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Physiological adaptations to interval training to promote endurance

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The physiological determinants of endurance exercise performance are complex but depend in part on the capacity of the cardiorespiratory system to transport oxygenated blood to working skeletal muscle, and the oxidative capacity of skeletal muscle, which is largely determined by mitochondrial content. Interval training — characterized by intermittent bouts of higher intensity exercise interspersed by periods of lower-intensity exercise or complete rest for recovery within a given session — enhances endurance exercise performance including in those who are already well trained, although the mechanisms may be different as compared to less-trained individuals. This brief review considers the evidence for cardiac and skeletal muscle responses to interval training that are associated with an improved capacity for whole-body aerobic energy provision, with a focus on recent findings.

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Introduction

Endurance refers to the capacity to perform prolonged exercise, and is typically characterized in terms of the highest velocity or power that can be sustained for a given period of time, or over a given distance. Numerous physiological factors interact to determine endurance capacity, and the precise mechanisms that regulate both training adaptation and the limits of human performance remain topics of considerable interest to researchers and practitioners [1,2]. One key determinant of endurance is maximal oxygen uptake (VO_{2max}), which largely reflects the capacity of the cardiovascular system to deliver oxygenated blood to working skeletal muscle, although the pulmonary system and other factors may be limiting in some instances [1,2]. Other key determinants of endurance include the 'lactate threshold', generally defined as the exercise intensity at which lactate starts to accumulate in blood, and critical power, which is derived from the relationship between power output and the time for which it can be sustained [1,2]. Both factors are related to skeletal muscle oxidative capacity, which in turn is primarily determined by mitochondrial volume density, although other mechanisms are involved.

Traditional endurance training, characterized by a high volume of moderate-intensity continuous training (MICT), improves endurance exercise performance in part by increasing maximal cardiac output and thus oxygen delivery to working skeletal muscle. MICT also stimulates mitochondrial biogenesis in skeletal muscle, which serves to increase the overall capacity for the oxidative metabolism of substrates [3]. In more highly trained individuals who already possess well-developed cardiovascular and muscle oxidative capacities, endurance exercise performance can be further enhanced through intensified training that typically incorporates intervals, although the mechanisms involved are likely different compared to less-trained individuals [4].

Interval training is characterized by intermittent bouts of higher intensity exercise interspersed by periods of lower-intensity exercise or complete rest for recovery within a given training session. Intensity can be gauged in numerous ways, including based on absolute or relative power output, speed, heart rate, or perceived exertion. The terminology used to characterize interval training can be complex, owing in part to the large number of variables that can be manipulated and which interact to determine the precise training impulse, especially when viewed through the lens of program prescription for high-level athletes [5]. A simpler classification scheme, and one often employed to broadly categorize studies examining physiological responses to interval training, distinguishes two main types: high-intensity interval training (HIIT), generally defined as relatively intense but submaximal efforts that elicit $\geq$80% of maximal heart rate, and sprint interval training (SIT), a more intense version in which bouts are performed in an 'all out' manner or at an absolute workload that elicits VO_{2max} [6].

This brief review considers cardiac and skeletal muscle responses to interval training that are associated with improved endurance exercise capacity. The focus is on recent findings from studies mainly conducted in healthy but not highly trained individuals, which have established

that interval training *per se* can induce physiological remodeling similar to or greater than MICT, often despite a reduced total exercise volume or with reduced training time commitment [6]. The interested reader is also referred to other reviews that more comprehensively examine the mechanistic basis for adaptation [7•,8••], the application for performance in highly trained individuals [9,10] and the potential to enhance indices of cardiometabolic health [11,12].

Cardiac responses to interval training

A systematic review and meta-analysis by Milanović *et al.* [13••] found that HIIT increases VO_{2max} superior to MICT in healthy individuals when total exercise volume or energy expenditure is matched. While the improved VO_{2max} after MICT is generally attributed to increased maximal cardiac output (Q_{max}) [14], largely mediated by haematological [15•] and cardiac adaptations [16•], the precise role of exercise intensity and volume in mediating these adaptations is not well understood. A recent study reported that a six week HIIT protocol involving four, 4-min efforts at ~90% of maximal heart rate (HR_{max}) was more effective than work-matched MICT at improving VO_{2max} and Q_{max} in healthy individuals, although the HIIT-induced improvement in Q_{max} was not explained by an increase in blood volume [17•]. Previously, Helgerud *et al.* [18] found that a similar HIIT protocol conducted for eight weeks was more effective than performing the same total work in a continuous manner at lower intensities for improving VO_{2max}, and this corresponded to an increase in stroke volume, suggesting a close link between the two. In contrast, another recent study found that six weeks of HIIT improved VO_{2max} but did not induce cardiac structural or functional adaptations [19]. Other studies have found that as little as six sessions of HIIT over two weeks can increase VO_{2max} in the absence of measurable changes in cardiac and haematological factors, suggesting enhanced skeletal muscle oxygen extraction might contribute in this regard [20]. The mechanisms explaining HIIT-induced changes in VO_{2max} including the magnitude and time course for potential cardiovascular responses requires further investigation.

With regards to SIT, another systematic review and meta-analysis [21] found this type of interval training can improve VO_{2max} similar to MICT despite reduced exercise volume and time commitment. Evidence regarding cardiovascular adaptations to SIT including the effect on Q_{max} are limited and equivocal. A four-week SIT intervention involving repeated 20-s intervals performed at ~170% of work rate at VO_{2max} did not change Q_{max}, despite improving VO_{2max} by 10% [22•]. Conversely, other studies have found that SIT improved stroke volume during submaximal exercise [23] and elicited a modest increase in Q_{max} when preceded by 10 sessions of HIIT [24]. These latter studies provide evidence for a potential effect of SIT on cardiovascular adaptations, which could in turn explain the observed increases in VO_{2max}. Stroke volume at submaximal exercise may not be an accurate reflection of Q_{max} [25] however, and thus SIT-induced improvements in submaximal stroke volume do not necessarily indicate that SIT is improving Q_{max}. In the study by Astorino *et al.* [24], the effect if SIT *per se* on changes in Q_{max} cannot be isolated given the study design. O'Driscoll *et al.* [26] provided support for an effect of SIT on cardiac adaptations and demonstrated a SIT-induced improvement in resting left ventricular end-diastolic function. Of note, there was no change in end-systolic function or ejection fraction [26], which suggests the potential SIT-induced improvement in Q_{max} could be the result of improvements in diastolic function and/or blood volume facilitating larger end-diastolic volumes as opposed to cardiac contractility *per se*. However, because Q_{max} was not measured in this study, the effect of these adaptations on Q_{max} cannot be established. Given the limited number of studies, conflicting findings, and divergent methodologies employed, the effect of SIT on Q_{max} and mechanisms underlying SIT-induced improvements in VO_{2max}, remain unclear.

Emerging evidence is exploring the minimal volume of brief intermittent exercise training that nonetheless induces physiological adaptation as reflected by an increased VO_{2max}. Interestingly, reducing the volume of a SIT protocol by half did not diminish the increase in VO_{2max} [27]. Further, when a very low volume SIT protocol involving two, 20-s bursts of 'all out' exercise was reduced to two, 10-s bouts, there was a blunted, yet measurable, increase in VO_{2max} [28]. Spreading three, 20-s vigorous bouts of activity in the form of stair climbing throughout the day, separated by one to four hours, was also recently shown to induce a modest improvement (~5%) in VO_{2max} [29]. As with MICT, there is also considerable inter-individual variability in the VO_{2max} response to interval training [30], with one study showing the incidence of 'non-response' to either a SIT or MICT protocol reduced by switching to the other training stimulus [31]. A recent multi-center comparison of VO_{2max} trainability between interval and traditional continuous training based on 677 participants across eight sites and involving 18 different interventions concluded that higher volume HIIT had more likely responders to improvements in VO_{2max} as compared to lower-volume HIIT/SIT and MICT [32]. Future research exploring the mechanistic basis of adaptation to various interval training protocols, including cardiac and haematological responses, is warranted.

Skeletal muscle responses to interval training

The precise role of exercise intensity, duration and volume in determining skeletal muscle responses to training, including the regulation of mitochondrial biogenesis, has also not been fully elucidated [33,34•]. Short-term

interval training can rapidly increase the oxidative capacity of human skeletal muscle as reflected by various biochemical measurements of mitochondrial components including the maximal activity or total protein content of mitochondrial enzymes and markers of mitochondrial respiration [7•,8••]. The potency of SIT in particular is evidenced by a study that showed as little as three, 20-s 'all out' sprints, set within a 10-min session that otherwise involved low-intensity cycling, increased mitochondrial content to a similar extent as a 50-min MICT protocol, when performed three times per week for 12 weeks [35]. An acute bout of SIT has also been shown to elicit greater activation of signaling cascades associated with mitochondrial biogenesis including the transcriptional coactivator peroxisome proliferator-activated receptor γ coactivator-1α (PGC-1α), as compared to a bout of traditional endurance exercise despite reduced time commitment [36,37]. Other work suggests that while SIT promotes greater and faster mitochondrial adaptations in skeletal muscle of moderately trained individuals, there may be a dissociation between training-induced changes in mitochondrial respiration and mitochondrial content [38,39]. Specifically, it has been proposed that intensity appears to be a key determinant of training-induced changes in mitochondrial respiration, whereas volume seems to be more important for changes in mitochondrial content [33]. The interested reader is referred to the recent review by Tschakert and Hofmann [9] that examines current controversies in the field and highlights some important methodological issues that need to be addressed to resolve existing conflicts.

Mindful of the individual variability in training responsiveness, MacInnis *et al.* [40•] employed a single-leg cycling model to facilitate a unique within-subject comparison of mitochondrial adaptation to a short-term HIIT or MICT protocol matched for total exercise volume and mean training intensity. Participants performed six sessions of training with each leg, which were randomized for dominance to perform 30 min of continuous exercise at 50% of single-leg peak workload, or four, 5-min intervals at 65% of peak workload interspersed by two minutes of active recovery. Both protocols increased mitochondrial content as indicated by the maximal activity of citrate synthase, but the increase was greater in the leg that performed HIIT as compared to MICT. These data suggest that exercise intensity, and/or the pattern of contraction, is an important determinant of exercise-induced skeletal muscle remodelling in humans. There is evidence from acute exercise studies that both parameters may influence the nature of the training adaptation. Intermittent exercise induces a greater activation of signaling pathways regulating PGC-1α when compared to a single bout of continuous exercise of matched work and intensity, which suggests metabolic fluctuations caused by the succession of on-transient and off-transient during intermittent exercise may be important for the adaptive response [41]. Other recent work suggests that, despite consisting of less total work than MICT or HIIT, SIT in particular is an effective stimulus for the activation of stress protein kinase signaling pathways linked to exercise-mediated adaptation of skeletal muscle [42]. Higher-intensity, intermittent exercise has also been shown to induce greater activation of AMP-activated protein kinase in type II fibres of human skeletal muscle, as compared to continuous exercise [43], suggesting the potential for fibre-type-specific adaptations to the two forms of training.

In addition to mitochondrial adaptations, both SIT and HIIT elicit improvements in other skeletal muscle factors that may contribute to enhanced oxygen extraction and oxidative energy metabolism such as increased capillary density [22•,44], including in both type I and type II fibres [45]. Particularly in more well-trained individuals, interval training can elicit further improvements in performance in the absence of a measurable changes in markers of mitochondrial content [4]. Skovgaard *et al.* [46] recently reported that training involving repeated 30-s sprints enhanced short-term exercise capacity in trained runners, in the absence of changes in mitochondrial protein markers but associated with increased expression of muscle proteins related to sodium/potassium transport and calcium reuptake. In contrast, another recent report by Gunnarsson *et al.* [47] found that including short 30-s sprints in a training program that otherwise involved MICT increased markers of mitochondrial protein content in trained individuals. Another recent report suggested the potential for improved running economy after intense intermittent but reduced volume training, which may be related to changes in the expression of proteins linked to energy consuming processes, primarily in type I muscle fibers [48]. Differences in study designs, including the training state of participants and specific nature and duration of the interventions, explain in part the divergent findings.

Conclusion

Interval training improves endurance exercise performance in part through cardiac and skeletal muscle remodeling that enhances the capacity for whole-body aerobic energy metabolism. In less-trained individuals, interval training *per se* can improve performance to a similar extent as traditional endurance training despite reduced total volume and time commitment. In more highly trained individuals, incorporating interval training leads to further gains in performance without increasing overall training volume. A complex myriad of factors regulate the overall response to interval training, and additional research is warranted to clarify the precise impact of specific interventions on specific physiological responses, as well as the identification of biomarkers of physiological responses that might provide insight into predicting training responsiveness [49,50].

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Conflict of interest statement

Nothing declared.

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