Upper Limb Circulatory Occlusion Improves Cycle Ergometer Time Trial Performance in Normoxia and Hypoxia

Original Research

S. Raj J. Trikha[1,2], Alissa A. Newman[1], Luke C. Hoskovec[1], Christopher Bell [1]

[1] Department of Health and Exercise Science, Colorado State University, Fort Collins, CO
[2] Department of Food Science and Human Nutrition, Colorado State University, Fort Collins, CO

Abstract

Introduction: The availability of blood and oxygen to exercising muscle is an important physiological determinant of endurance performance. This proof of concept study analyzed the ergogenic potential of a novel procedure: circulatory occlusion of inactive limbs. We hypothesized that upper limb circulatory occlusion would improve cycle ergometer performance and attenuate hypoxia-mediated decrements in endurance exercise.

Methods: 19 young, healthy adults (10 male, 9 female, age: 24 ± 3 years, mean$\pm$SD) completed four randomly ordered stationary cycle ergometer 5 km time trials in normoxia (fraction of inspired oxygen (FiO_2)=0.21) and hypoxia (FiO_2=0.15), with and without circulatory occlusion of the arms. Before each circulatory occlusion trial, participants held their arms above their head for 60 seconds, and automated blood pressure cuffs were rapidly inflated to 200 mmHg before participants lowered their arms.

Results: Time trial performances were: normoxia without occlusion 561.0 ± 65.4 s; normoxia with occlusion 555.6 ± 65.4 s; hypoxia without occlusion 594.6 ± 65.4 s; hypoxia with occlusion 586.2 ± 67.8 s. Statistical analysis revealed main effects of occlusion (faster with occlusion P=0.017), and inspired O_2 (slower in hypoxia P<0.001), but no interaction (occlusion x FiO_2 P=0.449).

Conclusion: These data provide support and proof of concept for an ergogenic effect of circulatory occlusion of inactive limbs during endurance exercise.

Key Words: Endurance, Ergogenic, Cycling

Corresponding author: S. Raj J. Trikha, trikhar@rams.colostate.edu

Introduction

Blood flow, and hence oxygen delivery, to active skeletal muscle has long been established as an important determinant of endurance exercise performance[1,2]. Physiological contributors to blood flow and oxygen delivery include total blood and/or plasma volume, total red blood cell volume, and oxygen carrying capacity. Consistent with this, interventions known to increase plasma volume, such as dextran, sodium-induced hypervolemia[3,4], and intravenous saline administration[5], or perturbations that enhance red blood cell volume, such as blood doping and administration of erythropoietin, have all been shown to increase maximal oxygen uptake (VO_{2max}) and improve performance in endurance events[6,7]. Aside from being contrary to the rules of most athletic governing bodies, and in addition to carrying clinically significant risks[8,9], blood doping and erythropoietin are impractical in that they require medical supervision and/or proficiency in blood collection and storage. Similarly, strategies promoting acute pre-exercise hypervolemia are also often impractical, involving invasive medical procedures, or evoking unfavorable gastrointestinal side effects. In the current study, we begin to explore the ergogenic potential of a novel

procedure that may temporarily promote the availability of blood to active skeletal muscle without actually increasing total blood or red cell volume: circulatory occlusion of non-active limbs.

The rationale for the approach is based on three observations. Circulatory occlusion of the legs with blood pressure cuffs accelerates oxygen uptake kinetics during the transition from rest-to-steady-state arm ergometry exercise[10]. Hughson and Imman argued that by occluding the non-working limbs, more blood, and hence oxygen, was available to the exercising skeletal muscle. Secondly, it has been demonstrated that increases in VO_{2max} following endurance training require only a small increase in blood volume[11]. Six weeks of endurance exercise training increased blood volume by ~380 ml, VO_{2max} by ~10%, and maximal cardiac output by ~1.5 L/min. When blood was removed via phlebotomy and blood volume returned to pre-training values, both VO_{2max} and maximal cardiac output were also returned to pre-training levels. These data illustrate that a 7% expansion of blood volume is sufficient to evoke an appreciable increase in VO_{2max}. Finally, and consistent with this prior observation, an autologous blood transfusion consisting of 135 mL of red blood cells improved cycle ergometer time trial performance[12]. Collectively, these results implicate that circulatory occlusion of the arms would only need to increase central blood volume by up to ~7% to elicit improvements in cycle ergometry endurance performance. Given that 12% of body mass can be attributed to the arms[13] it is feasible that circulatory occlusion of the arms should be sufficient to increase central blood volume by the magnitude necessary to improve performance.

Accordingly, the purpose of this proof of concept study was to investigate the hypothesis that upper limb circulatory occlusion would improve cycle ergometer time-trial performance. To further emphasize the critical contribution of oxygen delivery to performance, healthy adults were studied in both normoxia and hypoxia; we hypothesized that upper limb circulatory occlusion would attenuate hypoxia-mediated decrements in cycle ergometer time-trial performance, and that the magnitude of ergogenic effect of upper limb circulatory occlusion would be greater in hypoxia compared with normoxia.

Methods
The protocol was approved by the local institutional review board. All participants provided written informed consent prior to study initiation.

Participants
Young healthy, 18-30-year-old, men and women were invited to participate in the study. They self-identified as recreationally active (i.e. not-elite) and reported completing a minimum of 30-minutes of physical activity, 3 days per week, during the previous 12 months. Exclusion criteria included pregnancy (confirmed using a commercially available urine test kit for human chronic gonadotropin), previous cardio-pulmonary disease (self-report), anemia (confirmed by measurement of hemoglobin and hematocrit during the screening visit), history of venous thrombosis (self-report), resting peripheral oxygen saturation <95% (determined using a physiological monitor; IntelliVue MP5 Patient Monitor, Philips Healthcare, USA), and neuropathy in the arms/hands (self-report). Our laboratory is located at a moderate altitude of 1,525 m (5,003 feet) above sea level; usual barometric pressures are within the range ~630-640 mmHg. To avoid potentially confounding factors associated with acute exposure to altitude, all research participants were established local residents.

Protocol Overview
Following screening and habituation, participants completed four randomly ordered stationary cycle ergometer time trials, equivalent to 5 km, in normoxia (fraction of inspired oxygen (FiO_2)=0.21) and hypoxia (FiO_2=0.15), with and without circulatory occlusion of the arms. Assuming an average barometric pressure of 635 mmHg, then an FiO2 of 0.15 would simulate an altitude of approximately 4.1 km (or 13,500 ft); the US state in which our laboratory is located has over 300 mountains that are taller than 4.1 km, thus this simulated altitude has ecological relevance for our geographical location. Time trials were separated by 2-14 days. At the start of each occlusion trial, participants held their arms above their head; blood pressure cuffs were inflated to evoke upper limb circulatory occlusion.

Procedures
VO_{2max} was determined via indirect calorimetry (Parvo Medics, Sandy, Utah, USA) during incremental stationary cycle ergometer exercise to volitional fatigue, as previously described[14,15]. Body composition

(including whole and segmental total, lean and fat mass) was assessed using dual energy x-ray absorptiometry (DEXA: Hologic, Discovery W, QDR Series, Bedford, MA, USA). Protocol habituation involved completion of a practice time trial, without occlusion, that was otherwise identical to the experimental time trials. Time trials were completed on an electrically braked cycle ergometer (Dynafit Velotron; Racermate Inc., Seattle, Washington, USA), in a manner similar to that previously reported[14,15]. Following a brief opportunity for acclimation to the chamber comprising a warm-up (10 minutes, cycling at 100 W) participants completed stationary cycle ergometer exercise equivalent to 5 km as quickly as possible. During the time trial, all time cues were hidden from the participants but feedback regarding distance cycled was provided, as was standardized verbal encouragement (independent of experimental condition). Heart rate, peripheral oxyhemoglobin saturation (SpO_2; measured at the finger and ear lobe; IntelliVue MP5 Patient Monitor, Philips Healthcare, USA), and ratings of perceived exertion[16] were recorded every 5-minutes.

Following completion of the acclimation/warm-up and immediately prior to commencement of the time-trials, participants held their arms above their head for 60-seconds to create a negative hydrostatic column and encourage upper limb "draining". Automated blood pressure cuffs (D. E. Hokanson, Inc., Bellevue, Washington, USA) were then rapidly inflated to either 20 (Sham) or 200 mmHg before participants returned to cycling position. Circulatory occlusion was confirmed by the absence of a radial pulse and the inability to measure SpO_2 at the fingers. During the procedures incorporating hypoxia, the FiO_2 was manipulated using an environmental chamber (Colorado Altitude Training, Louisville, Colorado, USA), as previously described[14,15]. Participants were naïve to the FiO_2 within the chamber.

Experimental Considerations
Based on prior studies[14,15], we estimated that the time to complete a 5 km time trial would be ~10 minutes. We surmised a trial of this duration would permit us to test the effectiveness of the intervention while limiting the risk for injury associated with circulatory occlusion. Although circulatory occlusion can be uncomfortable, our laboratory has demonstrated that ischemia for up to 20 minutes is safe and well tolerated[17]. Further, to minimize the potential confounding influence of the expectations of our participants (i.e. a placebo effect) we incorporated a sham condition. The rationale for our choice of 20 mmHg as a control was based on our understanding that this pressure would be sufficient to be perceived by the participants, without influencing forearm venous draining[18,19]. In addition to this sham condition, participants remained naïve as to performance outcomes until study completion.

Statistical Analysis
A randomized, repeated measures, Latin-square design was utilized. The influences of circulatory occlusion of the arms and manipulations of FiO_2 were examined using two-way repeated measures analysis of variance (i.e. occlusion x FiO_2). Multiple comparisons of factor means were performed using the Holm-Sidak test. Habituation and control time-trial performances were compared using Student's paired T-Test. To provide initial insight into potential determinants of the time-trial response to circulatory occlusion of the arms, statistical relations were investigated using Pearson Product correlations. The level of statistical significance was set, a priori, as $P<0.05$. Data are reported as mean and standard deviation, unless otherwise indicated. Calculations were performed using commercially available software (SigmaStat 3.0, Systat Software Inc., San Jose, California, USA).

Results
Twenty-two adults were screened for participation. One female was excluded due to anemia (hemoglobin concentration: 10 mg/dL). Two males withdrew due to injury (sustained outside of the laboratory) and scheduling conflicts. One habituation trial was abandoned due to mechanical failure. Nineteen adults completed all remaining testing; physiological characteristics are presented in Table 1.

Table 1. Selected physiological characteristics of research participants (10 males, 9 females).

	VARIABLE (N = 19)
AGE (YEARS)	24 ± 3
BODY MASS (KG)	70.9 ± 12.5
HEIGHT (M)	1.73 ± 0.10
BODY MASS INDEX (KG/M²)	23.4 ± 2.1
LEAN MASS (KG)	55.4 ± 11.0
FAT MASS (KG)	15.1 ± 4.6
BODY FAT (%)	22.1 ± 6.9
ARM MASS (KG)	8.4 ± 2.3
ARM LEAN MASS (KG)	6.6 ± 1.9
RESTING BLOOD PRESSURE (MMHG)	124/78 ± 10/9
VO$_{2MAX}$ (L/MIN)	3.34 ± 0.83
VO$_{2MAX}$ (ML/KG/MIN)	47.1 ± 7.9

Mean ± Standard Deviation.
VO$_{2max}$: maximal oxygen uptake.

Prior to the four time trials in normoxia and hypoxia, participants completed a habituation trial, in normoxia without an occlusion cuff. Habituation data from each participant are presented in Figure 1. There was no difference between time trial performance during habituation and time trial in normoxia without occlusion (*n*=18; *P*=0.26).
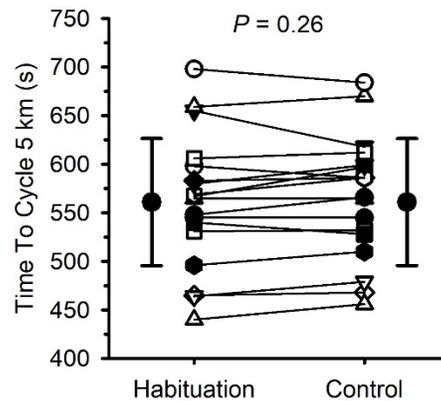

Figure 1. Individual participant time trial performance did not differ between habituation and control (n=18; *P*=0.26). Closed circles with error bars represent mean and SD.

Time trial performance data are presented in Figure 2A and 2B. There were main effects of occlusion (faster with occlusion, *P*=0.017), and FiO$_2$ (slower in hypoxia, *P*<0.001), but no interaction (occlusion x FiO$_2$, *P*=0.449). In normoxia, circulatory occlusion of the arms improved time trial performance in 11/19 participants (mean improvement: 5.3 s). In hypoxia, 14/19 experienced an ergogenic benefit of circulatory occlusion of the arms (mean improvement: 8.3 s). The magnitude of improvement was not different between normoxia and hypoxia (*P*=0.45).
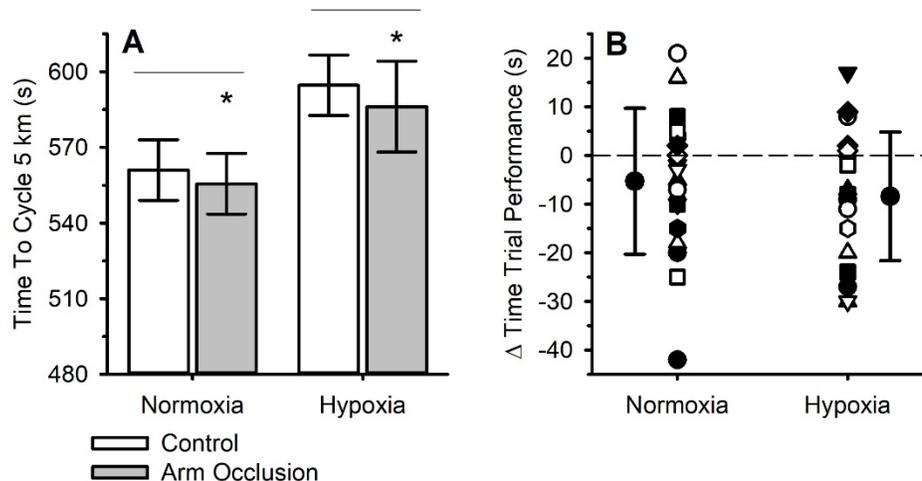
Figure 2. Upper limb circulatory occlusion improves time to cycle 5 kilometers (km). A) Average time to cycle 5 km in normoxia (FiO_2=0.21) and hypoxia (FiO_2=0.15) conditions improved with occlusion (n = 19). Data are mean and standard deviation. * indicates $P<0.05$. B) Individual change between time trial performance with and without upper limb circulatory occlusion. Closed circles with error bars represent mean and SD.

Following inspection of Figure 2B, it is clear the magnitude of time trial improvement in one participant was somewhat greater than the other participants. This participant's datum fell within three standard deviations of the mean (and median) change and thus was not considered an outlier[20]. To satisfy our remaining concern that the main effects reported in the previous paragraph were unduly influenced by this one participant, statistical analysis was repeated with this participant's data excluded; our interpretation was unchanged: main effects of occlusion (faster with occlusion $P=0.028$), and FiO_2 (slower in hypoxia $P<0.001$), but no interaction (occlusion x FiO_2 $P=0.327$).

Additional physiological and performance data are presented in Table 2. Heart rate appeared somewhat greater with circulatory occlusion of the arms, but this difference did not attain statistical significance (main effect: $P=0.062$). Peripheral oxygen saturation measured at the ear and finger, and pedal cadence and work rate were all lower in hypoxia ($P<0.001$). There were no main effects of occlusion (all $P>0.06$) and no interactions (FiO_2 x occlusion all $P>0.10$). SpO_2 was undetectable at the finger during circulatory occlusion of the arms.

Table 2. Physiological and performance parameters during each of the time-trials.

	NORMOXIA		**HYPOXIA**	
	Control (N = 19)	Occluded (N = 19)	Control (N = 19)	Occluded (N = 19)
HEART RATE (BEATS/MIN)	169 ± 9	171 ± 14	166 ± 13	170 ± 13
SPO$_2$ EAR* (%)	90 ± 8	89 ± 7	80 ± 8	84 ± 8
SPO$_2$ FINGER* (%)	91 ± 6	ND	80 ± 5	ND
RPE	17 ± 1	18 ± 1	18 ± 1	18 ± 1
PEDAL CADENCE* (REVOLUTIONS/MIN)	96 ± 12	97 ± 12	92 ± 12	92 ± 12
WORK RATE* (W)	198 ± 61	203 ± 64	174 ± 47	174 ± 45

Data: mean ± SD.
SpO_2: Peripheral oxygen saturation. RPE: Rating of perceived exertion (Borg Scale).
ND: Not detected.
* denotes main effect of hypoxia ($P<0.001$)

To provide initial insight into potential determinants of the ergogenic response to circulatory occlusion, statistical relations were investigated. None of the examined dependent variables predicted the magnitude

of improvement in normoxic time trial performance (all $P>0.10$). Examined variables included time trial performance in normoxia without occlusion, VO_{2max}, fat free mass, and total mass and fat free mass of the arms (estimated by DEXA). Further, the magnitude of improvement in normoxic time trial performance with occlusion of the arms was not different ($P=0.45$) between men (7.8 ± 15.0 s) and women (2.6 ± 14.8 s).

Discussion

The purpose of this proof of concept study was to investigate the hypothesis that upper limb circulatory occlusion would improve cycle ergometer time trial performance and attenuate hypoxia-mediated decrements in endurance exercise. Our data indicate that the time to cycle a distance equivalent to 5 km was faster during circulatory occlusion of the arms; this ergogenic effect was evident in both normoxia and hypoxia. Although variable, the mean magnitude of improvement in time trial performance with circulatory occlusion of the arms was approximately 7 seconds. Magnitudes of improvement smaller than this have been recognized as being sufficient to determine Olympic medal rankings in endurance events of up to ~8 minutes duration[21].

The manipulation of blood volume for ergogenic purposes has been previously explored[3-5,11,22-24] and has produced mostly favorable outcomes. In the current study, we did not attempt to increase total blood volume, rather, using a reallocation of resources approach, we believe we may have increased central blood volume via circulatory occlusion of inactive limbs.

The beneficial effects of blood flow occlusion prior to (e.g. (remote) ischemic preconditioning), or following exercise, have also been well described[25,26], as have the advantages of restricting blood flow during resistance training[27]. Additionally, attempts have been made to influence (both increase and decrease) blood flow to the legs during cycle ergometer exercise with a variety of techniques, including single-limb cycling[28,29], lower body negative pressure and postural changes, such as head up/down tilt[30,31]. In these basic science studies, the primary focus was physiological function and not athletic performance. To our knowledge, this is the first study in which circulatory occlusion of the non-active limbs to promote endurance performance has been explored. In this regard, we believe the proof of concept supported by our current data could stimulate a potentially fertile line of questioning. For example, in addition to mechanistic studies incorporating blood flow measurements, the circulatory occlusion of non-active limbs might promote athletic performance in activities other than cycling, such as running (with arm occlusion), or kayaking (with leg occlusion). Upper limb occlusion might also serve as a strategy to increase power output during training and/or promote recovery between sprints during high intensity interval training.

An additional question that remains to be answered pertains to the physiological characteristics of the athlete in whom non-active limb occlusion has the greatest ergogenic benefit. None of the variables considered in the current study, including sex, aerobic capacity, baseline time trial performance, and lean or total mass of the occluded arms predicted the magnitude of time trial improvement.

The rationale for our study was based on previous reports of accelerated VO_2 kinetics with circulatory occlusion of the legs during arm ergometry exercise[10], and the relatively small increase in blood volume required to increase VO_{2max}, maximal cardiac output and time trial performance[11,12]. It is important to emphasize that our purpose was to provide proof of concept only. We made no attempt to quantify central blood volume during upper limb circulatory occlusion, nor did we measure active limb (leg) blood flow. However, it seems unlikely that circulatory occlusion of the arms would improve cycle ergometer exercise performance for reasons other than increased central blood volume. It is possible that the expectations of our research participants contributed to improved time trial performance (i.e. a placebo effect). To minimize this potential confound we incorporated a sham (control) condition consisting of upper arm cuff inflation to 20 mmHg; a pressure we felt would be sufficient to be detected by the participants without influencing forearm venous draining[18,19]. We acknowledge that the perception of 20 *vs.* 200 mmHg is quite different with respect to the degree of numbness and paresthesia. In addition to the sham condition, we were careful to keep participants naïve as to performance outcomes until study completion. Moreover, use of a randomized, repeated measures, Latin-square experimental design, together with incorporation of a habituation trial should have minimized any further confounding influence of learning or conditioning. Indeed, as per Figure 1, the absence of a performance difference between the habituation and control time trials provides support our experimental approach.

From a practical and safety perspective, the activities best suited for non-active limb occlusion should be of sufficient duration to rely on a significant contribution from aerobic metabolism, but not so long as to risk tissue damage and injury due to extended ischemia and subsequent reperfusion. In this regard, our laboratory has previously shown that up to 20 minutes of forearm ischemia is generally well tolerated and does not result in significant injury, other than a brief increase in oxidative stress[17].

In summary, in normoxia and hypoxia, upper limb circulatory occlusion decreases the duration of time required to complete stationary cycle ergometer exercise equivalent to 5 km. We speculate that the mechanism explaining this ergogenic effect is improved blood and oxygen availability to the working muscle as a consequence of increased central blood volume, although this remains to be empirically investigated.

Media-Friendly Summary

Money, for many people, is often a limited commodity. With appropriate accounting, we may choose to forego purchasing an updated cell phone in favor of buying food. In the same way, blood may be considered a limited resource. In the current investigation, we demonstrated that if we temporarily stop blood flowing to the arms, there may be more blood available for the legs. Exploiting this principle, we were able to provide proof-of-concept for a novel strategy to improve short-duration endurance performance: circulatory occlusion of inactive limbs.

Acknowledgements

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