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RESEARCH ARTICLE

Low-volume HIIT and MICT speed $\dot{V}O_2$ kinetics during high-intensity "work-to-work" cycling with a similar time-course in type 2 diabetes

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Abstract

We assessed the rates of adjustment in oxygen uptake ($\dot{V}O_2$) and muscle deoxygenation [i.e., deoxygenated hemoglobin and myoglobin, (HHb + Mb)] during the on-transition to high-intensity cycling initiated from an elevated baseline (work-to-work, w-to-w) before training and at *weeks 3*, *6*, *9*, and *12* of low-volume high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) in type 2 diabetes (T2D). Participants were randomly assigned to MICT (n = 11, 50 min of moderate-intensity cycling), HIIT (n = 8, 10 × 1 min of high-intensity cycling separated by 1 min of light cycling) or nonexercising control (n = 9) groups. Exercising groups trained three times per week. Participants completed two w-to-w transitions at each time point consisting of sequential step increments to moderate- and high-intensity work-rates. [HHb + Mb] kinetics were measured by near-infrared spectroscopy at the vastus lateralis muscle. The pretraining time constant of the primary phase of $\dot{V}O_2$ ($\dot{V}O_2$ τ_p) and the amplitude of the $\dot{V}O_2$ slow component ($\dot{V}O_2$ A_s) of the high-intensity w-to-w bout decreased ($P < 0.05$) by a similar magnitude at *week 3* of training in both MICT (from 56 ± 9 to 43 ± 6 s, and from 0.17 ± 0.07 to 0.09 ± 0.05 L/min, respectively) and HIIT (from 56 ± 8 to 42 ± 6 s, and from 0.18 ± 0.05 to 0.09 ± 0.08 L/min, respectively) with no further changes thereafter. No changes were reported in controls. The parameter estimates of Δ[HHb + Mb] remained unchanged in all groups. MICT and HIIT elicited comparable improvements in $\dot{V}O_2$ kinetics without changes in muscle deoxygenation kinetics during high-intensity exercise initiated from an elevated baseline in T2D despite training volume and time commitment being ∼50% lower in the HIIT group.

NEW & NOTEWORTHY Three weeks of high-intensity interval training and moderate-intensity continuous training decreased the time constant of the primary phase of oxygen uptake ($\dot{V}O_2$) and amplitude of the $\dot{V}O_2$ slow component during a high-intensity exercise initiated from an elevated baseline, a protocol that mimics the abrupt metabolic transitions akin to those in daily life, in type 2 diabetes. These $\dot{V}O_2$ kinetics improvements were maintained until the end of the 12-wk intervention without changes in muscle deoxygenation kinetics.

exercise tolerance; exercise transitions; near-infrared spectroscopy; oxygen extraction; oxygen uptake slow component

INTRODUCTION

In healthy people, the initiation of a transition to high-intensity, constant work-rate upright cycling from moderate-intensity baseline cycling, referred to as work-to-work (w-to-w), elicits a significantly longer time constant of the primary phase of the oxygen uptake ($\dot{V}O_2$) kinetics response ($\dot{V}O_2$ τ_p) than initiating the same transition from rest or "unloaded" cycling (1–4). This prolonged $\dot{V}O_2$ τ_p translates to a compromised rate of oxidative energy transfer upon transition to the higher-intensity step of this protocol and has been attributed to constrained cellular respiration in the already active muscle fibers (5) and/or a larger recruitment of fast-twitch (type II) muscle fibers to meet the augmented metabolic demand (6).

Recently, Gildea et al. (7) observed that this slowing of $\dot{V}O_2$ τ_p during high-intensity w-to-w transitions is significantly greater in middle-aged individuals with type 2 diabetes (T2D) compared with their healthy counterparts, and that this effect is, at least in part, due to diabetes-induced limitations in peripheral oxygen (O_2) delivery to the working muscle. This is in agreement with consistent observations of blunted or slowed $\dot{V}O_2$ τ_p responses during on-transitions to moderate-intensity exercise from an unloaded baseline in young- and middle-aged individuals with T2D (8–12), that also appear to be influenced by impairments in O_2 delivery

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to active muscles (7, 12–16). W-to-w transitions replicate metabolic transitions from moderate to higher metabolic rates akin to those in daily life (such as abrupt velocity changes in walking/running/stair climbing, or changes in speed and/or gradient during cycling), and thus, interventions that may enhance $\dot{V}O_2$ kinetics during w-to-w transitions in T2D are of great relevance and warrant investigation. In this regard, short-term (~12 wk), traditional endurance training interventions, involving ~150 min of continuous exercise per week [intensities ranging from ~60% to 80% maximum heart rate (HR_{max})], have been shown to be effective at improving $\dot{V}O_2$ τ_p during moderate-intensity transitions initiated from an unloaded baseline in T2D (17–19). However, to our knowledge the effect of exercise training on $\dot{V}O_2$ τ_p during high-intensity w-to-w transitions in T2D has not been explored.

Accordingly, the purpose of the current study was to investigate the effects of 12 wk of two commonly used exercise training interventions on $\dot{V}O_2$ kinetics during high-intensity w-to-w cycling transitions in individuals with uncomplicated T2D. Specifically, we compared the effects of moderate-intensity (<ventilatory threshold, VT) continuous training (MICT) with low-volume, high-intensity interval training (HIIT), which typically involves ~75 min/wk of intermittent vigorous exercise, including less than 15 min of high-intensity efforts per session (20). Low volume HIIT was chosen for its time efficient nature (~50% lower time commitment) given "lack of time" is frequently cited as a key barrier for the well reported poor exercise adherence to current time-oriented physical activity guidelines in T2D (21). Although we have recently reported that low-volume HIIT and MICT elicit similar benefits in $\dot{V}O_2$ τ_p during moderate-intensity exercise transitions (22), interval training promotes greater oxidative enzyme adaptations in type II fibers (23), which are predominantly recruited during high-intensity efforts and might be expected to result in faster $\dot{V}O_2$ τ_p responses during high-intensity exercise transitions. Thus, we hypothesized that HIIT would be more effective at speeding $\dot{V}O_2$ kinetics during the high-intensity bouts of the w-to-w transitions. In an attempt to explore the mechanistic basis of any exercise-induced effect on $\dot{V}O_2$ kinetics in T2D, the rate of muscle deoxygenation (i.e., deoxygenated hemoglobin and myoglobin, HHb + Mb) was measured to assess the alterations on muscle fractional O_2 extraction. In addition, to assess the time course effects of these adaptations, physiological measurements were taken every 3 wk throughout the intervention (i.e., before training and at *weeks 3*, *6*, *9*, and *12*).

METHODS

Participants

Participants were recruited from the Diabetes Outpatient Clinics of St. Columcille's and St. Vincent's University Hospitals (Dublin). Participant's eligibility was initially checked following chart review. Specifically, participants were included if they had a clinical history of diabetes <11 years, were sedentary [≤1.5 h/wk of moderate-intensity exercise (<VT) and ≤1 structured exercise/wk in the preceding 6 mo, see *Testing*] (24), and had HbA_{1c} levels of <10%. Participants were excluded if they were treated by exogenous insulin, were smokers, had a disease contraindicating physical training, or demonstrated evidence of renal, liver, or cardiovascular disease. All individuals completed a 12-lead electrocardiogram treadmill stress test (Bruce protocol) at St. Columcille's Hospital before attending the laboratory tests.

Thirty-four participants completed the baseline laboratory assessments (see *Testing*) and were given opaque sealed envelopes randomly allocating them to one of the three intervention groups (MICT, initially n = 13; HIIT, initially n = 9; or Control, initially n = 12). Eight participants dropped out of the study for personal reasons unrelated to the experiment (MICT, n = 2; HIIT, n = 3; Control, n = 3). Participants in the Control group were offered re-randomization to one of the exercise training groups after the intervention period, of which two accepted (HIIT, n = 2) and subsequently completed the training intervention. The final study population consisted of 26 participants undergoing the intervention, of whom two underwent both Control and HIIT. Thus, 28 completed responses from the study intervention were included for statistical analysis (MICT, n = 11; HIIT, n = 8; Control, n = 9). All participants provided written informed consent before participation. The study was approved by the Faculty of Health Sciences' Research Ethics Committee, Trinity College Dublin, and St Vincent's Healthcare Ethics and Medical Research Committee, and conducted in accordance with the principles outlined by the Declaration of Helsinki.

Supervised Exercise Interventions

Overview.

Participants in the HIIT and MICT groups carried out a 12-wk supervised intervention, training three times per week on nonconsecutive days at a local health and fitness center in Co. Dublin. Participants in the Control group received no intervention and continued with their normal daily routine. All exercise training sessions were supervised by a study investigator. Training intensity was adjusted at 3-wk intervals (i.e., every 9 sessions) to reflect changes in fitness levels. Both exercise groups completed a 5-min warm up and 5-min cool down before and after each session on an aerobic machine of their choice (elliptical, treadmill, rower, or cycle ergometer). The main component of each training session was completed on a cycle ergometer as detailed in the following sections.

Low-volume high-intensity interval training.

The HIIT group completed 10 × 1-min bouts of high-intensity cycling interspersed with 1 min of light cycling. The high-intensity bout was completed at a power output equivalent to 70% of the difference between participant's peak power output (PO_{peak}) and the power output at ventilatory threshold (VT) (70% Δ) achieved during the ramp exercise test (see *Testing*), whereby participants were expected to exercise in the severe-intensity domain.

Moderate-intensity continuous training.

Each MICT session comprised of 50 min of cycling at a power output equivalent to ~80% VT as calculated from the ramp test (see *Testing*). The energy expenditure from the supervised exercise sessions was estimated based on the American College of Sports Medicine's equation (25).

Testing

Prior to the commencement of, and every 3 wk throughout the intervention, participants were required to attend the exercise testing laboratory on two separate occasions to complete a ramp incremental cycling test to exhaustion, three high-intensity calf plantar-flexion transitions, two to four moderate- and high-intensity cycling exercise transitions, and two w-to-w step transitions to high-intensity cycling exercise commencing from a baseline of moderate-intensity exercise. Data presented in the current manuscript are based on the cycling high-intensity w-to-w step transitions. Data on peak exercise responses obtained from the cycling ramp test (26) and moderate-intensity transitions (22) have been reported previously, whereas data on calf plantar-flexion transitions are not presented herein. For each participant, all tests were performed at the same time of day. All exercise tests were carried out in an upright position on an electrically braked cycle ergometer (Excalibur Sport; Lode B.V., Groningen, The Netherlands). Participants were asked to refrain from consuming alcohol, caffeine, and nonprescribed nutritional supplements as well as avoiding any strenuous exercise in the 24 h before testing. Prior to the intervention, activity levels were assessed by the use of 5-day RT3 triaxial accelerometry (Stayhealthy Inc., CA) (Table 1). The threshold for sedentary or inactive behavior (<1.5 metabolic equivalents or METs) was set as <100 counts/min, counts/min between 101 and 1,317 were considered light activity (1.5–3 METs); and counts/min >1,317 corresponded to moderate-to-vigorous physical activity (>3 MET) (27). At baseline (pretraining) and at the end of the intervention period (posttraining), fasting venous blood samples were collected to assess glycosylated hemoglobin (HbA_{1c}). Participants were familiarized with the ramp incremental test and constant work-rate tests before commencing the intervention.

Ramp incremental cycling tests.

The test started with an initial work-rate of 10 W for 2 min (i.e., "unloaded" cycling). This was followed by a progressive increase in power output at 10–25 W/min based on participants' activity levels. Pedaling rate was held constant at an individually selected cadence between 60 and 75 revolutions per minute (rpm) and was maintained throughout all further testing. Failure/exhaustion in a test was determined as a drop in cadence exceeding 10 rpm for >5 s. Peak work rate was the power output achieved at the point of failure. $\dot{V}O_{2peak}$ was the highest $\dot{V}O_2$ value (15-s average) attained during the test. The first ventilatory threshold (VT) was determined using the V-slope method (28); whereas the respiratory compensation point (RCP) was determined by identifying the second nonlinear increase of $\dot{V}E$ and $\dot{V}CO_2$, whereby an increase in $\dot{V}E/\dot{V}O_2$ is accompanied by an increase of $\dot{V}E/\dot{V}CO_2$ (29).

High-intensity work-to-work cycling exercise transitions.

All participants performed two separate w-to-w transitions to constant work-rate high-intensity cycling at 50% Δ (Δ50%; the sum of the power output at VT and 50% of the difference between the power output at VT and $\dot{V}O_{2peak}$ obtained during the ramp incremental test at the pretraining time point) each commencing from an elevated baseline of 80% VT (80% of each participant's VT). Therefore, for each participant the same absolute power output was used at all five

Table 1. *Physical characteristics, pretraining peak exercise values, and activity levels*

	MICT	HIIT	Control
n	11	8	9
Sex (male, female), *n*	7, 4	6, 2	4, 5
Age, yr	54 ± 10	51 ± 10	54 ± 9
BMI, kg/m^2	31.0 ± 5.7	28.8 ± 3.2	30.5 ± 3.6
Time since diabetes diagnosis, yr	6.6 ± 3.7	6.8 ± 3.7	6.6 ± 3.3
HbA_{1c}, %	6.9 ± 0.5	7.3 ± 0.5	6.8 ± 1.0
Fat layer of VL, mm	7.9 ± 4.2	6.5 ± 2.7	8.6 ± 3.2
Diabetes medication			
Diet only, *n*		1	1
Metformin, *n*	9	7	6
Sulfonylurea, *n*	2	3	2
DPP-4 inhibitor, *n*			2
GLP-1 analogues, *n*	1		1
Anti-hypertensive medication			
Angiotensin converting enzyme inhibitor, *n*		1	
Angiotensin II receptor blocker, *n*	1		1
Statins, *n*	5	3	3
Aspirin, *n*	3	1	2
PO_{peak}, W	160 ± 54	198 ± 41	148 ± 49
PO@ Δ50%, W	126 ± 43	161 ± 31	115 ± 36
PO@ 80% VT, W	74 ± 27	99 ± 17*†	66 ± 20
Habitual physical activity			
Inactive, h/day	17.4 ± 2.0	17.4 ± 2.9	17.9 ± 1.9
Light, h/day	5.8 ± 1.7	5.8 ± 2.6	5.4 ± 1.2
MVPA, h/day	0.8 ± 0.7	0.8 ± 0.3	0.7 ± 0.9

Data are means ± SD. *n* = no. of participants. BMI, body mass index; DPP-4, dipeptidyl-peptidase 4; GLP-1, glucagon-like peptide 1; HbA_{1c}, glycosylated hemoglobin; HIIT, high-intensity interval training; MICT, moderate-intensity continuous training; MVPA, moderate-to-vigorous physical activity; PO, power output; VL, vastus lateralis; VT, ventilatory threshold. A one-way ANOVA was used for the analysis. *Significantly different than Control ($P < 0.05$); †significantly different than MICT ($P < 0.05$).

time points during the intervention. The order of these bouts was fixed for all participants. Each transition consisted of 3 min of "unloaded" cycling at 10 W, immediately followed by 6 min of moderate-intensity (80% VT) cycling which in turn was immediately followed by 6 min of high-intensity (Δ50%) cycling. Exercise was performed continuously with changes in power output initiated as a step function without giving prior warning to the individual. There was a 45–60 min rest period between each of the cycling bouts. This resting period was sufficient for physiological parameters to return to baseline levels and subsequently not to influence $\dot{V}O_2$ kinetics parameters (measured in a subgroup of 12 participants with T2D, albeit using a single high-intensity w-to-w transition), and this is consistent with previous reports in healthy active individuals (30). Given that in the present study the mean response times of $\dot{V}O_2$ during the ramp cycle exercise (31) were not accounted for when calculating these target power outputs, power outputs at VT were overestimated. Five participants (MICT, n = 1; HIIT, n = 2; Control, n = 2) failed to complete 6 min of exercise at Δ50% during the w-to-w bouts at baseline, so only physiological responses collected over the same period (i.e., <6 min, range 3–5 min) during the subsequent time points were analyzed. Heart rate (HR), gas exchange/ventilatory variables, and muscle oxygenation and deoxygenation were continuously measured during each cycling bout.

Measurements

During exercise, participants wore a facemask to continuously collect expired air using an online metabolic system (Innocor, Innovision A/S, Odense, Denmark) that measured airflow using a pneumotachometer. Carbon dioxide analysis was performed by using a photoacoustic gas analyzer and oxygen was analyzed using an oxygen sensor (Oxigraf Inc.) based on the principle of laser diode absorption spectroscopy. The system was calibrated before each test as per manufacturer's recommendations. Both the oxygen sensor and photoacoustic gas analyzer require multipoint calibration that is routinely performed by the manufacturer every 6–12 mo. Analysis of expired air allowed determination of the rate of pulmonary O_2 uptake ($\dot{V}O_2$), CO_2 output ($\dot{V}CO_2$), minute ventilation ($\dot{V}E$), and the respiratory exchange ratio (RER) breath-by-breath. Heart rate (HR) was recorded every 5 s (Polar S610i, Polar Ltd., Finland), with peak HR defined as the highest HR attained within the last 15 s of termination of the test.

A continuous wave near-infrared spectroscopy (NIRS) system (Hamamatsu Niro 200Nx; Hamamatsu Photonics, Hamamatsu, Japan) was used to determine muscle oxygenation status noninvasively through the spatially resolved spectroscopy technique and modified Beer–Lambert principle with three wavelengths of emitting light (λ = 735, 810, and 850 nm). The theoretical basis of NIRS and its use in exercise measurements have been described in detail elsewhere (32) but briefly, this technique estimates the optical density changes of oxygenated (O_2Hb + Mb) and deoxygenated hemoglobin and myoglobin (HHb + Mb) based on the oxygen dependency of absorption changes for near-infrared light in these proteins. As the vastus lateralis (VL) muscle is a dominant locomotor muscle during cycling, the present study examined the concentration of HHb + Mb (Δ[HHb + Mb]), and tissue oxygenation index (TOI) of the right vastus lateralis (VL) muscle. After shaving, cleaning, and drying the skin, the probes were placed on the belly of the muscle, 10–16 cm above the lateral femoral condyle, parallel to the major axis of the thigh with a 3-cm spacing between the emitter and receiver. The probes were housed in a black rubber holder and secured on the skin surface with bi-adhesive tape and then covered with a dark elastic bandage, which minimized extraneous movement and the intrusion of stray light throughout the exercise protocol. Since the depth of the measured area was estimated to be approximately one-half the distance between the emitter and the receiver (~1.5 cm), the present study determined the thickness of the skin and adipose tissue at the site of the probe placement via two-dimensional (2-D) ultrasound operating in B-mode (Zonare Ultra Smart Cart, Software v. 4.7), to ensure that data largely represented absorption of near-infrared light in muscle tissue and not in subcutaneous fat. All individuals presented with adiposity <1.5 cm over the site of interrogation on the vastus lateralis.

Data Analysis

$\dot{V}O_2$ kinetics.

The breath-by-breath $\dot{V}O_2$ data for each transition were linearly interpolated to provide second-by-second values and time aligned such that *time 0* represented the onset of exercise. Data from each transition were ensemble-averaged to yield a single, average response for each individual and further time-averaged into 5 s bins (33). Data were then fitted to a monoexponential function (*Eq. 1*) or biexponential function (*Eq. 2*). During the high-intensity exercise bouts, responses were fitted to *Eq. 2*. During the moderate-intensity bouts, the majority of the 140 responses (90%) consisted of a single (primary) phase (visual inspection) and was fitted to *Eq. 1*. The remaining responses (10%) displayed a second phase ("slow component") and were fitted to *Eq. 2*. This second phase was observed in 14 responses (from 9 participants, Control, n = 3; HIIT, n = 3; MICT, n = 3), had a mean amplitude of 76 mL/min (SD = 21 mL/min), was only observed among control participants beyond *week 3* of the intervention, and was likely due to the fact that in the present study the mean response times of $\dot{V}O_2$ during the ramp cycle exercise were not accounted for when calculating the target power outputs (31). The equations are as follows:

$$\dot{V}O_2(t) = \dot{V}O_2\ \text{baseline} + A_p[1 - e^{(t-TD_p)/\tau_p}] \quad \text{F1} + A_s[1 - e^{(t-TD_s)/\tau_s}]\ \text{F2}, \tag{1}$$

$$\dot{V}O_2(t) = \dot{V}O_2\ \text{baseline} + A_p[1 - e^{(t-TD_p)/\tau_p}] \quad \text{F1} + A_s[1 - e^{(t-TD_s)/\tau_s}]\ \text{F2}, \tag{2}$$

where $\dot{V}O_2(t)$ represents the absolute $\dot{V}O_2$ at a given time t; $\dot{V}O_2$ baseline (for moderate-intensity, in *Eqs. 1* and *2*) is the mean $\dot{V}O_2$ in the final 30 s of unloaded cycling, whereas $\dot{V}O_2$ baseline (for high intensity, in *Eq. 2*) is the mean $\dot{V}O_2$ in the final 60 s of the moderate-intensity cycling exercise preceding the step transition to high-intensity cycling exercise. A_p and A_s are the amplitudes of the increase in $\dot{V}O_2$ for the primary and slow component phases; TD_p and TD_s are the time delays of these phases, and τ_p and τ_s are the time constants

of the phases, defined as the duration of time for which $\dot{V}O_2$ increases to a value equivalent to 63% of the amplitude. The conditional expressions F1 and F2 limit the fitting of the phase to the period at and beyond the time delay associated with that phase. The first 20 s of data after the onset of exercise (i.e., the phase I $\dot{V}O_2$ response) were deleted, while still allowing TD_p to vary freely [to optimize accuracy of parameter estimates (34)]. However, TD_s was constrained to avoid the possibility of including the slow component in the modeled fit for the fundamental phase of $\dot{V}O_2$. $\dot{V}O_2$ data were modeled from 20 s to 360 s of each step transition. The mean response time (MRT) was calculated through the fitting of a monoexponential curve from exercise onset to provide information on the "overall" $\dot{V}O_2$ kinetics during the high-intensity exercise bout, with no distinction made for the various phases of the response. The $\dot{V}O_2$ data were fit using a weighted least-squares nonlinear regression procedure (TableCurve 2D, Systat). Data points lying outside the 95% prediction interval during the initial fit of a model were excluded. For moderate-intensity exercise, only estimates representing the primary phase are presented. Although the presence of a slow component was detected in 14 responses during moderate-intensity exercise transitions, the presence of this phase does not appear to significantly affect the parameter estimates of the earlier phases (35). The end-exercise $\dot{V}O_2$ response, referred to as End A, was calculated as the averaged $\dot{V}O_2$ over the last 30 s. Because the asymptomatic value (A_s) of the exponential term describing the $\dot{V}O_2$ slow component may represent a higher value than is actually reached at the end of the exercise, the actual amplitude of the slow component was calculated as the absolute difference between the End A and $\dot{V}O_2$ baseline + A_p. The amplitude of the slow component was also described relative to the entire $\dot{V}O_2$ response [i.e., $A_s/(A_p + A_s)$]. The functional "gain" of the primary $\dot{V}O_2$ response (G_p) was calculated as the difference between $\dot{V}O_2$ A_p and $\dot{V}O_2$ baseline normalized to the difference in power outputs between the moderate-intensity exercise and unloaded cycling; and the functional gain of the entire response at the end of the high-intensity exercise bout (i.e., end-exercise gain) was calculated in a similar manner.

[HHb + Mb] kinetics and TOI.

To provide information on muscle deoxygenation throughout the protocol, we modeled the [HHb + Mb] response for moderate- and high-intensity exercise. As per the $\dot{V}O_2$ data, the NIRS-derived Δ[HHb + Mb] data for each transition were linearly interpolated to provide second-by-second values and time aligned. Data from each transition were ensemble-averaged to yield a single average response for each individual, and further time-averaged into 5-s bins. A time delay (TD) at the onset of exercise occurs in the [HHb + Mb] profile before it increases with an exponential-like time course (36). This was determined in the present study via visual inspection as a systematic increase above the pretransition level. For the moderate-intensity transitions, [HHb + Mb] data were fitted from the end of this TD to 180 s using a monoexponential (*Eq. 1*) function as per $\dot{V}O_2$. The shorter fitting window of 180 s was selected to counteract the previously reported variations in the NIRS signal between 180 and 360 s from exercise onset (also observed herein), from impacting the fitting of the on-transient response while permitting the reaching of a steady state (37, 38). For the high-intensity transitions, [HHb + Mb] data were fitted from the end of the TD to the end of the exercise bout using a biexponential (*Eq. 2*) function as per $\dot{V}O_2$. For the moderate- and high-intensity exercise, the time course for the primary phase of the Δ[HHb + Mb] response, referred to as the effective response time (τ'Δ[HHb + Mb]), was determined from the sum of the TD and τ from the onset of exercise. The amplitude change in TOI (TOI *A*) was calculated as the difference between baseline (30 s before each transition) and end-exercise (final 30 s) values.

Statistical Analysis

Physical characteristics and activity levels at baseline among groups were compared using a one-way ANOVA. Peak physiological responses, training intensity, TOI values, and kinetics parameter estimates for $\dot{V}O_2$ and [HHb + Mb] throughout the intervention were compared using a two-factor [time (pretraining, *week 3*, *week 6*, *week 9*, posttraining) vs. group (HIIT, MICT, CON)] mixed ANOVA. Body mass and HbA_{1c} results were also compared using a two-factor [time (pretraining, posttraining) vs. group (HIIT, MICT, CON)] mixed ANOVA. Differences were detected using a Student–Newman–Keuls post hoc test. Significance was set at $P < 0.05$. All values are expressed as means ± standard deviation (SD).

RESULTS

Physical Characteristics, Pretraining Peak Exercise Values, and Activity Levels

Participants' physical characteristics, peak exercise values, and activity levels at baseline are presented in Table 1. HbA_{1c} (%) (time × group interaction, $P < 0.012$) was reduced in the MICT (pre = 6.9 ± 0.5%, post = 6.6 ± 0.5%) and HIIT groups (pre = 7.3 ± 0.5%, post = 7.0 ± 0.6%) but not in the control (pre = 6.8 ± 1.0%, post = 7.0 ± 1.0%) group.

Exercise Adherence and Caloric Expenditure

The mean exercise adherence was 94 ± 6% (range 31–36 sessions) and 97 ± 4% (range 32–36 sessions) in the HIIT and MICT groups, respectively. The average training intensity (power output) increased significantly ($P < 0.05$) every 3 wk (i.e., after each laboratory testing session) in the MICT group (*weeks 1–3*, 84 ± 33 W; *weeks 4–6*, 102 ± 39 W; *weeks 7–9*, 113 ± 43 W; *weeks 10–12*, 122 ± 44 W) while it also significantly increased every 3 wk until *week 9*, but not between *week 9* and *12* in the HIIT group (*weeks 1–3*, 176 ± 35 W; *weeks 4–6*, 192 ± 37 W; *weeks 7–9*, 203 ± 38 W; *weeks 10–12*, 206 ± 40 W). The average energy expenditure and total work done per training session (including the warm up) was ~228 kcal and ~165 kJ for the HIIT group, and ~478 kcal and ~326 kJ for the MICT group. No adverse training effects to training were observed throughout the intervention period in either exercising group.

$\dot{V}O_{2peak}$ from Ramp Incremental Cycling

There was a significant time × group interaction ($P < 0.001$) for absolute $\dot{V}O_{2peak}$, so that $\dot{V}O_{2peak}$ did not increase in the control group ($\dot{V}O_{2peak}$ at pretraining = 1.86 ± 0.52 L/

min), but it significantly increased after 3 wk of MICT (from 2.08 ± 0.68 to 2.39 ± 0.68 L/min) and HIIT (from 2.42 ± 0.44 to 2.61 ± 0.47 L/min), with no further significant changes thereafter ($\dot{V}O_{2peak}$ at posttraining = 2.55 ± 0.73 L/min and 2.71 ± 0.54 L/min, respectively). Additional peak physiological responses have been reported in a companion paper (26).

$\dot{V}O_2$ Kinetics and NIRS-Derived Responses during High-Intensity Exercise of the W-to-W Transition

The parameter estimates of the $\dot{V}O_2$ kinetics response for the high-intensity exercise bouts throughout the intervention period are shown in Table 2, and responses for representative individuals are shown in Fig. 1. Individual $\dot{V}O_2$ τ_p and $\dot{V}O_2$ A_s responses throughout the intervention period are shown in Fig. 2. Pretraining $\dot{V}O_2$ τ_p and MRT values were similar among the three groups. After 3 wk of training, $\dot{V}O_2$ τ_p and MRT were significantly reduced in both the HIIT and MICT groups with no further significant changes thereafter. In contrast, $\dot{V}O_2$ τ_p and MRT were not changed throughout the 12-wk period in the control group (time × group interaction, $P < 0.01$). Similarly, $\dot{V}O_2$ A_s was significantly reduced after 3 wk of MICT and HIIT with no further changes thereafter, but it did not change (time × group interaction, $P < 0.01$) in the control group. The $\dot{V}O_2$ A_p or the functional $\dot{V}O_2$ gain were not different among groups and did not change throughout the intervention.

The kinetics parameters for Δ[HHb + Mb] as well as TOI values are displayed in Table 3 and Δ[HHb + Mb] responses for representative individuals are shown in Fig. 3. The effective response times of muscle deoxygenation (Δ[HHb + Mb] τ_p'), Δ[HHb + Mb] A_p, Δ[HHb + Mb] A_s, and the ratio of the modeled amplitudes of the primary phase Δ[HHb + Mb]/$\Delta\dot{V}O_2$ were not different among groups and did not change throughout the intervention (Table 3). The magnitude of the change in TOI during the high-intensity exercise transitions was not affected by the intervention in either group.

$\dot{V}O_2$ Kinetics and NIRS-Derived Responses during Moderate-Intensity Exercise of the W-to-W Transition

The parameter estimates of the $\dot{V}O_2$ kinetics response for the moderate-intensity exercise bouts throughout the intervention period are shown in Table 2. For $\dot{V}O_2$ τ_p, there was a significant time × group interaction ($P < 0.001$), so that $\dot{V}O_2$ τ_p did not change in the control group, but it was reduced after 3 wk of MICT and HIIT with no further changes thereafter. There was a main effect of group ($P < 0.05$) for $\dot{V}O_2$ A_p so that it was larger in the HIIT group compared with the other two groups. Kinetics parameters for Δ[HHb + Mb] as well as TOI values are displayed in Table 3. Exercise training did not affect the effective response time of the Δ[HHb + Mb] response or the ratio of the modeled amplitudes of the Δ[HHb + Mb]/$\Delta\dot{V}O_2$ in either group. There was a main effect of group ($P < 0.05$) for Δ[HHb + Mb] A_p so that it was larger in the HIIT compared with the control groups. The magnitude of the change in TOI during the moderate-intensity exercise transitions were not affected by the intervention in either group, and they were larger in the HIIT compared with the other two groups (main effect, group, $P = 0.025$).

DISCUSSION

To our knowledge this is the first study to investigate the time-course effects of low-volume HIIT and MICT on $\dot{V}O_2$ kinetics during high-intensity exercise initiated from an elevated baseline in individuals with uncomplicated T2D. The principal findings were that both HIIT and MICT significantly reduced $\dot{V}O_2$ τ_p as well as the amplitude of $\dot{V}O_2$ A_s during the transition to high-intensity cycling by *week 3* of training and that these effects occurred in the absence of changes in the dynamic response of Δ[HHb + Mb] suggesting an improved microvascular blood flow delivery. In contrast with our hypothesis, these adaptations were of a magnitude that was not different between exercising groups and were maintained without further improvements until the end of the 12-wk intervention period.

Time-Course Effects of Exercise Training on $\dot{V}O_2$ τ_p during High-Intensity Exercise of the W-to-W Transition

In the present study, despite training volume and time commitment being ~50% lower in the HIIT compared with the MICT group, both interventions significantly reduced $\dot{V}O_2$ τ_p after the 12-wk intervention period (31% MICT; 35% HIIT), with the reductions already apparent at the 3-wk time point (24% MICT; 26% HIIT). Although in a companion paper of the current investigation we have recently shown that the performance of both HIIT and MICT interventions elicit rapid (i.e., within 3 wk) adaptations in $\dot{V}O_2$ τ_p during transitions to moderate-intensity efforts from an unloaded/resting baseline in T2D (22), herein we report for the first time the effects of these interventions on $\dot{V}O_2$ kinetics upon step transitions to high-intensity exercise initiated from elevated metabolic rates in T2D. Among healthy participants, a number of studies have shown that HIIT and MICT interventions speed $\dot{V}O_2$ τ_p during transitions to moderate- and high-intensity efforts from an unloaded baseline (39–43); but to our knowledge, only one previous study has assessed $\dot{V}O_2$ kinetics responses during severe-intensity transitions initiated from a moderate-intensity baseline following HIIT and/or MICT. Specifically, consistent with our findings, Da Boit et al. (44) reported significant reductions in $\dot{V}O_2$ τ_p (26% and 22%) subsequent to 2 wk of either repeated sprint training (RST) (4–7, 30-s "all-out" sprints interspersed by 4 min of recovery) or MICT (60–110 min cycling at 90% VT). In addition, in agreement with Da Boit et al. (44) albeit during w-to-w exercise in the moderate-intensity domain (i.e., transitions from 45% VT to 90% VT), Williams et al. (45) reported a 40% reduction in $\dot{V}O_2$ τ_p (45 s to 25 s) in healthy untrained young males subsequent to 4 wk of HIIT (8–12 1-min cycling intervals at 110% WR_{max} interspersed by 1 min of unloaded cycling).

In the present study, the observed speeding of $\dot{V}O_2$ kinetics occurred without changes in the adjustment of muscle deoxygenation suggesting that these training-induced reductions in $\dot{V}O_2$ τ_p could partly be due to an improvement in microvascular O_2 delivery and/or enhanced intracellular O_2 utilization. Similarly, we have recently reported that the accelerated $\dot{V}O_2$ τ_p responses during transitions to moderate-intensity exercise following both HIIT and MICT in T2D were accompanied by no changes in [HHb + Mb] kinetics and with a simultaneous reduction in the normalized Δ[HHb + Mb]/$\Delta\dot{V}O_2$ ratio,

Table 2. *Dynamic response characteristics of $\dot{V}O_2$ during moderate-intensity and high-intensity cycling exercise of the work-to-work transitions for the MICT, HIIT, and Control groups*

	Pretraining	*Week 3*	*Week 6*	*Week 9*	Posttraining
Moderate intensity					
Baseline $\dot{V}O_2$, L/min					
MICT[a]	0.94 ± 0.21	0.94 ± 0.17	0.94 ± 0.24	0.96 ± 0.21	0.92 ± 0.17
HIIT	0.80 ± 0.23	0.84 ± 0.16	0.83 ± 0.09	0.84 ± 0.14	0.83 ± 0.12
Control	0.77 ± 0.18	0.73 ± 0.10	0.77 ± 0.15	0.76 ± 0.15	0.74 ± 0.13
$\dot{V}O_2$ A_p, L/min					
MICT	0.64 ± 0.32	0.60 ± 0.30	0.61 ± 0.24	0.61 ± 0.27	0.62 ± 0.29
HIIT[ab]	0.92 ± 0.29	0.88 ± 0.27	0.90 ± 0.18	0.87 ± 0.24	0.89 ± 0.18
Control	0.52 ± 0.22	0.55 ± 0.24	0.52 ± 0.25	0.51 ± 0.24	0.53 ± 0.22
$\dot{V}O_2$ G_p, mL/min·W					
MICT	9.8 ± 1.9	9.3 ± 1.7	9.8 ± 1.7	9.4 ± 1.1	9.6 ± 1.1
HIIT	10.2 ± 2.2	9.7 ± 1.8	10.1 ± 1.0	9.7 ± 1.5	10.0 ± 0.8
Control	9.3 ± 1.6	9.7 ± 1.2	9.2 ± 1.3	9.0 ± 0.9	9.5 ± 0.8
$\dot{V}O_2$ τ_p, s					
MICT	46 ± 12	33 ± 5*†	29 ± 11*†	27 ± 6*†	28 ± 6*†
HIIT	41 ± 7	32 ± 4*†	27 ± 4*†	26 ± 4*†	27 ± 4*†
Control	43 ± 7	41 ± 6	40 ± 7	41 ± 8	46 ± 7
CI_{95} $\dot{V}O_2$ τ_p, s					
MICT	4.4 ± 1.2	4.0 ± 1.5	4.1 ± 1.0	3.4 ± 1.1	3.3 ± 1.0
HIIT	4.4 ± 0.4	4.2 ± 1.1	4.0 ± 0.9	3.3 ± 0.9	3.8 ± 0.7
Control	4.0 ± 1.1	3.7 ± 0.5	3.8 ± 0.7	4.0 ± 1.2	4.8 ± 1.4
$\dot{V}O_2$ τ_p, s					
MICT	46 ± 12	33 ± 5*†	29 ± 11*†	27 ± 6*†	28 ± 6*†
HIIT	41 ± 7	32 ± 4*†	27 ± 4*†	26 ± 4*†	27 ± 4*†
Control	43 ± 7	41 ± 6	40 ± 7	41 ± 8	46 ± 7
High Intensity					
Baseline $\dot{V}O_2$, L/min					
MICT	1.58 ± 0.39	1.55 ± 0.35	1.54 ± 0.38	1.57 ± 0.38	1.54 ± 0.36
HIIT[a]	1.75 ± 0.31	1.73 ± 0.22	1.74 ± 0.19	1.71 ± 0.21	1.72 ± 0.20
Control	1.31 ± 0.32	1.30 ± 0.28	1.30 ± 0.31	1.31 ± 0.32	1.30 ± 0.30
$\dot{V}O_2$ A_p, L/min					
MICT	0.38 ± 0.15	0.44 ± 0.14	0.48 ± 0.16	0.47 ± 0.13	0.49 ± 0.16
HIIT	0.51 ± 0.17	0.54 ± 0.18	0.55 ± 0.16	0.56 ± 0.15	0.57 ± 0.13
Control	0.42 ± 0.15	0.41 ± 0.18	0.42 ± 0.15	0.40 ± 0.18	0.41 ± 0.21
$\dot{V}O_2$ τ_p, s					
MICT	56 ± 9	43 ± 6*†	41 ± 5*†	41 ± 7*†	39 ± 7*†
HIIT	56 ± 8	42 ± 6*†	40 ± 5*†	38 ± 4*†	37 ± 4*†
Control	54 ± 6	53 ± 4	52 ± 6	52 ± 7	52 ± 6
CI_{95} $\dot{V}O_2$ τ_p, s					
MICT	8.6 ± 2.5	8.9 ± 2.4	9.0 ± 2.5	8.3 ± 2.4	8.8 ± 1.7
HIIT	8.8 ± 2.8	9.0 ± 2.7	8.8 ± 2.2	8.8 ± 2.6	8.3 ± 2.6
Control	8.8 ± 2.3	8.8 ± 2.3	9.0 ± 2.8	9.0 ± 2.5	8.8 ± 2.2
$\dot{V}O_2$ A_s, L/min					
MICT	0.17 ± 0.07	0.09 ± 0.05*†	0.08 ± 0.06*†	0.08 ± 0.06*†	0.07 ± 0.05*†
HIIT	0.18 ± 0.05	0.09 ± 0.08*†	0.11 ± 0.06*†	0.10 ± 0.07*†	0.10 ± 0.08*†
Control	0.17 ± 0.05	0.17 ± 0.04	0.17 ± 0.06	0.17 ± 0.08	0.17 ± 0.05
$\dot{V}O_2$ A_s, %					
MICT	32 ± 11	16 ± 5*†	16 ± 9*†	14 ± 9*†	14 ± 9*†
HIIT	26 ± 5	14 ± 9*†	16 ± 7*†	15 ± 8*†	14 ± 9*†
Control	29 ± 7	30 ± 8	29 ± 9	31 ± 9	32 ± 10
$\dot{V}O_2$ MRT, s					
MICT	115 ± 8	73 ± 10*†	73 ± 11*†	70 ± 14*†	73 ± 15*†
HIIT	112 ± 8	76 ± 10*†	78 ± 13*†	80 ± 14*†	78 ± 12*†
Control	114 ± 13	118 ± 12	120 ± 11	119 ± 9	121 ± 11
End-exercise $\dot{V}O_2$ gain, mL/min·W					
MICT	10.2 ± 0.9	9.6 ± 1.2	10.1 ± 1.7	9.9 ± 0.8	10.1 ± 1.0
HIIT	10.8 ± 2.1	10.0 ± 1.6	10.4 ± 0.9	10.1 ± 1.1	10.3 ± 0.7
Control	10.7 ± 1.4	10.8 ± 1.3	10.6 ± 1.3	10.4 ± 0.6	10.8 ± 1.5

Data are means (SD). A, amplitude; CI_{95}, 95% confidence interval; Control, control (n = 9 participants); G, gain; HIIT, high-intensity interval training (n = 8 participants); MICT, moderate-intensity continuous training (n = 11 participants); MRT, mean response time; p, primary response; s, slow component phase; τ, time constant; $\dot{V}O_2$, oxygen consumption. A two-factor (time vs. group) mixed ANOVA was used for the analysis. *Significantly different from pretraining ($P < 0.05$); †significantly different from Control within the same time point ($P < 0.05$); [a]significantly different than Control ($P < 0.05$); [b]significantly different than MICT ($P < 0.05$).

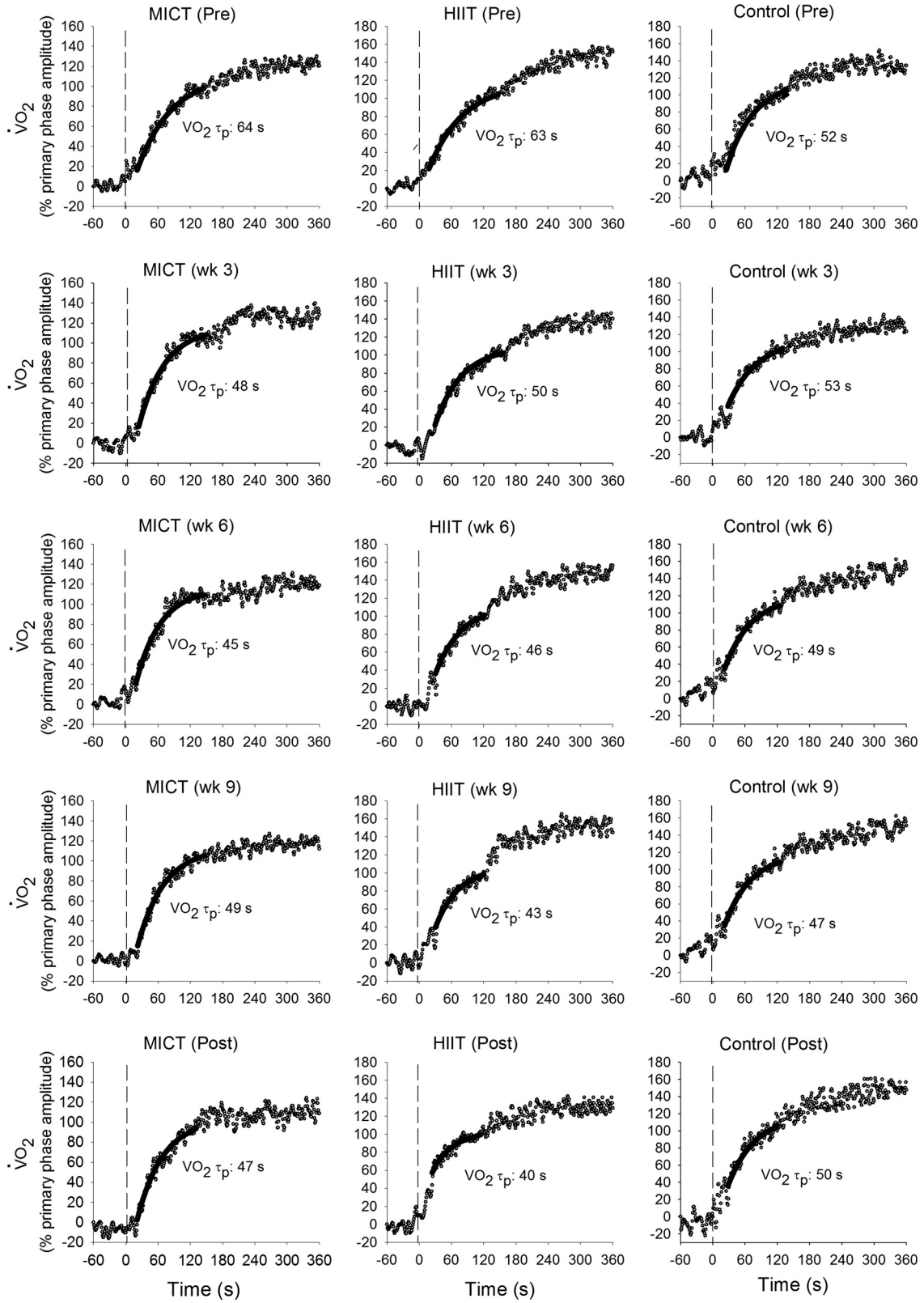

Figure 1. Representative time course of changes for the adjustment in normalized oxygen uptake ($\dot{V}O_2$; open circles) during the work-to-work cycling transitions for individuals in the moderate-intensity continuous training (MICT), high-intensity interval training (HIIT), and nonexercising control groups. The vertical line illustrates the abrupt transition to the higher work rate. The continuous black lines of best fit illustrate the primary phase of the $\dot{V}O_2$ response. Note the relatively faster time constant of the primary phase of the $\dot{V}O_2$ response ($\dot{V}O_2$ τ_p) and a reduced $\dot{V}O_2$ slow component beyond *week 3* of training in the participants from the HIIT and MICT groups, while $\dot{V}O_2$ τ_p and $\dot{V}O_2$ slow component are not affected by training in the participant from the control group.

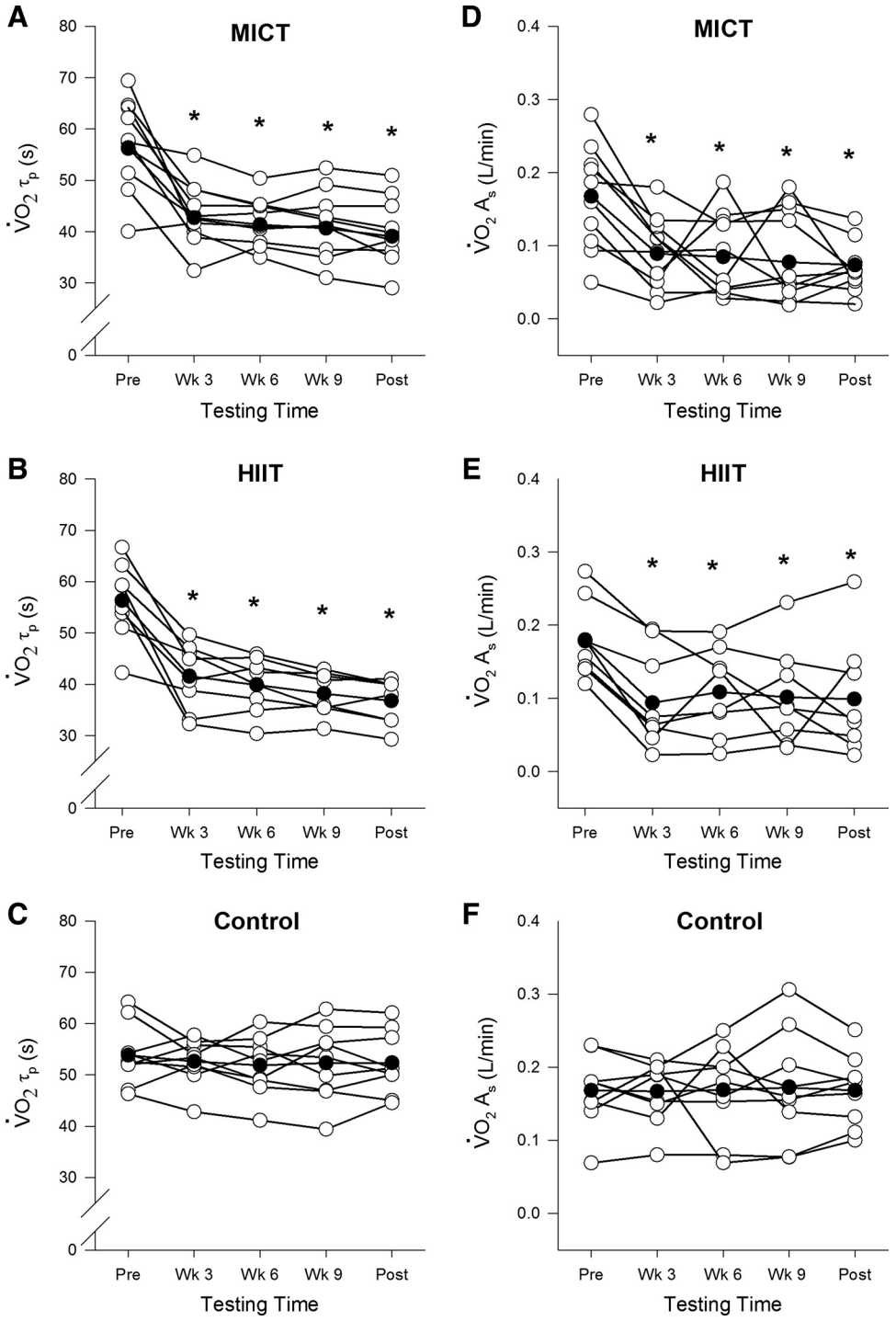

Figure 2. Individual time course of changes in the time constant of the primary phase of the oxygen uptake ($\dot{V}O_2$ τ_p) and amplitude of the $\dot{V}O_2$ slow component ($\dot{V}O_2$ A_s) in the moderate-intensity continuous training (MICT, *A* and *D*; n = 11 participants), high-intensity interval training (HIIT, *B* and *E*; n = 8 participants), and nonexercising control groups (*C* and *F*; n = 9 participants). Thin lines represent individual participants and thick lines, the mean change in each group. A two-factor (time vs. group) mixed ANOVA was used for the analysis. *Significantly different from pretraining ($P < 0.05$).

indicative of an increase in O_2 delivery relative to utilization within the microvasculature (22). These findings are also in agreement with Williams et al. (45) who showed in healthy individuals that the enhanced $\dot{V}O_2$ τ_p upon transition to w-to-w exercise in the moderate-intensity domain following HIIT was induced without changes in the adjustment of local muscle deoxygenation. It is possible that training enhanced blood flow kinetics and local blood flow distribution contributed to the faster $\dot{V}O_2$ kinetics. In this regard, substantial evidence exists to suggest that T2D is associated with impairments in the dynamic response of vasodilation (13, 16) and matching of capillary blood flow to metabolism (46) in contracting myocytes, whereas a short-term continuous endurance training intervention enhances leg vascular conductance kinetics at low contractile intensities, at least in females with T2D (47). This is consistent with previous reports of healthy populations showing faster conduit artery blood flow kinetics subsequent to a continuous aerobic training intervention (48).

Table 3. *Dynamic response characteristics of [HHb + Mb] and TOI during moderate-intensity and high-intensity cycling exercise of the work-to-work transitions for the MICT, HIIT, and Control groups*

	Pretraining	Week 3	Week 6	Week 9	Posttraining
Moderate intensity					
Baseline Δ[HHb + Mb], μMol·cm					
MICT	−67 ± 42	−72 ± 68	−84 ± 60	−60 ± 54	−62 ± 32
HIIT	−59 ± 44	−69 ± 35	−66 ± 41	−66 ± 38	−59 ± 35
Control	−55 ± 37	−52 ± 30	−53 ± 30	−60 ± 29	−54 ± 31
Δ[HHb + Mb] A_p, μMol·cm					
MICT	93 ± 36	104 ± 57	95 ± 40	91 ± 54	89 ± 32
HIIT[a]	183 ± 109	170 ± 105	169 ± 108	181 ± 108	179 ± 111
Control	73 ± 59	71 ± 52	66 ± 54	68 ± 55	68 ± 44
Δ[HHb + Mb] τ′, s					
MICT	29 ± 7	28 ± 5	27 ± 10	27 ± 12	27 ± 4
HIIT	23 ± 3	27 ± 5	23 ± 2	24 ± 9	23 ± 3
Control	26 ± 4	24 ± 6	26 ± 7	27 ± 5	26 ± 7
Primary phase Δ[HHb + Mb]/Δ$\dot{V}O_2$ μMol·cm·(L/min)					
MICT	149 ± 84	158 ± 76	153 ± 71	141 ± 72	140 ± 66
HIIT	174 ± 129	193 ± 110	170 ± 119	186 ± 133	186 ± 141
Control	122 ± 86	110 ± 67	113 ± 85	114 ± 77	120 ± 74
Baseline TOI, %					
MICT	71 ± 3	72 ± 5	72 ± 7	70 ± 5	73 ± 6
HIIT	71 ± 7	71 ± 8	71 ± 6	71 ± 9	72 ± 6
Control	71 ± 6	72 ± 7	71 ± 6	71 ± 7	74 ± 7
TOI *A*, %					
MICT	4.1 ± 3.5	4.9 ± 3.9	3.2 ± 2.3	2.8 ± 3.8	3.2 ± 3.8
HIIT[ab]	7.1 ± 6.5	9.1 ± 5.9	7.1 ± 5.2	7.4 ± 6.0	8.6 ± 6.0
Control	2.9 ± 3.6	3.4 ± 3.4	2.9 ± 3.3	2.7 ± 2.4	3.2 ± 4.8
High Intensity					
Baseline Δ[HHb + Mb], μMol·cm					
MICT	32 ± 42	31 ± 60	12 ± 47	36 ± 60	31 ± 46
HIIT[ab]	122 ± 130	123 ± 100	115 ± 130	125 ± 129	122 ± 137
Control	9 ± 68	23 ± 67	12 ± 84	7 ± 71	15 ± 50
Δ[HHb + Mb] A_p, μMol·cm					
MICT	60 ± 38	68 ± 31	69 ± 32	75 ± 48	65 ± 26
HIIT	78 ± 42	77 ± 51	86 ± 44	91 ± 97	80 ± 32
Control	42 ± 49	33 ± 36	39 ± 51	39 ± 48	35 ± 42
Δ[HHb + Mb] τ′, s					
MICT	30 ± 10	32 ± 5	33 ± 6	34 ± 7	33 ± 7
HIIT	32 ± 11	32 ± 11	32 ± 11	32 ± 9	32 ± 9
Control	28 ± 6	26 ± 11	29 ± 9	29 ± 13	28 ± 13
Primary phase Δ[HHb + Mb]/Δ$\dot{V}O_2$, μMol·cm·(L/min)					
MICT	163 ± 111	148 ± 58	141 ± 66	149 ± 84	132 ± 67
HIIT	135 ± 93	110 ± 68	134 ± 100	136 ± 97	122 ± 64
Control	83 ± 70	65 ± 53	82 ± 97	74 ± 60	73 ± 64
Δ[HHb + Mb] A_s, μMol·cm					
MICT	10 ± 6	15 ± 10	15 ± 15	14 ± 11	13 ± 10
HIIT	12 ± 7	12 ± 8	19 ± 12	17 ± 12	12 ± 8
Control	11 ± 7	12 ± 6	12 ± 8	13 ± 10	12 ± 10
Baseline TOI, %					
MICT	67 ± 5	67 ± 8	69 ± 8	68 ± 7	70 ± 9
HIIT	64 ± 12	62 ± 12	64 ± 11	63 ± 12	63 ± 11
Control	68 ± 9	68 ± 10	68 ± 8	68 ± 8	70 ± 10
TOI *A*, %					
MICT	3.1 ± 2.3	3.0 ± 2.6	4.6 ± 1.9	4.6 ± 2.2	3.6 ± 2.7
HIIT	3.7 ± 2.3	4.5 ± 3.4	6.3 ± 4.2	5.7 ± 4.9	4.3 ± 3.3
Control	3.0 ± 2.4	2.3 ± 2.4	2.0 ± 3.6	2.2 ± 2.9	2.2 ± 3.3

Data are mean (SD). *A*, amplitude; Control, control (n = 9 participants); [HHb + Mb], deoxygenated hemoglobin and myoglobin concentration; HIIT, high-intensity interval training (n = 8 participants); MICT, moderate-intensity continuous training (n = 11 participants); p, primary response; s, slow component phase; τ, time constant; τ′ [HHb + Mb], effective time constant (τ + time delay, TD); TOI, tissue oxygenation index; $\dot{V}O_2$, oxygen consumption. A two-factor (time vs. group) mixed ANOVA was used for the analysis. [a]Significantly different than Control ($P < 0.05$); [b]significantly different than MICT ($P < 0.05$).

Effect of Exercise Training on $\dot{V}O_2$ A_s during High-Intensity Exercise of the W-to-W Transition

Alongside reductions in $\dot{V}O_2$ τ_p, both training interventions also significantly reduced the amplitude of the $\dot{V}O_2$ slow component ($\dot{V}O_2$ A_s) during the high-intensity bout of the w-to-w transition at the same 3-wk time point and remained that way until the end of the interventions. This is in contrast to findings in healthy individuals, whereby 2 wk (i.e., 6 exercise sessions) of either RST or MICT did not elicit any changes in the $\dot{V}O_2$ A_s during severe-intensity work-to-work transitions despite eliciting significant reductions in $\dot{V}O_2$ τ_p (44). However, during transitions from unloaded to severe-intensity exercise, Bailey et al.

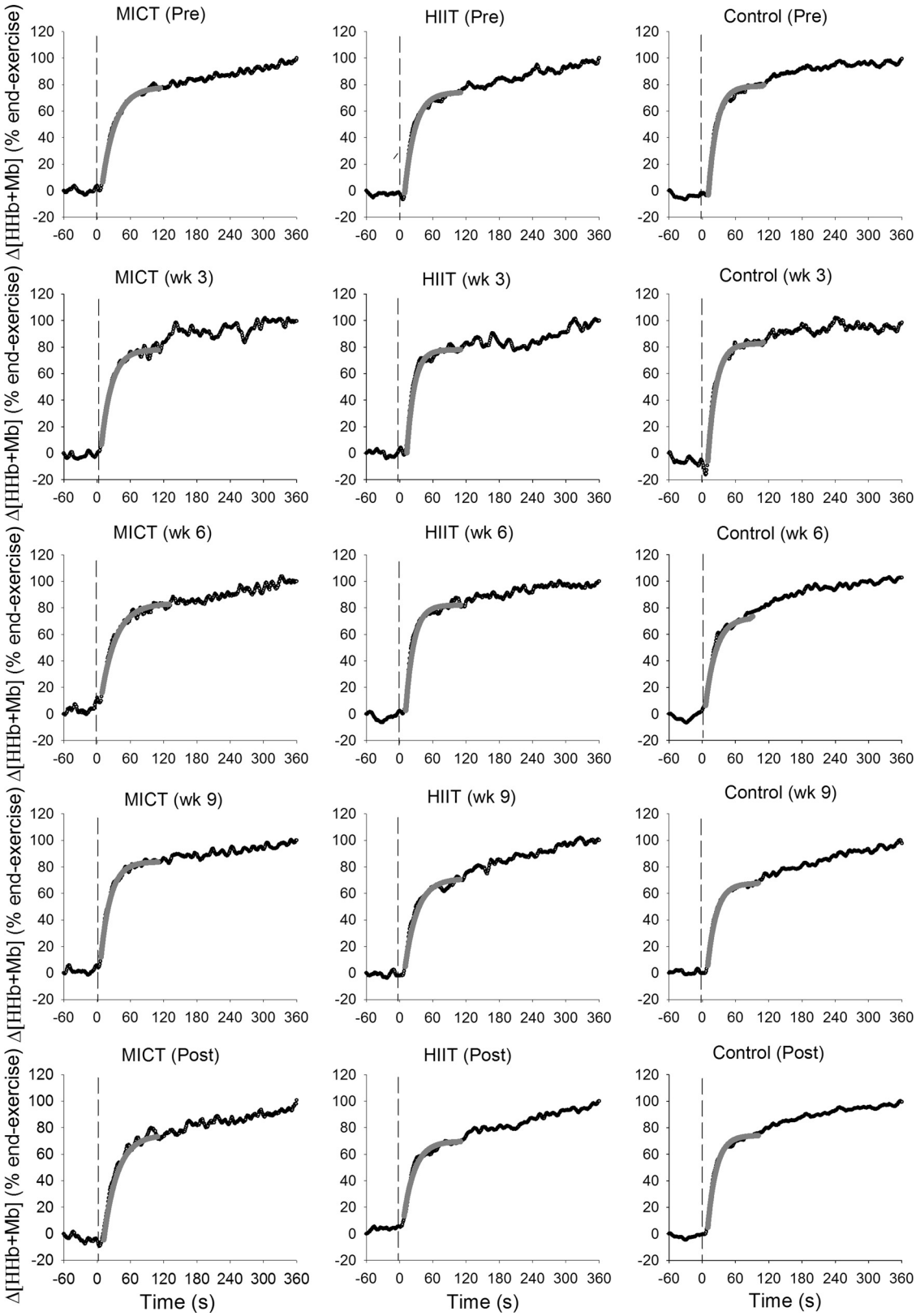

Figure 3. Representative time course of changes for the adjustment in normalized deoxygenated hemoglobin and myoglobin concentration (Δ[HHb + Mb]; open circles) during the work-to-work cycling transitions for representative individuals in the moderate-intensity continuous training (MICT), high-intensity interval training (HIIT), and non-exercising control groups. The vertical line illustrates the abrupt transition to the higher work-rate. The continuous gray lines of best fit illustrate the primary phase of the Δ[HHb + Mb] response. Note the time constant of the primary phase of the Δ[HHb + Mb] response (Δ[HHb + Mb] τ_p) is not affected by training in any of the three groups.

(40) reported that only 2 wk of RST (4–7, 30-s "all-out" sprints interspersed by 4-min rest), but not MICT (cycling at 90% VT for a duration that resulted in an equal work volume to RST), were sufficient to reduce $\dot{V}O_2$ A_s in healthy individuals. The fact that $\dot{V}O_2$ A_s is larger in severe-intensity transitions initiated from a resting baseline compared with a moderate-intensity baseline might suggest the potential to reduce $\dot{V}O_2$ A_s in the former, is likely larger. Therefore, authors suggested that a longer duration training program may be needed to allow for training-induced adaptations in the $\dot{V}O_2$ A_s during the moderate- to severe-intensity w-to-w transitions (44). On the other hand, in agreement with our findings, 6 wk of both HIIT (20 × 1-min at 90% $\dot{V}O_{2peak}$ interspersed by 60-s rest) or continuous aerobic training (30 min at 60% $\dot{V}O_{2peak}$) significantly decreased the amplitude of the $\dot{V}O_2$ A_s (from 0.41 to 0.30 L/min; and from 0.38 to 0.29 L/min, respectively) during severe-intensity exercise initiated from an unloaded cycling baseline in healthy populations (43).

The exercise-induced changes in the amplitude of the $\dot{V}O_2$ A_s herein can be, at least partially, attributable to adaptations in the skeletal muscle properties given the working skeletal muscle accounts for ~80% of the $\dot{V}O_2$ A_s (49). In this regard, in individuals with T2D, short-term continuous aerobic training has been shown to significantly increase oxidative enzyme activity and mitochondrial size and protein content (50). On the other hand, 2 wk of low-volume HIIT also increased mitochondrial oxidative activity (51) and, stimulated activity of peroxisome-proliferator activated γ coactivator (PGC-1α), shown to regulate mitochondrial content and respiration in diabetic skeletal muscle.

We had hypothesized that HIIT would speed $\dot{V}O_2$ τ_p to a greater extent than MICT given that during HIIT a greater proportion of type II muscle fibers are recruited during the repeated intervals above the VT. This would induce greater oxidative enzyme adaptations (23) compared with MICT, that predominantly involves the recruitment of type I oxidative muscle fibers. However, this was not the case herein, as both interventions speeded $\dot{V}O_2$ τ_p, (as well as reduced the $\dot{V}O_2$ A_s) by a magnitude not different among them. Importantly, participants herein were exercising at a lower relative exercise intensity at each testing time point throughout the interventions compared with pretraining, which likely reduced the proportion of type II fibers recruited. Similarly, in healthy populations, both continuous endurance training and HIIT interventions that provide sufficient stimulus for adaptation have also been shown to be equally effective at speeding $\dot{V}O_2$ kinetics during high-intensity transitions initiated from a moderate intensity (44) or resting (43) baseline, as well as during moderate-intensity transitions initiated from a resting baseline (41). As herein, in these studies participants used the same absolute power output during exercise transitions at all testing time points. Thus, it is plausible that in the present study both training interventions provoked rapid increases in the oxidative capacity of type I and II fibers and/or stimulated phenotypical shifts in type II muscle fibers, or indeed mechanism intrinsic to individual muscle fibers, and as such improved mitochondrial function or respiratory capacity. Such improvements would plausibly serve to improve metabolic stability, and subsequently negate the need to recruit higher level glycolytic fibers and thus reduce the amplitude of the $\dot{V}O_2$ A_s.

Effect of Exercise Training on $\dot{V}O_2$ τ_p during Moderate-Intensity Exercise of the W-to-W Transition

Consistent with findings from our recent companion paper (22), HIIT and MICT accelerated the $\dot{V}O_2$ kinetics during the moderate-intensity exercise transition after 3 wk of training with no additional changes thereafter, while there were no changes in any $\dot{V}O_2$ parameters in the control group. In addition, muscle deoxygenation kinetics responses were not altered throughout the intervention, suggestive of an improvement in the balance of O_2 delivery and utilization being a likely underlying mechanism of the accelerated $\dot{V}O_2$ kinetics. Indeed, it is likely that the training-enhanced $\dot{V}O_2$ kinetics and possibly the fatigability of muscle during the moderate-intensity baseline, contributed to speeding the $\dot{V}O_2$ kinetics of the high-intensity transition and reducing the fatigue-related and time-dependent increase in motor unit recruitment that underpins the slow component of $\dot{V}O_2$ during high-intensity exercise.

Limitations

A number of limitations of the present study must be acknowledged. First, the NIRS-derived findings herein relate to a single muscle, the VL, and therefore, interpretation of these data is limited to the site of interrogation (i.e., superficial sample of the VL). The established heterogeneity extant within a single muscle in terms of vascularity and fiber type, fiber recruitment, vascular control, and blood flow (52), likely extends to the VL, as well as the temporal and spatial heterogeneity in NIRS-derived responses extant both among and within muscles (53). Second, five participants did not complete the required 6 min of high-intensity cycling exercise during the w-to-w transitions at the pretraining time point. However, we believe this had little influence on the interpretation of our findings given that all participants showed a clear $\dot{V}O_2$ slow component phase, they were similarly distributed among groups (1–3 in each group) and only physiological responses collected over the same period during the subsequent time points were analyzed. In this regard, future studies should attempt to identify each individual's critical power to confirm that high-intensity exercise transitions were carried out within the same intensity domain for all participants (i.e., heavy or severe domain). Third, while in 14 responses (from 9 participants) a small $\dot{V}O_2$ slow component phase was observed during the moderate-intensity transitions, these participants were also similarly distributed among groups (3 in each group), thus, the influence on the interpretation of the current findings is likely minor. Fourth, herein the $\dot{V}O_2$ slow component was estimated using a second exponential response (*Eq. 2*), but it is also common practice to identify the onset of the slow component by fitting a monoexponential equation (*Eq. 1*) up to the point where residuals deviate from Gaussian distribution. We therefore carried out additional analyses to identify the onset of the slow component in line with the latter method, and these estimates coincided very closely (not

shown) with subsequent statistical outcomes unaffected. Finally, given that the current study is the first to report training-induced changes in $\dot{V}O_2$ kinetics during high-intensity w-to-w transitions in T2D, the overall trial was powered to detect changes in $\dot{V}O_{2peak}$ (26), so, we cannot exclude the possibility that the limited number of participants that completed the study precluded the observation of additional benefits in $\dot{V}O_2$ kinetics beyond the 3rd week of training.

Conclusions

The present study primarily demonstrated that both HIIT and MICT are safe and effective interventions that accelerate the $\dot{V}O_2$ kinetics response during high-intensity exercise initiated from an elevated baseline in individuals with uncomplicated T2D. Both forms of training induced a reduction in the amplitude of the $\dot{V}O_2$ A_s and an acceleration of $\dot{V}O_2$ τ_p without changes in [HHb + Mb] kinetics responses. Improvements in O_2 delivery during exercise are likely to have contributed to the observed reduction in $\dot{V}O_2$ τ_p with training, while the reduction in the amplitude of the $\dot{V}O_2$ A_s may have been caused by exercise-induced changes in skeletal muscle properties and motor unit recruitment patterns. From a practical perspective, investigating the training effects on the w-to-w protocol is of great relevance as it mimics the abrupt metabolic transitions akin to those in daily life such as abrupt walking/running/stair climbing velocity changes when for instance, people need to arrive on time to a place or an appointment. Moreover, individuals with T2D are being encouraged to actively commute to work by healthcare practitioners given the effectiveness of active commuting to improve body composition and cardiovascular health. In this regard, when people cycle to work, sudden changes in gradient and/or speed also mimic the w-to-w protocol investigated in the present study. Furthermore, given individuals with T2D perceive even light to moderate exercise as being more difficult than healthy counterparts (42), the perception of these w-to-w transitions is also likely harder that can ultimately result in a more sedentary lifestyle. Therefore, the present study yields promising results supporting the efficacy of time-saving low-volume HIIT in eliciting increases in exercise tolerance given a faster provision of aerobic metabolism will serve to reduce muscle fatigue during abrupt w-to-w transitions.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

N.G., J.R., D.O., S.G., and M.E. conceived and designed research; N.G., A.M., J.R., D.C., and A.N. performed experiments; N.G., A.M., and M.E. analyzed data; N.G., A.M., S.G., and M.E. interpreted results of experiments; N.G. and M.E. prepared figures; N.G. and M.E. drafted manuscript; N.G., A.M., J.R., D.C., A.N., D.O., S.G., and M.E. edited and revised manuscript; N.G., A.M., J.R., D.C., A.N., D.O., S.G., and M.E. approved final version of manuscript.

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