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Physiological mechanisms underlying enhanced performance with blood flow restriction training: neuromuscular, vascular and metabolic adaptations

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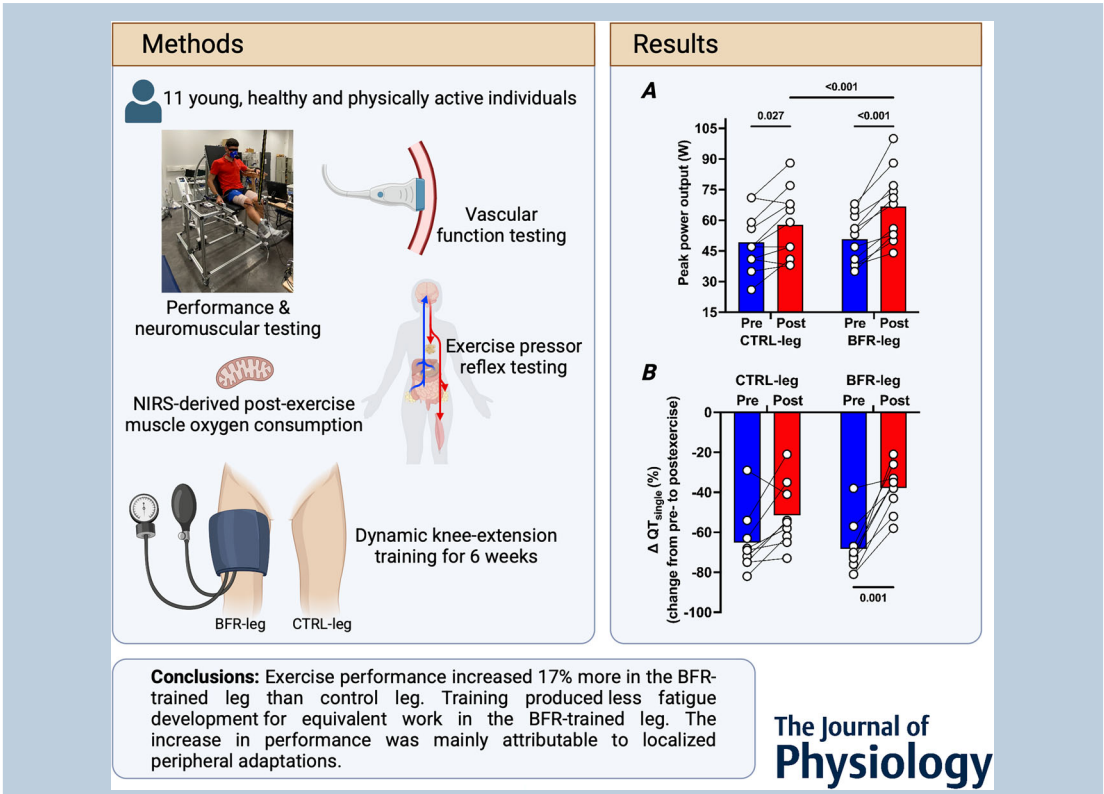

Abstract figure legend We investigated how 6 weeks of dynamic knee-extensor interval training with blood flow restriction (BFR-leg) and without (CTRL-leg) impacts performance and its mechanisms using non-invasive methods. Specifically, we used gold-standard methods to assess neuromuscular function, vascular function using Doppler ultrasound, and near-infrared spectroscopy (NIRS)-derived post-exercise recovery kinetics of muscle oxygen consumption as a surrogate for mitochondrial respiratory capacity and indices of the muscle metaboreflex, before and after training in each leg. We found that performance, assessed via incremental peak power output, increased in both legs; however, the increase in the BFR-leg was greater than in the CTRL-leg (*A*). The exercise-induced reduction in potentiated twitch force evoked by single electrical stimulation (QT_{single}) of the femoral nerve from before to 20 s after exercise was significantly lower following training in the BFR-leg, but not in the CTRL-leg (*B*). Findings further showed enhanced

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microvascular function with no increase in mitochondrial respiratory capacity with BFR training. Our results thus indicate that BFR training enhances performance by limiting the development of exercise-induced peripheral fatigue through integrated neuromuscular, vascular and metabolic adaptations.

Abstract We investigated how blood flow restriction (BFR) training enhances performance and neuromuscular function during dynamic exercise through adaptations in vascular function, mitochondrial respiratory capacity and metaboreflex-related haemodynamic responses. Eleven healthy active participants completed 6 weeks of interval training with one leg under BFR (BFR-leg; cuff pressure:165 ± 36 mmHg) and the other without (CTRL-leg). Before and after training, participants performed single-leg knee-extensor incremental tests to determine peak power output (W_{max}) and constant workload trials at 90% pre-training W_{max} to assess neuromuscular fatigue [maximal voluntary contraction (MVC) and evoked contractile force (QT)]. Blood flow responsiveness was evaluated using Doppler ultrasound during reactive hyperaemia (RH), passive leg movement (PLM) and rapid-onset vasodilatation (ROV). Mitochondrial respiratory capacity was estimated indirectly from post-exercise recovery kinetics of muscle oxygen consumption ($m\dot{V}_{O_2}$). Mean arterial pressure (MAP) and heart rate (HR) responses to metaboreflex activation during exercise and post-exercise circulatory occlusion (PECO) were measured. After training, W_{max} increased ∼17% more in the BFR-leg than in the CTRL-leg ($P < 0.001$). Exercise-induced reductions in MVC ($P < 0.001$) and QT forces ($P = 0.001$) were less in the BFR-trained leg than CTRL-leg, indicating less fatigue development. Femoral blood flow was higher in the BFR-leg during RH and ROV ($P < 0.001$), but not PLM. MAP ($P = 0.001$) and HR ($P < 0.001$) responses were lower in the BFR-leg during exercise with muscle metaboreflex activation, without training or leg differences during PECO ($P > 0.230$). The kinetics of $m\dot{V}_{O_2}$ improved similarly in both legs ($P < 0.007$). Compared to the control, BFR interval training elicited greater improvements in performance and less fatigue for equivalent exercise through integrated neuromuscular, vascular and metabolic adaptations.

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Key points

- Interval training with blood flow restriction (BFR) improves exercise performance by enhancing oxygen delivery and muscle homeostasis in contracting muscles, but its effects on neuromuscular fatigue and the underlying mechanisms are not fully understood.
- In a within-subject, unilateral design, participants trained one leg with BFR for 6 weeks while the contralateral leg served as a control. Before and after training, we assessed neuromuscular fatigue, vascular function, near-infrared spectroscopy (NIRS)-derived post-exercise recovery kinetics of muscle oxygen consumption ($m\dot{V}_{O_2}$, a surrogate for mitochondrial respiratory capacity) and muscle metaboreflex activation.
- BFR interval training attenuated neuromuscular fatigue development during high-intensity dynamic knee-extensor exercise, mainly by reducing impairments in peripheral (i.e. muscle) fatigue.
- After BFR training, leg blood flow was greater during vascular function tests compared to the control, suggesting enhanced haemodynamic function.
- Less fatigue for equivalent exercise occurred independently of changes in NIRS-derived $m\dot{V}_{O_2}$ and appears to be largely driven by peripheral neuromuscular and vascular adaptations.

Introduction

Blood flow restriction (BFR) training has become a well-recognized training modality shown to increase skeletal muscle strength and hypertrophy (Lixandrão et al., 2018; Loenneke et al., 2012; Slysz & Burr, 2018), as well as improve endurance capacity (Abe et al., 2010; Corvino et al., 2014; Paton et al., 2017) and maximal oxygen uptake ($\dot{V}_{O_2max}$) (Mitchell et al., 2019; Taylor et al., 2016). BFR is typically accomplished by inflating a pneumatic cuff around the most proximal region of the exercising limb(s) to reduce arterial blood flow and occlude venous outflow (Scott et al., 2015). Compression of the underlying vasculature during exercise can reduce skeletal muscle blood flow by ∼20–50% (Christiansen et al., 2019; Sundberg & Kaijser, 1992), leading to a transient lack of oxygen supply to the muscle (Corvino et al., 2017; Larkin et al., 2012; Manini & Clark, 2009). Cuff deflation in a subsequent resting phase results in a rapid rise in blood flow, approximately three times greater than during exercise without BFR and reperfusion-induced shear stress (Christiansen et al., 2019).

Compared to the same exercise performed without BFR, a single session of BFR exercise has notably been linked to greater perturbations in metabolic (e.g. H^+, P_i), ion (e.g. K^+) and redox muscle homeostasis (Christiansen et al., 2021), recruitment of type II muscle fibres (Fatela et al., 2016), discharge of mechanical and metabolic group III and IV muscle afferents (Nobrega et al., 2014), and activation of biochemical pathway responses such as AMPK and PGC1-α and production of reactive oxygen species (ROS) (Christiansen et al., 2018; Ferguson et al., 2021). Although such acute BFR-associated stimuli can transiently exacerbate neuromuscular fatigue development (Husmann et al., 2018; Lavigne et al., 2024), they may enhance long-term training adaptations (Burtin et al., 2012) and ultimately slow the rate of fatigue development for a given performance task.

In a series of recent studies, Christiansen et al. (2019–2021) described several beneficial effects of training with BFR compared to a training control. In these studies, performing interval cycling with BFR three times per week for 6 weeks increased arterial blood flow (Christiansen et al., 2019) and oxygen delivery (Christiansen et al., 2020), and lowered lactate production during dynamic exercise (Christiansen et al., 2021). It has also been documented that BFR-induced mechanisms elicit several other adaptations, including vascular remodelling (Hunt et al., 2013) and improved muscle perfusion (Kacin & Strazar, 2011). Production of ROS has been suggested to be related to repeated ischaemic episodes with interval BFR training, which in turn enhances gene expression associated with mitochondrial adaptations (Christiansen et al., 2018; Ferguson et al., 2021). This upregulated mitochondrial gene expression may enhance mitochondrial respiratory capacity, promote greater reliance on aerobic metabolic pathways for ATP resynthesis and support improved oxygen uptake. Moreover, repeated exposure to metabolite accumulation via localized hypoxic periods induced by BFR exercise may attenuate the exercise pressor reflex (Crisafulli et al., 2018; Sundblad et al., 2018), a key regulator of haemodynamic responses during exercise (Rowell & O'Leary, 1990; Seals et al., 1988), through the desensitization of group III and IV muscle afferents (Wang et al., 2012) and/or reduced metabolite production at a given work rate.

Collectively, these adaptations, mediated by increased convective O_2 delivery (Christiansen et al., 2020) and better maintenance of muscle ion homeostasis (Christiansen et al., 2021) via improved oxidative pathways (Christiansen et al., 2018; Pignanelli et al., 2021), suggest that BFR training may enhance exercise performance by delaying the development of exercise-induced neuromuscular fatigue. Neuromuscular fatigue manifests as a transient reduction in the ability of the contracting muscles to maintain force or power, resulting from impairments at both central and peripheral levels of the neuromuscular system (Bigland-Ritchie & Woods, 1984). Central fatigue refers to an exercise-induced decline in the ability to voluntarily activate muscles, whereas peripheral fatigue implies a reduction in the ability of the muscle fibres to generate force in response to neural input. In our previous study (Lavigne et al., 2024), we showed that a single session of BFR interval cycling evoked significantly larger decrements in exercise-induced neuromuscular fatigue compared to an intensity-matched control condition, due primarily to peripheral factors. However, the chronic effects of BFR training on the underlying peripheral and

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central components of neuromuscular fatigue during dynamic exercise remain unknown. This gap is important to address as neuromuscular fatigue plays a key role in determining exercise performance.

Accordingly, the present study aimed to investigate how neuromuscular, vascular and metabolic adaptations induced by BFR training contribute to improved exercise performance during dynamic knee-extensor exercise in healthy young adults. We used a comprehensive set of non-invasive assessments to examine adaptations in neuromuscular function, vascular responsiveness, near-infrared spectroscopy (NIRS)-derived post-exercise muscle oxygen consumption ($m\dot{V}_{O_2}$) as a surrogate for skeletal muscle mitochondrial respiratory capacity, and the exercise pressor reflex. It was hypothesized that: (1) BFR training would lead to greater improvements in exercise performance (reflected by time to task failure), and (2) for work- and duration-matched exercise, markers of neuromuscular fatigue (maximal voluntary contraction force, evoked forces and surface EMG) would be less impaired following BFR training compared to a volume-matched control. From a mechanistic standpoint, we further hypothesized that BFR training would improve vascular function and NIRS-derived post-exercise recovery kinetics of $m\dot{V}_{O_2}$ from knee-extensor exercise and attenuate the exercise pressor reflex during muscle metaboreflex activation, thereby contributing to less fatigue development for equivalent exercise, compared to a volume-matched control.

Methods

Ethical approval

This study was approved by the regional ethics committee (reference number: 2022-A01627-36) and was conducted in accordance with the standards set by the latest revision of the *Declaration of Helsinki*, except for registration in a database. Participants were informed of the study's requirements, benefits and potential risks both orally and in writing before providing their written informed consent to participate.

Participants

Two female and nine male healthy, physically active individuals (mean ± SD: age: 23 ± 3 years; height: 176 ± 10 cm; body mass: 71.0 ± 15.3 kg) completed the study. All participants passed a general medical assessment to ensure they could safely complete the exercise required in this study. Participants were: (1) free from diagnosed cardiovascular, neurological or musculoskeletal disorders; (2) self-identified non-smokers; (3) not taking any medications; and (4) normally physically active (range: recreational activity to competitive amateur sport) university students. Using power analysis software (G*Power version 3.1), the minimal sample size required for an 80% statistical power and an alpha error probability of 5% (two-tailed; effect size $F = 0.40$; non-sphericity correction = 1; ANOVA with repeated measures within factors) was 10 participants. This sample size is comparable to those of previous studies using a within-participant design to investigate training adaptations to BFR exercise between limbs (Christiansen et al., 2019, 2020; Sundblad et al., 2018).

Experimental design

Participants visited the laboratory for four experimental sessions prior to and five experimental sessions following the training intervention. All exercise was performed on a custom-built dynamic knee-extensor ergometer designed to isolate quadriceps muscle work in a 'kicking' motion (Andersen & Saltin, 1985). Each participant completed two familiarization sessions. During the first familiarization session, anthropometric measurements were collected, and participants completed two graded incremental single-leg exercise tests to task failure (initial workload: 3 W; workload increment: 3 W min^{-1}; cadence: 60 rpm), separated by a 30 min rest period. The power output attained during the last completed stage was determined as the estimated peak power output (W_{max}). During the second familiarization session, participants performed practice submaximal and maximal bouts of dynamic knee-extensor exercise with each leg. During the submaximal period, participants performed three, 3 min bouts of knee-extension exercise continuously. The intensities of each exercise bout were 20, 30 and 40% of W_{max}, respectively. Next, following 5 min of rest, participants performed a maximal exercise bout at 90% W_{max} to task failure. Participants were instructed to: (1) always exercise at 60 rpm to ensure a constant work rate, (2) completely relax during knee flexion and (3) keep hips as still as possible during the protocol. Participants also practised the neuromuscular function assessment protocol (described below) before and after the practice exercise tests.

A study overview is presented in Fig. 1. During the first experimental session, quadriceps muscle mitochondrial respiratory capacity was estimated non-invasively in each leg by measuring NIRS-derived post-exercise $m\dot{V}_{O_2}$ recovery kinetics, followed by an incremental knee-extensor exercise test to task failure to determine peak power output and whole-body peak oxygen uptake ($\dot{V}_{O_2peak}$). $\dot{V}_{O_2peak}$ was determined during every incremental knee-extensor exercise test to task failure, defined as the highest 30 s average of recorded oxygen uptake values. In the second experimental session,

single-leg knee-extension exercise was performed to task failure at 90% of W_{max} to examine the development of neuromuscular fatigue following exercise. In these experiments, central and peripheral fatigue were quantified via pre-/post-exercise decreases in superimposed and potentiated single and doublet electrical femoral nerve stimulations. In the third experimental session, cardiovascular and cardiorespiratory responses were measured during single-leg knee-extensor exercise with concomitant muscle metaboreflex stimulation via graded muscle occlusion and post-exercise circulatory occlusion (PECO) to evaluate whether BFR training would reduce the sensitivity of the exercise pressor reflex. During the fourth experimental session, multiple assessments of vascular function specific to the leg, determined by reactive hyperaemia (RH), flow-mediated

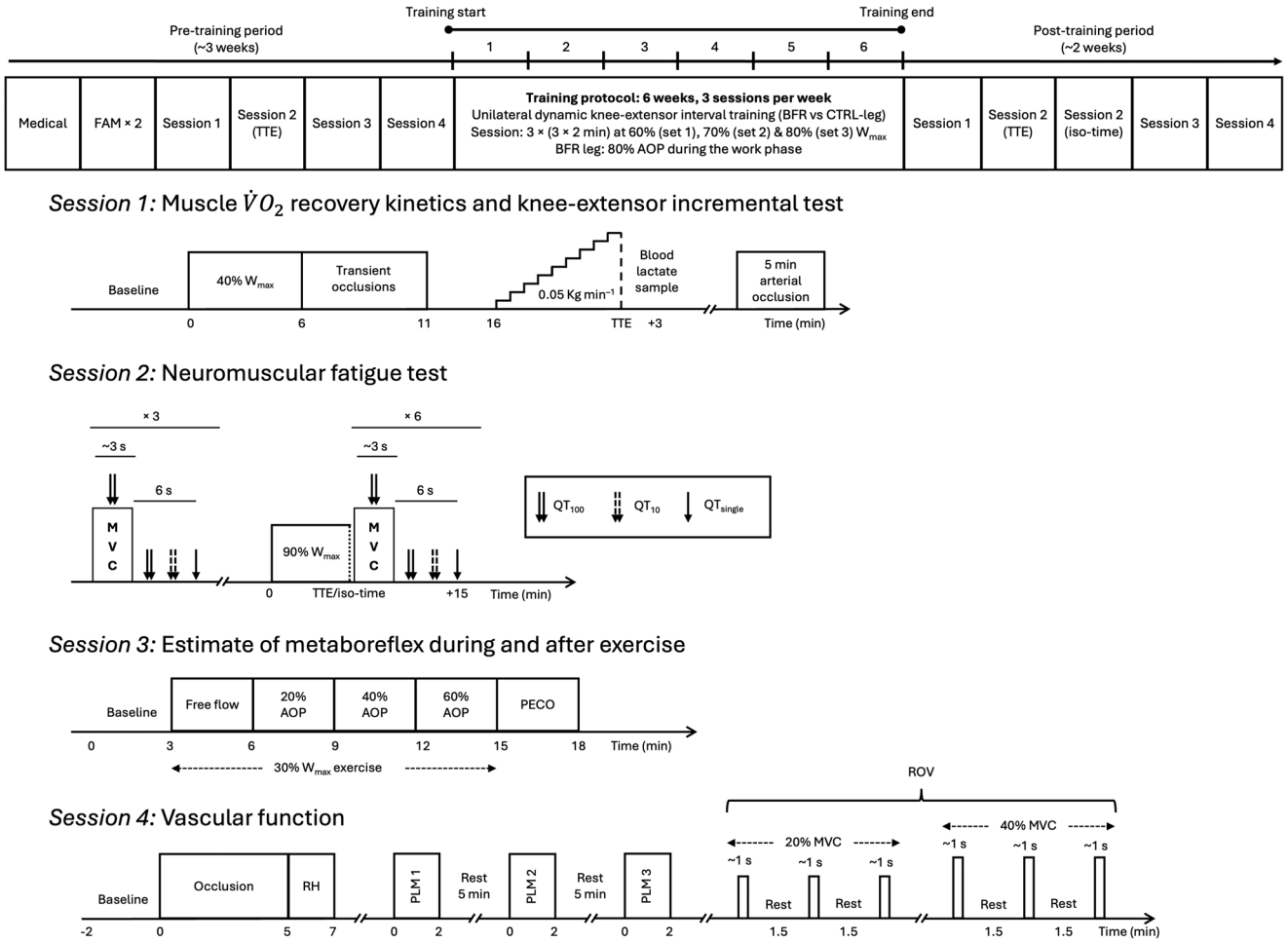

Figure 1. Schematic representation of the study timeline and testing protocols for each experimental visit

A diagram illustrating the study timeline, including the familiarization, pre-training testing, training period and post-training testing periods is shown along the top of the figure. Session 1: protocol used to estimate NIRS-derived post-exercise recovery kinetics of $m\dot{V}_{O_2}$ (a surrogate for mitochondrial respiratory capacity) and determine single-leg knee-extensor peak power output (W_{max}) and peak oxygen uptake ($\dot{V}_{O_2peak}$). Session 2: protocol used to quantify neuromuscular fatigue development. Session 3: protocol used to estimate leg metaboreflex activation. Session 4: protocol used to estimate leg vascular function using tests of reactive hyperaemia (RH), passive leg movement (PLM) and rapid-onset vasodilatation (ROV). Participants performed each test with one leg then the other (randomized order) and this order was kept the same for each participant before and after the training period. Abbreviations: AOP, arterial occlusion pressure; BFR, blood flow restriction; FAM, familiarization; FF, free-flow exercise; iso-time, the exercise task maintained until the duration completed before training was matched; $m\dot{V}_{O_2}$, muscle oxygen consumption; MVC, maximal voluntary contraction; NIRS, near-infrared spectroscopy; PECO, post-exercise circulatory occlusion; PLM, passive leg movement; RH, reactive hyperaemia; TTE, time to exhaustion; QT_{10}, potentiated quadriceps twitch evoked with supramaximal electrical 10 Hz paired stimulation; QT_{100}, potentiated quadriceps twitch evoked with supramaximal electrical 100 Hz paired stimulation; QT_{single}, potentiated twitch peak force evoked by single electrical stimulation of the femoral nerve.

dilatation (FMD), passive leg movement (PLM) and rapid onset vasodilatation (ROV), were performed using Doppler ultrasound to determine whether vascular adaptations occur in the femoral artery because of knee-extensor BFR training. On each occasion, both limbs underwent experimental testing separately, first with one leg and after a minimum of 30 min of rest with the other leg. The order of legs was randomized prior to the first experiment and kept consistent for each participant before and after the training period.

After the pre-training experimental sessions, the legs of participants were randomly assigned to a 6 week training intervention consisting of dynamic interval knee-extensor exercise with BFR for one leg (BFR-leg) and with free flow for the other leg (CTRL-leg). Randomization was performed using an open-source, web-based minimization program (Saghaei & Saghaei, 2011) and considered sex (i.e. male/female) and the dominant limb (i.e. right/left). During training, the legs were trained simultaneously, and their force output and cadence were matched every training session. Before training, each participant's arterial occlusion pressure was measured while sat upright on the knee-extensor ergometer. A 13 cm pneumatic cuff (Hokanson Inc., Bellevue, WA, USA) was applied proximally around the thigh and inflated with a rapid inflation system (Hokanson E20 cuff inflator; Hokanson). Cuff pressure was increased gradually until femoral arterial blood flow was no longer detectable by Doppler ultrasound using a linear transducer (see 'Ultrasound data analysis' for details). The pressure recorded as full occlusion was the cuff pressure that resulted in cessation of femoral artery blood flow distal to the cuff. Arterial occlusion pressure was measured three times per leg, with ≥2 min between measurements, and the mean value was used for subsequent BFR prescriptions. During the training intervention, BFR was applied at 80% of the pressure required for full arterial occlusion.

After training, each experimental session was replicated. All exercise intensities were matched according to the participants' pre-training levels. The intense exercise bout of the second experimental session (i.e. 90% of pre-training W_{max}) was terminated after the same duration at which task failure was reached before training. Participants returned for a fifth visit to perform exercise to task failure at 90% pre-training W_{max}. Post-training assessments began a minimum of 72 h (and maximum of 168 h) after the training period to allow for sufficient recovery from the final training session.

All experimental procedures and training interventions were performed under standard environmental conditions (temperature ∼20°C; relative humidity ∼40%). All experimental sessions were separated by ≥48 h to allow full recovery from exhaustive exercise (Carroll et al., 2017). All experimental measurements were performed at a similar time of day (±2 h) to minimize diurnal variations in maximal muscle performance (Tamm et al., 2009). Participants were instructed to abstain from fatiguing/high-intensity exercise and alcohol consumption for 24 h and caffeine for 12 h before each experimental session.

NIRS-derived $m\dot{V}_{O_2}$ measurements

Quadriceps mitochondrial respiratory capacity was estimated non-invasively via NIRS as the recovery rate of post-exercise muscle oxygen consumption ($m\dot{V}_{O_2}$) following the method previously proposed (Ryan et al., 2014). The NIRS probe was placed over the vastus lateralis and the BFR cuff was secured proximally around the leg to transiently occlude blood flow after exercise. The protocol began with two measurements of resting $m\dot{V}_{O_2}$ by inflating the blood pressure cuff (∼250–300 mmHg) for 30 s. Following the resting measurements, participants performed 6 min of constant work rate submaximal exercise at 40% W_{max} (adapted from Zuccarelli et al., 2020), chosen to achieve steady state in $m\dot{V}_{O_2}$. Immediately upon relaxation, a series of repeated supramaximal arterial occlusions were performed with the following timings: five occlusions lasting 5 s each, separated by 5 s with free flow; five occlusions lasting 7 s each, separated by 7 s with free flow; and 10 occlusions lasting 10 s each, separated by 10 s with free flow. Each NIRS datapoint was corrected for small changes in blood volume (Ryan et al., 2012). Resting baseline and post-exercise $m\dot{V}_{O_2}$ were calculated as the rate of change (i.e. slope) of the deoxygenated haemoglobin (HHb) signal using simple linear regression over the first 3 s (150 data points) of each individual occlusion. This short window was chosen because the deoxyhaemoglobin response is approximately linear during the initial seconds of an occlusion, improving signal-to-noise ratio. The two values from the resting measurements were averaged to obtain a resting baseline $m\dot{V}_{O_2}$ value. The repeated post-exercise $m\dot{V}_{O_2}$ measurements were fit to a mono-exponential curve (Ryan et al., 2014), and the fitting rate constant k and the corresponding time constant tau (τ) were calculated. The k-constant and τ values correlate with the maximal rate of skeletal muscle respiration determined via high-resolution respirometry (Ryan et al., 2014) and phosphocreatine (PCr) recovery kinetics via ^{31}P magnetic resonance spectroscopy (MRS) (Ryan et al., 2013), respectively. Following the incremental test, an ischaemic calibration of the NIRS signal was performed by inflating a pneumatic cuff (∼300 mmHg) for 5 min, or until the deoxygenated haemoglobin signal plateaued for 30 s, while participants remained seated upright in the ergometer with their feet off the ground. This procedure was used to obtain complete deoxygenated NIRS values

and normalize the [HHb] signal to each participant's maximal physiological value.

Assessment of exercise pressor reflex

After a 3 min baseline period, participants commenced 12 min of single-leg dynamic knee-extensor exercise corresponding to 30% of their pre-training W_{max}. Exercise began with 3 min of unrestricted flow. Thereafter, the thigh cuff was inflated to induce graded muscle ischaemia via occlusion at 20, 40 and 60% of the pressure required for full arterial occlusion. Each of these intensities comprised a 3 min exercise period. At the end of the exercise portion, the thigh cuff was inflated to a pressure of ∼300 mmHg to ensure full blood flow occlusion (i.e. PECO) for 3 min, followed by a 3 min recovery/reperfusion period. A 30 min rest period separated the metaboreflex activation trials of the first and second leg.

Assessments of vascular function

For all testing procedures, superficial femoral artery diameter, blood velocity and fingertip photoplethysmogram signals were recorded continuously at baseline and throughout the entire procedure. During a pre-training reproducibility assessment, across 11 participants (two visits, three repeats/day), the between-day coefficient of variation at baseline was 1.98 ± 1.79% for femoral artery diameter and 13.7 ± 10.2% for femoral artery velocity. The three tests described below were conducted on the same day.

Reactive hyperaemia and flow-mediated dilatation. The hyperaemic response following arterial occlusion release, referred to as RH, provides valuable insight into microvascular function (Philpott & Anderson, 2007). Additionally, endothelial function can be indirectly evaluated by measuring the vasodilatory response after a short period of cuff occlusion, known as FMD (Harris et al., 2010). Participants were positioned supine on a treatment table at rest for 20 min before the start of data collection and remained in this position for the remainder of the test. A pneumatic cuff measuring 9 cm in width (Hokanson) was positioned on the upper leg just proximal to the knee cap. Doppler ultrasound measurements were recorded with the probe placed ∼10 cm proximal to the cuff. After resting baseline, the pneumatic cuff was rapidly inflated to a supra-systolic pressure of ∼250 mmHg for 5 min. Haemodynamic measurements were performed for a minimum of 30 s prior to the release of the cuff and for 2 min immediately following pneumatic cuff deflation.

Passive leg movement. Several studies have demonstrated that the hyperaemic response to passive leg movement (PLM) is dependent on nitric oxide (NO) bioavailability (Gifford & Richardson, 2017; Hanson et al., 2020; Mortensen et al., 2012), making PLM a useful paradigm for assessing vascular function. Accordingly, PLM was performed as previously described (Hanson et al., 2020). Briefly, participants were placed seated upright at rest and remained in this position for the remainder of the test. Following baseline superficial femoral artery and peripheral haemodynamic measurements, PLM was performed for 60 s at a frequency of 1 Hz (i.e. 60 passive knee extensions per minute) using a metronome. PLM was achieved by a member of the research team manually moving the participant's lower leg through a range of motion from 90° to 180° at the knee joint. Participants were instructed to remain relaxed throughout the test and to not resist or assist with the movement. This procedure was replicated three times each leg with a ∼10 min rest period between each trial.

Rapid-onset vasodilatation. ROV, an index of the vascular responsiveness to a single muscle contraction, has also been shown to be dependent on NO bioavailability (Casey et al., 2013). ROV was assessed having participants perform single 1 s isometric quadriceps contractions at 20% and 40% of their pre-training maximal voluntary contraction (MVC) in the isometric dynamometer. Participants received commands to contract and relax, and real-time force feedback was displayed to a computer monitor placed in front of the subject. Each contraction was monitored to ensure proper contraction intensity and duration. Three contractions were performed at each intensity with rest intervals of ≥90 s given between contractions to allow haemodynamics to return to baseline, and ≥5 min between intensity blocks (Crecelius et al., 2013). Haemodynamic measurements were performed prior, during and for 45 s following contraction.

Training intervention

Supervised training consisted of 18 sessions over 6 weeks, performed three times per week on non-consecutive days, with an adherence rate of 100%. Each training session consisted of a 5 min warm-up at 30% W_{max}, followed by three sets of 3 × 2 min intervals. Passive recovery was given for 1 min between intervals and for 5 min between sets. The intensities were set at 60% (32 ± 7 W), 70% (37 ± 9 W) and 80% W_{max} (42 ± 10 W) for the first, second and third sets, respectively. Unlike the previous studies by Christiansen et al. (2019, 2020), the external workload was increased throughout the training period by up to an additional ∼10–15% of W_{max} per set, since some of our participants were highly fit (i.e. competitive amateur track & field, volleyball or mixed martial arts athletes). The legs were trained concurrently, and the force generated

by each leg was matched using s-beam force transducers (LC101-500 Omegadyne, Sunbury, OH, USA). Force and cadence of each leg were displayed on a computer monitor placed in front of the participant to provide real-time visual feedback.

Blood flow to the working muscles of the BFR-leg was intentionally restricted during each interval by inflating the BFR cuff, placed around the most proximal part of the leg, to 80% of the pressure required for full arterial occlusion (165 ± 36 mmHg). A previous study on leg BFR training using a similar cuff pressure reported an ∼50% reduction in blood flow during exercise (Christiansen et al., 2019). The cuff was immediately inflated at the start of each interval and deflated at the end to facilitate local muscle ischaemia during exercise bouts and reperfusion during recovery periods. Previous studies have shown that this type of protocol is ideal for optimizing training adaptations, as it imposes optimal metabolic, ionic and redox stress on peripheral tissues (Christiansen et al., 2018, 2021).

Data collection and analyses

Neuromuscular assessment of quadriceps function. The set-up for the neuromuscular assessment of quadriceps function and force acquisition in our laboratory has been described previously (Lavigne et al., 2024). Briefly, subjects were seated upright on a custom-made isometric dynamometer with both the trunk–thigh angle and knee joint angle at ∼90°. A non-compliant strap attached to a calibrated load cell (model LC101, Omega Engineering Inc, Norwalk, CT, USA) was fixed to the subject's ankle, just superior to the malleoli. Wireless surface EMG sensors (Trigno Wireless EMG system, Delsys, Boston, MA, USA) were placed at the muscle belly of the vastus lateralis (VL), vastus medialis (VM), rectus femoris (RF) and biceps femoris (BF) (Hermens et al., 2000). The EMG signals were digitized at a sampling rate of 2000 Hz using a data acquisition system (PowerLab 16/35, ADInstruments, Australia), recorded using commercially available software (Labchart v8.1.25, ADInstruments) and stored for further off-line analysis. Percutaneous electrical stimulation was delivered to the femoral nerve via a cathode electrode (30 × 30 mm, Ag-AgCl, Mini-KR; Contrôle Graphique, Brie-Comte-Robert, France) secured in the inguinal triangle with gauze and tape. The anode, a 50 × 90 mm electrode (Durastick Plus; DJO Global, Vista, CA, USA) was placed on the gluteal fold. A constant current stimulator (DS7A; Digitimer, Welwyn Garden City, UK) was used to deliver a square-wave stimulus of 1 ms in duration. Optimum stimulus intensity was determined as the current that did not elicit an increase in quadriceps resting twitch and compound muscle action potentials (M_{max}) following two successive 10 mA increments at rest. To ensure maximal spatial recruitment of motor units during the neuromuscular tests, this intensity was multiplied by 130%. The mean ± SD stimulus intensity was not different between legs (70 ± 19 *vs.* 68 ± 20 mA, $P = 0.407$) for all visits.

Neuromuscular assessments were conducted before and immediately after every exercise protocol using a standardized set of contractions. In each set, participants performed a 3 s MVC during which superimposed paired stimuli at 100 Hz (QT_{100} superimposed) were delivered at the peak force of the MVC to determine voluntary activation (VA) of the quadriceps (Merton, 1954). Then, potentiated quadriceps twitch forces evoked by paired 100 Hz (QT_{100}), paired 10 Hz (QT_{10}) and single (QT_{single}) electrical stimulations of the femoral nerve were elicited 2, 4 and 6 s after each MVC, respectively. At baseline (i.e. before single-leg knee-extensor exercise), three standardized sets of contractions, separated by 1 min, were performed following a brief quadriceps warm-up routine. After exercise, to capture the rapid recovery from fatigue that occurs within the first minutes after exercise termination, the same standardized sets of contractions were performed at exactly 20 s and 1, 2, 4, 8 and 15 min after exercise.

Peak force was determined for all MVC, QT_{100} and QT_{10} measurements. For all QT_{single} measurements, peak force, contraction time to peak force (CT), maximal rate of force development (MRFD, maximal value of the first derivative of the force signal) and half-relaxation time (HRT, time to obtain half the decline in maximal force) were determined. The $QT_{10:100}$ ratio (i.e. QT_{10}/QT_{100}) was calculated and interpreted as an index of prolonged low-frequency force depression (Martin et al., 2004). Quadriceps VA during MVCs was calculated as follows (Merton, 1954).

$$\text{VA } (\%) = \left(1 - \frac{QT_{100\ \text{superimposed}}}{QT_{100}}\right) \times 100$$

The greatest baseline MVC, QT_{single}, QT_{10}, QT_{100}, $QT_{10:100}$, VA and MRFD values and the lowest baseline CT and HRT values from the pre-exercise standardized sets of contractions were used for analysis (Ducrocq & Blain, 2022). Pre- to post-exercise differences in MVC, VA, QT_{single}, QT_{10}, QT_{100} and $QT_{10:100}$ (expressed as a percentage change from pre-exercise) were calculated to quantify and characterize the origin of exercise-induced neuromuscular fatigue.

Evoked M_{max} responses of VL, VM and RF muscles were analysed from the QT_{single} stimulation for peak-to-peak amplitude. The root mean square of the EMG signal recorded during each MVC (RMS_{MVC}) was analysed as the highest 500 ms average produced during voluntary effort. During exercise, each EMG burst from

the VL, VM and RF was identified using a custom-written MATLAB script (MathWorks Inc., Natick, MA, USA). The RMS of each EMG burst was calculated during exercise. RMS values were then normalized to the highest RMS value of the pre-exercise MVC ($RMS_{\%MVC}$) and 30 s bin averaged.

Central haemodynamics. Beat-by-beat heart rate (HR) and blood pressure variables (systolic blood pressure, SBP; diastolic blood pressure, DBP; mean arterial pressure, MAP) were recorded continuously via a non-invasive dual finger photoplethysmography unit (Human NIBP Nano System, ADInstruments). The left hand was held on a custom-made support at the level of the heart and photoplethysmography cuffs were placed on the third and fourth fingers. A software extension (Non-Invasive Cardiac Output, ADInstruments) was added to the LabChart 8 software to estimate stroke volume from the blood pressure waveform and subsequently cardiac output (stroke volume × HR) with the ModelFlow algorithm (Windkessel model, ADInstruments).

Ultrasound data analysis. Blood velocity and vessel diameter of the superficial femoral artery were measured using a Doppler ultrasound system (ArtUs EXT-1H, Telemed Medical Systems, Vilnius, Lithuania) equipped with a linear array transducer (L12-5N40-A4, Telemed Medical Systems) operating in duplex mode at a B-mode imaging frequency of 12 MHz and Doppler frequency of 4 MHz. Data were acquired using commercially available software (EchoWave II, v.3.4.4, Telemed Medical Systems). Blood velocity measurements were obtained with the transducer positioned to maintain an insonation angle $\leq 60°$, with the sample volume maximized and centred according to vessel size. Femoral artery B-mode images and pulsed-wave Doppler waveforms were recorded as video files, stored digitally and analysed off-line with custom-written MATLAB scripts (Meste et al., 2024). Frame-by-frame analysis was conducted for vessel diameter using automated edge detection at a perpendicular angle along the central axis of the artery and for blood velocity based on pixel intensities modelled as a probability density function. Diameter and velocity data were then synchronized, which enabled the calculation of blood flow and shear rate. Femoral blood flow was calculated using the equation:

$$\begin{aligned} &bloodflow\left(\mathrm{ml}\cdot min^{-1}\right) \\ &= \left\{\left(\text{mean blood velocity } \left(\mathrm{cm}\cdot s^{-1}\right)\right)\right. \\ &\quad \left.\times\left[\pi \times (\text{vessel radius } (\mathrm{cm}))^2\right]\times 60\right\} \end{aligned}$$

and shear rate (SR) was calculated as:

$$\mathrm{SR}\ \left(\mathrm{s}^{-1}\right) = \frac{4 \times \text{mean blood velocity } \left(\mathrm{cm}\cdot s^{-1}\right)}{\text{diameter } (\mathrm{cm})}$$

For RH and PLM, blood flow data were subsequently bin-averaged into 1 s bins corresponding to 1 s averaged velocities and diameters and smoothed. For ROV, blood flow data were bin-averaged into one-cardiac cycle bins corresponding to one-cardiac cycle averaged velocities and diameters. Resting diameter (cm) was averaged over 30 s. The dilatory response (i.e. FMD) during RH was established as the percentage change from baseline to peak arterial diameter (3 s average value) and calculated with the equation:

$$\mathrm{FMD}\ (\%) = \frac{\text{peak diameter} - \text{baseline diameter}}{\text{baseline diameter}} \times 100$$

while peak flow during the protocols was identified as the highest 1 s average, and area under the curve (AUC) was calculated for blood flow and shear rate. Limb vascular conductance (LVC) was calculated as:

$$LVC\left(ml\cdot min^{-1}\cdot mmHg^{-1}\right) = bloodflow\left(ml\cdot min^{-1}\right) / MAP\left(mmHg\right)$$

Cardiorespiratory and metabolic variables. Gas exchange and ventilatory variables were collected using a calibrated breath-by-breath portable gas analyser (Cortex MetaMax 3B, Cortex GmbH, Leipzig, Germany). HR was recorded using a chest strap heart rate monitor (Polar H7, Polar Electro Oy, Kempele, Finland). Oxygen uptake ($\dot{V}_{O_2}$), carbon dioxide output ($\dot{V}_{CO_2}$), $\dot{V}_{CO_2}/\dot{V}_{O_2}$, minute ventilation ($\dot{V}_E$), $\dot{V}_E/\dot{V}_{O_2}$, $\dot{V}_E/\dot{V}_{CO_2}$, breathing frequency (f_B), tidal volume (V_T) and HR were recorded during all experimental exercise sessions. Data were cleaned and interpolated to 1 s intervals with MATLAB custom-written scripts before bin analysis. Except for HR, which was computed as a 5 s average, all cardiorespiratory variables were computed using the last 30 s of each exercise phase.

Finger prick blood samples (5 µl) were collected at 3 min after exercise and analysed by a portable lactate meter (LactatePro2, Arkray, Kyoto, Japan) to determine blood lactate concentration ([La]b).

Near-infrared spectroscopy. Concentrations of oxygenated haemoglobin [O_2Hb], deoxygenated haemoglobin [HHb] and total haemoglobin ([tHb] = [O_2Hb] + [HHb]) were measured using a continuous wave NIRS device (OxyMon; Artinis Medical Systems, Elst, The Netherlands) as previously described (Van Beekvelt et al., 2001). Wavelengths of 765 and 855 nm were emitted from photodiodes secured in optode holders, fixed longitudinally over the vastus

lateralis, approximately two-thirds between the greater trochanter and superior border of the patella, which allowed for multiple optode distances between 25 and 55 mm. Adhesive tape secured the optode holders to the skin, and an optically dense black cloth and an elastic tensor bandage were used to limit any extraneous light or movement from interfering with the device. The skin underneath the probes was shaved and cleansed with an isopropyl alcohol swab. Skinfold thickness was measured using a Harpenden Skinfold Caliper (Baty International, UK) to ensure that the depth of light penetration was sufficient to effectively interrogate the underlying muscle at a depth more than twice the skinfold thickness beneath the optode holder (Barstow, 2019). Data were recorded continuously at 50 Hz via an online data acquisition system OxySoft (Artinis Medical Systems). Given that NIRS signals measure absolute changes from a set baseline, haemoglobin signals were set to zero following collection, and values were calculated as micromolar changes from rest. The raw signals were filtered with a moving Gaussian smoothing algorithm and data were extracted in .xlsx format and processed using custom-written scripts in MATLAB.

Statistical analysis

Data are presented as mean ± SD unless otherwise stated. Normality of dependent variables were assessed using the Shapiro-Wilks test. A random-intercepts linear mixed-effects model (LMM) was conducted to assess the main effects of condition and time, and condition × time interaction effects on all dependent variables data. This modelling framework incorporates all sampled data rather than just the mean values from each participant, thereby preserving variability both within and across participants. For variables that were assessed repeatedly and/or bin averaged over time, analyses were performed separately for the condition main effects of training (pre-training *vs.* post-training) and differences with training between legs (CTRL-leg *vs.* BFR-leg) and time (repeated samples) as fixed factors. For variables assessed at a single time point before and after the training period, a two-way (2 × 2) repeated-measures ANOVA was performed to evaluate differences between training (pre-training *vs.* post-training) and leg (CTRL-leg *vs.* BFR-leg). An alpha-level of $P < 0.05$ was used to indicate statistical significance. F values are reported for main and interaction effects (Cohen, 1988). *Post hoc* analyses were performed using Tukey's HSD test to examine differences from baseline for each condition and for differences between conditions within the same timepoint. Effect size for ANOVA (partial eta squared, ${}_{p}\eta^2$) was interpreted based on Cohen's conventions, where <0.06, 0.06–0.14 and >0.14 were considered as a small, medium and large effect, respectively (Cohen, 1988). Effect size for *post hoc* analysis (Cohen's d) was interpreted as trivial (<0.2), small (0.2–0.5), moderate (>0.5–0.8) and large (>0.8) (Cohen, 1988). All statistical tests were performed using RStudio (version 2024.12.0+467).

Results

Adverse effects of BFR training

Twelve participants were initially recruited in this study. However, one was withdrawn during the training phase due to the development of an encapsulated, isolated and non-vascularized haematoma in the medial saphenous compartment, attributed to cuff-related trauma. The remaining 11 participants completed the full protocol without reporting any adverse effects.

Performance, metabolic and cardiorespiratory responses to exercise

W_{max} increased in both legs (CTRL-leg: $P = 0.005$, $d = 1.58$; BFR-leg: $P < 0.001$, $d = 2.90$), with 17 ± 11% greater improvements in the BFR-leg ($P = 0.003$, $d = 1.62$). Time to task failure at 90% pre-training W_{max} increased by 118 ± 78% in the CTRL-leg (pre: 298 ± 86 s, post: 665 ± 375 s; $P = 0.010$, $d = 1.76$) and 234 ± 83% in the BFR-leg (pre: 293 ± 74 s, post: 997 ± 420 s; $P < 0.001$, $d = 3.37$), with the BFR-leg outperforming the CTRL-leg by 65% ($P = 0.022$, $d = 1.59$). Performance changes were not correlated between legs (both $r \leq 0.33$, $P > 0.321$), suggesting that the improvement in performance observed in the CTRL-leg was independent of those in the BFR-leg. Metabolic and cardiorespiratory adaptations (see Table 1*A*, Supplementary Appendix) occurred only in the BFR-leg. During the incremental test, $\dot{V}_{O_2peak}$ ($P = 0.004$, $d = 1.59$), $\dot{V}_E$ ($P = 0.002$, $d = 1.73$), HR ($P = 0.004$, $d = 1.61$), and post-exercise blood lactate (5.6 ± 2.0 to 7.7 ± 2.2 mM; $P = 0.031$, $d = 1.63$) increased, whereas the CTRL-leg showed no changes (all $P > 0.514$).

Neuromuscular responses

Work- and duration-matched exercise. In both legs, training had no effect on baseline MVC, potentiated twitch parameters, M_{max}, VA and RMS_{MVC} ($F = 0.02$–3.69, all $P > 0.089$, all ${}_{p}\eta^2 < 0.09$). In both legs, training attenuated exercise-induced fatigue from work rate- and duration-matched exercise at 90% pre-training W_{max}, as evidenced by a lesser reduction in MVC (BFR-leg: $F = 204.52$, $P = < 0.001$; CTRL-leg: $F = 61.58$, $P < 0.001$),

QT_{single} (BFR-leg: $F = 416.08$, $P < 0.001$; CTRL-leg: $F = 98.68$, $P < 0.001$), QT_{10} (BFR-leg: $F = 315.18$, $P < 0.001$; CTRL-leg: $F = 102.2$, $P < 0.001$), QT_{100} (BFR-leg: $F = 138.17$, $P < 0.001$; CTRL-leg: $F = 62.94$, $P < 0.001$) and $QT_{10:100}$ (BFR-leg: $F = 188.12$, $P < 0.001$; CTRL-leg: $F = 46.25$, $P < 0.001$) throughout recovery (Fig. 2). Training also attenuated the exercise-induced decline in MRFD (BFR-leg: Δ27%, $F = 257.02$, $P < 0.001$; CTRL-leg: Δ16%, $F = 65.06$, $P < 0.001$) and the extent to which exercise impaired CT throughout the recovery period (BFR-leg: Δ−12%, $F = 39.83$, $P < 0.001$; CTRL-leg: Δ−5%, $F = 38.30$, $P < 0.001$). These improvements were greater in the BFR-leg than CTRL-leg for MVC (∼6%, $F = 34.16$, $P < 0.001$), QT_{single} (∼8%, $F = 29.48$, $P = 0.001$), QT_{10} (∼6%, $F = 102.2$, $P = 0.001$), QT_{100} (∼7%, $F = 30.67$, $P = 0.001$), $QT_{10:100}$ (∼6%, $F = 23.95$, $P = 0.001$) and MRFD (∼15%, $F = 65.06$, $P < 0.001$). There was no exercise-induced reduction in VA in either leg, before or after training ($P > 0.279$).

Training decreased $RMS_{\%MVC}$ in all muscles during the work- and duration-matched exercise in both the BFR-leg (VL: ∼15%, $F = 11.12$, $P = 0.001$; VM: ∼35%, $F = 32.74$, $P < 0.001$; RF: ∼49%, $F = 48.17$, $P < 0.001$) and the CTRL-leg (VL: ∼12%, $F = 13.17$, $P = 0.001$; VM: ∼17%, $F = 22.67$, $P < 0.001$; RF: ∼49%, $F = 33.64$, $P < 0.001$), with no difference between legs (Fig. 3).

Constant work rate time to task failure exercise. Despite the large increases in performance after training, when exercise was performed to exhaustion, reductions in QT_{single}, QT_{10} and QT_{100} and recovery from fatigue remained unchanged compared to pre-training in both legs (BFR-leg: $F = 0.44$–0.78, all $P > 0.380$; CTRL-leg: $F = 0.10$–3.61, all $P > 0.061$). In the BFR-leg, the exercise-induced decrease in MVC force decreased less at post- compared to pre-training times during recovery (∼4%, $F = 4.47$, $P = 0.038$). In the CTRL-leg, $QT_{10:100}$ declined more after training than before training during recovery (∼−4%, $F = 14.01$, $P < 0.001$). After training, the pre- to post-exercise reductions in HRT and CT were attenuated throughout the recovery period compared to pre-training (i.e. improved) in both the BFR-leg (HRT: ∼21%, $F = 20.41$, $P < 0.001$; CT: ∼7%, $F = 8.38$, $P = 0.005$) and CTRL-leg (HRT: ∼16%, $F = 51.50$, $P < 0.001$; CT: ∼16%, $F = 17.94$, $P < 0.001$), without any difference between legs (both $P > 0.112$). Training did not change MRFD in either leg (both $P > 0.862$). Before training, neither leg showed an exercise-induced reduction in VA ($P > 0.541$). After training, VA declined in both legs (CTRL-leg: 95 ± 4 to 89 ± 7%, $P = 0.010$, $d = 1.01$; BFR-leg: 98 ± 2 to 84 ± 14%, $P = 0.030$, $d = 1.33$), with no between-leg differences ($P > 0.444$). In contrast, training did not significantly affect VL, VM or RF RMS_{MVC} across the recovery period (all $P > 0.056$).

Vascular function

Reactive hyperaemia. There were no differences for baseline arterial blood flow, diameter and shear rate between legs either before or after training (all $P > 0.473$), nor were they affected by training in the legs (both $P > 0.064$). On average, RH femoral blood flow increased in the BFR-leg (∼26%, $F = 236.12$, $P < 0.001$) and decreased in the CTRL-leg from pre- to post-training (∼−11%, $F = 56.88$, $P < 0.001$). Accordingly, after training, the RH blood flow response was greater in the BFR-leg than in the CTRL-leg (∼32%, $F = 453.50$, $P < 0.001$) (Fig. 4*A* and *B*). Likewise, training increased mean RH LVC in the BFR-leg from 9.3 ± 7.4 to 11.3 ± 10.2 ml min^{-1} $mmHg^{-1}$ ($F = 100.87$, $P < 0.001$), but was lower from pre- to post-training in the CTRL-leg (pre: 10.6 ± 8.0 ml min^{-1} $mmHg^{-1}$, post: 7.4 ± 6.9 ml min^{-1} $mmHg^{-1}$; $F = 180.33$, $P < 0.001$). After training, mean RH LVC was higher in the BFR-leg than in the CTRL-leg ($F = 484.05$, $P < 0.001$).

During the RH response, peak blood flow increased by ∼27% with training in the BFR-leg, but not in the CTRL-leg (Fig. 4*C*). After training, peak RH blood flow was higher in the BFR-leg than in the CTRL-leg by ∼30%. An interaction effect ($F = 11.99$, $P = 0.002$) revealed that peak LVC was higher in the BFR-leg than in the CTRL-leg (∼28%, $P = 0.041$, $d = 1.25$). Training did not change the overall time to peak flow in the legs (13 ± 3 s; range: 6–18 s; $F = 0.09$, $P = 0.771$) or FMD ($F = 0.043$, $P = 0.838$). The peak shear rate, blood flow AUC and shear rate AUC were not different with training or between legs (Fig. 4*D*–*F*).

Passive leg movement. Time course changes in femoral blood flow during PLM are shown in Fig. 5. Mean blood flow increased from pre- to post-training in both legs (CTRL-leg: ∼8%, $F = 11.84$, $P < 0.001$; BFR-leg: ∼6%, $F = 5.14$, $P = 0.024$). LVC during PLM slightly increased from pre- to post-training in the CTRL-leg (pre: 1.6 ± 1.1 ml min^{-1} $mmHg^{-1}$, post: 1.7 ± 1.2 ml min^{-1} $mmHg^{-1}$; $F = 13.42$, $P < 0.001$), but did not change in the BFR-leg (pre: 1.9 ± 1.3 l min^{-1} $mmHg^{-1}$, post: 1.9 ± 1.2 l min^{-1} $mmHg^{-1}$; $F = 0.05$, $P = 0.818$). PLM peak blood flow, peak shear rate, blood flow AUC and shear rate AUC were not different with training and were also not different between legs (Fig. 5*C*–*F*).

Rapid onset vasodilatation. Figure 6*A*–*D* illustrates the time course changes in absolute femoral blood flow responses following single-leg contraction at 20% and 40% MVC. The mean hyperaemic response was not different between legs at pre-training for either intensity ($F = 0.10$–2.38, $P > 0.123$). At the 40% MVC trial, blood flow increased from pre- to post-training in the BFR-leg (∼9%, $F = 9.82$, $P = 0.002$), but not in the CTRL-leg ($F = 2.36$, $P = 0.125$). After training, mean blood flow was,

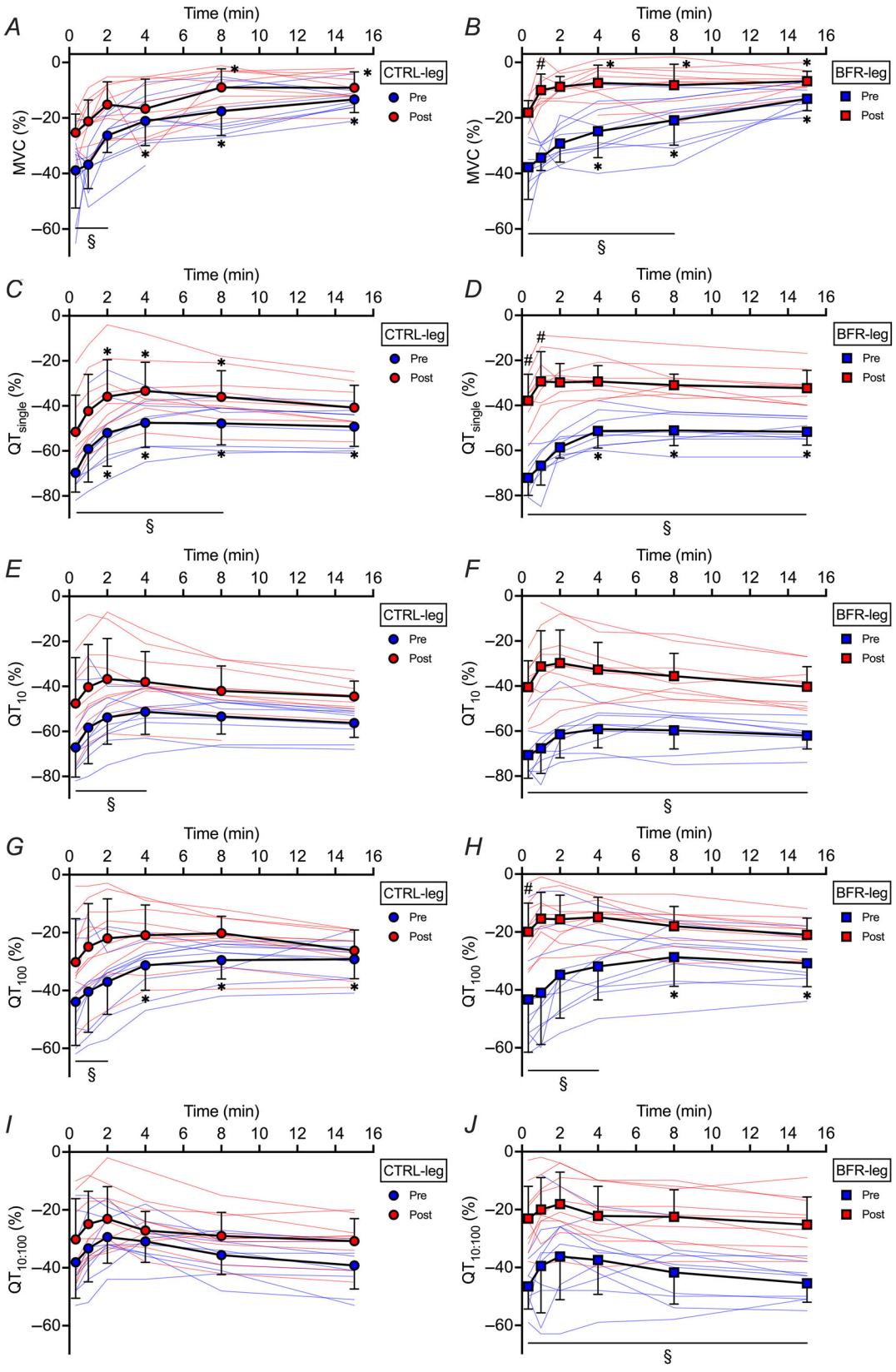

Figure 2. Effect of training on quadriceps neuromuscular fatigue and recovery following high-intensity exercise at the same workload and for the same duration
Line and scatter plots displaying the transient reduction and subsequent 15 min recovery period of quadriceps neuromuscular fatigue indices by comparing the measurements performed after to before dynamic knee-extensor

exercise in the control leg (CTRL-leg, left panels) and the leg that trained with BFR (BFR-leg, right panels). Before training (Pre, blue symbols), exhaustion was reached after ∼3–8 min of exercise at 90% W_{max}. After training (Post, red symbols), exercise at 90% of the pre-training W_{max} was terminated after the same time at which exhaustion was reached Pre. Symbols (circles: CTRL-leg; squares: BFR-leg) and error bars represent the mean ± SD and lines indicate individual participants. Abbreviations: MVC, maximal voluntary contraction; QT_{10}, potentiated quadriceps twitch evoked with supramaximal electrical 10 Hz paired stimulation; QT_{100}, potentiated quadriceps twitch evoked with supramaximal electrical 100 Hz paired stimulation; $QT_{10:100}$, low-frequency fatigue ratio (QT_{10}/QT_{100}); QT_{single}, potentiated twitch peak force evoked by single electrical stimulation of the femoral nerve. Differences between time points that were statistically significant are shown for outcomes based on *post hoc* testing. $^{*}P < 0.05$, different from 20 s post-exercise for the condition and at the time point indicated; $^{\S}P < 0.05$, Post different from Pre; $^{\#}P < 0.05$, different from CRTL-leg at Post.

on average, higher in the BFR-leg than in the CTRL-leg for both trials (20% MVC: ∼10% $F = 7.02$, $P = 0.008$; 40% MVC: ∼13%, $F = 16.68$, $P < 0.001$). In both legs, training did not change peak blood flow at 20% MVC (Fig. 6*E*); however, a peak hyperaemic training effect was observed at 40% MVC (Fig. 6*F*). The blood flow AUC at 20% and 40% MVC were not different with training or between legs (Fig. 6*G* and *H*).

Muscle mitochondrial respiratory capacity

Group mean $m\dot{V}_{O_2}$ recovery kinetics curves, k values and τ values are shown in Fig. 7*A* and *B*. From pre- to post-training, individual k values increased and τ values decreased in both legs, indicating that the NIRS recovery rate and time constants improved with training, without differences between legs (Fig. 7*C* and *D*).

Leg metaboreflex activation

As illustrated in Fig. 8, training did not affect central cardiovascular responses during free flow exercise with both legs (all $P > 0.057$), without differences between legs (all $P > 0.155$). Over graded BFR exercise, HR for the BFR-leg and CTRL-leg were respectively ∼13% and ∼5% less at post- compared to pre-training (both $P < 0.001$). In the BFR-leg only, SBP ($F = 25.56$, $P < 0.001$), DBP ($F = 15.06$, $P < 0.001$) and MAP ($F = 17.10$, $P < 0.001$) decreased from pre- to post-training. After training, these variables were lower during exercise with the BFR-leg compared to the CTRL-leg (SBP: $F = 15.47$, $P < 0.001$; DBP: $F = 17.92$, $P < 0.001$; MAP: $F = 17.99$, $P < 0.001$; HR: $F = 7.66$, $P = 0.008$). Cardiovascular responses during PECO were unchanged after training in both legs (all $P > 0.230$), with no difference between legs (all $P > 0.234$).

Discussion

The aim of this study was to examine the extent to which BFR interval training influences exercise performance and fatigue development in response to dynamic exercise, and to identify the physiological mechanisms underlying these effects. We found that training with BFR led to greater improvements in single-leg exercise performance and less exercise-induced neuromuscular fatigue than training without BFR. This enhancement was evidenced by less of a decrement in maximum force-generating capacity following training with BFR compared to the CTRL-leg after constant workload exercise performed at the same intensity (90% of the pre-training W_{max}) and duration as before training. After training, contractile function, assessed via the amplitude of evoked twitches, also improved more in the BFR-leg, indicating less peripheral fatigue throughout the 15 min post-exercise recovery period compared to the control. Relative to control, BFR interval training enhanced vascular function, as shown by increased blood flow responsiveness during tests of RH, PLM and ROV. Lastly, $m\dot{V}_{O_2}$ recovery kinetics improved similarly in both legs from before to after training. Overall, these integrative data suggest that BFR training attenuates fatigue during intense exercise, in part via improved neuromuscular and vascular adaptations, rather than changes in estimated mitochondrial respiratory capacity.

Effects of BFR training on exercise performance

This study showed that training with a reduction in blood flow to exercising muscles led to substantially greater improvements in exercise capacity compared to training without BFR, despite both legs performing the same amount of work during the training period. In comparison to the control, BFR training elicited a nearly twofold larger increase in peak power output during incremental single-leg dynamic knee-extension exercise to task failure (Table 1*A*, Supplementary Appendix). We also showed a twofold larger increase in time to task failure during constant work rate single-leg dynamic knee-extension exercise at 90% pre-training W_{max}. In agreement with our results, bilateral interval cycling (3 × 3 × 2 min with each set performed at 60, 70 and 80% of maximal aerobic power) with blood flow to exercising muscles of one leg reduced by ∼50% (cuff pressure: ∼180 mmHg) three times per week for 6 weeks resulted in a twofold greater increase in single-leg incremental peak power output than the training control (Christiansen et al., 2019). Similarly, bilateral cycling (15 min at 40% $\dot{V}_{O_2max}$) with reduced

blood flow to both legs (pressure: 160–220 mmHg), performed three times per week for 8 weeks, resulted in a 15% improvement in cycling time to exhaustion during an incremental test, whereas, by contrast, no performance change was observed in the non-BFR training control despite a two-thirds higher training volume (Abe et al., 2010). Our findings further support that BFR training at light and moderate to vigorous exercise intensities, applied over a short period (6–8 weeks), elicits substantially greater improvements in exercise performance than training at the same exercise intensity without BFR. This is particularly relevant in situations where individuals

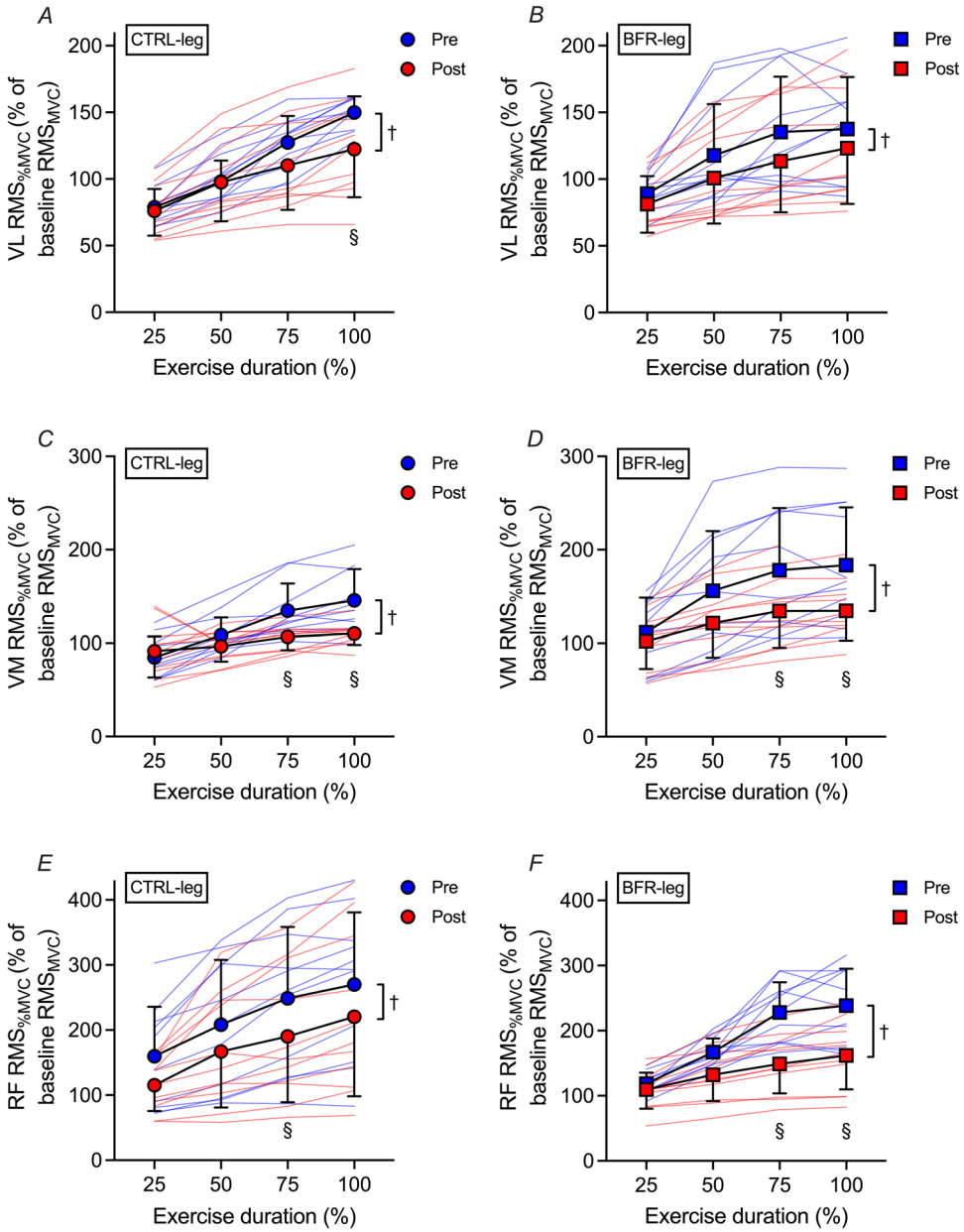

Figure 3. Effect of training on quadriceps muscle activation during high-intensity exercise at the same workload and for the same duration
Line and scatter plots displaying root-mean-square EMG normalized to the RMS recorded during pre-exercise MVC ($RMS_{\%MVC}$) for the vastus lateralis (VL) (*A* and *B*), vastus medialis (VM) (*C* and *D*) and rectus femoris (RF) (*E* and *F*) in the control leg (CTRL-leg, left panels) and the leg that trained with BFR (BFR-leg, right panels). Before training (Pre, blue symbols), exhaustion was reached after ∼3–8 min of exercise at 90% W_{max}. After training (Post, red symbols), exercise at 90% of the pre-training W_{max} was terminated after the same time at which exhaustion was reached Pre. Each data point represents the average over the preceding quarter section of the exercise bout. Symbols (circles: CTRL-leg; squares: BFR-leg) and error bars represent the mean ± SD and lines indicate individual participants. †Significant main effect of training; §$P < 0.05$, Post different from Pre.

are unable to tolerate higher mechanical loads, such as in the case of injury, joint pain or rehabilitation, yet still require an effective training stimulus to improve functional capacity.

Effects of BFR training on exercise-induced fatigue

After training, the BFR-trained leg exhibited less neuromuscular fatigue during recovery after being exercise-matched for work rate and duration compared to both its pre-training condition and the control leg after training (Fig. 2). Also, during recovery from high-intensity exercise performed to exhaustion, neuromuscular fatigue in the BFR-trained leg was comparable to both legs before training and to the control after training, despite the BFR-trained leg performing substantially more work after training. Together, these data provide strong evidence that BFR training delayed/limited the rate of fatigue development to a greater extent than the training control, suggesting that the BFR-leg was more resistant to fatigue. Regarding the latter observation, these findings appear consistent with previous studies showing that exercise performance is tightly regulated by the development of peripheral fatigue, which is constrained to a critical level associated with a certain level of intramuscular metabolic perturbation (Amann & Dempsey, 2008; Amann et al., 2006). Most neuromuscular adaptations were of peripheral origin, as evidenced by the attenuated exercise-induced decline in evoked twitch forces (QT_{single}, QT_{10} and QT_{100}) for the same amount of work performed after *vs.* before training. The absence of a training effect on M_{max} indicates that the enhanced preservation of force in the BFR-trained leg was not attributable to improved

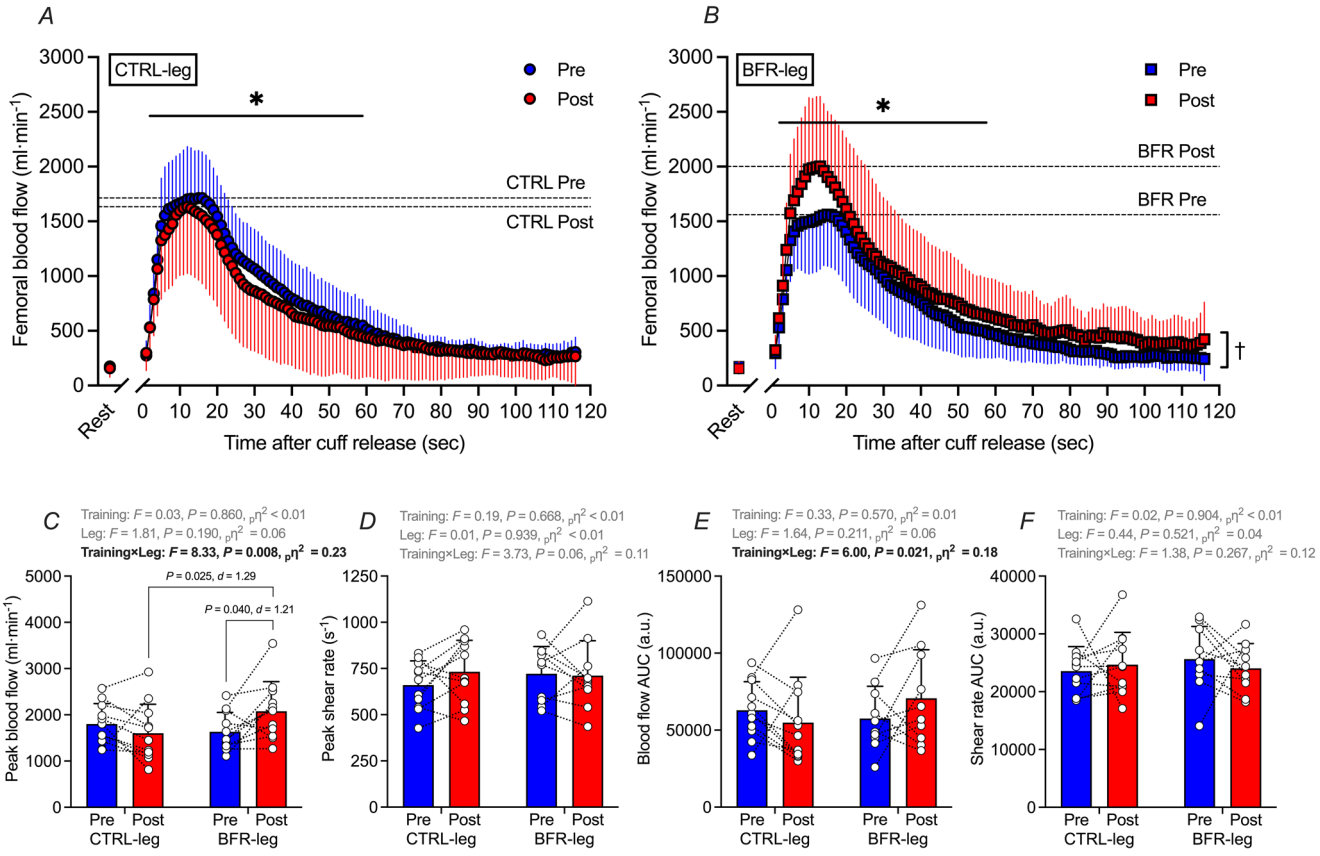

Figure 4. Effect of training on reactive hyperaemia leg blood flow and wall shear rate responses
Resting baseline and post-ischaemic blood flow during ∼120 s of reactive hyperaemia is shown in the leg that trained without BFR (CTRL-leg) (*A*) and with BFR (BFR-leg) (*B*). *C* and *D*, absolute peak post-ischaemic blood flow and wall shear rate, respectively. *E* and *F*, area-under-the-curve (AUC) for post-ischaemic blood flow and wall shear rate, respectively. For *A* and *B*, symbols and error bars represent the mean ± SD and the horizontal dashed lines represent average peak blood flow values for each condition. For *C*–*F*, coloured bars are the mean, error bars are ±SD and each open dot indicates individual participants. Pre-training (Pre) data are plotted in blue and post-training (Post) data in red. *F*-values, *P*-values and $_p\eta^2$ for the main effects of training, leg and the training × leg interaction, as determined with a two-way 2 × 2 repeated-measures ANOVA, are shown above each panel. Significant ($P < 0.05$) main effects and interaction effects are shown in bold, black text. †Significant main effect of training on averaged blood flow; *$P < 0.05$, different from rest.

membrane excitability (Fuglevand et al., 1993). In contrast, the smaller exercise-induced reduction for $QT_{10:100}$ in the BFR-trained leg compared to the control suggests that BFR training elicits peripheral adaptations that help preserve excitation–contraction coupling and muscle Ca^{2+} handling/sensitivity during exercise (Martin et al., 2004), potentially by mitigating ROS-mediated impairments (Bruton et al., 2008). In our previous study (Lavigne et al., 2024), we demonstrated that exercise-induced peripheral fatigue was twofold greater with BFR compared to exercising with free flow during low-intensity cycling exercise at 40% W_{max}. We hypothesize that the reduced peripheral fatigue observed in the BFR-trained leg compared to the control is attributable to adaptations induced by repeated exposure to higher levels of exercise-induced fatigue and intramuscular metabolite accumulation during training sessions. These adaptations may involve substantial increases in oxidative enzymes, such as citrate synthase, cytochrome *c* oxidase and 3-hydroxyacyl-CoA dehydrogenase, as previously reported following repeated 30 s sprint training (Burgomaster et al., 2005, 2006, 2008).

Central contributions to the attenuated neuromuscular fatigue after BFR training appear negligible. In time- and work-matched exercise, VA did not decline in either leg. In constant-workload trials to task failure before training, VA was likewise maintained, indicating no exercise-induced central fatigue. Following training, VA was significantly reduced at task failure, but the reduction was similar in the control and BFR legs, indicating no BFR-specific central adaptation. We interpret the lower VA at task failure after training as a consequence of the longer time to exhaustion, which are from ∼5 min before training to ∼11 min and 16.6 min in the control and BFR leg, respectively. This is consistent with previous findings showing that central fatigue is more pronounced after exercise of longer compared to shorter durations (Ducrocq & Blain, 2022; Thomas et al., 2015). Specifically, results from our

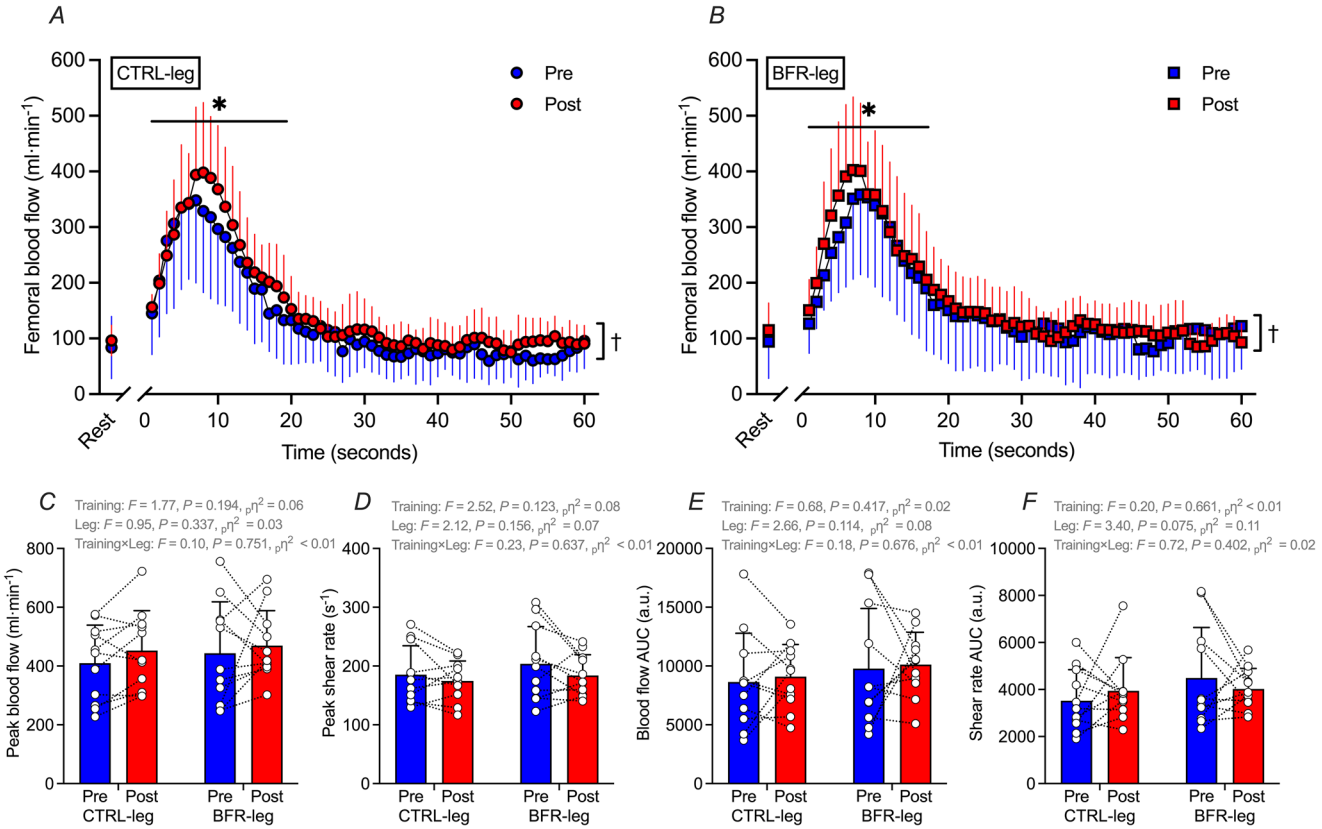

Figure 5. Effect of training on passive leg movement blood flow and wall shear rate responses
Resting baseline and single passive leg movement (PLM) blood flow over 60 s is shown in the leg that trained without BFR (CTRL-leg) (*A*) and with BFR (BFR-leg) (*B*). *C* and *D*, absolute peak PLM blood flow and wall shear rate, respectively. *E* and *F*, area-under-the-curve (AUC) for PLM blood flow and wall shear rate, respectively. For *A* and *B*, symbols and error bars represent the mean ± SD. For *C*–*F*, coloured bars are the mean, error bars are ±SD and each open dot indicates individual participants. Pre-training (Pre) data are plotted in blue and post-training (Post) data in red. *F*-values, *P*-values and $_p\eta^2$ for the main effects of training, leg and the training × leg interaction, as determined with a two-way 2 × 2 repeated-measures ANOVA, are shown above each panel. Significant ($P < 0.05$) main effects and interaction effects are shown in bold, black text. †Significant main effect of training on averaged blood flow; *$P < 0.05$, different from rest.

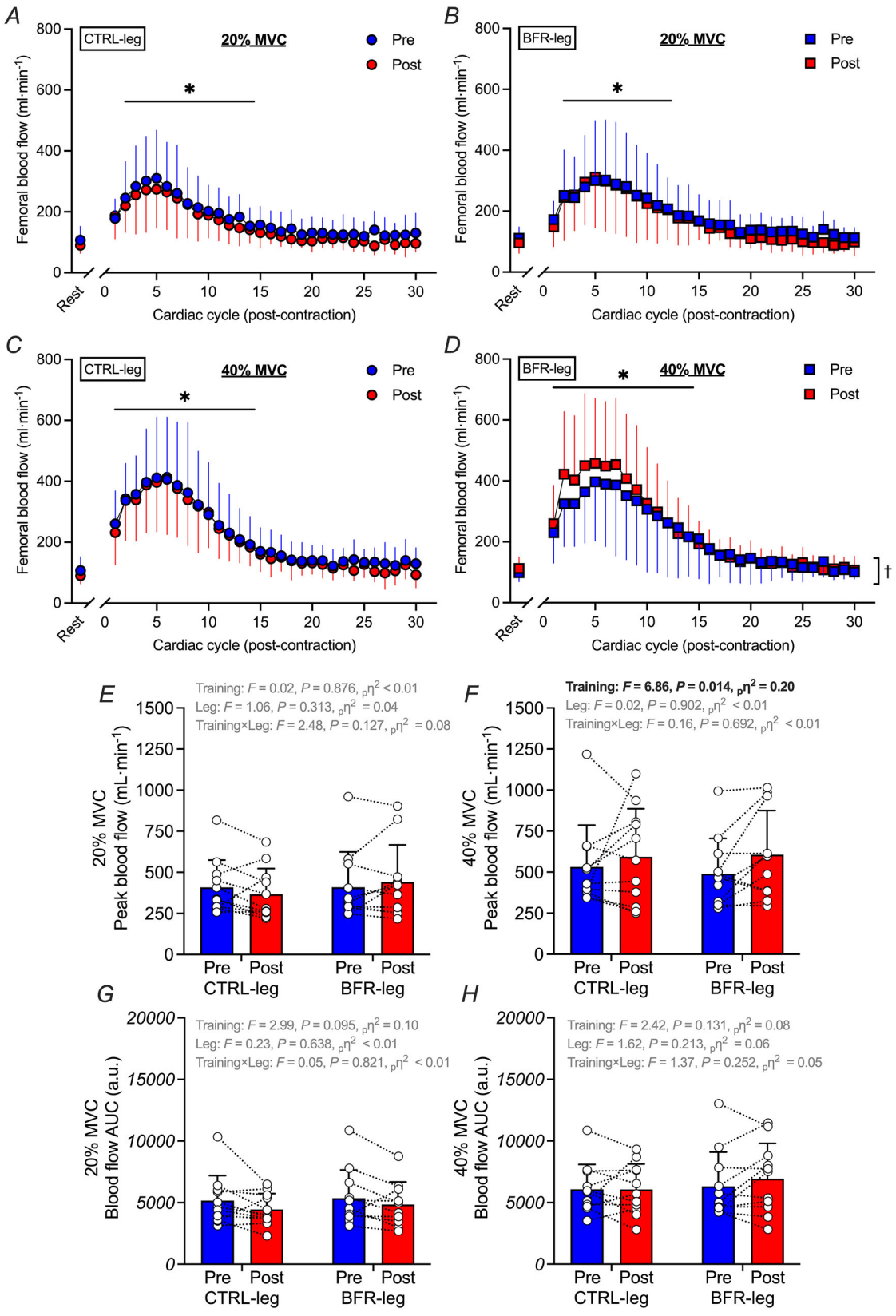

Figure 6. Effect of training on blood flow following single-leg isometric knee-extensor contractions
Resting baseline and the femoral blood flow response over 30 cardiac cycles following single-leg isometric knee-extension contractions at 20% (*A* and *B*) and 40% (*C* and *D*) of the pre-training maximal voluntary contraction

(MVC) are shown for the leg that trained without BFR (CTRL-leg) and with BFR (BFR-leg). *E* and *F*, 20% and 40% MVC absolute peak blood flow. *G* and *H*, area-under-the-curve (AUC) of the 20% and 40% MVC. For *A–D*, symbols and error bars represent the mean ± SD. For *E–H*, coloured bars are the mean, error bars are ±SD and each open dot indicates individual participants. Pre-training (Pre) data are plotted in blue and post-training (Post) data in red. *F*-values, *P*-values and $_p\eta^2$ for the main effects of training, leg and the training × leg interaction, as determined with a two-way 2 × 2 repeated-measures ANOVA, are shown above each panel. Significant ($P < 0.05$) main effects and interaction effects are shown in bold, black text. †Significant main effect of training on averaged blood flow; *$P < 0.05$, different from rest.

lab have shown no significant central fatigue (i.e. VA unchanged from before to after exercise) for 3–10 min exercise bouts, but a significant VA reduction at 15 min (ΔVA $\approx -12\%$) (Ducrocq & Blain, 2022). Furthermore, after the training period, quadriceps $RMS_{\%MVC}$ decreased by ∼12–49% during exercise matched for time and work rate, with slightly greater reductions in the BFR-trained leg, suggesting that the same amount of external work was achieved with a lower relative neural drive and is consistent with improved neuromuscular efficiency. The more pronounced reduction of $RMS_{\%MVC}$ in the BFR-trained leg may be explained by improved oxidative pathways leading to a reduction in the accumulation of fatigue-inducing metabolites and/or a greater capacity to buffer these metabolites during sustained exercise (Christiansen et al., 2021).

Together, these findings indicate that improvements in muscle contractile function were driven by mechanisms that helped preserve muscle homeostasis and delay neuromuscular fatigue primarily by attenuating the development of peripheral fatigue (e.g. enhanced excitation–contraction coupling or myofibrillar Ca^{2+}

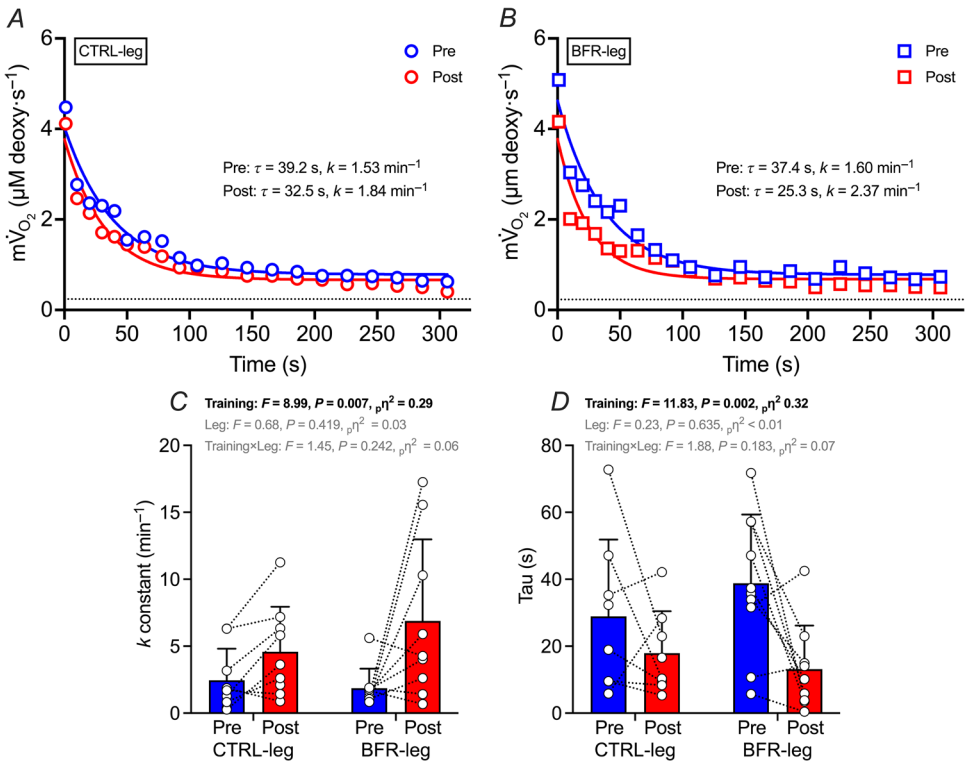

Figure 7. Effect of training on $m\dot{V}_{O_2}$ recovery kinetics by NIRS following exercise at 40% W_{max}
Group mean muscle $\dot{V}_{O_2}$ ($m\dot{V}_{O_2}$) recovery kinetics of the vastus lateralis following 6 min of constant workload exercise at 40% W_{max} are shown in the leg that trained without BFR (CTRL-leg; circles) (*A*) and with BFR (BFR-leg; squares) (*B*). Means ± SD and individual values of the *k* constant (*C*) and time constant (D) are shown for $m\dot{V}_{O_2}$ recovery kinetics. Data measured during each post-exercise arterial occlusion episode were fit to a monoexponential function to calculate the *k* constant and tau (indexes of mitochondrial respiratory capacity). For *A* and *B*, the dotted horizontal lines indicate the resting $m\dot{V}_{O_2}$ baseline values. For *C* and *D*, coloured bars are the mean, error bars are ±SD and each open dot indicates individual participants. For all data, pre-training (Pre) data are plotted in blue and post-training (Post) data in red. *F*-values, *P*-values and $_p\eta^2$ for the main effects of training, leg and the training × leg interaction, as determined with a two-way 2 × 2 repeated-measures ANOVA, are shown above each panel. Significant ($P < 0.05$) main effects and interaction effects are shown in bold, black text. Abbreviations: *k*, velocity constant; τ, time constant.

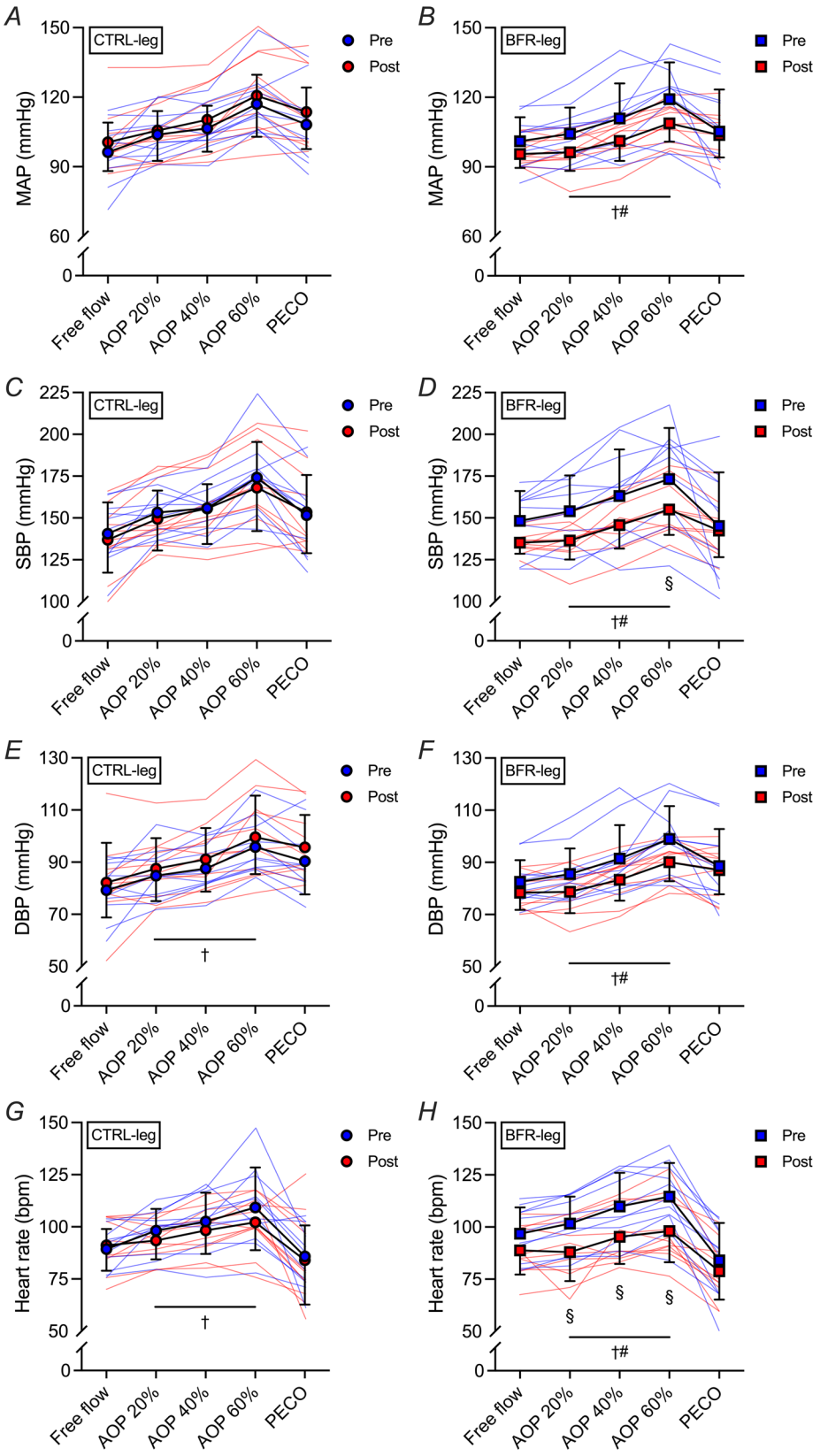

Figure 8. Effect of training on cardiovascular responses during dynamic knee-extensor metaboreflex activation
Line and scatter plots displaying: *A* and *B*, mean arterial pressure (MAP); *C* and *D*, systolic blood pressure (SBP); *E* and *F*, diastolic blood pressure (DBP); and *G* and *H*, heart rate in the leg that trained without BFR (CTRL-leg, left panels)

and with BFR (BFR-leg, right panels). Pre-training (Pre) data are plotted in blue and post-training (Post) data in red. Symbols (circles: CTRL-leg; squares: BFR-leg) and error bars represent the mean ± SD and lines indicate individual participants. †Significant main effect of training; #significant main effect of leg at post-training; §$P < 0.05$, Post different from Pre.

sensitivity) (Messonnier et al., 2007; Sostaric et al., 2006) but also by improving drive to motor units during exercise (Sidhu et al., 2017).

Vascular function

In the present study, we examined the effect of BFR interval training on leg vascular function, assessed by RH, PLM, ROV and FMD, to explore how the different underlying mechanisms of these tests may contribute to limiting fatigue development. No training- or leg-related differences were found when considering FMD data, which is considered a reliable tool for the non-invasive evaluation of conduit artery endothelial function (McCully, 2012). By contrast, an increase in femoral blood flow responsiveness was observed following BFR training for RH, PLM and ROV, indicating improved vascular function. Specifically, both the absolute and peak RH response was greater in the BFR-trained leg compared to the training control (Fig. 4), which primarily reflects skeletal muscle blood flow capacity and is minimally mediated by NO (Limberg et al., 2020). We also found that LVC increased by ∼21% during the same test, with no change in the control, suggesting that vascular resistance was reduced in the BFR-trained leg. ROV, which measures the contraction-induced rapid hyperaemic and vasodilatory response via endothelial (Crecelius et al., 2013), mechanical (Kirby et al., 2007) and adrenergic signals (Casey & Joyner, 2012), also demonstrated a greater absolute blood flow response during the 40% MVC trials after training with BFR compared to the control. By contrast, PLM, which predominately assesses endothelial NO function (Mortensen et al., 2012), revealed modest but significant training increases in absolute blood flow in both legs, without differences between legs. The leg-specific improvements in flow during RH and ROV of the BFR-trained leg suggests that vascular adaptations were driven primarily by improved peripheral microvascular function (Hanson et al., 2020; Philpott & Anderson, 2007; Rosenberry & Nelson, 2020) and metabolic vasodilation (Casey et al., 2013; Crecelius et al., 2013), rather than by NO-dependent endothelial function (Mortensen et al., 2012). These adaptations are consistent with physiological angiogenesis (i.e. structural remodelling occurring at the distal end of the vasculature tree) (Hunt et al., 2013). Angiogenic remodelling in response to BFR training appears to be mediated primarily by peripheral stimuli, including repeated bouts of tissue hypoxia and shear stress, both of which are known to promote skeletal muscle capillary growth (Hudlicka & Brown, 2009; Lundby et al., 2009). Together, these vascular adaptations may reflect enhanced tissue perfusion and O_2 delivery during exercise, thereby contributing to less fatigue development in the BFR-trained leg.

NIRS-derived post-exercise $m\dot{V}_{O_2}$

Following the training period, the rate constant (k) was significantly higher and the time constant (τ) was significantly lower in both legs compared to pre-training (Fig. 7), suggesting that, on average, the recovery rate of post-exercise $m\dot{V}_{O_2}$ improved. Because post-exercise $m\dot{V}_{O_2}$ recovery kinetics, as estimated here, tracks PCr recovery kinetics measured by *in vivo* ^{31}P-MRS (Ryan et al., 2013) and *in situ* mitochondrial respiratory capacity measured by high-resolution respirometry (Ryan et al., 2014), we interpret the observed training-induced acceleration in $m\dot{V}_{O_2}$ recovery as evidence of improved skeletal muscle mitochondrial function. We also observed no significant differences in k or τ between legs, indicating that improvements in mitochondrial respiratory capacity occurred to a similar extent in both the BFR-trained leg and control leg. Our finding that BFR training did not elicit a superior effect on estimated muscle mitochondrial respiratory capacity aligns with previous studies showing no changes in mitochondrial enzyme protein content, such as OXPHOS, following interval knee-extensor exercise training with BFR in recreationally trained men (Christiansen et al., 2020). Despite the absence of greater improvement in $m\dot{V}_{O_2}$ following BFR compared to CTRL training, $\dot{V}_{O_2peak}$ during incremental exercise to volitional exhaustion was ∼13% higher in the BFR-trained leg compared to the control leg. Together, our $m\dot{V}_{O_2}$, $\dot{V}_{O_2}$ and blood flow results suggest that improved leg aerobic power following BFR training is driven primarily by enhanced O_2 utilization via increased convective O_2 transport, rather than mitochondrial adaptations, *per se*. This is consistent with previous findings showing that BFR interval training augments convective O_2 delivery and attenuates lactate release, thereby improving the fraction of $\dot{V}_{O_2max}$ that can be sustained during exercise (Christiansen et al., 2020).

Leg metaboreflex activation responses to BFR training

We also investigated whether BFR interval training modulates the exercise pressor reflex via graded metaboreflex activation during dynamic single-leg knee-extensor exercise to explore if potential adaptations

in cardiovascular haemodynamic regulation, in conjunction with vascular improvements, could contribute to the improvements in exercise performance and in limiting fatigue development. We observed that blood pressure and HR responses were reduced during submaximal dynamic knee-extensor exercise-matched absolute workloads and levels of arterial occlusion following BFR training (Fig. 8). In contrast, no significant training effect was observed during post-exercise circulatory occlusion, a manoeuvre used to activate afferent signals of group IV metabosensitive neurons in isolation from central command and group III mechanoreflex afferents (Crisafulli et al., 2011).

The findings of the present study appear consistent with previous studies showing that training with BFR reduces the cardiovascular responses to exercise (Crisafulli et al., 2018; Sundblad et al., 2018), without changing metaboreflex sensitivity (Crisafulli et al., 2018). Specifically, Sundblad et al. (2018) observed a reduction in MAP and HR during a sustained isometric knee-extension contraction following BFR training, particularly in the later stages of the contraction when the highest concentration of intramuscular metabolites would be expected. Similarly, Crisafulli et al. (2018) showed that BFR training reduced MAP during rhythmic handgrip exercise yet did not provoke lowered metaboreflex activity during post-exercise circulatory occlusion.

We interpret the attenuated cardiovascular responses during exercise to reflect peripheral adaptations that reduce accumulation of metabolites following BFR training, probably attributable to both enhanced oxidative capacity and muscle perfusion, thereby reducing the metabolic strain for a given workload. This latter result suggests that the sensitivity of the metaboreflex was not different following BFR training. These results may have important clinical relevance for the potential application of BFR training in populations with exaggerated sympathetic nerve activity and impaired vascular function, such as individuals with hypertension, heart failure or peripheral artery disease, because of its ability to improve haemodynamic function. This, however, must be interpreted with caution as the BFR-induced transient augmentation of the exercise pressor reflex could increase the risk of potential deleterious cardiovascular events (Cristina-Oliveira et al., 2020; Spranger et al., 2015).

Translational perspective

This study demonstrates that training with BFR over 6 weeks, in comparison with an exercise control, improved exercise performance in our experimental model, which is consistent with previous work showing improvements in incremental peak power and time to exhaustion across different BFR training modalities and intensities (Abe et al., 2010; Christiansen et al., 2019, 2020, 2021). We also observed an increase in vascular responsiveness, consistent with prior work despite differences in exercise modality and conduit artery examined (Hunt et al., 2013). Another novel result was that training with BFR resulted in blunted cardiovascular responses during constant workload exercise with graded occlusion, which corroborates knee-extensor and handgrip findings of reduced pressor responses without altered metaboreflex sensitivity (Crisafulli et al., 2018; Sundblad et al., 2018). Our original data show that these adaptations translate into a more robust neuromuscular response and a delay in fatigue development during exercise. Collectively, these findings support BFR as a potent stimulus for improving exercise performance primarily via peripheral adaptations. Given that one of the main benefits of BFR training is acquiring adaptations at lower mechanical loads than conventional high-intensity training, BFR may be particularly relevant when higher loads are not tolerated (e.g. injury, joint pain, rehabilitation). In parallel, concerns that BFR can transiently augment the exercise pressor reflex warrant caution, especially in populations with overactive sympathetic activity (Cristina-Oliveira et al., 2020; Spranger et al., 2015). In this sense, an adapted single-leg knee-extensor BFR protocol reduces cardiorespiratory burden and, as training lowers metabolic stress, further attenuates the exercise pressor reflex, as evidenced in our study, which can benefit individuals with limited cardiorespiratory reserve.

Limitations

The current investigation provides important information regarding physiological adaptations to BFR interval training. Nevertheless, study limitations are worth noting. First, this study used a within-participant design by which one leg trained with BFR and the other without. This raises the possibility of a BFR training cross-over effect (Bowman et al., 2019, 2020; Wong et al., 2024), either through systemic influences, which are thought to occur via upregulation of various cellular signalling pathways and hormonal responses to both ischaemic/hypoxic environments and periods of shear stress (Ferguson et al., 2021; Madarame et al., 2008; Reeves et al., 2006), or by neural mechanisms involving the activation of motor pathways that project to the contralateral limb from unilateral training (Carroll et al., 2006). However, several outcome measures mitigate this concern. Notably, $\dot{V}_{O_2peak}$ improved only after training in the BFR-leg, without training-induced changes in the training control leg. Moreover, in comparison to the control, the BFR-trained leg demonstrated greater improvements in performance, including higher peak power output during maximal incremental exercise and a longer time to task

failure during high-intensity constant work rate exercise. These improvements, which were accompanied by less neuromuscular fatigue, were not correlated between legs, suggesting that any adaptations occurring in the control leg were, at least in part, independent of those induced by BFR interval training. Any residual cross-leg influence would probably have enhanced the control leg, leading to a conservative (underestimated) estimate of the BFR effect in between-leg comparisons.

As a second consideration, our study was not designed to include the measurement of blood flow during high-intensity exercise. While such data would have strengthened the mechanistic interpretation of our findings, the observed improvements in vascular function support, at least in part, an improvement in muscle perfusion and in oxygen delivery capacities.

Finally, we were unable to directly assess mitochondrial respiratory capacity via high-resolution respirometry from muscle biopsies (Perry et al., 2013). While this approach is considered the gold-standard for evaluating mitochondrial function *in situ*, we utilized a validated NIRS protocol involving repeated arterial occlusions to non-invasively estimate mitochondrial respiratory capacity from $m\dot{V}_{O_2}$ recovery kinetics. This NIRS-derived test has been shown to correlate well with high-resolution respirometry as well as PCr recovery kinetics measured by *in vivo* ^{31}P-MRS, a reliable index for skeletal muscle oxidative capacity (Ryan et al., 2013), supporting its use as a functionally relevant alternative for measuring mitochondrial function in humans.

To extend our findings, studies integrating our functional and mechanistic measures with complementary molecular- and cellular-level markers of neuromuscular (E–C coupling/Ca^{2+} handling), vascular (NO signalling/microvascular remodelling) and mitochondrial (biogenesis) pathways are warranted.

Conclusion

Our findings provide strong evidence that BFR interval training is a highly effective strategy for enhancing exercise performance and limiting fatigue development beyond what is achieved with conventional training during equivalent exercise tasks. These benefits appear to arise mainly from preserved muscle contractile capacity and improved microvascular function, rather than by greater mitochondrial respiratory improvements. Collectively, these physiological adaptations support BFR interval training as a powerful modality for enhancing functional capacity, particularly in contexts where high mechanical loading is not feasible, such as in rehabilitation settings or in individuals with joint or musculoskeletal limitations.

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Additional information

Data availability statement

The data are available upon reasonable request from the corresponding author.

Competing interests

The authors declare no conflict of interest.

Author contributions

All authors contributed to the conception and design of the study and the acquisition, analysis and/or interpretation of the data. C.L. wrote the first draft of the manuscript, and all other authors critically revised the manuscript for intellectual content. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved. All persons listed as authors qualify for authorship, and all those who qualify for authorship are listed.

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Keywords

blood pressure, central fatigue, exercise pressor reflex, ischaemia, metaboreflex, mitochondria, peripheral fatigue, reactive hyperaemia

Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the HTML view of the article. Supporting information files available:

Peer Review History
Table 1*A*