ARTICLE

Metabolic Adaptations to Short-term High-Intensity Interval Training: A Little Pain for a Lot of Gain?

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GIBALA, M.J., and S.L. MCGEE. Metabolic Adaptations to Short-term High-Intensity Interval Training: A Little Pain for a Lot of Gain? *Exerc. Sport Sci. Rev.*, Vol. 36, No. 2, pp. 58–63, 2008. *High-intensity interval training (HIT) is a potent time-efficient strategy to induce numerous metabolic adaptations usually associated with traditional endurance training. As little as six sessions of HIT over 2 wk or a total of only approximately 15 min of very intense exercise (~600 kJ), can increase skeletal muscle oxidative capacity and endurance performance and alter metabolic control during aerobic-based exercise.* **Key Words:** exercise, skeletal muscle, mitochondria, oxidative capacity, substrate metabolism, cell signaling

INTRODUCTION

Regular endurance training improves performance during tasks that rely mainly on aerobic energy metabolism, in large part by increasing the body's ability to transport and use oxygen and altering substrate metabolism by working skeletal muscle. In contrast, high-intensity "sprint"-type training is generally believed to have less of an effect on oxidative energy metabolism and endurance capacity. However, many studies have shown that a sufficient volume of high-intensity interval training (HIT), performed for at least 6 wk, increases peak oxygen uptake ($\dot{V}O_{2peak}$) and the maximal activity of mitochondrial enzymes in skeletal muscle (16,21). Recent evidence suggests that a number of metabolic adaptations usually associated with traditional high-volume endurance training can be induced faster than previously thought with a surprisingly small volume of HIT. The present article briefly summarizes work from our laboratory (5–8,11) and others (18,21) that sheds new light on the potency of HIT to induce rapid changes in exercise capacity and skeletal muscle energy metabolism.

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WHAT IS HIGH-INTENSITY INTERVAL TRAINING (HIT)?

Although there is no universal definition, HIT generally refers to repeated sessions of relatively brief intermittent exercise, often performed with an "all-out" effort or at an intensity close to that which elicits $\dot{V}O_{2peak}$ (*i.e.*, ≥90% of $\dot{V}O_{2peak}$). Depending on the training intensity, a single effort may last from a few seconds to up to several minutes, with multiple efforts separated by up to a few minutes of rest or low-intensity exercise. In contrast to strength training in which brief intense efforts are usually performed against a heavy resistance to increase skeletal muscle mass, HIT is normally associated with activities such as cycling or running and does not induce marked fiber hypertrophy (21). A common HIT intervention — and the model used in our recent studies — is the Wingate test, which involves 30 s of all-out maximal cycling against a high braking force on a specialized ergometer. Our standard protocol involved subjects repeating the Wingate test four to six times — separated by 4 min of recovery — for a total of only 2 to 3 min of very intense exercise per training session, with three training sessions performed each week for 2 to 6 wk (5–8,11). The most unique aspect of our work has been the very low training volume, equivalent to approximately 300 kJ of very intense exercise per week. All studies were performed on healthy college-aged men and women who were habitually active but not engaged in any sort of structured training program.

HIT RAPIDLY IMPROVES EXERCISE CAPACITY

One of the most remarkable findings from our recent studies was the dramatic improvement in exercise performance

during tasks that rely mainly on aerobic energy metabolism, despite the very low training volume. In our initial study (8), subjects doubled the length of time that exercise could be maintained at a fixed submaximal workload — from approximately 26 to 51 min during cycling at 80% of pretraining $\dot{V}O_{2peak}$ — after only 6 HIT sessions over 2 wk (Fig. 1). The validity of this finding was bolstered by the fact that a control group showed no change in performance when tested 2 wk apart with no training intervention (Fig. 1). Subsequent work confirmed that 2 wk of HIT improved performance during tasks that more closely resemble normal athletic competition, including laboratory time trials that simulated cycling races lasting from approximately 2 min to approximately 1 h (5,6,11). There was no measurable change in $\dot{V}O_{2peak}$ after 2 wk of Wingate-based HIT (5,6,11), which suggests that "peripheral" adaptations were largely responsible for the improved exercise capacity. Other investigators have reported an increased $\dot{V}O_{2peak}$ after 2 wk of HIT (19,22); however, the total work performed in those studies was considerably greater than in our recent investigations (5,6,8,11). As noted by Talanian *et al.* (22) and discussed further later, this finding supports the idea that a minimum volume of HIT may be necessary to increase $\dot{V}O_{2peak}$ and stimulate other adaptations such as an increased capacity for fat oxidation.

SKELETAL MUSCLE ADAPTATIONS TO SHORT-TERM HIT

The factors responsible for training-induced improvements in exercise capacity are obviously complex and determined by numerous physiological (*e.g.*, cardiovascular, ionic, metabolic, neural, respiratory) and psychological attributes (*e.g.*, mood, motivation, perception of effort). Our studies have used the needle biopsy technique to examine changes in selected markers of skeletal muscle metabolic control. We

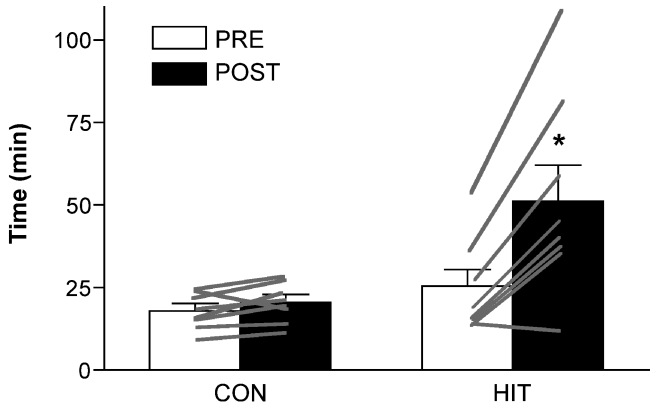

Figure 1. Cycle time to exhaustion at 80% of pretraining peak oxygen update before (PRE) and after (POST) six sessions of high-intensity interval training (HIT) over 2 wk or equivalent period without training (control; CON). Individual and mean (±SE) data are plotted for eight subjects in each group. *$P < 0.05$ versus PRE within same condition. [Adapted from Burgomaster, K.A., S.C. Hughes, G.J.F. Heigenhauser, S.N. Bradwell, and M.J. Gibala. Six sessions of sprint interval training increases muscle oxidative potential and cycle endurance capacity. *J. Appl. Physiol.* 98:1895–1990, 2005. Copyright © 2005 The American Physiological Society. Used with permission.]

have consistently found an increased muscle oxidative capacity (assessed using the maximal activity or protein content of mitochondrial enzymes such as citrate synthase and cytochrome oxidase) ranging from approximately 15% to 35% after six sessions of HIT over 2 wk (6,8,11). In one study (11), we directly compared a group of subjects who performed our standard HIT protocol versus a group who performed 6 sessions of continuous cycling at 65% $\dot{V}O_{2peak}$ for 90–120 min·d^{-1}. Total training time commitment over 2 wk was approximately 2.5 and 10.5 h for the sprint and endurance groups, respectively, and total exercise volume was approximately 90% lower for the HIT group. The two diverse training protocols induced remarkably similar adaptations in exercise performance and skeletal muscle oxidative capacity (Fig. 2). Although a few other studies have compared interval versus continuous training using matched-work designs (see references in (11)), to our knowledge, this was the first study to demonstrate that HIT is indeed a very time-efficient strategy to induce adaptations normally associated with endurance training (11).

Our recent human data are supported by previous work on rats that examined changes in skeletal muscle oxidative capacity in response to various forms of exercise training (9,23). Dudley *et al.* (9) reported similar increases in cytochrome oxidase maximal activity after 6 wk of training with either short bouts of intense running or prolonged periods of continuous running at lower work intensities. Given the large difference in training volume between groups, the authors concluded: "the typical endurance-training response of a biochemical change in mitochondrial content can be achieved at relatively intense exercise (*i.e.*, exceeding $\dot{V}O_{2max}$) maintained for relatively short durations… for the same adaptive response, the length of daily exercise necessary to bring about the change becomes less as the intensity of training increases" (9). More recently, Terada *et al.* (23) showed that 8 d of high-intensity intermittent swim training (lasting <5 min·d^{-1}) increased citrate synthase maximal activity in rat skeletal muscle to a level similar to that induced by 6 h of daily low-intensity training.

In addition to an increased skeletal muscle oxidative capacity after 2 wk of HIT, we have also detected changes in carbohydrate metabolism that are normally associated with traditional endurance training (Fig. 3), including an increased resting glycogen content, a reduced rate of glycogen utilization and lactate production during matched-work exercise, and increased total muscle glucose transporter 4 protein content (5,6). Selected markers of lipid metabolism, including the maximal activity of β-hydroxyacyl-CoA dehydrogenase (HAD) and the muscle contents of fatty acid translocase (FAT/CD36) or plasma membrane–associated fatty acid binding protein ($FABP_{pm}$), were unchanged after 2 wk of Wingate-based training intervention (5,6). In contrast, Talanian and coworkers (22) recently reported that seven sessions of HIT over 2 wk increased the maximal activity of HAD, the muscle protein content of $FABP_{pm}$, and whole-body fat oxidation during 60 min of cycling at 65% pretraining $\dot{V}O_{2peak}$. A major discrepancy between our recent studies (6,8,11) and the work of Talanian *et al.* (22) was the nature of the HIT stimulus. Subjects did not perform all-out sprints in the latter study, however, each training

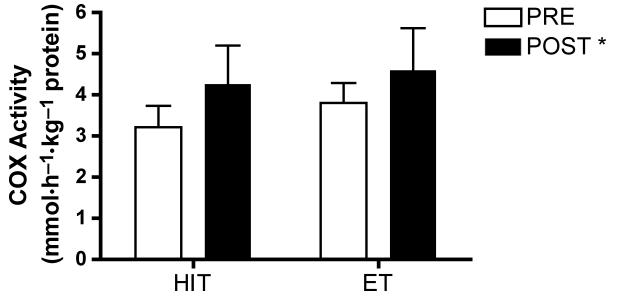

Figure 2. Maximal activity of cytochrome *c* oxidase (COX) measured in resting human skeletal muscle biopsy samples obtained before (PRE) and after (POST) six sessions of high-intensity interval training (HIT) or continuous moderate-intensity training (ET) over 2 wk. Total training time commitment was approximately 2.5 and 10.5 h for the sprint and endurance groups, respectively, and total exercise volume was approximately 90% lower for the HIT group. Values are means ± SE for eight subjects in each group. *$P < 0.05$ versus PRE (main effect for time). [Adapted from Gibala, M.J., J.P. Little, M. van Essen, G.P. Wilkin, K.A. Burgomaster, A. Safdar, S. Raha, and M.A. Tarnopolsky. Short-term sprint interval versus traditional endurance training: similar initial adaptations in human skeletal muscle and exercise performance. *J. Physiol.* 575(Pt 3):901–911, 2006. Copyright © 2006 Blackwell Publishing. Used with permission.]

session consisted of 10 times 4-min bouts of cycling at 90% of $\dot{V}O_{2peak}$, with 2 min of rest between intervals. Total training time commitment (~5 h) and exercise volume (~3000 kJ) over the 2-wk training period was thus substantially higher than in our recent studies that have used Wingate-based exercise training (6,8,11). Recently, we conducted a 6-wk training study (7) and compared two groups who performed either 4–6 Wingate tests with 4.5 min recovery per d 3 d·wk^{-1} (HIT group) or 40–60 min of continuous cycling at approximately 65% $\dot{V}O_{2peak}$ per d 5 d·wk^{-1} (endurance training group). Despite a markedly lower weekly training time commitment (~1.5 vs ~4.5 h) and training volume (~225 vs ~2250 kJ·wk^{-1}), both protocols induced similar increases in mitochondrial markers for skeletal muscle carbohydrate (pyruvate dehydrogenase E1α protein content) and lipid oxidation (HAD maximal activity) (Fig. 4). Glycogen utilization and phosphocreatine utilization during exercise were also reduced after training, and calculated rates of whole-body carbohydrate and lipid oxidation were decreased and increased, respectively, with no differences between groups (7).

POTENTIAL SIGNALING MECHANISMS INVOLVED IN SKELETAL MUSCLE REMODELING AFTER HIT

The potency of HIT to elicit rapid changes in skeletal muscle oxidative capacity is no doubt related to its high level of muscle fiber recruitment and potential to stress Type II fibers in particular, but the underlying mechanisms are unclear. From a cell-signaling perspective, exercise is typically classified as either strength or endurance, with short-duration high-intensity work usually associated with increased skeletal muscle mass and prolonged low- to moderate-intensity work associated with increased mitochondrial mass and oxidative enzyme activity (3). Indeed, the distinct pathways that regulate either cell growth or mitochondrial biogenesis intersect at a number of points in an inhibitory fashion, resulting in a response that is largely exclusive for one type of exercise or the other (3). Relatively little is known regarding the intracellular signaling events that mediate skeletal muscle remodeling in response to HIT that, unlike traditional strength training, is not characterized by marked skeletal muscle hypertrophy (21). Rather, given the oxidative phenotype that is rapidly up-regulated by HIT (Fig. 2), it seems likely that metabolic adaptations to this type of exercise could be mediated in part through signaling pathways normally associated with endurance training.

A key regulator of oxidative enzyme expression in a number of cell types, including skeletal muscle, is the peroxisome proliferator–activated receptor-γ coactivator 1 alpha (PGC-1α). PGC-1 is a transcriptional coactivator that recruits histone acetyltransferase (HAT) enzymes to a number of specific DNA-bound transcription factors within gene regulatory promoter regions (15). Recruitment of HATs to these regions alters the local chromosome structure to one that favors transcription. The effect of PGC-1α on skeletal muscle phenotype can be dramatic, with genetic overexpression of PGC-1α inducing a fast to slow fiber–type conversion (17). This change in phenotype is accompanied by enhanced mitochondrial enzyme expression and an increase in time to fatigue when electrically stimulated (17). Endurance exercise increases PGC-1α activity (18) and expression (26), suggesting that PGC-1α could be a critical component of the adaptive response to this form of training. Recently, we (7) found that 6 wk of low-volume HIT increased PGC-1α protein content in human skeletal muscle similar to high-volume endurance training (Fig. 5). The potency of interval-based training in this regard is supported by the work of Terada *et al.* (23), who showed increased skeletal muscle PGC-1α protein content after a single bout of high-intensity intermittent swim exercise in rats.

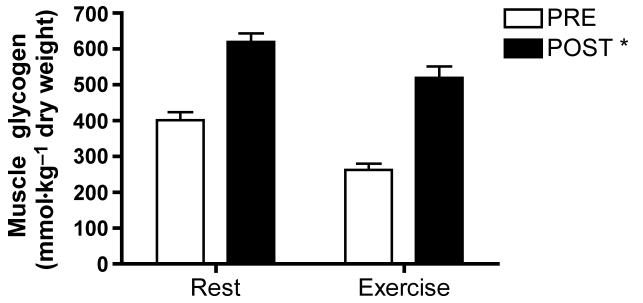

Figure 3. Glycogen content measured in human skeletal muscle biopsies obtained at rest and after 20 min of matched-work exercise before (PRE) and after (POST) 2 wk of high-intensity interval training. Exercise consisted of 10 min at 60% of peak oxygen uptake ($\dot{V}O_{2peak}$) followed by 10 min at 90% of $\dot{V}O_{2peak}$ at the same absolute workload before and after training. Values are means ± SE, n = 8. *Main effect for trial (Posttraining > pretraining, $P < 0.05$). Net muscle glycogenolysis during the exercise bout was also lower posttraining versus pretraining ($P < 0.05$). [Adapted from Burgomaster, K.A., G.J.F. Heigenhauser, and M.J. Gibala. Effect of short-term sprint interval training on human skeletal muscle carbohydrate metabolism during exercise and time trial performance. *J. Appl. Physiol.* 100:2041–2047, 2006. Copyright © 2006 The American Physiological Society. Used with permission.]

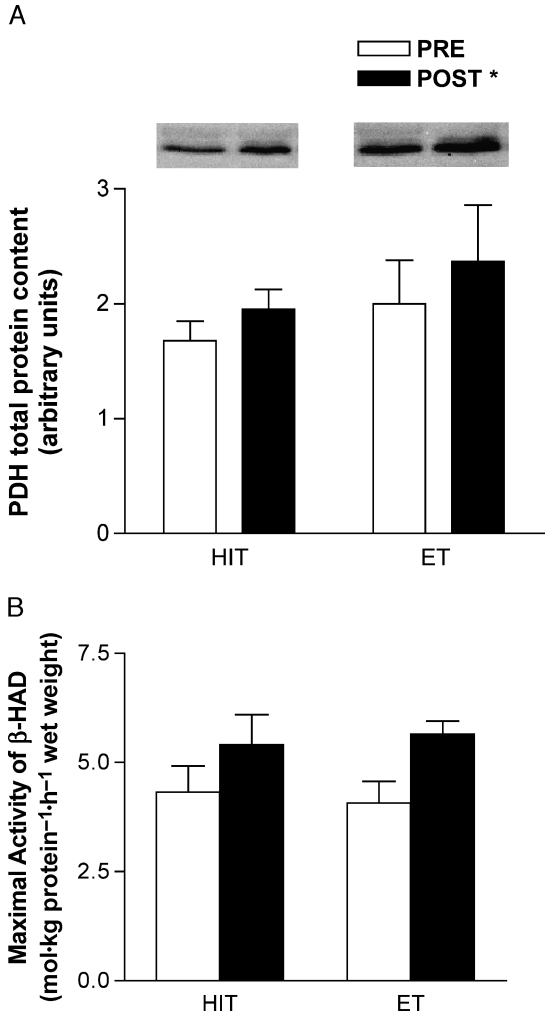

Figure 4. Total protein content of pyruvate dehydrogenase (PDH) E1α subunit (A) and maximal activity 3-hydroxyacyl-CoA dehydrogenase (β-HAD; B) measured in human skeletal muscle biopsy samples obtained before (PRE) and after (POST) 6 wk of high-intensity interval training (HIT) or 6 wk of endurance training (ET). Total weekly training time commitment was approximately 1.5 and 4.5 h for the sprint and endurance groups, respectively, and total exercise volume was approximately 90% lower for the HIT group (~225 vs ~2250 kJ·wk^{-1}). Values are means ± SE (n = 10 per group). *Main effect for condition ($P < 0.05$), such that POST is greater than PRE. [Adapted from Burgomaster, K.A., K.R. Howarth, S.M. Phillips, M. Rakobowchuk, M.J. MacDonald, S.L. McGee, and M.J. Gibala. Similar metabolic adaptations during exercise after low volume sprint interval and traditional endurance training in humans. *J. Physiol.* 586:151–160, 2008. Copyright © 2008 Blackwell Publishing. Used with permission.]

PGC-1α activity is acutely regulated by p160myb, a powerful repressor of PGC-1α function (10). Phosphorylation of PGC-1α disrupts the interaction with p160myb, allowing PGC-1 to associate with transcriptional regulators, which augments PGC-1α activity. The p38 mitogen-activated protein kinase (MAPK) is one kinase that can phosphorylate PGC-1α and thereby regulate PGC-1α activity (10). This pathway is a member of the larger MAPK family and is activated by cellular stresses including aerobic-type exercise (25). Although the exact mechanism by which exercise activates p38 MAPK is unknown, it likely involves phosphorylation by an upstream kinase cascade. Indices of PGC-1α activation during exercise are associated with increases in p38 phosphorylation in the nucleus (18). Furthermore, constitutive activation of p38 MAPK in fast muscle fibers results in enhanced mitochondrial enzyme expression (1), suggesting that p38 MAPK is an important mediator of the adaptive response to exercise.

Exercise is also a powerful regulator of PGC-1α expression, with significant increases in PGC-1α protein detected 3 h after exercise in rat skeletal muscle (26). Analysis of the PGC-1α gene promoter region reveals that conserved domains for the myocyte enhancer factor 2 (MEF2) and 3′-5′-adenosine monophosphate response element binding protein (CREB) are required for exercise-induced increases in PGC-1α expression (2). Whereas CREB is largely controlled by sympathetic nervous system activity, MEF2 seems to be regulated by the energy-sensing enzyme adenosine monophosphate–activated protein kinase (AMPK). Activation of AMPK is associated with PGC-1α and mitochondrial enzyme expression and has been hypothesized to be a main mediator of skeletal muscle adaptation to exercise (13). The p38 MAPK pathway also plays a role in regulating PGC-1α expression during exercise (1), likely through the regulation of PGC-1α activity. Together, these data indicate that the p38 MAPK and AMPK pathways are key mediators of increased skeletal muscle oxidative capacity in response to exercise training. Although the precise signaling events involved in the skeletal muscle response to HIT are unclear, the marked increase in oxidative enzyme expression and improved endurance capacity suggest that HIT potently activates these same signaling pathways. Additional research is warranted to clarify the effect of different acute exercise impulses on molecular signaling events in human skeletal muscle and the precise time course and mechanisms responsible for adaptations induced by short-term HIT.

IMPLICATIONS: HOW MUCH EXERCISE IS ENOUGH?

Although there is consensus regarding the importance of physical activity, the minimum dose necessary to improve health status is unclear (4). Public health guidelines generally recommend 30–60 min of moderate-intensity exercise on most days of the week. However, despite overwhelming scientific evidence that regular physical activity is effective in the prevention of chronic diseases and premature death, most adults fail to meet even the minimum physical activity guidelines. Countless studies have shown that the most commonly cited reason for not exercising is a "lack of time" (12). This finding is ubiquitous; regardless of age, ethnicity, sex, or health status, people report that a lack of time is the primary reason for their failure to exercise on a regular basis. Given that lack of time is such a common barrier to exercise participation, exercise prescription innovations that yield benefits with minimal time commitments represent a potentially valuable approach to increasing population activity levels and population health. HIT is often dismissed outright as unsafe, unpractical, or intolerable for many individuals. However, there is growing appreciation of the potential for intense interval-based training

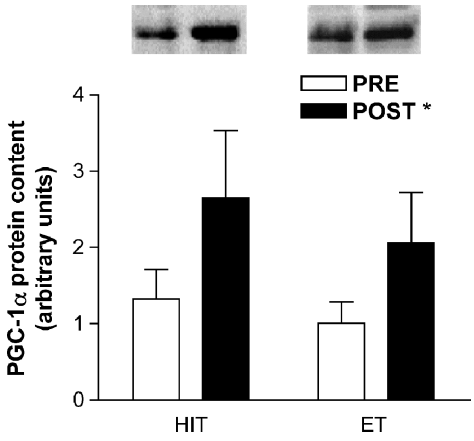

Figure 5. Total protein content of peroxisome proliferator–activated receptor-γ coactivator 1 alpha (PGC-1α) measured in human skeletal muscle biopsy samples obtained before (PRE) and after (POST) 6 wk of high-intensity interval training (HIT) or 6 wk of endurance training (ET). Total weekly training time commitment was approximately 1.5 and 4.5 h for the sprint and endurance groups, respectively, and total exercise volume was approximately 90% lower for the HIT group (~225 vs ~2250 kJ·wk^{-1}). Values are means ± SE (n = 10 per group). *Main effect for condition ($P < 0.05$), such that POST is greater than PRE. (Reprinted from Burgomaster, K.A., K.R. Howarth, S.M. Phillips, M. Rakobowchuk, M.J. MacDonald, S.L. McGee, and M.J. Gibala. Similar metabolic adaptations during exercise after low volume sprint interval and traditional endurance training in humans. *J. Physiol.* 586:151–160, 2008. Copyright © 2008 Blackwell Publishing. Used with permission.)

to stimulate improvements in health and fitness in a range of populations, including persons with various disease conditions (20,24). In addition, some data suggest that a low-frequency high-intensity approach to training is associated with greater long-term adherence as compared with a high-frequency low-intensity program (14).

LIMITATIONS AND PERSPECTIVE

Our recent studies should not be interpreted to suggest that low-volume interval training provides all of the benefits normally associated with traditional endurance training. The duration of the training programs in most of our published work to date was relatively short (up to 6 wk), and it remains to be determined whether similar adaptations are manifest after many months of low-volume interval and high-volume continuous training. It is possible that the time course for physiological adjustments differs between training protocols; the very intense nature of interval training may stimulate relatively rapid changes, whereas the adaptations induced by traditional endurance training may occur more slowly. Second, the Wingate-based training model that we have used requires a specialized ergometer and an extremely high level of subject motivation. Given the extreme nature of the exercise, it is doubtful that the general population could safely or practically adopt the model. Like the recent work by Talanian *et al.* (22), future studies should examine modified interval-based approaches to identify the optimal combination of training intensity and volume necessary to induce adaptations in a practical time-efficient manner. Finally, to date, we have only examined selected variables in skeletal muscle, and future studies should examine whether low-volume interval training induces other physiological adaptations normally associated with prolonged periods of moderate-intensity training. HIT may differ from traditional endurance training with respect to changes induced in the cardiovascular and respiratory systems, metabolic control in other organs (*e.g.*, liver, adipose tissue), and protection from disorders associated with chronic inactivity (*e.g.*, insulin resistance, lipid dysregulation).

CONCLUSIONS

Elite endurance athletes have long appreciated the role of high-intensity interval exercise as part of a comprehensive training program. Recent evidence suggests that — in young healthy persons of average fitness — intense interval exercise is a time-efficient strategy to stimulate a number of skeletal muscle adaptations that are comparable to traditional endurance training. However, fundamental questions remain regarding the minimum volume of exercise necessary to improve physiological well-being in various populations, the effectiveness of alternative (less extreme) interval-training strategies, and the precise nature and magnitude of adaptations that can be elicited and maintained over the long-term. A comprehensive evaluation of the physiological adaptations induced by different interval-training strategies in a wide range of populations will permit evidence-based recommendations that may provide an alternative to current exercise prescriptions for time-pressed individuals.

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