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CROSSTALK

CrossTalk opposing view: High intensity interval training does not have a role in risk reduction or treatment of disease

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Moderate-intensity continuous exercise has been used in clinical settings for decades and is known to have a plethora of benefits. The beneficial effects of endurance exercise are well documented: exercise adaptations result in mitochondrial biogenesis, increased skeletal muscle capillarization, improved vascular compliance, and increased stroke volume and cardiac output (Holloszy, 1973; Clausen, 1977). As a result, chronic endurance training (ET) is a well-known primary and secondary prevention tool for various pathologies, including, but not limited to, diabetes mellitus (Boule *et al.* 2001), hypertension (Cornelissen & Smart, 2013) and heart failure (HF) (Pina *et al.* 2003).

Given the well-documented benefits of exercise on health, and the increasing incidence of lifestyle-related diseases, there is renewed interest in identifying the optimal exercise prescription. Two broad types of aerobic training have largely been represented in the literature: ET (∼50–80% $\dot{V}_{O_2max}$) and higher-intensity/explosive type training. The latter is further delineated as either sprint interval training (SIT; short bursts at > 100% $\dot{V}_{O_2max}$) or high-intensity interval training (HIIT; ∼90% $\dot{V}_{O_2max}$), characterized by brief, repeated bursts of intense exercise separated by periods of rest or low-intensity exercise ('active recovery'). Recently, these programmes have been described as time efficient alternatives to traditional ET, as only 3–10 min of active exercise is required (Gillen & Gibala, 2014). To date, the majority of studies investigating the effects of HIIT have utilized young, healthy subjects, and therefore more research is required to elucidate the effects of HIIT in older and clinical populations (Gist *et al.* 2014). To examine the appropriateness of HIIT clinical settings of secondary prevention, we pose the following questions. What is the 'goal' of exercise training for clinical populations? Are the documented adaptations in skeletal and cardiac muscle following ET and HIIT comparable in models of cardiovascular disease?

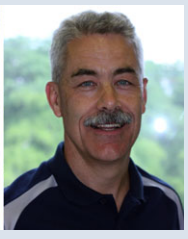
Exercise as a secondary prevention tool

The overarching goal of secondary prevention programmes is risk factor reduction (e.g. reducing blood pressure (BP), blood glucose, etc.). Two important effects of ET are post-exercise hypotension and improved glucose tolerance, both of which are maintained for 12–24 h after an exercise bout. Given these effects, and their powerful role in risk reduction, it stands to reason that frequent exercise would be required to sustain any benefit derived, and the current recommendation for ET on 'most, if not all, days of the week' supports this supposition. However, while the recommendation for HIIT of 2–3 days per week plays a role in disease prevention, clinical populations may not benefit from the above-described effects on BP and glucose tolerance if HIIT is used in isolation. Reductions of 8.3 mmHg in systolic BP and 5.2 mmHg in diastolic BP have been documented in hypertensive individuals in response to ET (Cornelissen & Smart, 2013); however, the long-term effects of HIIT on BP are less clear. The Osaka Gas Company questionnaire showed that low-intensity walking had profound effects on the susceptibility to hypertension, and concluded that every 10 min increase in daily walking decreased the risk of hypertension by 12% (Hayashi *et al.* 1999). These data suggest that while 2–3 days of exercise at a higher intensity may be appropriate in healthy individuals, the use of HIIT alone is not optimal if reducing BP is a major goal of exercise training in a clinical population.

Endurance versus high intensity interval training

In young, healthy subjects the metabolic effects of ET and HIIT appear to be equivalent in human skeletal muscle. Acutely, both types of exercise similarly activate signalling pathways that induce skeletal muscle adaptation (Gibala *et al.* 2009). Chronically, ET and HIIT result in comparable increases in skeletal muscle mitochondrial content, maximal activities of oxidative enzymes, the expression of plasma membrane transport proteins, glycogen content and 24 h post-exercise energy expenditure (Helgerud *et al.* 2007; Burgomaster *et al.* 2008; Skelly *et al.* 2014). However, in contrast to ET, the effects of HIIT on central parameters (e.g. stroke volume, cardiac output) are equivocal (Bacon *et al.* 2013; Gist *et al.* 2014; Weston *et al.* 2014), and there is limited evidence indicating the cellular effects of HIIT in rodent heart tissue and no evidence in human hearts.

Tanya M. Holloway completed her PhD training with Lawrence L. Spriet at the University of Guelph, Canada and recently began her postdoctoral training with Luc van Loon in Human Movement Sciences at Maastricht University, The Netherlands. Her research interests include investigating the effects of various cardiovascular diseases on skeletal and heart muscle, as well as examining if and how exercise may augment the effects of disease in these tissues. Her research interests are influenced by the 10 years she spent as a clinical exercise physiologist working with various cardiovascular patient populations including heart failure, pre/post-heart transplant and congenital patients. **Dr. Lawrence L. Spriet** is a Professor and Chair of the Department of Human Health and Nutritional Sciences in the College of Biological Science at the University of Guelph in Guelph, Canada. His research examines how skeletal muscle generates the large amounts of energy needed to perform whole-body exercise in sport and work situations. The pathways that metabolize carbohydrate and lipid as fuel to produce energy are studied in human skeletal muscle. He also examines how moderate aerobic training and high-intensity intermittent training can augment the ability of skeletal and heart muscles to provide the energy needed to improve performance.



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While the evidence on the effects of HIIT in complex clinical populations (e.g. HF) is sparse, a study by Wisloff *et al.* (2007) reported in patients with post-infarction HF that HIIT was superior to moderate ET with regards to left ventricular remodelling, aerobic capacity, endothelial function and quality of life. However, it is important to note that while infarctions affecting a large portion of the left ventricle (LV) are undoubtedly a basis for HF, the aetiology, disease progression and molecular fingerprint are fundamentally different from hypertrophy-related (hypertensive) HF. Of the limited studies that do exist, the data are difficult to interpret and inconsistent. HIIT was superior to ET in stable coronary artery disease patients; however, the ET was lower than what is generally clinically used (Rognmo *et al.* 2004), which is likely to explain why others have found no difference between HIIT and ET utilized in cardiac rehabilitation (Currie *et al.* 2014; Tschentscher *et al.* 2015). Smaller scale studies have demonstrated HIIT to be effective in overweight and obese individuals (Gillen *et al.* 2013) and those with type II diabetes mellitus (Gillen *et al.* 2012).

High intensity interval training in secondary prevention

Significant knowledge gaps exist on the effects of HIIT on cardiac morphology and disease progression in hypertension-induced HF, with only 200 combined HF patients studied to date (Pinkstaff, 2015). Despite the knowledge gaps identified, HIIT is recommend in the setting of cardiovascular diseases (Gielen *et al.* 2015). There is acknowledgement, however, regarding risk in low fitness populations: 'it may also be prudent to include a preconditioning phase of training (moderate intensity endurance exercise) prior to initiating HIIT' (Gillen & Gibala, 2014). This is an essential message, as higher baseline fitness level reduces risk associated with exercise-induced ischaemic events in clinical populations (Thompson *et al.* 2007).

While clinicians and scientists await data elucidating the cellular and molecular effects of HIIT in human heart tissue, rodent studies have revealed a cautionary tale. Negative adaptations within rodent hearts as a result of exhaustive (Schultz *et al.* 2007; Benito *et al.* 2011; da Costa Rebelo *et al.* 2012), but not low intensity exercise training (Chicco *et al.* 2008) have been documented, eluding to the existence of an 'intensity threshold' in underlying pathological conditions. While ET decreases fibrosis and prevents pathological hypertrophy in rodent models of HF (Miyachi *et al.* 2009), the effects of HIIT on these molecular adaptations were largely unknown until recently. Our laboratory has provided evidence that in a rodent model of hypertension, ET had overall beneficial effects in both skeletal (Holloway *et al.* 2015*a*) and cardiac muscle (Holloway *et al.* 2015*b*), while in contrast HIIT did not. Specifically, in skeletal muscle, HIIT promoted a transition towards a more glycolytic phenotype and a reduced capillary-to-fibre ratio (Holloway *et al.* 2015*a*). In cardiac muscle, ET protected against LV hypertrophy and fibrosis, and promoted increased LV capillary-to-fibre ratios; however, HIIT promoted pathological adaptations in the LV of hypertensive rats (Holloway *et al.* 2015*b*). Therefore, it remains to be determined if HIIT represents an optimal secondary prevention strategy in the presence of existing cardiovascular disease.

In summary, while ET has extensive effects in health and disease on both skeletal and cardiac muscle, the overall impact of HIIT remains to be fully elucidated in the presence of underlying pathology. Therefore, the positive effects of ET and the fact it can safely be performed daily should not be overlooked or forgotten. Furthermore, considering hypertension is the most common form of cardiovascular disease, it may be prudent to consider the evidence for an intensity threshold, before widely prescribing HIIT for risk reduction or treatment of disease.

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Additional information

Competing interests

The authors have no competing interests.

Author contributions

All authors have approved the final version of the manuscript and agree to be accountable for all aspects of the work. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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