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Effect of Blood Flow Restriction on Tissue Oxygenation during Knee Extension

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[1]Beckman Laser Institute and Medical Clinic, School of Medicine, University of California, Irvine, CA; [2]Department of Pediatrics, Irvine School of Medicine, University of California, Irvine, CA; [3]Department of Orthopedic Surgery, University of California, Irvine, CA; and [4]Department of Kinesiology, California State University, Long Beach, CA

ABSTRACT

GANESAN, G., J. A. COTTER, W. REULAND, A. E. CERUSSI, B. J. TROMBERG, and P. GALASSETTI. Effect of Blood Flow Restriction on Tissue Oxygenation during Knee Extension. *Med. Sci. Sports Exerc.*, Vol. 47, No. 1, pp. 185–193, 2015. **Purpose**: Time-resolved near-infrared spectroscopy was used to quantify tissue oxy- and deoxyhemoglobin concentrations ([HbO_2] and [HbR]) and O_2 saturation (stO_2) in the oblique fibers of the vastus medialis muscle and brain prefrontal cortex during knee extension with and without blood flow restriction (BFR). **Methods**: Six young healthy males performed three sets of knee extensions on a dynamometer (50% one-repetition maximum) separated by 90-s rest periods in three conditions: 1) until fatigue without BFR (fatigue), 2) until fatigue with BFR (100 mm Hg cuff constriction around thigh (BFR)), 3) same number of repetitions from condition 2 without BFR (matched). Each condition was performed on a separate visit. **Results**: BFR was associated with higher [HbR] at the oblique fibers of the vastus medialis muscle (rest 1: 57.8 (BFR) vs 35.0 μM (matched); $P < 0.0001$) and a significantly lower stO_2 during recovery periods between sets (7.5%–11.2 % lower than non-BFR conditions for rest 1 and 2, $P < 0.0001$). Using a piecewise linear spline method, a spike in [HbR] was observed before the onset of HbR clearance during recovery, causing HbR clearance to begin at a higher concentration (81 (BFR) vs 62 μM (matched), $P = 0.029$). [HbO_2] kinetics during recovery were also affected by BFR, with longer duration (BFR, 51 s; matched, 31 s; $P = 0.047$) but lower rate of increase (BFR, 58 $\mu M \cdot min^{-1}$; matched, 89 $\mu M \cdot min^{-1}$; $P = 0.004$) during recovery. In the prefrontal cortex, BFR was associated with increased [HbR], diminished increase in [HbO_2], and higher subjective exertion. **Conclusions**: These findings yield insight into possible physiological mechanisms of BFR and suggest a role of time-resolved near-infrared spectroscopy in monitoring and optimization of BFR exercise on an individual basis. **Key Words:** RESISTANCE TRAINING, EXERCISE, BLOOD FLOW RESTRICTION, FATIGUE, DIFFUSE OPTICS, TISSUE OXYGENATION

In recent years, considerable attention has been drawn to the potential use of blood flow restriction (BFR) in enhancing the skeletal muscle response to resistance exercise. Exercise with BFR (sometimes called Kaatsu training [33]) has been observed to cause greater increases in muscle size compared with non-BFR resistance exercise of comparable intensity/duration (22,39). American College of Sports Medicine guidelines recommend sets of exercise at 70%–85% of one-repetition maximum (1RM) to achieve hypertrophy in untrained individuals (2), whereas it has been shown that intensities as low as 20% 1RM can induce hypertrophy with concomitant BFR (37). These and other published findings suggest a use of BFR in treatment of muscle atrophy (6,19,40).

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The molecular mechanisms for BFR enhancement of training are being actively investigated. Among the proteins with postulated signaling roles are mammalian target of rapamycin, heat shock proteins, and nitric oxide synthase (23). However, it is not known precisely how BFR exerts an effect on these signaling pathways. We hypothesized that measurements of muscle hemodynamics and oxygenation during BFR and similar non-BFR exercise would provide insight into this process.

Near-infrared spectroscopy (NIRS) is a noninvasive technique used to measure tissue concentrations of oxy- and deoxyhemoglobin ([HbO_2] and [HbR]), which together provide information about tissue-specific O_2 availability and use as well as blood flow. NIRS has numerous applications in sports science (13). Considerable work has been done to characterize muscle NIRS responses in a variety of resistance exercise conditions (9,29). NIRS has also been used to assess cerebral function during resistance exercise (24). On the basis of the range of currently available commercial instrumentation, most studies have used continuous-wave NIRS (CW-NIRS) techniques (29), which report relative changes in tissue hemoglobin concentration and oxygen saturation (stO_2). In contrast to CW-NIRS, time-resolved NIRS (TR-NIRS) is able to quantitatively separate light absorption from scattering and

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measure absolute hemoglobin concentrations in tissue. This is accomplished by measuring and fitting the temporal point spread function of emitted light signals to a model of light transport in tissue (26). These features make TR-NIRS particularly attractive for the current study because it allows compensation for differences in path length (PL) and scattering (14) that might occur with large changes in blood volume and would therefore result in more accurate measurements.

To gain insight into physiological mechanisms for the effect of BFR, we conducted a study on isokinetic knee extension exercise with and without partial BFR (occlusion pressure of 100 mm Hg) using a two-channel commercial TR-NIRS instrument (TRS-20; Hamamatsu KK, Japan) (41). For the muscle studies, we measured the oblique fibers of the vastus medialis muscle (VMO). These muscle fibers insert medially on the patella and are thought to be important in preventing injuries such as subluxation and lateral displacement of the patella and in assessing patellofemoral pain syndrome (28,31). There have been efforts to study the VMO using EMG (33), but to our knowledge, no published studies use NIRS to assess VMO oxygenation in knee extension. There is ongoing interest in whether therapies can specifically target VMO for hypertrophy (34).

This study also included TR-NIRS measurements of cerebral oxygenation. Blood flow and oxygenation in critical cerebral areas, such as the prefrontal cortex (PFC), have been hypothesized as determinants in the ability to sustain longer exercise challenges. This may be especially relevant during conditions of BFR when the subjective perception of fatigue may be amplified (17). We hypothesized that if BFR exercise results in greater subjective exertion, it may also alter the PFC oxygenation response to exercise when compared with control, non-BFR exercise.

METHODS

This study was conducted under an institutional-approved human subject protocol and carried out in the human performance laboratory at the University of California (Irvine, CA). Seven healthy male subjects were enrolled, and each provided a written informed consent.

Familiarization period. Each subject was familiarized with all elements of the experimental protocol before the first testing condition. During the first visit, body mass and resting blood pressure were measured and each subject was screened for possible contraindications to exercise. The Biodex dynamometer (System 3; Biodex Corp., Shirley, NY) was used for all exercise sessions and measurements. Isokinetic extension of the dominant knee joint was conducted at 30° per second with a range of motion of 90°. Maximal torque production for knee extension (1RM) was obtained from the highest torque produced during five repetitions. Subjects were familiarized with real-time visual feedback of peak torque production until they could reliably produce torque as close to 50% of 1RM as possible, which was used for all subsequent testing.

Testing visits. Testing sessions were conducted during morning hours in a fasted state. The three conditions for this exercise study are as follows: 1) exercise to volitional fatigue without BFR (fatigue), 2) exercise to volitional fatigue with BFR (BFR), and 3) exercise without BFR with the same number of repetitions as that in the BFR condition (matched). The subjects were randomly chosen to perform the three conditions in one of two orders: 1) BFR, matched, and fatigue or 2) fatigue, BFR, and matched, with each session separated by at least 48 h. Each exercise test was preceded by a brief warm-up. Rest periods between sets were 90 s, and the minimum number of repetitions per set was 10. For the BFR and fatigue conditions, sets were terminated when two consecutive repetitions produced torque >10% lower than 50% 1RM. For the BFR condition, an 85-cm cuff was wrapped around the proximal thigh and connected to a rapid inflator (E20 Rapid Cuff Inflator; Hokanson, Inc.) set to 100 mm Hg. Cuff inflation occurred 30 s before the start of the first set, and deflation occurred immediately after cessation of the third set. The number of repetitions achieved during the BFR condition was used to determine the number of repetitions in the matched condition. The protocol for the fatigue condition was identical to that for BFR but does not include cuff inflation. At the end of each exercise set, subjects were asked to provide an RPE, expressed as a number between 6 and 20 (3). One subject was excluded from data analysis because of failure to adequately follow experimental instructions regarding consistent torque production.

TR-NIRS measurements. Before exercise testing, TRS-20 silicone fiber holders were placed over the VMO (parallel to muscle fibers) and PFC (superolateral forehead) and secured directly to the skin with a double-sided clear tape. The VMO probe was further secured with an overlying tape, and the PFC probe, with an elastic headband to prevent motion. Source–detector separation was 30 mm for the VMO and 40 mm for the PFC. Continuous measurements in both tissues were made in parallel every 3 s. TR-NIRS, as implemented in the TRS-20 and described in a recent publication (41), uses a single-photon counting method to record individual reflected pulses from tissue. From these, the intensity of reflectance, optical PL, and absorbance change can all be derived without model assumptions. A least square method is used to fit a curve derived from the diffusion equation to the obtained reflectance, allowing determination of reduced scattering coefficient (μ_s') and absorption coefficient (μ_a). From absorption coefficients, PL calculations and known molar extinction coefficients at the three wavelengths, [HbO_2], [HbR], total hemoglobin ([THb]), and stO_2 are calculated using the Beer–Lambert law (41). stO_2 is defined as the ratio [HbO_2]/[THb] and is expressed as a percentage.

Data analysis. Repetitions, RPE, and total work output were recorded and tabulated for each set. All TR-NIRS output variables ([HbR], [HbO_2], [THb], and stO_2) were averaged for the baseline period, all sets, and all rest periods in both tissues. Average values were calculated for each set and

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rest period and tabulated using Prism (version 6; GraphPad Software, San Diego, CA). The same program was also used for ANOVA and subsequent multiple Bonferroni-corrected comparisons. Mean optical PL and μ_s' at 796 nm in VMO were also analyzed using coefficients of variation (CV) calculated over the course of the whole exercise challenge in the BFR and matched conditions. CV values were compared between conditions using a paired two-tailed *t*-test. For analysis of oxygenation kinetics, [HbO_2] and [HbR] for the first set and recovery period of exercise by each subject were imported to MATLAB (version R2013A; MathWorks). The beginning of the rapid phase of deoxygenation for both [HbR] and [HbO_2] was identified and used as the starting point for subsequent fitting. The Shape Language Modeling tool (12) was used to apply a sequential piecewise linear model to each [HbO_2] and [HbR] curve. We chose to apply this method in the first set and recovery because it was the longest set in repetitions and it would allow for determination of the effect of BFR independent of any prolonged effects of occlusion. The output of each of these fits is an *R*-squared value and a series of "breakpoints" (BP) time *t*, which represent the optimized times (and corresponding concentrations) of transition between the phases. Using this approach, [HbR] and [HbO_2] were modeled as following two-phase kinetics during both exercise and recovery: an initial fast phase, followed by a longer phase, and a slower second phase. The values for fit parameters (transition concentrations and rapid-phase slopes) were averaged for all subjects across two conditions (BFR and matched, the conditions in which overall timing was similar because of similar number of repetitions) and compared using paired two-tailed *t*-tests.

RESULTS

Exercise parameters. The fatigue condition was associated with a higher number of repetitions ($P < 0.001$) (Fig. 1A) and, therefore, higher total work (Fig. 1B), as compared with the other two conditions. There was not a significant difference in work output between BFR and matched conditions (Fig. 1B). BFR was associated with a significantly higher RPE (Fig. 1C) than the matched condition for all sets (16.8 vs 13.6 for set 1, 18.4 vs 12.8 for set 2, and 18.6 vs 13.0 for set 3, $P < 0.0001$) but only higher than the fatigue condition in set 2 (18.4 vs 16.8, $P = 0.0128$).

VMO oxygenation. In Figure 2, average values for each stage of exercise across six subjects are shown. For all four variables, there were significant *F*-values for interaction between exercise condition and stage of exercise. BFR exercise was associated with a significantly higher average [THb] than other conditions at each stage from the first rest period until the end of the third set when occlusion was released ($P < 0.0001$ in all cases) (Fig. 2A). During rest periods 1 and 2, this was driven by a significantly higher [HbR] in exercise with BFR over other conditions (Fig. 2C) (BFR vs fatigue: rest 1 and rest 2 ($P < 0.0001$ for both), BFR vs matched: rest 1 and rest 2 ($P < 0.0001$)). During sets 2 and 3, the increased [THb] was driven by a higher [HbO_2] (Fig. 2D) (sets 2 and 3: BFR vs matched and fatigue, $P < 0.01$ for all). The average [HbO_2] was also significantly higher in the fatigue condition than that in the BFR condition in the third rest period ($P = 0.0008$) after release of the occlusion. BFR was associated with nearly 10% lower average stO_2 during rest periods 1 and 2 than that in the other conditions (Fig. 2B) ($P < 0.0001$ in both cases). Reduced scattering coefficient (μ_s') and PL at 796 nm were also analyzed in the BFR and matched conditions. It was found that the CV for PL was significantly higher for BFR than that for the matched condition over the whole duration of exercise (4.9% vs 3.0%, $P = 0.002$). There was also a trend toward a difference in CV of μ_s' at

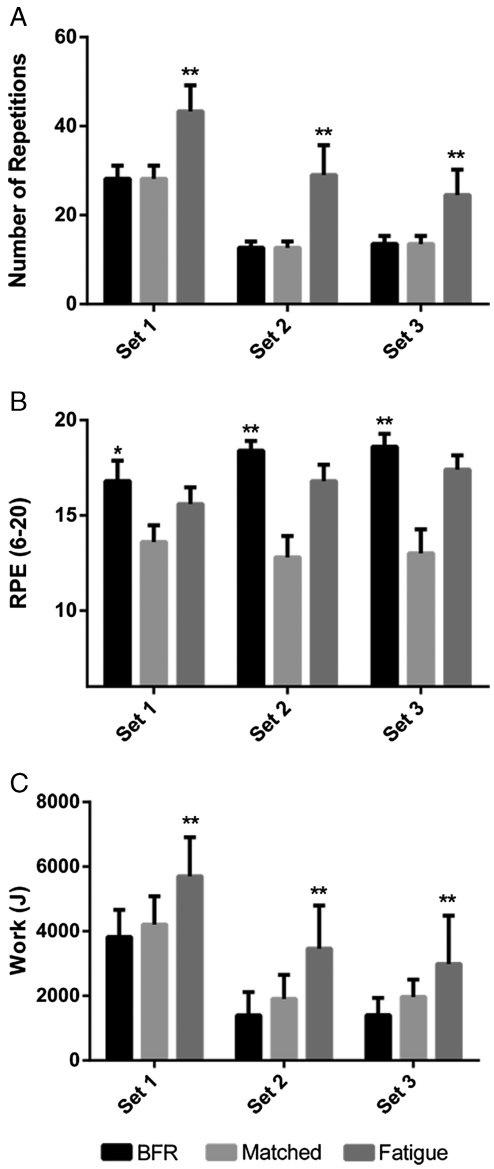

FIGURE 1—Average number of repetitions (A), total work output (B), and RPE (C) during three sets of isokinetic knee extension in six healthy subjects. The three sets were performed by each subject in three conditions: to exhaustion without BFR (fatigue), to exhaustion with BFR (BFR), and without BFR matching the workload in BFR (matched). *$P < 0.05$, BFR vs matched. **$P < 0.05$, BFR versus both other conditions.

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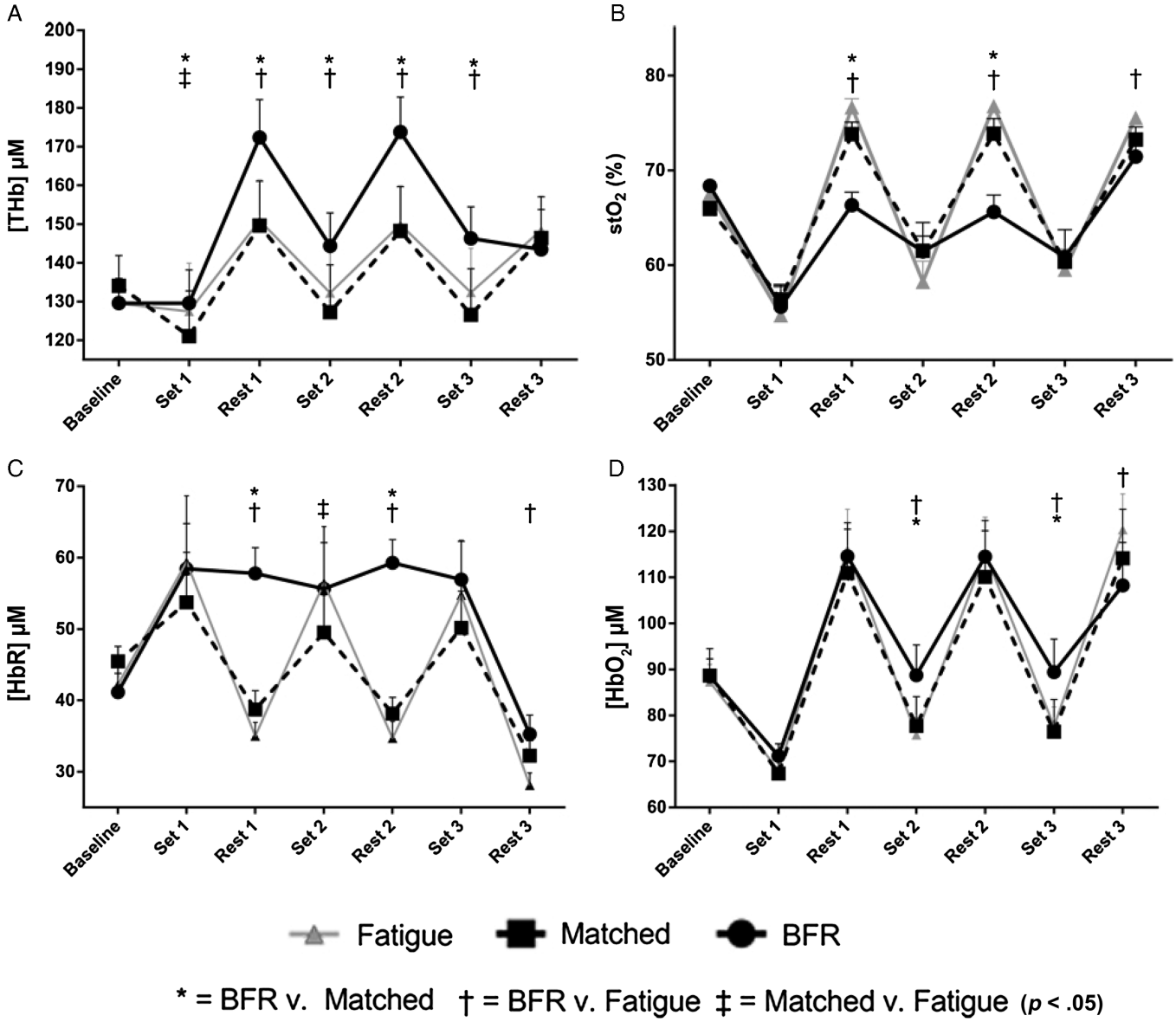

FIGURE 2—Average absolute [THb] (A), stO_2 (B), [HbO_2] (C), and [HbR] (D) in the VMO muscle during three sets of isokinetic knee extension in six healthy subjects. The three sets were performed by each subject in three conditions: to exhaustion without BFR (fatigue), to exhaustion with BFR (BFR), and without BFR matching the workload in BFR (matched).

796 nm, but it did not reach statistical significance (6.0% for BFR vs 4.0% for matched, $P = 0.09$). Finally, in comparison with the matched condition, the percentage change in PL from baseline to final recovery was different (−2.7% for BFR vs −0.6% for matched, $P = 0.03$).

Two-phase linear fitting results. Figure 3 shows representative results from a single subject for two-phase piecewise linear fitting of [HbO_2] and [HbR] during set 1 and rest 1. Panels A and B show data for [HbO_2] in matched and BFR conditions, respectively, whereas panels C and D show [HbR] fits in the same conditions. For all variables, the slope and duration of the rapid first phase (phase 1) and the concentration at the transition between phases during both exercise and recovery were analyzed, as shown in Table 1. In subject 6, the rapid phases in [HbO_2] seemed to occur faster than the measurement time of the TRS (3 s), and therefore, parameters for this phase were not included in the analysis. Significantly different fit parameters were identified in analysis of [HbR] during rest 1. Specifically, the concentrations at which both rapid and slow phases of [HbR] clearance began were higher in the presence of BFR ($P = 0.029$ and $P = 0.011$, respectively). This reflected the fact that in BFR, the rapid phase of [HbR] clearance during recovery was preceded by a "spike" of [HbR], contributing to the higher average concentration (Fig. 2C). To accommodate this, an extra BP was included in the fitting procedure for the BFR condition. This [HbR] "spike" was detected in all six subjects analyzed in the BFR condition and to some extent in the matched condition for only 2 subjects. For [HbO_2] during recovery, the duration of the first phase was significantly longer in BFR versus that in matched conditions

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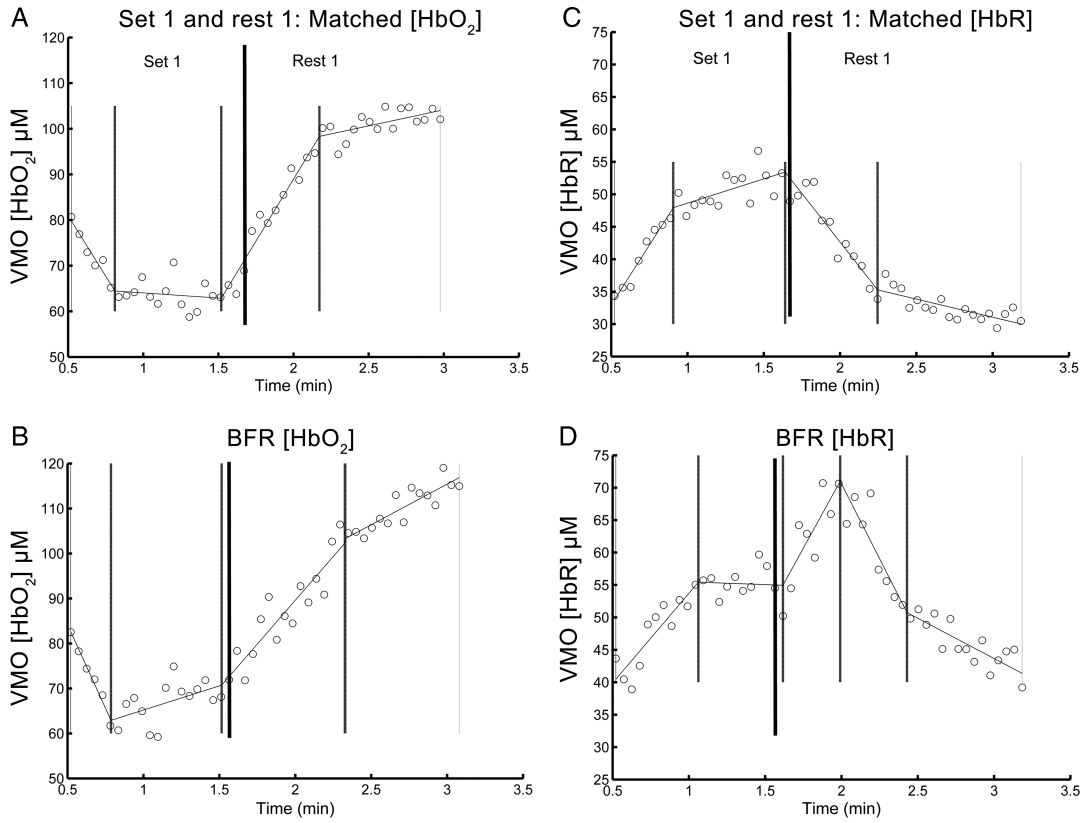

FIGURE 3—Representative single-subject results using piecewise linear spline fitting of the first set and rest periods. Panels A and B show the results of [HbO_2] goodness of fit for matched (A, $R^2 = 0.952$) and BFR conditions (C, goodness of fit: $R^2 = 0.888$). Panels B and D show results of [HbR] for matched (C, $R^2 = 0.976$) and BFR (D, $R^2 = 0.965$). *Solid black lines* represent event markers for division between exercise and recovery. *Vertical narrow lines* represent the position in time of optimally fitted BP between linear phases. The *circles* represent raw data points, and the *solid lines* represent the fitted linear segments.

(51 vs 31 s, $P = 0.047$). However, the slope of [HbO_2] increase was also significantly lower (56 vs 89 $\mu M \cdot s^{-1}$, $P = 0.004$). Finally, in the BFR condition (but not matched) there was a correlation between the magnitude of increase in [THb] from the first set of exercise to recovery and the slope of rapid-phase clearance of [HbR] during recovery ($r = -0.88$, $P = 0.02$).

PFC oxygenation. Figure 4 shows results for PFC oxygenation parameters. Panels A and B show representative BFR and matched raw data for [HbR] in two subjects, with the whole three sets of exercise shown by *dashed lines*. Generally, exercise was associated with small but consistent increases in both PFC [HbR] and [HbO_2], as shown by maximal changes from baseline (Δ[HbR] and Δ[HbO_2]) in Figure 4C and D. The BFR condition was associated with a significantly lower Δ[HbO_2] than the matched and fatigue conditions during all sets (Fig. 4C) and the second rest period ($P < 0.01$ for all). During the first rest period, the Δ[HbO_2] was lower in BFR than that in matched ($P = 0.0008$). BFR was associated with a significantly higher Δ[HbR] (Fig. 4D) than matched during the first rest period and all subsequent stages ($P = 0.0014$ for set 2, $P < 0.0001$ for others). Δ[HbR] was higher in BFR than that in fatigue during rests 2 and 3, as well ($P < 0.0001$ and $P = 0.02$, respectively). Panels E–G

TABLE 1. Summary of mean ± SEM of fitting parameters for all subjects for the first set and rest periods.

		Initial Concentration (μM)		First Phase Duration (s)		Transition Concentration (μM)		First Phase Slope ($\mu M \cdot s^{-1}$)	
	Condition	BFR	Matched	BFR	Matched	BFR	Matched	BFR	Matched
[HbR] set 1	Average ± SEM	40 ± 4	34 ± 4	25 ± 5	30 ± 7	60 ± 7	56 ± 7	69 ± 29	63 ± 20
(average $R^2 = 0.895$)	*P* value	0.059		0.330		0.187		0.599	
[HbR] rest 1	Average ± SEM	81 ± 8	62 ± 6	25 ± 5	27 ± 7	58 ± 5	37 ± 3	−62 ± 13	−57 ± 9
(average $R^2 = 0.940$)	*P* value	*0.029*		0.781		*0.011*		0.717	
[HbO_2] set 1	Average ± SEM	93 ± 4	88 ± 7	15 ± 2	17 ± 2	65 ± 4	63 ± 5	−133 ± 48	−94 ± 27
(average $R^2 = 0.959$)	*P* value	0.371		0.296*		0.638		0.279*	
[HbO_2] rest 1	Average ± SEM	71 ± 2	67 ± 4	51 ± 7	31 ± 2	114 ± 9	111 ± 9	56 ± 10	89 ± 14
(average $R^2 = 0.977$)	*P* value	0.307		*0.047*[a]		0.441		*0.004*[a]	

Paired two-tailed *t*-tests were used to compare mean values between two conditions: BFR and matched. *P* values for significant differences are italicized.
[a]One subject was excluded from this comparison because the fitted first phase was shorter than the TRS-20 measurement interval.

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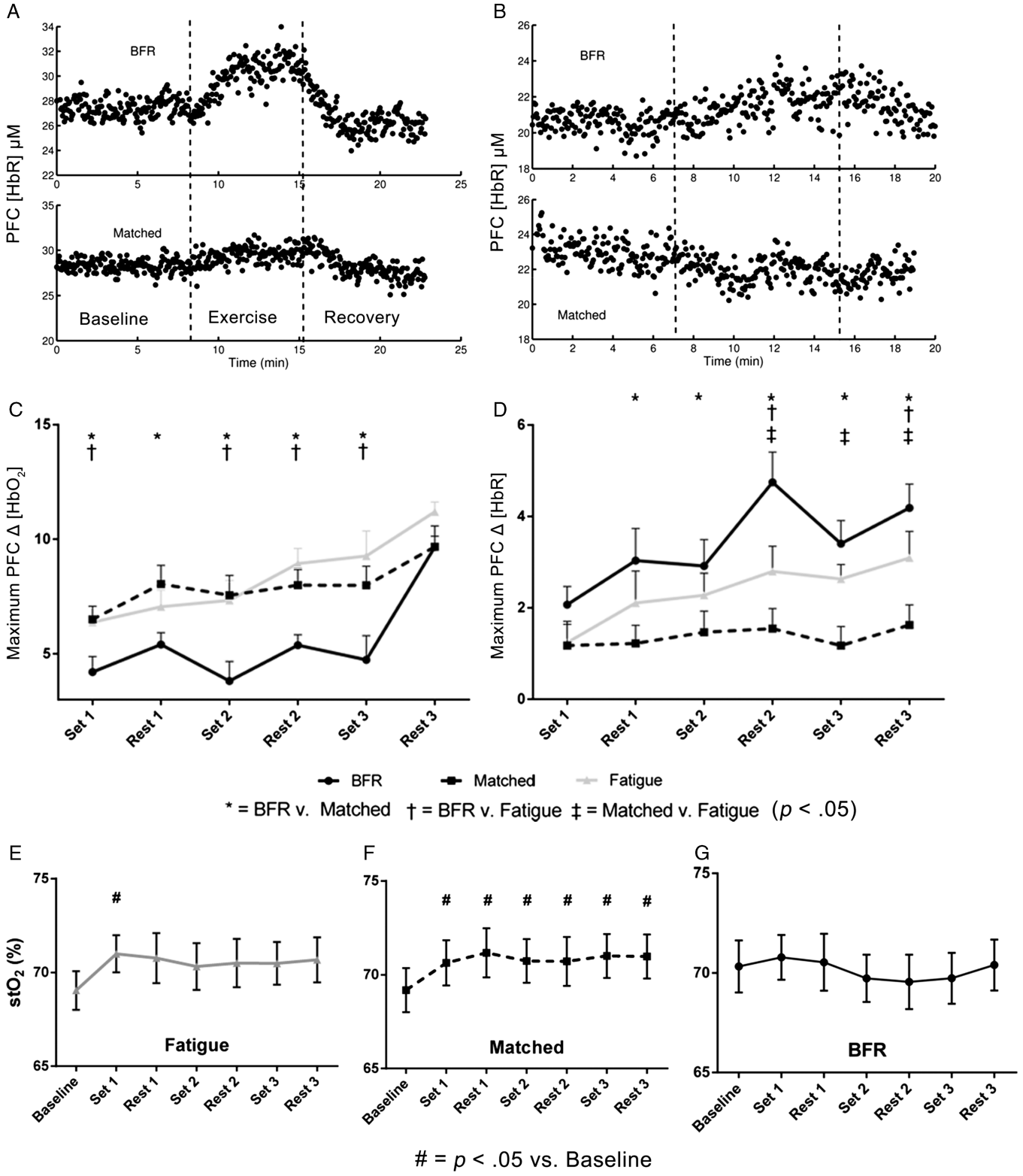

FIGURE 4—Sample tracings in two subjects for [HbR] in BFR (above) and matched (below) conditions (A and B). For each exercise stage, the maximal difference from baseline was calculated for [HbO_2] and [HbR] and group averages are shown in panels C and D. Panels E to G show average stO_2 values at each stage of exercise analyzed separately in the three experimental conditions.

show average absolute stO_2 at each experimental stage, with conditions analyzed separately by one-way ANOVA and *post hoc* Dunnett test against baseline values. For the fatigue condition (Fig. 4E), there was a significant increase in stO_2 during set 1 ($P = 0.0176$). For the matched condition (Fig. 4F), stO_2 at every stage was higher than those at

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baseline ($P < 0.01$ for all). There were no PFC stO_2 changes with BFR (Fig. 4G).

DISCUSSION

VMO oxygenation. We have assessed tissue hemoglobin content and oxygenation using TR-NIRS with and without BFR to understand the effects of occlusion on muscle oxygenation during knee extension. The typical patterns observed during NIRS measurements of exercising muscles are shown in the matched condition in Figure 3. Exercise is associated with increased [HbR] and reduced [HbO_2], with both reversing during recovery. Recovery is associated with a hyperemic supraexercise [HbO_2] and stO_2 because of both vasodilation and increased demand to pay back O_2 deficit. [HbR] and [HbO_2] together reflect the balance between O_2 use and muscle blood flow (15). To our knowledge, there are few published studies on muscle oxygenation during BFR exercise and none on the VMO muscle. In a 2011 study, Kacin and Strazar (18), using a CW-NIRS system, compared oxygenation dynamics of the vastus lateralis before and after a BFR training program. They reported no acute differences in vastus lateralis oxygenation with full arterial occlusion (230 mm Hg), but training resulted in larger increases in exercise-associated [THb] and [HbO_2] during non-BFR exercise. They did not report kinetics of oxygenation during recovery (18). We observed that knee extension with subsystolic BFR (100 mm Hg) results in exposure of the VMO to substantially decreased stO_2 values (range, 7.5%–11.2% lower) during recovery from each set. This reduction in stO_2 occurs in the context of greater [THb], perhaps indicating an increased capacity for postexercise O_2 consumption. Part of this phenomenon may be driven by increased downstream muscle O_2 demand in the period immediately after exercise. Analysis of exercise and recovery kinetics of [HbO_2] and [HbR] showed that although BFR slowed VMO [HbO_2] hyperemia during recovery (56 $\mu M \cdot min^{-1}$ in BFR vs 89 $\mu M \cdot min^{-1}$ in matched, $P = 0.004$), it did not inhibit the average increase in [HbO_2]. BFR exercise was, however, associated with a spike in [HbR] before the onset of rapid clearance during recovery, contributing to the higher average [HbR] (49% higher for BFR during rest 1). To come to these conclusions, we used an empirical piecewise regression approach to identify transitions between VMO oxygenation phases. Typically, muscle [HbR] kinetics are modeled with phasic monoexponential regression (4,11,20). Recent work has shown, in the context of cycling ramp exercise, that piecewise linear fitting may be a valid approach (35). Qualitatively, the piecewise approach provides an advantage of greater descriptive use and potentially useful comparisons between parameters such as phase duration and slope. Although VMO [HbR] and [HbO_2] kinetics in knee extension have not been extensively characterized, our results would seem to indicate that the piecewise approach is valid. However, our study was limited by the acquisition time of the TR-NIRS instrument (approximately 3 s per measurement) and, therefore, a loss of sensitivity to transient changes.

We also observed differences in measured PL between experimental conditions. The CV for PL at 796 nm was significantly higher in BFR versus matched, indicating greater variability over the course of exercise and recovery. There were also larger oscillations in μ_s' in BFR, although the CV difference was not statistically significant ($P = 0.09$). This observation is likely due to larger blood volume oscillations in BFR exercise, with a likely contribution of other molecular species (14), which accumulate to a higher degree in the BFR state. In addition, the change in PL from baseline to final recovery (after release of BFR) was larger in BFR than that in matched, perhaps indicating a persistent effect on VMO optical properties after BFR exercise. Both PL and μ_s' can affect reported [HbO_2] and [HbR] by the Beer–Lambert law. Another issue that must be considered is the effect of skin and subcutaneous adipose tissue on measured optical properties. Although all reflectance NIRS measurements include nonnegligible contributions from the superficial layers, several factors mitigate this fact in this case. Firstly, the overlying tissue above the VMO is relatively thin (3–6 mm, G. Ganesan, author's unpublished observations, 2013) compared with the source–detector separation (30 mm). Secondly, the time-resolved approach discriminates between early- and late-arriving photons, which allows for greater intrinsic sensitivity to absorption in deeper tissues. Finally, the level of [THb] recorded in this study (baseline VMO [THb], 148.5 ± 6.8 μM) is consistent between subjects, indicating similar distribution of muscle in the sample volume. Although the influence of superficial changes in blood flow and blood volume on reported kinetics cannot be discounted (8), others have shown these to be minimal in the case of brain TR-NIRS measurements (1). Furthermore, it has been shown that using spatially resolved NIRS, another technique capable of compensating for changes in PL, reduces sensitivity to skin blood flow in muscle [THb] measurements (25). Future studies may help quantify the effects of subcutaneous adipose tissue thickness and skin blood flow on kinetics of VMO TR-NIRS signals, similar to what has been done with other muscle groups (5).

Mechanisms of BFR effect. One hypothesis for the increased BFR-induced training adaptation and hypertrophy in muscles is the effect of metabolite accumulation in venous blood (23) and subsequent release of circulating factors (6,38). It is thought that reduced O_2 delivery is also likely to contribute to the BFR effect because systemic hypoxia during resistance exercise has been shown to enhance hormonal responses (21). Given the persistently low muscle stO_2 during recovery with BFR, hypoxic signaling may be stimulated in this condition. However, although we observed a decrease in [HbO_2] recovery slope, there is no evidence to suggest an O_2 delivery limitation during BFR because there was no overall reduction in [HbO_2] during exercise or rest. In fact, [HbO_2] is elevated during sets 2 and 3 of exercise in BFR over other conditions. It is possible that BFR, by slowing the egress of

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deoxygenated blood-facilitated O_2 use, contributed to the observed [HbR] spike. Further studies are required to determine whether the lower stO_2 observed during recovery leads to hypoxic signaling or it is simply a consequence of greater O_2 availability and extraction.

In addition, it has been demonstrated that BFR training can enhance postocclusive hyperemic blood flow in the muscle (27) possibly as a result of increased angiogenesis. The persistent increase in blood volume caused by BFR, as evidenced by elevated [THb], may act to enhance the shear stimulus on the vessel wall, thereby promoting angiogenesis (18,30). The level of hypertrophy achieved with a given dosage of resistance exercise is also dependent on the duration of rest periods, with shorter intervals likely inducing larger gains (10). It is possible that the spike in [HbR] we observe in BFR exercise acts in a way analogous to reduction in recovery time, i.e., by slowing metabolite clearance.

PFC oxygenation. We have also shown small but consistent increases in [HbR] and [HbO_2] in the PFC of subjects with and without BFR. In BFR and fatigue conditions, when RPE is higher, this increase in PFC [HbR] is relatively larger, suggesting that PFC [HbR] may be related to activity-dependent fatigue (12,36). In addition, during BFR, the increase in [HbO_2] during exercise is smaller than that in the other conditions and, therefore, stO_2 does not increase. Our results correspond to published data indicating that knee extension is associated with increases in PFC stO_2 and blood volume ([THb]) (24). The observation that BFR abolished the PFC stO_2 increase during exercise suggests that it causes a different metabolic response for a given increase in [THb]. It has been observed (17) that lighter exercise with moderate occlusion is associated with perceptual responses akin to heavier-load, non-BFR exercise possibly because of increased compression of peripheral nerves. In a 2003 study, it was shown that cycling exercise with occlusion could alter cerebral metabolism (7) possibly by altered sensory input from the skeletal muscle. It is not clear whether small PFC stO_2 changes (<5%) such as those we observed would affect perception of fatigue. It seems that at minimum, moderate exercise with BFR can affect O_2 use and blood flow in the PFC in a manner that correlates with increased RPE. In summary, the results of these studies indicate that muscle hemodynamics and oxygenation may play a role in the enhancement of resistance exercise outcomes by BFR and that BFR can modulate exercise-induced changes in PFC hemodynamics in combination with perceived exertion during isokinetic resistance exercise.

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The results of this study do not constitute endorsement of the techniques used by the American College of Sports Medicine.

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