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High but not moderate-intensity endurance training increases pain tolerance: a randomised trial

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Abstract

Purpose: To examine the effect of high-intensity interval training (HIIT) compared to volume-matched moderate-intensity continuous training (CONT) on muscle pain tolerance and high-intensity exercise tolerance. *Methods:* Twenty healthy adults were randomly assigned (1:1) to either 6 weeks of HIIT (6-8 x 5 min at halfway between lactate threshold and maximal oxygen uptake [50%Δ]) or volume-matched CONT (~60-80 min at 90% lactate threshold) on a cycle ergometer. A tourniquet test to examine muscle pain tolerance and two time to exhaustion (TTE) trials at 50%Δ to examine exercise tolerance were completed pre- and post-training; the post-training TTE trials were completed at the pre-training 50%Δ (same absolute-intensity) and the post-training 50%Δ (same relative-intensity). *Results:* HIIT and CONT resulted in similar improvements in markers of aerobic fitness (all $P \geq 0.081$). HIIT increased TTE at the same absolute- and relative-intensity as pre-training (148% and 43%, respectively) to a greater extent than CONT (38% and −4%, respectively) (both $P \leq 0.019$). HIIT increased pain tolerance (41%, $P < 0.001$) whereas CONT had no effect (−3%, $P = 0.720$). Changes in pain tolerance demonstrated positive relationships with changes in TTE at the same absolute- ($r = 0.44$, $P = 0.027$) and relative-intensity ($r = 0.51$, $P = 0.011$) as pre-training. *Conclusion:* The repeated exposure to a high-intensity training stimuli increases muscle pain tolerance, which is independent of the improvements in aerobic fitness induced by endurance training, and may contribute to the increase in high-intensity exercise tolerance following HIIT.

Key words: Central nervous system; exercise tolerance; high-intensity interval training; muscle fatigue; muscle pain.

Introduction

Endurance exercise induces acute muscle pain (O'Connor and Cook 1999) which increases with the intensity and duration of the exercise (Borg et al. 1985; Cook et al. 1997; Hamilton et al. 1996; Ljunggren et al. 1987). Group III/IV sensory muscle afferents send nociceptive signals from the periphery to the central nervous system (CNS) in response to mechanical pressure, heat, cold and intramuscular metabolites produced during muscular contractions (e.g. hydrogen, potassium, adenosine triphosphate, bradykinin and prostaglandins) (O'Connor and Cook 1999; Pollak et al. 2014), and have been implicated in the acute responses to exercise (Amman? Sidhu?). The ability to tolerate exercise-induced muscle pain is therefore considered an important contributing factor to high-intensity exercise tolerance (Mauger 2013; Mauger 2014; O'Connor and Cook 1999).

Trained individuals may be able to better tolerate muscle pain and therefore perform closer to the limits of their maximum capacity (Mauger 2013; Mauger 2014; O'Connor and Cook 1999). Whilst cross-sectional data supports that those engaged in endurance activities have greater pain tolerance despite unaltered pain sensitivity compared to controls (Ord and Gijsbers 2003; Scott and Gijsbers 1981; Tesarz et al. 2012), only a limited number of studies have shown that endurance training increases pain tolerance (Anshel and Russell 1994; Jones et al. 2014). Jones et al. (2014) demonstrated that six weeks of cycling endurance training increased ischaemic muscle pain tolerance in the untrained upper limb. However, the training and control groups were self-selected resulting in different baseline levels of aerobic fitness (maximal rate of oxygen uptake [$\dot{V}O_{2max}$]) between groups. The control group did not perform any training and therefore any behavioural artefacts associated with completing a supervised training programme cannot be excluded as a mechanism. Finally, the training was completed at 75% heart rate (HR) reserve, an intensity that likely produces different perceptual and metabolic

stress amongst individuals (Mann et al. 2013; Scharhag-Rosenberger et al. 2010). Therefore, it is unclear whether the exercise intensity is important in increasing pain tolerance. An attractive theory is that repeated exposure to painful training or regularly approaching the limits of performance in training, such as that induced by high-intensity exercise, will improve pain tolerance (O'Connor and Cook 1999), however this has yet to be tested.

High-intensity interval training (HIIT) is more effective at improving high-intensity exercise tolerance (i.e. the time for which a pre-determined exercise intensity can be sustained until volitional exhaustion) than moderate-intensity continuous training (CONT) (Daussin et al. 2008; Seiler et al. 2013). However, when matched for work completed, HIIT and CONT produce similar improvements in aerobic fitness (lactate threshold [LT] and $\dot{V}O_{2max}$) (Edge et al. 2006; Poole and Gaesser 1985), suggesting other mechanisms contribute to the greater increase in exercise tolerance. Considering the proposed role of exercise-induced muscle pain in impairing exercise tolerance (Mauger 2013; O'Connor and Cook 1999), and the importance of exercise intensity in eliciting muscle pain (Cook et al. 1997), it is important to understand the effect of the intensity of an endurance training intervention on muscle pain tolerance and the relationship with exercise tolerance.

Accordingly, the aim of the present study was to examine the effect of endurance training intensity on ischaemic muscle pain tolerance. We compared HIIT and volume-matched CONT in a randomised trial. Secondary aims were to investigate the relationship between the changes in pain tolerance and high-intensity exercise tolerance following training. It was hypothesised that although markers of aerobic fitness would increase similarly in both groups, a greater enhancement of ischaemic muscle pain tolerance would be seen following HIIT, which would also be accompanied by greater improvements high-intensity exercise tolerance. We have

previously reported the central and peripheral fatigue adaptations in response to the training in a previous publication (O'Leary et al. 2017).

Methods

Participants

Twenty healthy adults (four women) volunteered to participate in this two-arm parallel group single-blind randomised study (Table 1). The study was approved by the institutional ethics review board and carried out in accordance with the Declaration of Helsinki. Participants were recruited in Oxford, UK via advertisements and word of mouth. Before taking part, each participant completed health history questionnaires to confirm the absence of any cardio-respiratory, neurological or neuromuscular disorder, and provided written informed consent. All participants were non-smokers, not taking any medications and were not engaged in endurance training (≤ 30 min per session, ≤ 2 sessions per week), as confirmed by initial interview. Although not assessed in the present study, it is possible that participants had experience of cycling during activities of daily living. After completing the pre-training experimental trials, participants were allocated the next available study number that related to a computer-generated block randomisation list. Participants were randomised (1:1) into either a HIIT group or a group completing work-matched CONT stratified according to the LT and $\dot{V}O_{2max}$ (Table 1). The list was held by an investigator not involved in the experimental trials who supervised the training intervention. Whilst participants could not be blinded, they were naïve to the study hypotheses and therefore neither intervention was presented to be superior. Group allocation was concealed from the assessor until the end of the study and participants were instructed to refrain from discussing their training programme. All experimental trials were therefore completed by a blinded assessor with group allocation only revealed after data analysis.

Experimental Procedures

Each participant completed three experimental trials before and after 6 weeks of either HIIT or CONT (Fig. 1). All trials were separated by 48 - 72 h and performed at the same time of day. Each participant was instructed to arrive at the laboratory 2 h postprandial and after abstaining from caffeine (12 h), alcohol (24 h) and exhaustive exercise (48 h). During the first visit participants completed a modified tourniquet test to examine ischaemic muscle pain tolerance. This was followed by a submaximal and maximal exercise test for the determination of the LT, lactate turn-point (LTP) and $\dot{V}O_{2max}$. The second visit involved the completion of a high-intensity exercise tolerance cycling test (time to exhaustion [TTE]) at an intensity halfway between LT and $\dot{V}O_{2max}$ (50%Δ) which served as a familiarisation trial. During the third visit participants repeated the exercise tolerance test which served as the experimental trial. Following the completion of the third baseline experimental trial, participants were allocated to the HIIT or CONT intervention which was initiated within 2 - 5 days. At follow-up the three experimental trials were repeated within 2 - 4 days of completing training, however the familiarisation trial was replaced by an exercise tolerance trial at the pre-training 50%Δ (same absolute-intensity [post-abs]) whilst the second exercise tolerance trial was completed at the post-training 50%Δ (same relative-intensity [post-rel]). This allowed a comparison of exercise tolerance at the same absolute work rate as well as the same relative-intensity as pre-training.

Pain Tolerance

A modified tourniquet test was employed to examine the effect of endurance training on ischaemic muscle pain tolerance (Jones et al. 2014). Participants performed repeated isometric hand-grip contractions with their right hand using a grip force transducer (MLT004/ST, ADInstruments, UK) whilst securely strapped into a chair. The force was digitised (1000Hz,

PowerLab 4/26, ADInstruments, UK) and displayed on a computer screen in front of each participant at eye level (LabChart 7, ADInstruments, UK). Each participant first completed a series of ~5 s maximal voluntary contractions (MVC) in order to determine peak hand-grip force. A minimum of three MVCs were performed until force plateaued with each MVC separated by 1 min of rest. A cuff was then placed around the upper arm (SC10D, Hokanson, USA) which was then exsanguinated by being raised above the level of the heart for 60 s. The cuff was then inflated to 200 mmHg (E20, Hokanson, USA) before the arm returned to horizontal. Repeated contractions were performed under ischaemic conditions at 30% MVC for 4 s separated by 4 s rest to the limit of tolerance. Each contraction was prompted by an auditory stimulus and monitored by visual feedback. Participants were blinded to elapsed time and pain tolerance was the total time the contractions could be sustained before voluntary termination of the test. Pain was rated every ~30 s using a 0 - 10 scale. The assessment of pain tolerance in an untrained limb (arms) allows the central adaptations to be determined independently of any training-induced peripheral adaptations, and has shown to be reliable and sensitive to endurance training-induced increases in pain tolerance (Jones et al. 2014).

Exercise Tests

All exercise tests were completed on an electromagnetically braked cycle ergometer (Excalibur Sport, Lode, Netherlands) at a self-selected cadence above 60 rpm. HR was monitored using online telemetry (T31, Polar, Finland) and expired gases were recorded breath-by-breath using an online gas analyser (Metalyzer 3B, Cortex, Germany). Blood lactate concentrations ($[La^-]$) were measured from whole blood finger-tip capillary samples (Lactate Pro, Arkray, Japan). Perceived exertion (RPE) was determined using the Borg Scale (6 - 20).

Aerobic Fitness

Participants first completed an incremental submaximal exercise test for the determination of the LT and LTP. The exercise started at 50 W for men and 30 W for women with the power output increased by 20 W every 4 min. [La^-] was measured at the end of each stage and the test was terminated once [La^-] reached ≥4 $mmol \cdot l^{-1}$. The LT and LTP were determined by visual inspection of the power output and [La^-] relationship by two blinded independent reviewers. The LT was defined as the first sudden and sustained increase in [La^-] and the LTP was defined as the appearance of a second sudden increase in [La^-] between the LT and $\dot{V}O_{2max}$. Following 20 min rest, a maximal ramp test was completed for the determination of $\dot{V}O_{2max}$. The maximal test began with cycling for 1 min at 100 W for men and 50 W for women followed by a ramp increase of 25 $W \cdot min^{-1}$ for men and 20 $W \cdot min^{-1}$ for women until 60 rpm could no longer be maintained. Expired gases and HR were measured throughout the exercise tests. $\dot{V}O_{2max}$ and peak power output ($\dot{W}_{max}$) were taken as the highest 30 s average of the recorded $\dot{V}O_2$ and power output, respectively. The power output at $\dot{V}O_{2max}$ was calculated from linear extrapolation of the $\dot{V}O_2$ and power output relationship at sub-LT intensities and used for calculating the intensity at 50%Δ.

Exercise Tolerance

High-intensity exercise tolerance was examined with a series of TTE trials. All trials were preceded by a submaximal 5 min self-paced warm-up. Each trial was completed at a self-selected cadence above 60 rpm and terminated when a cadence of 60 rpm could not be maintained for 5 s or if the participant fell below this cadence three times. Participants were blinded to elapsed time and verbally encouraged to continue as long as possible. The trials were completed at 50%Δ in order to target an intensity above maximal lactate steady state (Pringle and Jones 2002) and to induce significant central and peripheral fatigue (O'Leary et al. 2016).

The 50%Δ was recalculated after training so the post-training TTE trials could be completed at both the pre-training 50%Δ (post-abs) and post-training 50%Δ (post-rel) (Fig. 1).

Training

All training sessions were completed on a cycle ergometer (either Excalibur Sport or Corival, Lode, Netherlands) and supervised by an investigator not involved in the experimental trials. Participants were instructed to maintain normal habitual activity throughout the training. Both the HIIT and CONT training groups completed 3 training session per week for 6-weeks (18 total sessions) with each session separated by a minimum of 24 h. An adapted HIIT protocol was used (Weston et al. 1997) which involved 6 repeats of 5 min cycling at 50%Δ, each separated by 1 min rest, which was progressed to 8 repeats during weeks 4 - 6. The CONT protocol involved continuous cycling at 90% of the power output at LT. The duration was prescribed so that the same volume of work (kJ) that would have been completed in the HIIT protocol was completed at the power output equal to 90% of LT. Training near the LT provides an aerobic stimulus but prevents the non-linear increase in metabolic and perceptual stress seen with exercise above the LT (Jones and Carter 2000). Training intensities were prescribed relative to metabolic thresholds in order to elicit disparate metabolic and perceptual demands between groups (Mann et al. 2013; O'Leary et al. 2016). HR and RPE were measured at 5 min intervals throughout each training session. Intensity was re-assessed every 2 weeks (session 7 and 13) and increased if necessary to ensure HR and RPE were consistent with baseline values throughout training. The full characteristics of the training interventions have been reported in a previous publication (O'Leary et al. 2017).

Statistical Analysis

Data are displayed as mean ± SD in the tables and text, and mean ± SE in the figures unless stated otherwise. Statistical analyses were completed in SPSS (v.23, SPSS Inc., USA). All data were tested for normality. Total training volume and baseline measures of aerobic fitness, exercise tolerance and pain tolerance were compared between groups with independent samples t-tests. A series of 2 × 2 (group [HIIT and CONT] × time [pre-training and post-training]) mixed-design ANOVAs were used to compare training interventions for aerobic fitness, ischaemic pain tolerance and exercise tolerance. Pain ratings during the pain tolerance test were compared between groups using a 2 × 2 × 4 (group [HIIT and CONT] × trial [pre-training and post-training] × time ([30 s, 60 s, 90 s, 120 s]). Where the assumption of sphericity was violated, Greenhouse-Geisser corrections were applied. Where an ANOVA revealed a significant main effect or interaction, post-hoc contrasts and t-tests were used to test for differences within and between groups where appropriate. Effect sizes were calculated with partial eta squared (ηp^2) and Cohen's D. Pearson's correlation coefficients were used to test associations between changes in pain tolerance and exercise tolerance. A stepwise multiple linear regression was used to better understand how the change (%) in $\dot{V}O_{2max}$ ($l \cdot min^{-1}$), LT (W), LTP (W) and pain tolerance integrate to predict the change (%) in TTE during the post-abs and post-rel trials. Significance was accepted as $P \leq 0.05$.

Results

Training Intensity, Training Volume and Aerobic Fitness

The characteristics of the training protocols and the aerobic fitness adaptations have previously been reported (O'Leary et al. 2017). In brief, all participants successfully completed the training intervention (98% and 99% of HIIT and CONT sessions completed, respectively). Total training volume was similar between groups (HIIT: 7918 ± 1541 kJ vs CONT: 8105 ± 2036

kJ, P = 0.809). There were no differences in power output, HR or RPE progression between groups (group × time interactions, all P ≥ 0.303). HR and RPE were higher during HIIT compared with CONT (main effects of group, both P < 0.001). There were no differences between groups for pre-training measures of LT, LTP, $\dot{V}O_{2max}$ or $\dot{W}_{max}$ (all P ≥ 0.506) or training-induced changes in these measures (group × time interactions, all P ≥ 0.081, $\eta_p^2 \leq$ 0.159). Both HIIT and CONT increased the power at LT, power at LTP, $\dot{W}_{max}$ and $\dot{V}O_{2max}$ ($l \cdot min^{-1}$) (main effects of time, P < 0.001, $\eta_p^2 \geq 0.580$) (Fig. 2). The $\dot{V}O_2$ (%$\dot{V}O_{2max}$) at LT and LTP showed a similar pattern of change.

Exercise Tolerance

The coefficient of variation for TTE between the familiarisation and the pre-training experimental trial was 11.8%. The pre-training trials were completed at 202 ± 47 W (80 ± 6 %$\dot{V}O_{2max}$) and 189 ± 52 W (79 ± 5 %$\dot{V}O_{2max}$) for the HIIT and CONT groups, respectively. There were no differences between groups for pre-training TTE (HIIT: 26:04 ± 9:10 mm:ss vs CONT: 24:49 ± 10:40 mm:ss P < 0.05). HIIT and CONT increased the power at 50%Δ by 11 ± 5% (223 ± 50 W, 80 ± 5 %$\dot{V}O_{2max}$) and 6 ± 10% (201 ± 51 W, 78 ± 6 %$\dot{V}O_{2max}$,), respectively (main effect of time, P < 0.001, $\eta_p^2 = 0.621$) with no difference between groups (group × time interactions, P = 0.144, $\eta_p^2 = 0.115$). There was a significant group × trial interaction for the post-abs TTE (P < 0.001, $\eta_p^2 = 0.523$) and post-rel TTE (P = 0.019, $\eta_p^2 = 0.269$). Post-hoc analysis revealed that HIIT increased TTE by 148 ± 74% during the post-abs trial (pre-training: 26:04 ± 9:10 mm:ss vs post-abs: 63:04 ± 22:59 mm:ss, P < 0.001, D = 2.112) and 43 ± 56% during the post-rel trial (pre-training: 26:04 ± 9:10 mm:ss vs post-rel: 34:54 ± 11:15 mm:ss, P = 0.011, D = 0.854). For the CONT group, TTE was increased by 38 ± 52% in the post-abs trial (pre-training: 24:49 ± 10:40 mm:ss vs post-abs: 32:45 mm:ss, P = 0.018, D = 0.747), however TTE was not different between the pre-training and post-rel trials (pre-training: 24:49

± 10:40 mm:ss vs post-rel: 20:37 ± 6:36 mm:ss, P = 0.342, D = 0.472). The significant group × trial interactions demonstrate the increase in TTE was greater after HIIT compared with CONT for both the post-abs and post-rel trial.

Pain Tolerance

There was no difference in pre-training ischaemic muscle pain tolerance time between groups (P = 0.544). Isometric hand grip MVC was unaffected by HIIT (pre-training 467 ± 123 N vs post-training 467 ± 122 N) or CONT (pre-training 446 ± 118 N vs post-training 431 ± 109 N) (main effect of trial, P = 0.332, $\eta_p^2 = 0.052$) with no difference between groups (main effect of group, P = 0.598, $\eta_p^2 = 0.016$) and no group × trial interaction (P = 0.351, $\eta_p^2 = 0.049$). There was a significant group × trial interaction for pain tolerance time (P = 0.001, $\eta_p^2 = 0.460$). Post-hoc analysis revealed that pain tolerance was increased following HIIT (39 ± 29%, P < 0.001, D = 1.497) but not CONT (4 ± 16%, P = 0.720, D = 0.049) with a significant difference between groups (Fig. 3). There was no effect of trial (P = 0.077, $\eta_p^2 = 0.173$), no group × trial interaction (P = 0.763, $\eta_p^2 = 0.005$) and no group × trial × time interaction (P = 0.446, $\eta_p^2 = 0.045$) for ratings of pan (Fig. 4). There were significant associations between change in pain tolerance and change in TTE during the post-abs (r = 0.44, P = 0.027) and post-rel trial (r = 0.51, P = 0.011) (Fig. 5). When each group was considered independently, these relationships were abolished (HIIT post-abs: r = 0.12, P = 0.375 and post-rel: r = 0.48, P = 0.079; CONT post-abs: r = −0.11, P = 0.385 and post-rel: r = 0.09, P = 0.400). Multiple linear regression could be used to successfully predict the change in post-rel TTE only (P = 0.021), however, the change in pain tolerance was the only predictor explaining 26% of the variance. The regression equation was: change in post-rel TTE (%) = 0.953 change in pain tolerance (%) – 1.101.

Discussion

The aim of this study was to examine the effect of endurance training intensity on ischaemic muscle pain tolerance. The main findings are that HIIT, but not work-matched CONT, resulted in improvements in ischaemic muscle pain tolerance. Ratings of pain during the ischaemic test were unchanged after training, which suggests that pain sensitivity was unaffected and a similar level of pain was tolerated for longer. The similar increases in LT, LTP and $\dot{V}O_{2max}$ between groups demonstrate the improvements in pain tolerance were independent of changes in aerobic fitness. HIIT also resulted in greater improvements in exercise tolerance (TTE) at the same power output as pre-training (post-abs trial) and the same relative-intensity as pre-training (post-rel trial). Significant associations between the change in pain tolerance and change in TTE suggest an increase in pain tolerance may contribute, in some part, to the increase in exercise tolerance.

To date, the majority of research examining pain tolerance in response to training has been cross-sectional (Ord and Gijsbers 2003; Ryan and Kovacic 1966; Scott and Gijsbers 1981; Tajet-Foxell and Rose 1995; Tesarz et al. 2012) and there has been limited experimental data. Jones et al. (2014) reported that endurance training increased the tolerance of ischaemic muscle pain, however our study is the first randomised trial demonstrating this adaptation is training intensity dependent and to also provide accompanying exercise tolerance data. It has previously been suggested that regular exposure to exercise that provides a sufficient metabolic disturbance, and therefore noxious stimulus (i.e. high-intensity) (Jones et al. 2014; O'Connor and Cook 1999), or regularly approaching the limits of performance in training (O'Connor and Cook 1999), may increase pain tolerance due to familiarisation to the noxious stimuli. It therefore stands to reason that training intensity would be important in increasing pain tolerance, however this hypothesis had yet to be tested.

Ischaemic muscle pain tolerance, measured as the duration for which submaximal hand-grip contractions could be performed under ischaemic conditions, was increased by HIIT but not CONT. Although the tourniquet test has been suggested to stimulate sensory afferents in a similar way to exercising muscle (Jones et al. 2014), this assumption has been questioned (Amann et al. 2015). Separate subtypes of group III/IV afferents, namely metaboreceptors and metabo-nociceptors, have been identified with the former responding to innocuous levels of intramuscular metabolites present during exercise, whereas the latter are activated by higher noxious metabolite concentrations present during ischaemia but not exercise (for review see Amann et al. (2015)). Whilst there are structural and functional differences between these receptors, it is unclear whether they have different effects at supraspinal sites. However, they appear to contribute independently to sensations of muscle pain and fatigue (Pollak et al. 2014). As the activity of these receptors was not measured, it is not possible to comment on the exact mechanisms underpinning our results.

There are a number of general mechanisms plausible for the increase in pain tolerance. Firstly, the pain signal may be attenuated in response to the stimulus (Jones et al. 2014). However, as the pain tolerance test was performed on the arm, which was not involved in the training intervention, and the occlusion of blood flow excludes any central circulatory influence, the nociceptor stimulus is likely the same pre- and post-training (Jones et al. 2014). In support of this, training did not impact the pain ratings during the ischaemic contractions and dampened pain sensitivity is therefore an unlikely mechanism. These data instead demonstrate a similar degree of pain was tolerated for longer suggesting better central tolerance of nociception rather than a down regulation of peripheral afferent firing. Although high-intensity exercise may induce a post-exercise analgesic effect compared to moderate-intensity exercise (Hoffman et

al. 2004), previous research supports that endurance training has no effect on pain sensitivity (Jones et al. 2014).

Both HIIT and CONT increased markers of aerobic fitness to a similar extent in agreement with previous work-matched HIIT and CONT studies (Edge et al. 2006; Poole and Gaesser 1985). By matching groups for aerobic fitness at baseline, employing a randomised design and controlling the volume of training completed, the training-induced increase in aerobic fitness and any behavioural biases associated with completing a training intervention can be excluded as an underlying mechanism. The intensity of the HIIT was set at 50%Δ in order to target an intensity above LTP (no steady-state), whereas the CONT intensity was set at 90%LT and was therefore in the moderate-intensity domain (steady-state). High-intensity exercise causes a noxious biochemical stimuli combined with a high intramuscular pressure (O'Connor and Cook 1999). Exercise-induced muscle pain demonstrates an exponential relationship with cycling intensity with an onset at ~50% $\dot{V}O_{2max}$ in untrained individuals (Cook et al. 1997), an intensity similar to the LT in our study. Whilst it is possible that the intensity of HIIT may accustom individual to exercise-induced pain, it is likely that the afferents stimulated during exercise are different to those tested with the tourniquet test, as discussed previously. Our 'within-training' data (O'Leary et al. 2017) also supports that the HIIT group routinely approached the limits of their exercise tolerance during training whereas the CONT group did not. For example, all participants reached an RPE of 19 or 20 during the last 5 min of each session in the HIIT group but none above 15 during CONT. The increase in pain tolerance could therefore be due to regularly approaching the limit of exercise tolerance, rather than due to training intensity per se, and it is unclear whether moderate-intensity exercise training to the limit of tolerance has similar effects.

The implications of our results are that a greater tolerance of pain could affect the willingness to endure exercise (Cook et al. 1997) and allow exercise tolerance closer to maximal capacity (O'Connor and Cook 1999). Although the mechanisms of fatigue and exhaustion are multifactorial, inhibitory feedback from group III/IV muscle afferents to the CNS is thought to contribute (Amann 2011; Amann et al. 2015; Mauger 2013; Nybo and Secher 2004; Smirmaul 2012; Taylor et al. 2016). Despite similar improvements in aerobic fitness, HIIT resulted in markedly greater increases in exercise tolerance during the post-abs trial compared with CONT, in agreement with previous work (Daussin et al. 2008; Seiler et al. 2013). When the exercise tolerance test was repeated at the same relative-intensity as pre-training (post-rel trial), only HIIT resulted in improvements in exercise tolerance. The similar HR, [La^-] and RPE responses during the post-rel trial compared with pre-training, reported previously (O'Leary et al. 2017), demonstrate a similar physiological strain was tolerated for longer. As the HIIT group trained at the same intensity as the exercise tolerance trials, these greater improvements in TTE could be expected due to the specificity of the training. However, significant associations between improvements in pain tolerance and exercise tolerance during both the post-abs and post-rel trial suggests an increase in pain tolerance following HIIT could contribute to improvements in exercise tolerance. It is therefore possible that an increase in central tolerance of group III/IV muscle afferent feedback allows greater exercise tolerance. However, the strength of the associations ($r = 0.44$ - 0.51) should be considered, with the variance in the improvement in pain tolerance only able to explain a small proportion of the variance in the improvements in TTE. Furthermore, when assessed within each group these associations were abolished and multiple linear regression could only successfully predict some of the variance in the change in post-rel TTE, with the change in pain tolerance the only predictor. Nevertheless, these cannot be confirmed as mechanisms from the methodology employed here and the role of group III/IV afferents in exercise tolerance is unclear.

The results from this study should be considered alongside the following limitations. As previously discussed, there are likely to be differences in the subtypes of sensory afferents that are stimulated by the exercising muscle during whole-body locomotor exercise compared to ischaemic contractions (Amann et al. 2015). These afferents are also likely to have functional and structural differences, thus limiting our ability to comment on the exact mechanism by which HIIT increases pain tolerance. Additionally, the pain induced by one type of experimental stimulus may not transfer to other forms of pain (O'Connor and Cook 1999) and therefore the results reported here may not translate to other forms of induced pain and further work is warranted in this area.

Conclusion

This study demonstrates that 6 weeks HIIT resulted in improvements in ischaemic muscle pain tolerance whereas work-matched CONT had no effect. It is possible this increase in pain tolerance contributes, in some part, to the accompanying improvements in exercise tolerance. The mechanism is independent to the improvements in aerobic fitness and is likely through the repeated exposure to high metabolic stress and the accompanying noxious exercise stimulus induced by high-intensity exercise.

Author Contributions: The study was designed by TJO, MGM and JC; TJO and MGM collected and analysed the data; TJO, MGM, JC and KH all contributed to preparation of the manuscript. The final manuscript was approved by all authors. The authors declare no conflicts of interest.

Conflicts of Interest

The authors declare no conflicts of interest.

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Abbreviations

CNS	central nervous system
CONT	moderate-intensity continuous training
HIIT	high-intensity interval training
HR	heart rate
[La^-]	blood lactate concentration
LT	lactate threshold
LTP	lactate turn-point
MVC	maximal voluntary contraction

post-abs	same absolute-intensity as pre-training
post-rel	same relative-intensity as post-training
RPE	rating of perceived exertion
TTE	time to exhaustion
$\dot{V}O_2$	oxygen uptake
$\dot{V}O_{2max}$	maximal oxygen uptake
$\dot{W}_{max}$	peak power output
50%Δ	intensity equivalent to halfway between LT and $\dot{V}O_{2max}$

Figure Legends

Fig. 1 Overview of the study design.

CONT, moderate-intensity continuous endurance training; HIIT, high-intensity interval training; post-abs, same absolute-intensity as pre-training; post-rel, same relative-intensity as pre-training; TTE, time to exhaustion; 50%Δ, halfway between lactate threshold and maximal oxygen uptake.

Fig. 2 Aerobic fitness at the pre-training and post-training time-points. a, maximal oxygen uptake; b, peak power output; c, lactate threshold; d, lactate turn-point. Data are mean ± SE.

*P < 0.05 vs pre-training.

Fig. 3 Ischaemic muscle pain tolerance before and after 6 weeks of high-intensity interval training (HIIT) or moderate-intensity continuous training (CONT). Data are mean ± SE.

*P < 0.05 vs pre-training; #P < 0.05 vs CONT.

Fig. 4 Pain ratings throughout the pain tolerance tests before and after for 6 weeks of high-intensity interval training (a) or moderate-intensity continuous training (b). Data are mean ± SD.

Fig. 5 Relationships between change in pain tolerance (%) and change in exercise tolerance (time to exhaustion) during the post-abs (a) and post-rel trial (b) following 6 weeks of high-intensity interval training (HIIT) and moderate-intensity continuous training (CONT). Relationships are for the HIIT and CONT data grouped.