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THE COGNITIVE INHIBITORY RESPONSE TO ACUTE EXERCISE WITH AND WITHOUT BLOOD FLOW RESTRICTION AND FULL BODY COOLING

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ABSTRACT

The production and utilization of lactate has been suggested as a potential mechanism to increase interference control, a core executive function. Although blood flow restricted exercise has been shown to acutely increase blood lactate concentration, the effect of this exercise on interference control is unknown. Higher intensity exercise tends to have a greater benefit on interference control, but this is not always the case, which may be due to an increase in body temperature. Cooling may prevent this elevation and reinforce the exercise-induced benefit on interference control. The purpose of this thesis was twofold: 1) to evaluate the effect of acute interval exercise with and without blood flow restriction and cooling on interference control and 2) to evaluate whether changes in blood lactate mediate changes in interference control. 85 participants (44 males, 41 females; 22 ± 3 years) completed all 6 visits. The initial visit consisted of paperwork and familiarization with the cognitive task and the Vasper™ exercise device. For the rest of visits, participants completed 5 separate exercise conditions, including non-exercise control (Con), exercise only (Ex), exercise with blood flow restriction (ExB), exercise with cooling (ExC), and exercise with blood flow restriction and cooling (ExBC) in random order. The measurement of lactate, and the Stroop Color Word Test was performed before and after the exercise protocol. The protocol consisted of 5 minutes of warmup, 10 minutes of moderate intensity exercise, and five 20 second sprints separated by 40 seconds of light exercise. Bayes Factors (BF_{10}) quantified evidence for or against the null. The MEMORE macro was used for within subject statistical mediation with the threshold for statistical significance being set at $p \leq 0.05$. Bayesian pairwise comparisons found that only ExC [σ: -0.37 (-0.59, -0.15)] and ExBC [σ:

-0.3 (-0.53, -0.09)] produced changes in incongruent reaction time different from that of Con. There was also evidence that all exercise conditions produced blood lactate (BF_{10} = 8.65e+29 – 1.9e+32) and congruent reaction time (BF_{10} = 4.01 – 15.371) different from that of Con. Mediation analysis did not find evidence that changes in lactate mediated the change in incongruent reaction time. Our results found that exercise with cooling and exercise with blood flow restriction and cooling both saw favorable changes in incongruent reaction time (a marker of interference control), which might not be explained by the changes in systemic blood lactate. Given that both favorable conditions included cooling, it would be worth further exploring the cooling aspect of VASPER technology. Future work could also potentially investigate the use of relative pressure for the blood flow restriction. It is possible that applying a more uniform pressure to each individual might further improve this marker of executive function.

LIST OF ABBREVIATIONS AND SYMBOLS

BF_{10}	Bayesian Factor
BDNF	Brain Derived Neurotrophic Factor
Con	Time-matched non-exercise control
EEG	Electroencephalogram
Ex	Exercise
ExB	Exercise with blood flow restriction
ExC	Exercise with cooling
ExBC	Exercise with blood flow restriction and cooling
ICC	Intraclass Correlation Coefficient
1RM	One repetition maximum
PAR-Q	Physical activity readiness questionnaire
Q/Q Plot	Quantile-quantile plot

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CHAPTER I: INTRODUCTION

The importance of exercise has been emphasized in literature not only to enhance the musculoskeletal, cardiovascular (Nystoriak & Bhatnagar, 2018), and respiratory system (Holloszy, 1967), but to also promote cognitive functions (Edwards & Loprinzi, 2018). Investigation of exercise on cognition is an emerging area of research. Cognitive function encompasses a variety of capabilities including attention, memory, processing speed, language, and perceptual abilities (Douris et al., 2018). One component of cognition also relates to executive function, which governs basic cognitive functions (e.g. inhibitory control, working memory, and task flexibility) and builds higher order of mental processes such as reasoning, problem solving, and planning (Diamond, 2013). The Stroop task tests interference control (specifically, prepotent response inhibition), a component of basic cognitive functions necessary for organizing executive function and has been shown to improve following certain forms of exercise (Hashimoto et al., 2018). A novel mechanism for these effects may be related, in part, to the production and utilization of lactate. Previous work suggests that while the brain relies on glucose at rest, the brain may become more dependent upon lactate for fuel during exercise. Since the infusion of lactate has been shown to result in an increase in brain derived neurotrophic factor (BDNF) (Schiffer et al., 2011), this might explain some (certainly not all) of the benefits of acute exercise on cognitive inhibitory control. Interestingly, although high intensity exercise can result in a large release of lactate, this intensity of exercise is not always associated with improved general cognitive functions (Chang, Labban, Gapin, & Etnier, 2012). This suggests that other factors may also be occurring which may have a dampening effect on cognitive enhancement. For example, the negative effects of excessive increases in norepinephrine and dopamine in the dorsal prefrontal cortex during/after high intensity exercise on working memory has been discussed in literature (Arnsten, 2011; Arnsten et al., 2012; Tillman & Loprinzi, 2019). High doses of norepinephrine and dopamine in the dorsal prefrontal cortex excessively excite β-adrenoceptors and D_1 receptor, which activate calcium-cAMP signaling, opening nearby K^+ channels; the release of K^+ depolarizes action potentials, weakening the synaptic inputs, which may impair dorsolateral prefrontal cortex function related to cognitive inhibitory control (Arnsten et al., 2012; Tillman & Loprinzi, 2019). Thus, while traditional high intensity exercise may improve many aspects of health, the lack of consistent improvement in cognitive inhibitory control is an important consideration moving forward; particularly in the current climate where more emphasis is being placed on mental health.

As noted previously, although high intensity exercise can result in a large release of lactate (a secondary fuel source for the brain), this intensity of exercise is not consistently associated with improved general cognitive functions (Arnsten, 2011; Arnsten, Wang, & Paspalas, 2012; Tillman & Loprinzi, 2019). This might be related, in part, to the rise in body temperature, which has previously been shown to reduce cognitive inhibitory processing (Shibasaki et al., 2016). This may also explain why a previous study found cognitive benefits to low load resistance training (Sardeli et al., 2017) but not that of traditional high load exercise or low load resistance exercise with blood flow restriction (Sardeli et al., 2017). It is possible, though currently unknown, that the application of cooling to these conditions may remove the proverbial brake on the exercise induced increase in cognitive inhibitory control. In addition, it is not known if aerobic exercise with blood flow restriction can improve inhibitory control over that of the same exercise without restriction. Due to the large changes in lactate associated with this form of exercise (Jensen et al., 2016), it is possible that the addition of blood flow restriction may provide the necessary substrate to the brain in order to observe a favorable effect of exercise on cognition. It is also possible, but not currently known, if the cooling would be required in order to realize the effects of blood flow restriction, due to the potential negative cognitive effects of elevated body temperature.

Purpose

The purpose of this study was to evaluate the acute cognitive responses (interference control) to high intensity interval exercise alone, high intensity interval exercise with cooling, high intensity interval exercise with blood flow restriction, and high intensity interval exercise with blood flow restriction and cooling by utilizing Stroop Color Word Test.

Research Question

What is the impact of high intensity interval exercise on interference control?

Is the change in the cognitive marker affected by cooling, blood flow restriction, or cooling and blood flow restriction?

If there is a change in the cognitive marker, is it related to the change in lactate?

Significance

Exercise with and without blood flow restriction has been show to produce beneficial changes in muscle size, strength, and physical function across a wide range of populations (untrained, trained, injured) (Patterson et al., 2019). Although the majority of evidence is centered on the effects of low load resistance training, aerobic exercise has also been shown to produce cardiovascular adaptations; in addition to increases in muscle size and strength. However, one area that has received little attention is the impact of blood flow restricted exercise on cognitive performance (Törpel et al., 2018). Cognitive health is of interest across the life span, and any drug-free and time efficient method for cognitive enhancement would be of immediate interest to those in business, education, and/or any situation where individuals could benefit from enhanced brain function. Though mental health is important in and of itself, it is also an important consideration in business settings where there is a need for cognitive optimization. Although some forms of traditional exercise have demonstrated small but meaningful enhancements in general cognitive functions (Chang et al., 2012), this form of exercise may augment core temperature during exercise (Lim et al., 2008). In an effort to maintain normal temperature, the individual will sweat which may reduce the viability of this type of exercise in a workplace setting. In addition to sweating, rising core body temperature may also reduce the cognitive enhancing effects of exercise (Shibasaki et al., 2016). One potential solution is the Vasper™ exercise program. This is a novel training technique that couples blood flow restricted aerobic exercise with full body cooling in an effort to achieve the results of traditional exercise with less time (20 minutes) and without the elevation in body temperature associated with higher intensity exercise. Whether this form of exercise is capable of improving cognition is not currently known. Understanding the specific impact of exercise, cooling, and blood flow restriction on cognition as well as an investigation into one of the mechanisms associated with improving cognition is of great importance for further innovation of the Vasper™ exercise program and for the scientific literature in general, improving the cognition of people.

Assumptions

1. Participants will maintain all normal daily activities and dietary habits during the study.
2. Participants will comply with all food, caffeine, and exercise restrictions prior to testing.

3. Participants will answer all questions truthfully.

Delimitations

1. The results of the acute study were only applicable to healthy males and females between the ages of 18-35 years.
2. The participants were volunteers recruited from the university community and may not represent a true random sample of the population.
3. We assessed inhibitory control to a prepotent response from the result of the Stroop Color Word Test; therefore, this study design did not answer how other cognitive functions change with this exercise protocol.

Limitations

1. We measured acute effects; therefore, we cannot answer the chronic effects of the exercise protocol on cognitive functions and whole blood lactate.
2. The degree of blood flow restriction during exercise was maintained between absolute pressure (60-80 mmHg). Since this was not a quantification of the amount of blood flow, no assumptions can be made on the actual percent reduction in blood flow caused by the cuff inflation pressure.

Operational Definitions

1. Blood flow restriction – The application of pneumatic cuffs, elastic wraps, or fluid pressure placed around the proximal portion of a limb with the goal of reducing arterial flow to a muscle and occluding venous flow out of the limb.
2. Vasper^{TM} exercise program – combination of compression, liquid cooling, and high intensity interval training with low-impact movement lasting about 20 minutes.

3. Stroop Color Word Test – a conventional neuropsychological test widely utilized for assessing the ability to inhibit predominant (habitual) response during decision-making task. During the test, individuals react to the color of words as quickly and accurately as possible. The meaning of words can be identical (congruent) or different (incongruent) to/from the color of the words.

CHAPTER II: BACKGROUND

HISTORY OF BLOOD FLOW RESTRICTION

The application of blood flow restriction with the goal of increasing muscle size and strength was popularized by Yoshiaki Sato. The story goes that he came up with the idea of blood flow restriction for augmenting muscle size and strength when he felt numbness after sitting for prolonged periods during a Buddhist ceremony (Sato, 2005). He also experimented with this technique to attenuate muscle atrophy after an injury induced period of immobilization (Sato, 2005). Sato invented his first blood flow restriction device (Kaatsu) specifically for muscle hypertrophy and strength enhancement in 1983. However, the effects of blood flow restriction were driven based on personal experiences; therefore, experimental work on blood flow restriction was needed to better understand the benefits and possible risks of blood flow restriction. The first published paper on blood flow restriction in combination with exercise occurred in 1998 and investigated whether factors other than high mechanical stress can induce substantial muscle adaptation. (Shinohara, Kouzaki, Yoshihisa, & Fukunaga, 1998). Shinohara et al. (1998) reported that 4 weeks of low-intensity resistance training (isometric knee extension at 40% of maximal voluntary contraction) induced greater strength gain and maximal rate of torque development on the leg with tourniquet ischemia compared to the other leg without tourniquet ischemia. With the positive impact of blood flow restriction on muscular strength, the study suggested several research questions for possible mechanisms of strength gain using blood flow restriction (e.g. increases in neuromuscular activity through afferent feedback and metabolic activities).

To date, research has been completed for blood flow restriction alone, in combination with low intensity aerobic exercise, and in combination with low load resistance exercise. Blood flow restriction alone attenuated the decrease in cross-sectional are of the thigh (Takarada, Takazawa, & Ishii, 2000). The application of blood flow restriction with low intensity aerobic exercise increased cardiovascular fitness (Abe, Fujita, et al., 2010; Abe, Kearns, & Sato, 2006; Park et al., 2010) as well as muscle size and strength (Abe, Kearns, & Sato, 2006; Ozaki et al., 2011; Abe et al., 2010). In addition, blood flow restriction with low-load resistance training promoted skeletal muscle hypertrophy and muscular strength gain (Takarada, Takazawa, Sato, et al., 2000). Because of these beneficial effects with less mechanical stress compared to moderate-high load resistance training, the research interest in blood flow restriction has increased not only within the exercise and sport performance field but also within the clinical and rehabilitative field.

SAFETY OF BLOOD FLOW RESTRICITON

The benefits associated with blood flow restriction should be interpreted within the context of safety to ensure that the exercise technique is both safe and effective. Blood clotting and muscle damage are two commonly cited concerns with blood flow restriction. The effects of blood flow restriction on coagulation factors has been investigated in healthy adults (Clark et al., 2010; Madarame et al., 2010; Nakajima et al., 2007), older adults (Shimizu, 2016; T Yasuda et al., 2013.; Tomohiro Yasuda, 2015) with arterial stiffness (Yasuda et al., 2015) and those with stable ischemic heart disease (Madarame et al., 2012). None of these studies found an increase in coagulation or a decrease in fibrinolytic potential. In addition, a critical review of the literature by Loenneke et al. (2014) concluded that blood flow restriction exercise resulted in minimal to no muscle damage. However, the majority of the safety work has been completed on healthy individuals and the safety of this within clinical populations is limited.

APPLICATION OF BLOOD FLOW RESTRICTION

Throughout the blood flow restriction literature, numerous different devices, cuff widths, and cuff materials are used to restrict blood flow. The cuff or wrap is placed around the proximal portion of a limb with the goal of reducing arterial flow to a muscle and occluding venous flow out of the limb (Jessee, Mattocks, et al., 2018). In early blood flow restriction literature, a wide range of absolute restrictive pressures was utilized such as 110 ± 7.1 mmHg (Takarada, Sato, & Ishii, 2002), 160-230 mmHg (Abe et al., 2006), and 214 ± 7.7 mmHg (Takarada et al., 2000). In addition, many of these pressures have been applied without considering individual limb structure and the cuff been applied. These factors can have a major impact on the blood flow restriction stimulus.

Individual characteristics, such as limb circumference and composition, have been observed to have a large impact on the arterial occlusion pressure. Loenneke et al. (2015) and Jessee et al. (2016) investigated several factors that might play a role in determining the arterial occlusion pressure. They found that limb circumference had the largest impact on predicting arterial occlusion pressure. Additionally, Shaw & Murry (1982) found as leg circumference increased, the percentage of tourniquet pressure to achiever mean tissue pressure decreased. Thus, these results indicated that larger the limb is, greater the arterial occlusion pressure is needed.

Cuff width has also been shown to have a large impact on the arterial occlusion pressure (Loenneke et al., 2013). A narrow cuff (5cm wide) requires higher restrictive cuff pressure to completely occlude arterial blood flow compared to wider cuff (13.5 cm wide) (Loenneke et al., 2013). The result showed that lower restrictive cuff pressure was needed to restrict arterial blood flow when applying wider cuff compared with narrower cuff. The difference in arterial occlusion pressure between narrow and wide cuff widths can be explained by the transmission from restrictive pressure to soft-tissue pressure. About 64% of restrictive pressure was transmitted to deeper tissues for an 8 cm cuff, whereas about 95% of restrictive pressure was transmitted to deeper tissues for a wider cuff (12 and 18 cm) (Crenshaw et al., 1988). This result indicates that a wider cuff might transmit the pressure to tissue more efficiently; that is, less cuff pressure is needed to achieve arterial occlusion pressure when using a wider cuff.

The cuff type/material is another potential factor that might impact the arterial occlusion pressure. Resting arterial occlusion pressure in a supine position was measured with the same cuff width (5 cm) but different cuff materials (nylon and elastic) and there was no significant difference in resting arterial occlusion pressure between the two cuff materials (Loenneke et al., 2013). Furthermore, Buckner et al. (2017) found there was no significant difference in the acute skeletal muscle and perceptual responses to blood flow restriction exercise with similar cuff widths but different cuff materials (nylon, 5 cm: elastic, 3 cm) despite a higher resting arterial occlusion pressure for the elastic cuff compared to that of the nylon cuff. This suggests that cuff width has a greater impact on arterial occlusion than cuff material.

Given the impact of limb circumference and cuff width on the arterial occlusion pressure, it is important to apply a pressure that accounts for both of these factors. Loenneke et al. (2013) recommended to apply a cuff pressure based on a percentage of resting arterial occlusion pressure to account for differences cuff width and limb circumferences. The current literature has shifted to the use of relative cuff pressure based on resting arterial occlusion pressure (Laurentino et al., 2012; Kim et al., 2017; Conceição & Ugrinowitsch, 2019; Bowman et al., 2019). With this, several studies have investigated the "optimal" percentage of resting arterial occlusion pressure to provide the greatest benefits with the lowest cuff pressure (Counts et al., 2016; Lixandrão et al., 2015). More recently, Jessee et al. (2018) assessed the muscular adaptations following very low-load resistance training (15% 1RM) with moderate blood flow restriction (40% resting arterial occlusion pressure) and with high blood flow restriction (80% resting arterial occlusion pressure). In that study, there was no significant differences in muscle size and strength between the two training groups. This result indicated that the high blood flow restriction may not be needed for muscle adaptation when the exercise is taken to or near task failure. On the other hand, Mouser et al. (2019) found that higher pressures may be needed for vascular adaptations (e.g. limb conductance). Thus, with low load resistance exercise, moderate arterial occlusion pressure might be needed to cause muscle adaptation, but not enough circumferential strain to cause chronic vascular adaptation. Therefore, with low load resistance exercise, high arterial occlusion pressure might be useful to cause both muscle and vascular adaptation.

PHYSIOLOGICAL ADAPTATIONS TO BLOOD FLOW RESTRICTION

Blood flow restriction alone has been shown to attenuate the reduction in muscle size/limb circumference (Takarada, Takazawa, & Ishii, 2000; Kubota, Sakuraba, Sawaki, Sumide, & Tamura, 2008) and muscle strength (Kubota et al., 2011) associated with immobilization. Takarada et al. (2000) conducted a 2-week training intervention on patients following anterior cruciate ligament (ACL) reconstruction. A smaller reduction in muscle size was observed in the blood flow restriction group than in the time matched control group. Furthermore, Kubota et al. (2008) investigated the effect of blood flow restriction application on limb size, strength, and serum concentration of growth hormone in healthy male participants.

With 14 days of immobilization, a greater decrease in thigh and leg circumference and greater decreases in knee extensor/flexor/ankle planter flexor tongue were found in the control group compared to the blood flow restriction group despite of no significant change in serum concentration of growth hormone in all three groups. The results of these studies provided some evidence for the idea that the application of blood flow restriction can slow down the loss of atrophy and maintain function.

With low intensity aerobic training, blood flow restriction has been shown to increase muscle size and volume (Abe, Fujita, et al., 2010; Abe, Sakamaki, et al., 2010; Ozaki et al., 2011), muscular strength and functional performance (Abe, Sakamaki, et al., 2010; Ozaki et al., 2011), aerobic capacity (Abe, Fujita, et al., 2010; Park et al., 2010), and anaerobic capacity (Park et al., 2010). Abe, Sakamaki, et al. (2010) conducted 6 weeks of walking training intervention (one a day, 5 days per week) on physically active men and women aged 60-78 years. Participants walked at 4 km/h for 20 minutes with or without blood flow restriction set at 160 mmHg on the first week of training. The pressure was increased by 10 mmHg each week until a final belt pressure reached 200 mmHg. After the training intervention, the blood flow restriction training group increased muscle size/volume, isokinetic/isometric strength, and physical function over a group performing the same exercise without blood flow restriction. Notably, no change in maximal aerobic capacity was observed in either group. In the same year, Abe, Fujita, et al. (2010) published a study which investigated the effects of low intensity cycling training on muscle size/volume, strength, and maximal oxygen uptake in physically active young men aged 20-26 years. The participants cycled at 40% of their pre VO_{2max} for 15 minutes with blood flow restriction or for 45 minutes without blood flow restriction. The blood flow restriction group increased muscle cross-sectional area and muscle volume, and maximal aerobic capacity; while, there was no significant changes in these dependent valuables in non-blood flow restriction training group from baseline to the end of the training intervention. Ozaki et al. (2010) recruited sedentary women aged 57-73 years and provided support for the greater increases in muscle size/volume, isokinetic strength, functional ability, and maximal oxygen intake in the group walking with blood flow restriction compared to a group doing the same walking without blood flow restriction (45% of heart rate reserve). Park et al. (2010) found greater effects of treadmill walking with blood flow restriction on aerobic/anaerobic capacity than treadmill walking alone in male college basketball athletes but did not observe changes in strength. Taken together, the application of blood flow restriction with low intensity aerobic exercise may be a method to induce both muscular and cardiovascular adaptations in certain populations.

Although high-load resistance training (>75% 1RM) has traditionally been considered as the optimal method for muscle growth and strength gain, low-load resistance training (<50% 1RM) with blood flow restriction has been showed to induce similar changes in muscle size and strength as high-load resistance training (Kim et al., 2017). Laurentino et al. (2012) also observed that high-load training group and low-load training with blood flow restriction group had a similar increase in muscle size and maximal dynamic strength. Nevertheless, the increase in strength still often favors high-load resistance training rather than low-load resistance training with blood flow restriction training due to specificity of training (Kim et al., 2017). This means that a high-load training group practices closer to the 1RM test compared to a low-load training group so that the high-load group is more likely to improve the ability to lift a heavier weight. Still, blood flow restriction with blood flow restriction can be quite useful when individuals cannot or do not want to perform high-load resistance training (e.g. injured, patients with musculoskeletal diseases).

The available literature to date suggests that blood flow restriction can serve as a useful technique to enhance musculature and strength from immobilization to the phase where individuals can regularly perform resistance training (Loenneke et al., 2012). Application of blood flow restriction alone within the rehabilitative treatment during the immobilized phase can slow down the decrease in muscle volume and strength, which may accelerate the next gradual weight-bearing phase of rehabilitation. The augmented muscle growth and aerobic/anerobic capacity in low intensity aerobic exercise program with blood flow restriction may further prepare individuals for the next weight-loading phase of rehabilitation. The muscle adaptation in low-load resistance training with blood flow restriction may hasten the rehabilitation process to bring the patients back to baseline. Moreover, low load resistance training (30% 1RM) with blood flow restriction combined with high load resistance training (75% 1RM) induced similar hypertrophic adaptation but greater isometric and dynamic muscular strength compared to low load resistance training with blood flow restriction alone. Of note, the strength and hypertrophic adaptation in low load resistance training with blood flow restriction combined with high load resistance training was similar to high load resistance training alone (Yasuda et al., 2011). This suggests that the combination of low-load resistance training with blood flow restriction and high load resistance training could be useful to bridge the gap between low-load resistance training with blood flow restriction alone and high load resistance training alone.

MECHANISM OF SKELETAL MUSCLE HYPERTROPHY

The mechanisms of attenuating muscle atrophy and weakness during immobilization by blood flow restriction without exercise are not clearly known yet. However, potential mechanisms of maintaining muscle mass were suggested, such as muscle cell swelling. During blood flow restriction, arterial blood flow is restricted to active muscle tissues and venous blood flow leaving the muscle tissues is occluded, both of which increase the pressure gradients from blood vessel/capillary to muscle tissues, causing a potential fluid shift from the blood to muscle tissues (Jessee, Buckner, et al., 2018). The fluid shift could stimulate the intrinsic volume sensors that have been hypothesized to stimulate anabolic signaling or/and attenuate catabolic signaling, resulting in slowing down muscle atrophy. Another possible mechanism that may explain the attenuation of muscle mass by blood flow restriction is beta-adrenoceptor signaling. Occlusion of venous blood flow decreases venous return, which may activate baroreceptors located in the carotid sinus and in the aortic arch (Iida et al., 2007). The activation of baroreceptors induces the increase in norepinephrine release, which may trigger the beta-adrenoceptor signaling (Loenneke et al., 2012). The change in beta-adrenoceptor associate with the change in beta-adrenoceptor agonists. The beta-adrenoceptor agonists can induce skeletal muscle growth and fat loss (Lynch & Ryall, 2008). Thus, muscle cell swelling, and beta adrenoceptor could be the mechanisms for the muscle adaptation by BFR without exercise, but these are still not completely clear mechanisms.

The potential mechanisms of augmented muscular adaptation by blood flow restriction with low intensity aerobic training would be similar to the mechanisms without exercise but greater changes in muscle size and strength. The greater accumulation of metabolic byproducts was observed in low intensity cycling with blood flow restriction than without blood flow restriction, but to a lesser extent to that of high intensity cycling (Thomas et al., 2018). This greater accumulation of metabolic byproducts during blood flow restriction may cause greater muscle cell swelling and/or muscle activation compared to without blood flow restriction. Also, due to the greater cardiac output compared to same aerobic exercise without blood flow restriction, there would be greater blood volume in working muscle, which might cause greater fluid shift into muscle cells (Loenneke et al., 2012). Thus, accumulation of metabolites in exercising muscle and muscle cell swelling may be the mechanism of muscle hypertrophy by blood flow restriction during low aerobic training.

The mechanism of muscle adaptation in low-load resistance training with blood flow restriction has been most studied phase in the literature. The stimulation of both type I and type II muscle fibers activate anabolic signaling pathway such as mTORC1 (Fujita et al., 2007; Fry et al., 2010) and MAPK signaling pathways (Fry et al., 2010). Gundermann et al. (2014) highlighted the essential role of mTORC1 signaling pathway on muscle protein synthesis by showing that rapamycin-induced inhibition of mTORC1 signaling pathway blocked the muscle protein synthesis response following low load resistance exercise with blood flow restriction. Also, low load resistance training with blood flow restriction decreased the activity of myostatin signaling (Laurentino et al., 2012), which decreases muscle protein synthesis. Moreover, Nielsen et al. (2012) compared the muscle biopsy samples before and after low resistance training intervention with or without blood flow restriction. The greater increases in myogenic stem cells, numbers of myonuclei, and myofiber sizes were observed in blood flow restriction training with blood flow restriction. The increase in numbers of myonuclei induced by satellite cells (myogenic stem cells) could explain the mechanism of greater muscle hypertrophy with blood flow restriction than without blood flow restriction at the low load. Thus, low load resistance training program combined with blood flow restriction promotes muscle hypertrophy by augmenting anabolic signaling pathways similar to that of traditional high load resistance training regimen.

MECHANISM OF STRENGTH

The mechanism of strength has been traditionally discussed as “neural adaptation first, followed by hypertrophy.” This indicates that the early phase of strength change is due to neural adaptation and later on hypertrophy plays a role of increasing strength. The traditional statement of strength adaptation was established by Sale (1988) mainly based on two commonly cited studies (Ikai & Fukunaga, 1970; Moritani & deVries, 1979). Ikai & Fukunaga (1970) observed both increases in cross-sectional area and muscular strength following the resistance training intervention; therefore, they suggested the increase in strength might be explained by increase in muscle size and neural discharge even though they did not measure neural discharge. Moritani & DeVries (1979) observed that the slope of muscle activation gradually leaned rightward during the resistance training intervention. Therefore, they concluded that dominant factor of strength gain shifted from neural adaptation to muscle hypertrophy after 3-5 weeks of 8 weeks resistance training regimen even though they did not measure muscle size in the study. Also, it may be difficult to conclude the change in the contribution factor of strength from the shift of slope in muscle activation due to possible large inter-individual error. Later on, other studies supported the idea that hypertrophy plays an important role on strength adaptation by using correlations (Bowman et (Bowman et al., 2019; Conceição & Ugrinowitsch, 2019; Jeremy P. Loenneke et al., 2013)al., 2019; Conceição & Ugrinowitsch, 2019; Jeremy P. Loenneke et al., 2013)(Balshaw et al., 2017; Erskine et al., 2014). These results could tell that individuals who have larger muscle tend to be stronger; however, it is important to note that the correlation does not indicate causation. Thus, although it is widely thought that neural adaptation and muscle hypertrophy contribute to strength adaptation, the cited literature for the effect is not capable of supporting such a causal claim.

Recently, the mechanism of strength gain has been revisited and other hypotheses have been put forth. For example, the increase in strength following resistance training could be potentially explained by either neural adaptation and/or local level muscle adaptations (Loenneke et al., 2019). Previous research suggested several possible locations where the neural adaptation could occur. Aagaard et al. (2002) investigated the evoked V-wave and H-reflex response during maximal muscle contraction before and after 14 weeks of heavy weight-lifting strength training (total of 38 sessions) in 14 untrained male participants. The results showed that both evoked V-wave and H-reflex responses during maximal voluntary isometric contraction increased after the training intervention. The results indicated that an enhanced drive in descending pathways from higher motor centers occurred in supraspinal level as well as increased motoneuron excitability and/or changes in presynaptic Ia afferent inhibition occurred in spinal levels. Also, these neural changes occurred with increases in maximal concentric muscle strength, suggesting that the neural adaptation in spinal cord could contribute to the strength gain. Another study observed increases in motor evoked potential amplitude and maximal isometric strength of tibialis anterior muscle after 4 weeks of resistance training at a stimulation intensity of 20% above threshold during a baseline contraction of 10% maximal voluntary contraction (Griffin & Cafarelli, 2007). Griffin & Cafarelli (2007) concluded that the increased central nervous system excitability in the primary motor cortex might be associated with higher initial motor unit firing rates and lower motor unit recruitment, resulting in a faster and greater muscle force production following resistance training.

The mechanisms of strength change may also occur peripherally. For example, there might be adaptations occurring between neurons and muscle fibers and/or within the muscle fibers themselves. Casolo et al. (2019) assessed the change in muscular strength and motor unit conduction velocity, which refers to how fast the action potentials can propagate along the muscle fibers innervated by individual motor neurons, in healthy, recreationally active and non-smoking young men following a combination of ballistic and sustained isometric strength training. The exercise group increased the motor unit conduction velocity of higher threshold motor units, indicating that peripheral adaptation in the electrophysiological properties of muscle . membrane occurred at higher-threshold motor units might related to increased maximal isometric force production (Casolo et al., 2019). This authors suggested that enhanced activity in Ka^+-K^+-pump and/or release of Ca^{2+} from sarcoplasmic reticulum may associate with the increased motor unit conduction velocity. In another study, the effects of a 12-week progressive resistance training regimen on maximal dynamic strength as well as the function of the myosin molecule in young and elderly participants by assessing the velocity of sliding of the unregulated actin on myosin (Canepari et al., 2005). Following this training intervention, the speed of actin filaments on myosin isoforms and muscle dynamic strength increased in both young and elderly subjects; therefore, the myosin shortening velocity could relate to an increase in strength.

In conclusion, the increases in strength following resistance training might be related to an enhanced neural adaptation in the primary motor cortex and spinal cord as well as local adaptation at the junction between neurons and muscle membrane and the within the muscle itself.

ACUTE EXERCISE AND COGNITION

The relationship between acute exercise and cognition has been widely studied and been of great interest to those in research and the general population. The current literature supports that exercise is one method used to enhance cognition, although the effects are likely to be small (Etnier et al., 1997). However, the interaction between exercise and cognition is complex and can be influenced by many factors such as the types of cognitive task, exercise intensity, timing of cognitive assessment, fitness level, and time of day (Chang et al., 2012; Lambourne & Tomporowski, 2010).

There are many studies which support the positive effects of acute exercise on specific types of cognitive tasks (Chang et al., 2012; Yanagisawa et al., 2010; Ferris, Williams, & Shen, 2007). Acute exercise has small-moderate positive effects on cognition in executive function, reaction time, information processing (Chang et al., 2012) and memory (Loprinzi, Blough, et al., 2019; Roig et al., 2013) but not in other types of cognitive tasks such as, Wechsler Adult Intelligence Scale, a task to indicate crystallized intelligence (Chang et al., 2012). In addition, the acute exercise-induced changes in cognition differed between specific cognitive tasks (Chang et al., 2012). The result showed that among commonly utilized cognitive tasks of executive function, improvements were observed in Stroop interference, verbal fluency, incompatible reaction time, and decision-making, whereas impairment was found with the digit span task. Thus, acute exercise could differently impact performance on the cognitive tasks. This suggests that each cognitive task may evaluate different aspects of cognitive function and each aspect of cognitive function could have a unique mechanism. Therefore, when investigators assess the cognitive effects of acute exercise, it is important to select a test that reflects the specific cognitive function of interest.

Exercise intensity affects the exercise-induced changes in cognition differently depending on the timing of the cognitive task in relation to the bout of exercise. Some studies reported the changes in cognition were different between exercise intensities (Fontana et al., 2009; Mehren et al., 2019); however, they did not specify the timing for when the cognitive tests were taken. The meta-analysis by Chang (2012) and the empirical study by Crush & Loprinzi and (2019) suggested that the timing of the cognitive task may play an important role in the exercise-cognition interaction. A meta-analysis showed that when cognitive tasks dependent to prefrontal cortex are tested during high intensity exercise, there is an impairment of the cognitive tasks

(Jung et al., 2021). This outcome could be because metabolic and cognitive resources are preferably used to sustain movement (i.e., transient hypofrontality effect) (Loprinzi, Day, et al., 2019). However, exercise intensities affected cognitive functions differently when cognitive function tests were conducted after exercise. Positive benefits of cognition were more likely to be observed in light/moderate exercise intensity immediately following exercise. However, additional time (11-20 minutes) appears to be needed in order to realize cognitive enhancement following moderate/high intensity exercise. Further, moderate/high intensity exercise appears to benefit cognitive function to a greater extent compared to very light and light exercise intensity (Chang et al., 2012). The physiological and psychological reasoning as to why the effects of exercise intensity on changes in cognition differ depending on the timing of cognitive tests is equivocal, but central fatigue and internal temperature could possibly explain the results.

Differences in baseline fitness level have also been shown to impact the effects of acute exercise on cognitive functions. Individuals with higher aerobic fitness had greater positive effects in cognitive functions from a single bout of exercise than individuals with lower aerobic fitness (Chang et al., 2012). However, this may not occur for all cognitions (e.g., memory) (Roig et al., 2013). In addition, physically fit individuals tends to have better baseline cognitive function (Buck et al., 2008), including working memory capacity, an important component of cognitive inhibition. Further, higher baseline fitness is associated with enhanced brain activation (Mehren et al., 2019) and gray and white matter in medial-temporal, parietal, and frontal areas (Gordon et al., 2008). Not only fitness level, but also aging could affect the interaction between exercise and cognitive function. A meta-analysis found that high-school aged individuals and older adults had greater improvement on cognitive functions after acute exercise compared to the overall population, but again, this may be moderated by the specific cognitive task (Chang et al., 2012). Thus, fitness level, cognitive task, and age-group should be considered when investigators assess the interaction between acute exercise and cognition.

Whilst many studies have studied a variety of influence of exercise intensities and exercise modes on cognitive performance assessed from different cognitive tasks, only one study has investigated the effects of blood flow restriction exercise on cognition. Sardeli et al. (2018) compared Stroop-test-based cognitive function between control and resistance exercise protocols with a high load, low load, and low load with blood flow restriction in untrained healthy older adults. The study showed that the greatest reduction in the reaction time from neutral stimuli was observed in the low load group only. However, it is important to note that the change in reaction time occurs typically in incongruent stimuli, but not in neutral stimuli for the Stroop test (Yanagisawa et al., 2010). Since the effects of blood flow restriction exercise on the acute change in cognitive function have not been clear, further studies for blood flow restriction exercise and cognition need to be developed for both resistance and aerobic exercise.

UNDERSTANDING OF BRAIN ACITIVTY DURING A COGNITIVE TASK

The measurement of brain activity during cognitive tasks increased following the introduction of the electroencephalogram (EEG) in the 1930's (Woodman, 2010). EEG presents the raw data of electrical activity in brain. Early studies assessed brain activity by comparing raw EEG data during the performance of simple tasks such as opening and closing the eyes (Davis, 1939). However, the random noise from EEG measurement made it difficult for investigators to identify the actual brain activity.

In the 1960s, the event-related potentials were able to be quantified from the EEG measurement (Woodman, 2010). Current studies accept that the event-related potential technique with EEG measures electrical potentials from postsynaptic activity of neural ensembles such as flow of ions between cell membranes through the extracellular fluid and from neurotransmitter release (Logothetis et al., 2001; Woodman, 2010). Event-related potentials consist of C1, P1, N1, P2, N2 (N200), and P3 (P300) components and others such as N400. The early components, which are C1, P1, or N1, may indicate sensory and perceptual processing (Woodman, 2010). P2 is not well understood in the current literature but may be related to wakefulness into sleep (Crowley & Colrain, 2004). N2 and P3 appear to associate with categorization of the visual stimulus (Folstein & Van Petten, 2007; Kutas et al., 1977). Also, it is commonly known that P3 (or P300) component could be a marker of brain activity required to perform cognitive performance such as immediate memory (Polich & Kok, 1995). In addition to EEG, the development of neuroimaging techniques such as functional magnetic resonance imaging and functional near-infrared spectroscopy have helped researchers to define the activated brain region in response to a certain cognitive task. For example, executive functional tasks such as Stroop interference activate the anterior cingulate cortex, lateral prefrontal cortex, and dorsolateral prefrontal cortex (Keil & Kaszniak, 2002). Thus, the brain activity related to cognitive tasks has been developing as the measurements of assessment continue to evolve.

MECHANISM OF EXERCISE-COGNITION

While previous literature consistently shows what neural components affect cognition and where the neural activity occurs during a certain cognitive task, the mechanism of how acute exercise affects cognitive functions remains unclear. Also, as mentioned previously, the term "cognition" covers a wide range of cognitive functions, each of which may have a unique mechanism with acute exercise or may interact with other mechanisms. Therefore, it is difficult to cover all the mechanisms for each cognitive function. Since the Stroop task will be used for our experiment, we will specifically review the potential mechanism of how acute exercise could influence interference control. Specifically, the test assess prepotent response inhibition, one of the basic cognitive inhibitory controls, which builds a high-order of executive function with other cognitive functions such as reasoning, problem solving, and planning (Diamond, 2013; Etnier & Chang, 2009). Prepotent response inhibition, a cognitive ability to inhibit predominant responses, is often measured by the Stroop task (MacLeod, 1991). During the incongruent trials, the color of words does not match with the meaning of words. Individuals need to inhibit a predominant response to the meaning of word and select the key that corresponds with color of the word; therefore, individuals respond slower and make more errors compared to congruent trials (the meaning of words and the color of the words are identical) (Diamond, 2013).

The possible mechanism of exercise-induced changes in interference control is explained from psychophysiological, neurophysiological, and physiological approaches. The exercise-induced change in interference control might be related to arousal (Byun et al., 2014), sympathoadrenal system and hypothalamic-pituitary-adrenal axis (McMorris et al., 2009), brain dopamine availability (Stroth et al., 2010), and central and peripheral lactate (Hashimoto et al., 2018), but likely not related to cerebral blood flow (Lucas et al., 2012; Ogoh et al., 2014). These responses occur when cognitive changes are observed, although this does not necessarily mean that these responses cause the changes in cognition. However, among these responses, central and peripheral lactate production has received recent interest as a potential mechanism for these cognitive effects.

The increased cerebral lactate utilization could be associated with improvement in inhibitory control of a prepotent response. Hashimoto et al. (2018) compared the changes in Stroop task interference score, cerebral blood flow/perfusion, cerebral substrate utilization (oxygen, glucose, and lactate), responses of neurohumoral substrates (e.g. BDNF and adrenaline) and psychological factors (e.g. arousal and fatigue) at pre and post two high intensity exercise protocols as well as during 60 minutes of recovery following the two exercise protocols. In this study, greater Stroop test interference and decreased cerebral lactate utilization were found during the recovery after the second exercise bout compared to the first exercise bout; whilst the change in other variables (e.g. BDNF and adrenaline) did not differ between the two exercise protocols. Glycogen depletion after the first bout might be related to the reduction in cerebral lactate concentration, which may lead to the decreased cerebral lactate utilization. This result does not mean that the reduction in cerebral lactate utilization causes the impaired inhibitory control of a prepotent response but indicates that there may be a relationship between cerebral lactate utilization and interference control.

The increased systemic level of lactate during ($r^2 = 0.81$) and after ($r^2=0.75$) exercise was associated with elevated cerebral lactate utilization (Hashimoto et al., 2018). Glucose is used as an energy source for the brain (neuronal glycolysis) at rest (Kemppainen et al., 2005), and cerebral glucose utilization increases during exercise. However, during high intensity exercise, slower energy production from oxidative energy production from astrocyte-derived lactate compensates the margin of required energy in which neuronal glycolysis cannot fill to sustain the movement (Díaz-García & Yellen, 2019). This increase in cerebral lactate utilization was related to an increase in arterial lactate, produced as a by-product mainly from muscle glycogen during high intensity exercise (Hashimoto et al., 2018). This result indicates that peripherally produced lactate might be transferred to brain through the blood stream and utilized as a cerebral energy source during and after high intensity interval exercise. In addition, Bergersen suggested (2015) that as blood lactate levels increase during exercise, lactate flows from the blood stream into the brain by monocarboxylate transporters (MCTs), supporting energy production.

Taking the two paragraphs together, the elevated peripheral lactate production during and after exercise, especially with high intensity exercise, may be related to cerebral lactate utilization as well as enhancement of interference control (a basic cognitive function for organizing executive function). The mechanism of how exercise-induced increases in cerebral lactate affects the neural activity required for interference control is unknown. However, a mice model study showed that increased lactate utilization in the brain during exercise induced hippocampal BDNF expression, which associated with improved spatial learning and memory retention (El Hayek et al., 2019). This could be a possible mechanism for improving cognitive inhibition, but further studies are needed to confirm the mechanism(s) by assessing tasks related to interference control in humans.

CHAPTER III: METHODOLOGY

PARTICIPANTS

All participants were recruited from the University of Mississippi Community and surrounding area through word of mouth, recruitment flyers, and classroom announcements. Overtly healthy participants (men and women) aged 18-35 were recruited for the study. This age range was chosen because of convenience, low risk associated with studying this population, and previous data suggesting improvements in this age group following acute exercise (Hashimoto et al., 2018). Upon visiting the laboratory, before engaging in any testing procedures, all participants were asked to complete an exclusionary criteria checklist to identify any characteristics that would prohibit them from participation. Afterwards, participants were informed of all testing procedures and time commitments required for the completion of the study, and they were given the opportunity to read the informed consent form as well as ask any questions. If they consented to participate in the study, they were asked to complete a Physical Activity Readiness Questionnaire (PAR-Q). If participants are not identified as at risk for health complications, they began the testing procedures. The study was approved by the Institution of Review Board at the University of Mississippi.

INCLUSION CRITERIA

- Between the ages of 18 – 35 years old.
- Do not regularly use tobacco at least 6 months prior to the study.

- Do not currently take medication to control hypertension.
- Abstain from caffeine 8 hours prior to testing.
- Abstain from alcohol 24 hours prior to testing.
- Abstain from exercise 24 hours prior to testing.
- Abstain from eating within 2 hours.
- Free from orthopedic injury that might prevent exercise.

EXCLUSION CRITERIA

- Outside the age range of 18 – 35 years.
- Regular use of Tobacco at least 6 months prior to study.
- Currently taking medication to control hypertension.
- Being color blind
- Have caffeine within 8 hours prior to testing.
- Have alcohol within 24 hours prior to tastings.
- Engage in exercise 24 hours prior to testing.
- Consumed food within 2 hours.
- Have an orthopedic injury that might prevent exercise.
- Meet 2 or more of the following risk factors for thromboembolism:
- Diagnosed with Crohn's Disease or Inflammatory Bowel Disease.
- Past fracture of hip, pelvis, femur.
- Major surgery within the last 6 months.
- Varicose veins.
- Family history of deep vein thrombosis.

- Personal history of deep vein thrombosis.
- Family history of pulmonary embolism.
- Personal history of pulmonary embolism.

EXPERIMENTAL DESIGN

Participants reported to the laboratory on six separate occasions with each visit lasting approximately 45 minutes. The initial visit began with paperwork, such as exclusion criteria, informed consent, and PAR-Q. If the participant consents and does not meet any exclusion criteria, we then measured standing height and body mass. Following the measurement, participants were familiarized with the cognitive tests and the Vasper™ exercise device. For visits 2–6, participants were scheduled to complete 5 separate exercise conditions across 5 separate days (in a random counterbalanced order). The conditions are as follow: (1) non-exercise control; (2) exercise only; (3) exercise + blood flow restriction; (4) exercise + cooling; and (5) exercise + cooling + blood flow restriction. Each visit started out with 5 minutes of seated rest, a measurement of lactate, baseline test of cognition and then the exercise protocol. Similar to a previous study (Jensen et al., 2016), participants warmed up for 5 minutes (<100 W) followed by 10 minutes of moderate intensity (100-150 W) exercise. The session concluded with five 20 seconds sprints separated by 40 seconds of light (<100 W) exercise. Participants were instructed to complete each sprint at a maximal effort for all exercise conditions. Instead of the exercise, the participant had a light conversation with two investigators for 20 minutes (matched with the time of exercise) in control condition. The light conversation was selected as a control in order to account for the social interaction component during the exercise. Following last sprint cycle, the blood flow restriction conditions had the cuffs removed. Two minutes following the final sprint cycle, lactate was reassessed. Eleven-minutes following exercise, cognition was reassessed. Participants were scheduled for the next visit which would be completed a minimum of 3 days later but no more than 10 (at the same time of day).

Table 1. An overview of all conditions included within this study.

	Control	Exercise 1	Exercise 2	Exercise 3	Exercise 4
Pressure	-	-	+	-	+
Cooling	-	-	-	+	+
Exercise	-	+	+	+	+

The symbol (−) means that the procedure was not applied for the condition, whereas the symbol (+) means that the procedure was applied for the condition.

PARTICIPANT HEIGHT AND BODY MASS

Standing height was measured to the nearest 0.1 cm using a stadiometer. Participants were asked to stand with heels together, while looking forward, standing tall, and holding a deep breath. Body mass was measured to the nearest 0.1 kg using a standard digital scale. Prior to both measurements participants were asked to remove all headwear, shoes, jackets, and items from their pockets.

EXERCISE PROTOCOLS

Each participant performed 20 mins of exercise on a modified NuStep recumbent cross trainer (NuStep Inc, Ann Arbor, MI, USA), which involves contralateral elbow flexion/extension and knee flexion/extension as previously explained (Jensen et al., 2016). The exercise began with a 5-minute warm-up (50–100W), followed by 10 minutes of moderate intensity (100–150W) exercise. The last 5 minutes of exercise consisted of five 20s sprints separated by 40s of active recovery (~25W). When this exercise was performed with blood flow restriction and cooling, the seat was covered with a cooling mat (Vasper Systems, Mounntain View, CA, USA), and the liquid compression cuffs (Vasper Systems, Mounntain View, CA, USA) were applied to the proximal portion of each arm (cuff width: 14 cm) and thigh (cuff width: 22 cm). The pressure of the compression cuffs was maintained at 40 mmHg for the arm and 65 mmHg for the thigh. The refrigerated liquid (7.2–10 °C) was circulated through a seating mat, compression cuffs, and foot plates. The foot plates of the NuStep are made of copper. During the exercise, the participants placed their bare feet on each plate. The purpose of exercising with bare feet is to cool the feet, the crucial thermoregulator of the human body, during the cooling sessions. The cooling system of the foot plates was turned off and covered with a fabric cloth, and the cooling mat was removed except for during the cooling sessions. Since compression cannot be applied with cooling, towel and t-shirts were wrapped around the arm and thigh under the cuffs to prevent the cooling.

WHOLE BLOOD LACTATE MEASUREMENT

Whole blood lactate was indirectly measured using a handheld analyzer after 5 minutes of seated rest and 2 minutes after exercise (Loenneke et al., 2012). For the control visit, after initial whole lactate measurement participants kept the seated rest for 20 minutes; then, the second whole lactate measurement was conducted. Fingertip whole blood lactate samples of approximately 0.7 µL by volume was collected by the same investigator using the manufacture guidelines for testing. The participant' finger was cleaned with alcohol prior to testing. Fingertips were punctured with a lancet, and the first drop of blood was wiped off to decrease the chance of contamination. The finger was lightly squeezed to form a second drop of blood, and when the drop appears, the end of the test strip touched the blood drop until the test strip was filled.

COGNITIVE ASSESSMENT

The Stroop Color Word Test has been widely used to assesses an aspect of interference (or inhibitory) control, called prepotent response inhibition, the ability to intentionally suppress dominant, automatic, or prepotent responses (Diamond, 2013; Friedman & Miyake, 2004). This test has been highly associated ($r = 0.68 \pm 0.18$) with different aspect of interference control (i.e., resistance to distractor interference) (Friedman & Miyake, 2004); therefore, the performance in Stroop Color Word Test is likely related to the overall interference control performance. In addition, the unity/diversity framework developed from a research group found that inhibition (same as interference control) was visually perfectly correlated with common executive function (i.e., a combination of what is common to all three-executive function) and did not possess the inhibition-specific component (Miyake & Friedman, 2012). This finding indicates that interference control is a basic ability necessary for any executive functioning tasks.

The Stroop Color Word Test was performed using PsyToolKit, a computerized software (Stoet, 2017a, 2017b). Specifically, we used the Stroop Color Word testing with keyboard responding. Participants were given words written in color and asked to indicate the color of the word (not its meaning) by pressing the corresponding keys (r,g,b,y for red, green, blue, and yellow stimuli). Participants were instructed to accomplish this as quickly and accurately as possible. PsyToolKit Stroop Task presented 80 trials with sixteen combinations, consisting of 4 colors (red, green, blue, yellow) by 2 color-stim congruencies (congruent and incongruent) (Li et al., 2019). In each trial, a combination of word and color was randomly selected by the computer (approximately 20 trials from congruent, 60 trials from incongruent). There is a 0.5 second interstimulus interval between trials, and the stimuli remained on the screen until the key response or for a maximal of 2 seconds, with latencies measured from the onset of the stimuli. At the end of each trial, visual feedback (“CORRECT” or “WRONG” for 0.5 seconds) was provided based on the participant’s response. The total experiment time was within 80-240 second (1.4 - 4 minutes).

The congruent trials involved the color word and the color it was presented being the same; incongruent trials involved the color word being different than the color it was presented in (e.g., it read GREEN, but this word was not in the green color). The outcome measure were the average latency [in milliseconds (ms)] of the correctly identified and error rate in congruent and incongruent conditions (Ouankhamchan & Fujinami, 2019). Stroop score was calculated by subtracting correct average congruent latency from correct average incongruent latency (Li et al., 2019). In a familiarization session, a set of 40 trials was performed until participants became comfortable with the test at least 3 times. In testing sessions, two sets of 80 trials were performed before exercise and a set of 80 trials was performed 11 minutes after exercise. For a control condition, participants performed two sets of 80 trials, rest for 31 minutes, and then retest a set of 80 trials.

Previous study showed that Stroop Color Word Test is a validated cognitive task (Crush & Loprinzi, 2017). The reliability of Stroop Color Word Test was determined by 1-2 week test-retest reliability tests among young adults (intraclass correlation coefficient (ICC) = 0.78, 0.92, for congruent and incongruent, respectively; Vora, Varghese, Weisenbach, & Bhatt, 2016), young- to middle-age adults (ICC = 0.91; Beglinger et al., 2005), and older adults (ICC = 0.80; Lemay, Bédard, Rouleau, & Tremblay, 2004). The validity of Stroop Color Word Test was confirmed by the highly correlated total time of completion and accuracy with conventional executive function tests (r = 0.79, r = 0.72, for congruent and incongruent, respectively; Vora et al., 2016).

STATISTICAL ANALYSIS

A Bayesian repeated measures analysis of variance (ANOVA) was completed on the pre-post change scores. The r-scale fixed effects were set at an uninformed prior of 0.5. Evidence for or against the null was quantified with Bayes Factor's. A Bayes Factor of 0.33 and below indicated that the null model predicts the data better. A Bayes Factor of 3 and above will indicate that the alternative model predicts the data better. In the event that the Bayes Factor is over 3, follow up Bayesian paired sample t-tests was completed to determine where the differences lie. Uninformed priors of 0.707 centered on zero was used (Cauchy distribution) and the same Bayes Factor thresholds were used. When the outcome variables were not normally distributed (visually confirmed by QQ-plot), we elected to use non-parametric Wilcoxon signed-rank tests (results based on data augmentation algorithm with 5 chains of 10000 iterations). We also ran a within-subject mediation model using the MEMORE macro in SPSS. This was done to test whether changes in lactate mediated changes in incongruent reaction time. Emphasis was placed on the indirect effect and the 95% confidence interval of that estimate.

CHAPTER IV: RESULTS

DEMOGRAPHICS

111 participants were recruited in this study. 26 participants withdrew from this study due to the following reasons; COVID-19-related issue (n=11), could not reschedule within 3–10 days (n=4), did not find it interesting to participate in the study after the familiarization visit (n=5), busy schedule (n=1), injury outside of this study (n=1), car accident (n=1), breathing issues (n=1), fear of needles (n=1), and exceeded the body mass limit (180 kg) of the exercise device (n=1). Therefore, 85 participants completed all the visits (Table 2).

Table 2. Study demographics.

Demographics (n=85)	**Mean (SD)**
Sex (male/female)	44/41 (n of each)
Age (years)	22 (3)
Height (cm)	171.9 (8.5)
Body mass (kg)	76.3 (19)

PERFORMANCE VARIABLES

Performance descriptive (i.e., average watts, stride per minute, sprint average watts, and sprint stride per minute) can be found in Table 3. The workload was numerically lower in the blood flow restriction conditions, indicating that the restriction may allow for results at an overall lower workload.

Table 3. Performance variables separated by condition (n=85 except for Exercise + Blood Flow Restriction + Cooling which had a missing data in stride/minute (n=84)). The mean with standard deviation (SD) were provided for each of the five conditions. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; and ExBC: Exercise + Blood Flow Restriction + Cooling. Avg: Average; Min: minute.

Condition	Avg Watts	Stride/Min	Sprint Avg Watts	Sprint Stride/Min
Ex	104.4 (14.6)	116.70 (5.8)	393.5 (141.7)	167.8 (17.9)
ExB	97.6 (15.1)	116.83 (9)	353.9 (130.3)	162.4 (18)
ExC	104.6 (12.8)	117.08 (5)	388.7 (129.3)	167.4 (18)
ExBC	98.7 (15.3)	116.63(5.3) (n=84)	356.8 (131.1)	162.9 (18.2)

INCONGRUENT REACTION TIME

Changes in incongruent reaction time were not normally distributed (visually confirmed by QQ-plot, in Figure 1), therefore, we elected to compare changes with a non-parametric Wilcoxon signed-rank test (results based on data augmentation algorithm with 5 chains of 10000 iterations). Changes in incongruent reaction time are found in Table 4 and Figure 2. The difference between conditions and the variability of that difference is found in Table 4 and Figure 3. Since there is not a readily available Bayesian non-parametric omnibus test, we included the p value for the Frequentist Friedman test. The Friedman test was statistically significant ($p=0.066$), providing additional justification for our pairwise comparisons. Bayesian pairwise comparisons found that only Exercise with Cooling [σ: -0.37 (-0.59, -0.15)] and Exercise with Blood Flow Restriction and Cooling [σ: -0.3 (-0.53, -0.09)] produce changes in incongruent reaction time different from that of the non-exercise control condition. There was no evidence that any of the exercise conditions differed from each other.

Figure 1. Model Averaged Q-Q Plot for Incongruent Reaction Time. This plot was generated on the comparison of change scores using the Bayesian Repeated Measures ANOVA analysis. Since this plot illustrates that the data is not normally distributed, we elected to use non-parametric analysis which is an analysis that does not require a normal distribution.

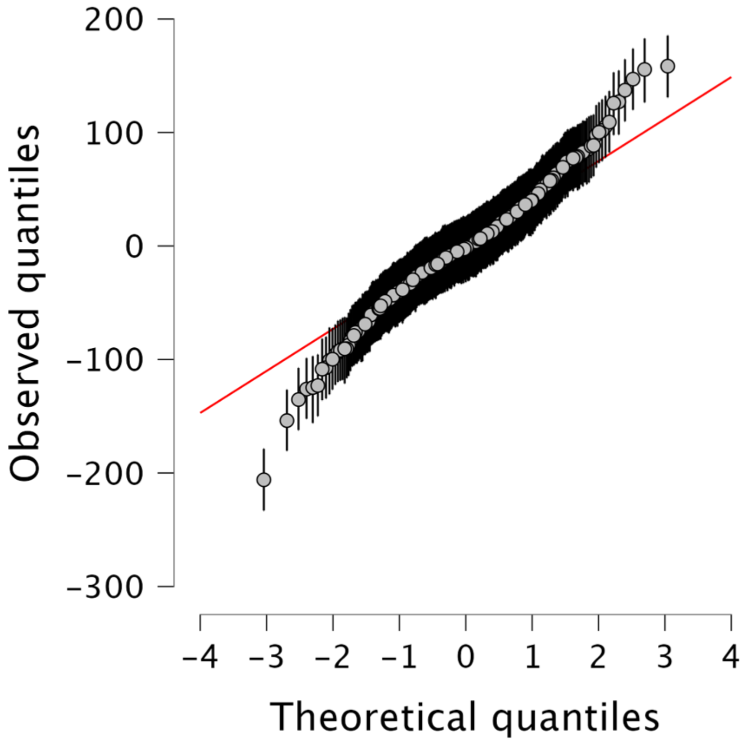


Table 4. Incongruent Reaction Time (n=85) separated by condition. Pre, Post, and within condition change scores are provided for each of the five conditions. The inferential statistics are provided in the bottom half of the table. Each condition is compared head to head and the difference values and the variability of that difference is provided as a 95% credible interval. The Bayes Factor provides evidence for or against the null hypothesis. Anything below 0.33 is evidence for the null hypothesis (medians do not differ) and anything above 3 is evidence for the alternative hypothesis (medians differ). Importantly, Bayes Factors should be interpreted as a continuous variable. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise

+ Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.

Condition	Pre (ms)	Post (ms)	Change Score (SD)
Ex	682.01	666.46	-15.55 (52.01)
ExB	695.75	675.46	-20.28 (62.22)
ExC	692.28	669.81	-22.48 (44.05)
ExBC	690.09	668.43	-21.66 (44.26)
Con	688.34	686.09	-2.26 (43.81)
Comparison	*Difference (ms)*	*95% credible interval*	*Bayes Factor*
Ex vs. ExB	4.4	-13.52, 22.6	0.126
Ex vs. ExC	6.6	-6.3, 19.8	0.25
Ex vs. ExBC	5.8	-7.5, 19.2	0.195
Ex vs Con	-12.57	-25.8, 0.64	0.91
ExB vs. ExC	1.99	-13.4, 17.4	0.19
ExB vs. ExBC	1.24	-15.3, 18.07	0.122
ExB vs. Con	-17.2	-33.3, -1.1	2.24
ExC vs. ExBC	-.78	-13.9, 12.1	0.131
Ex C vs. Con	-19.43	-33, -5.8	33.41
ExBC vs. Con	-18.6	-32.4, -4.6	6.7

Figure 2. Within condition changes (n=85) in Incongruent Reaction Time (ms). This is provided as a visual representation for the change and this is meant only to provide descriptive information. The difference between conditions and the variability of that difference is provided in Table 4 and Figure 3. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.

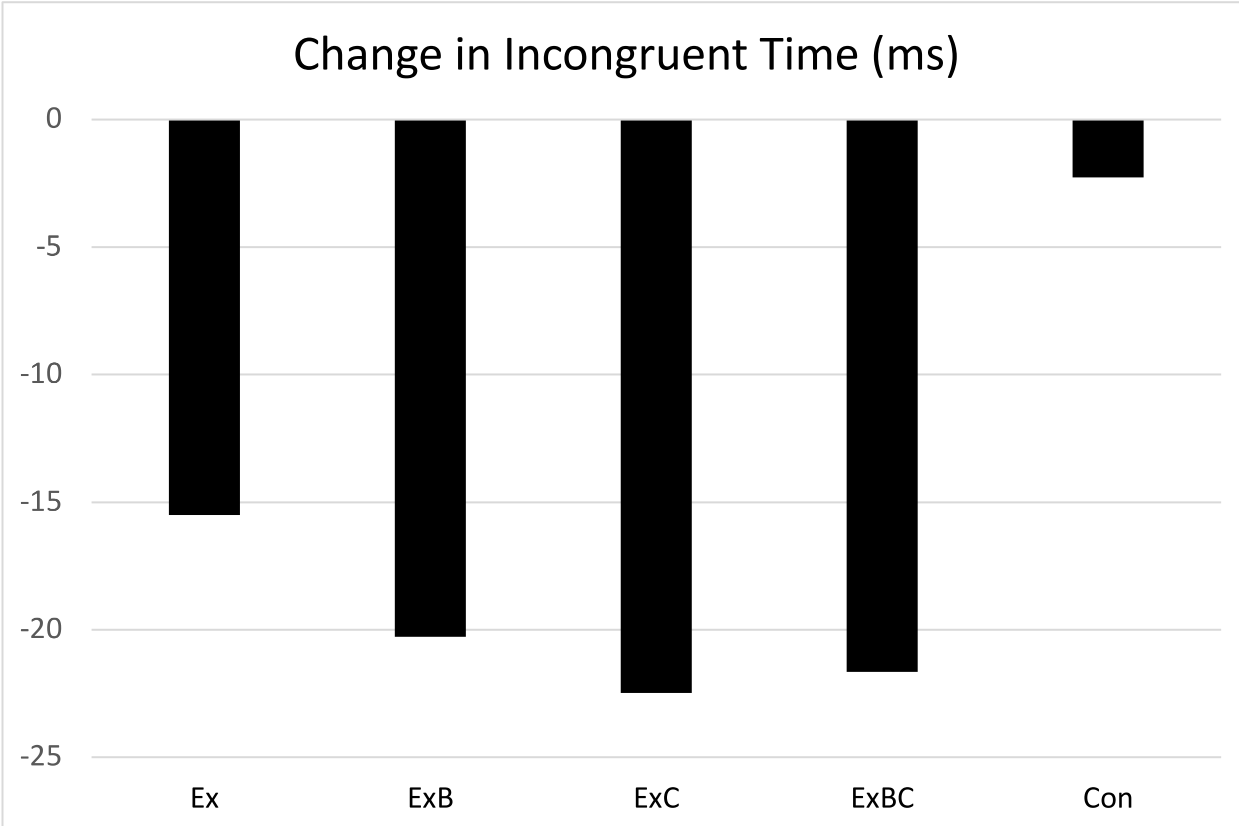
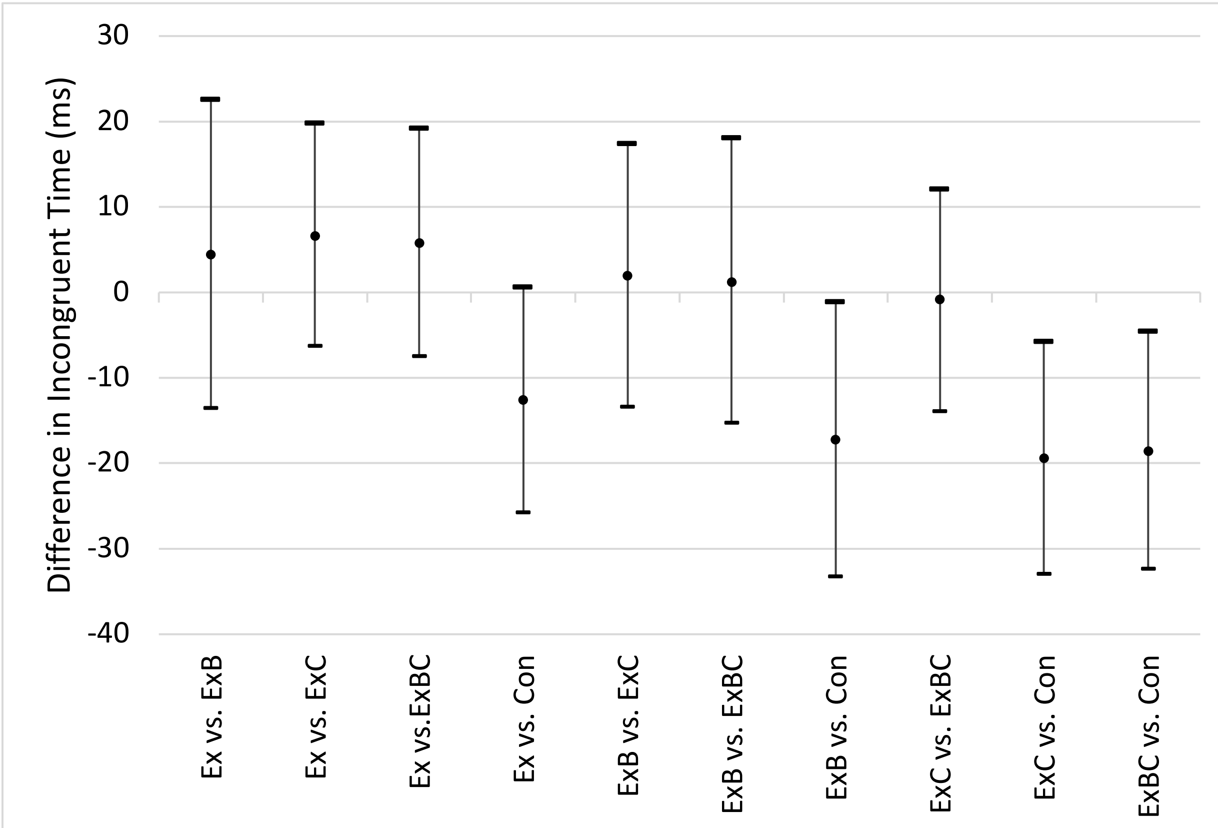


Figure 3. Incongruent reaction time differences between each condition. The x-axis indicates the comparison being made. The first variable listed is being subtracted from the second variable. Thus, a positive value indicates that the first condition in the comparison has a higher score and a negative value indicates that the second condition in the comparison has a higher score. The Bayes Factors associated with each comparison are found in Table 4. The middle dot represents the median difference surrounded by the 95% credible interval of the posterior distribution. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.



CONGRUENT REACTION TIME

Changes in congruent reaction time were not normally distributed (visually confirmed by QQ-plot, in Figure 4), therefore, we elected to compare changes with a non-parametric Wilcoxon signed-rank test (results based on data augmentation algorithm with 5 chains of 10000 iterations). Changes in congruent reaction time are found in Table 5 and Figure 5. The difference between conditions and the variability of that difference is found in Table 5and Figure 6. Since there is not a readily available Bayesian non-parametric omnibus test, we included the p value for the Frequentist Friedman test. The Friedman test was statistically significant ($p=0.005$), providing additional justification for our pairwise comparisons. Bayesian pairwise comparisons found that Exercise [σ: -0.34 (-0.55, -0.12)], Exercise with Blood Flow Restriction [σ: -0.29 (-0.50, -0.07)], Exercise with Cooling [σ: -0.31 (-0.53, -0.09)], and Exercise with Blood Flow Restriction and Cooling [σ: -0.28 (-0.50, -0.07)] produce changes in congruent reaction time different from that of the non-exercise control condition. There was no evidence that any of the exercise conditions differed from each other.

Figure 4. Model Averaged Q-Q Plot for Congruent Reaction Time. This plot was generated on the comparison of change scores using the Bayesian Repeated Measures ANOVA analysis. Since this plot illustrates that the data is not normally distributed, we elected to use non-parametric analysis which is an analysis that does not require a normal distribution.

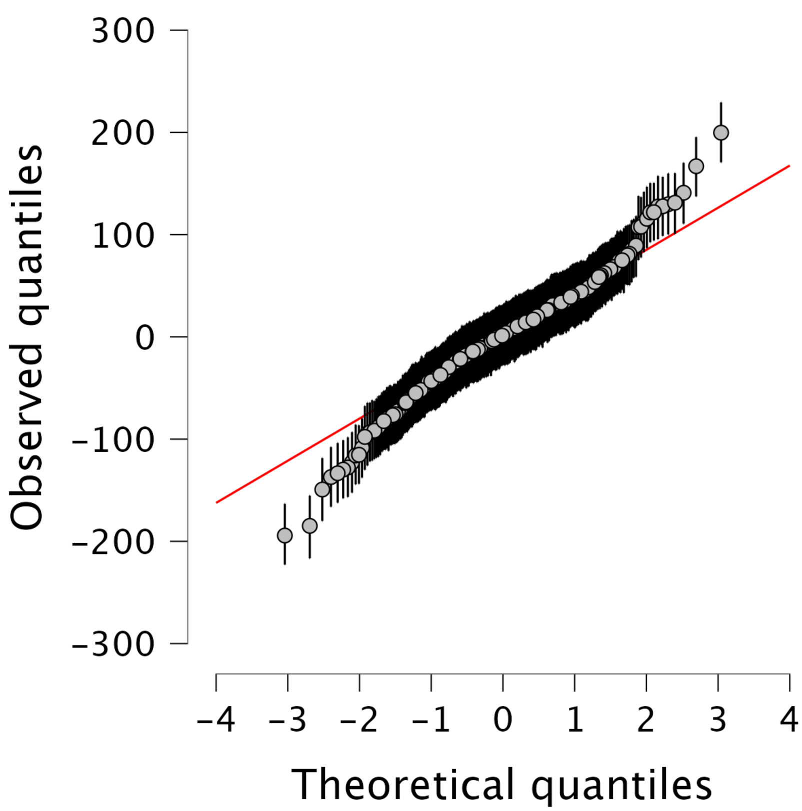


Table 5. Congruent Reaction Time (n=85) separated by condition. Pre, Post, and within condition change scores are provided for each of the five conditions. The inferential statistics are provided in the bottom half of the table. Each condition is compared head to head and the difference values and the variability of that difference is provided as a 95% credible interval. The Bayes Factor provides evidence for or against the null hypothesis. Anything below 0.33 is evidence for the null hypothesis (medians do not differ) and anything above 3 is evidence for the

alternative hypothesis (medians differ). Importantly, Bayes Factors should be interpreted as a continuous variable. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.

Condition	**Pre (ms)**	**Post (ms)**	**Change Score (SD)**
Ex	618.66	592.64	-26.01 (48.29)
ExB	618.41	595.63	-22.78 (65.12)
ExC	617.88	593.70	-24.18 (53.31)
ExBC	617.19	595.40	-21.79 (45.73)
Con	613.52	608.85	-4.68 (50.11)
Comparison	*Difference (ms)*	*95% credible interval*	*Bayes Factor*
Ex vs. ExB	-3.01	-20.67, 14.40	0.142
Ex vs. ExC	-1.66	-17.13, 14.13	0.122
Ex vs. ExBC	-4.10	-17.21, 8.62	0.152
Ex vs Con	-20.49	-34.88, -5.94	15.371
ExB vs. ExC	1.26	-14.24, 17.46	0.120
ExB vs. ExBC	-0.97	-17.01, 14.82	0.129
ExB vs. Con	-17.41	-36.19, 1.13	4.053
ExC vs. ExBC	-2.09	-16.51, 12.07	0.131
Ex C vs. Con	-18.72	-35.74, -2.11	6.782
ExBC vs. Con	-16.60	-29.14, -3.25	4.010

Figure 5**.** Within condition changes (n=85) in Congruent Reaction Time (ms). This is provided as a visual representation for the change and this is meant only to provide descriptive information. The difference between conditions and the variability of that difference is provided in Table 5 and Figure 6. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.

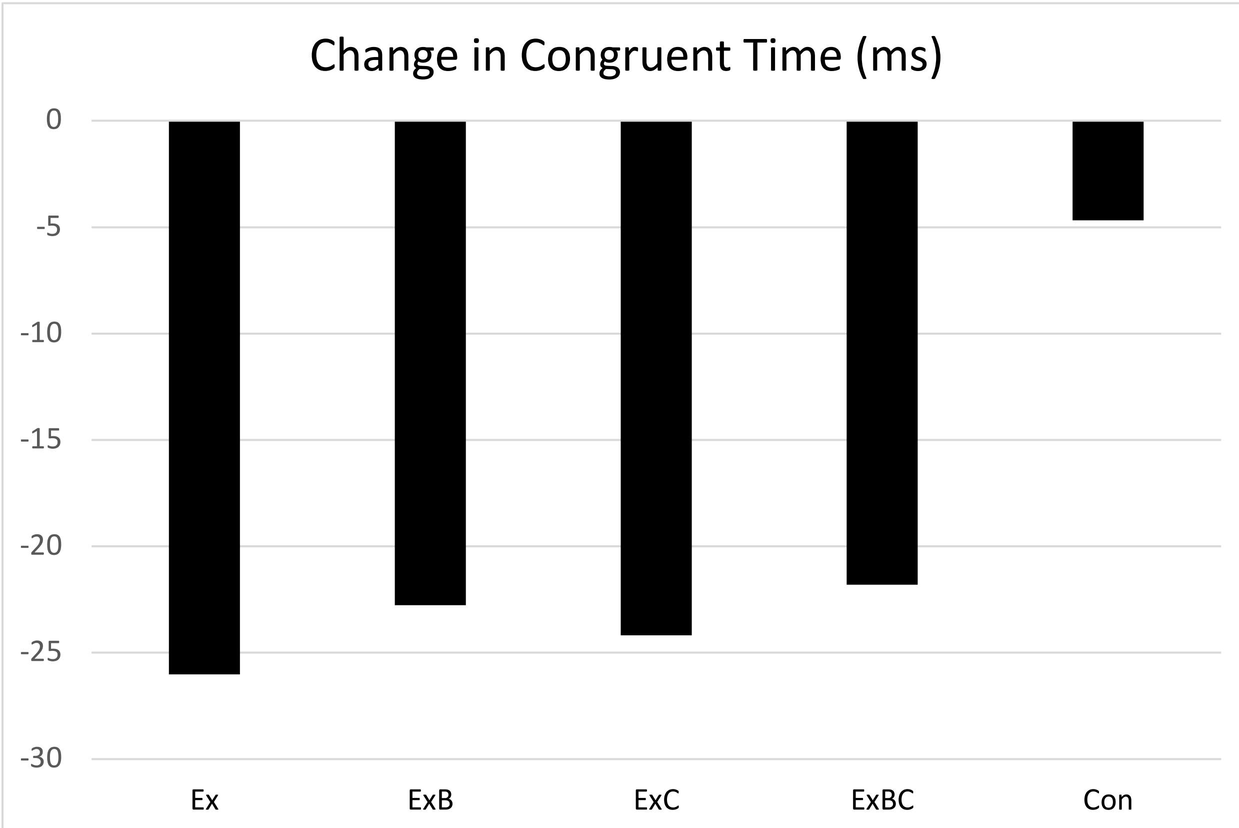
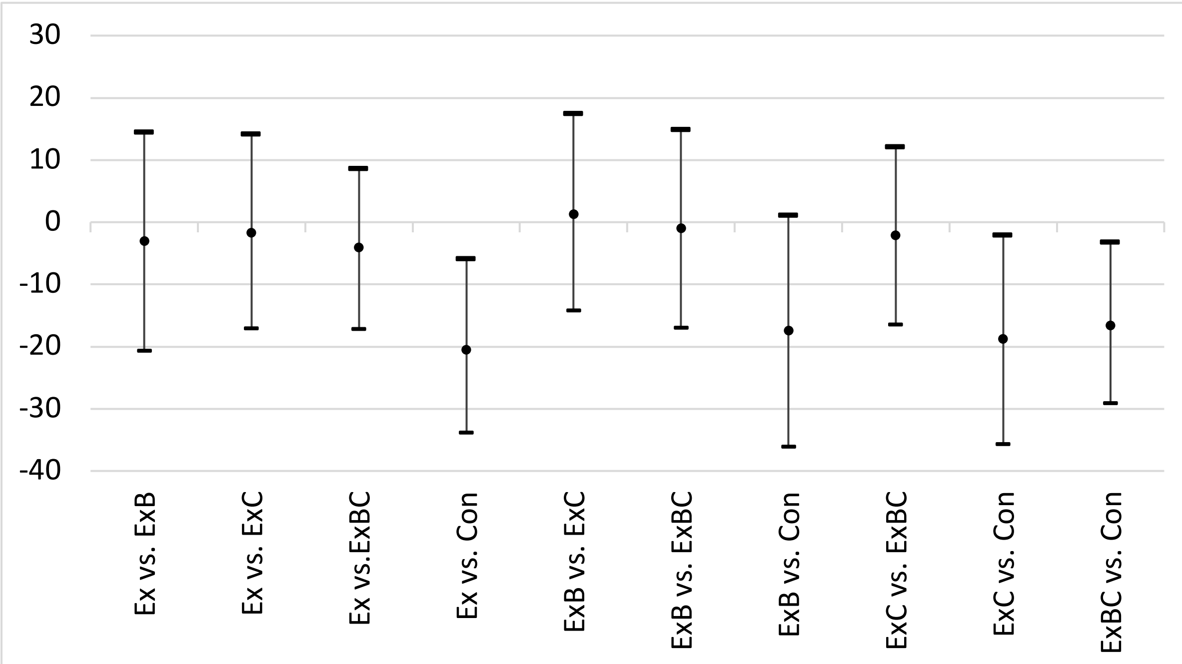


Figure 6. Congruent Reaction Time differences between each condition. The x-axis indicates the comparison being made. The first variable listed is being subtracted from the second variable. Thus, a positive value indicates that the first condition in the comparison has a higher score and a negative value indicates that the second condition in the comparison has a higher score. The Bayes Factors associated with each comparison are found in Table 5. The middle dot represents the median difference surrounded by the 95% credible interval of the posterior distribution. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC:

Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control



STROOP SCORE

Changes in the Stroop score were not normally distributed (visually confirmed by QQ-plot, in Figure 7), therefore, we elected to compare changes with a non-parametric Wilcoxon signed-rank test (results based on data augmentation algorithm with 5 chains of 10000 iterations). Changes in Stroop score are found in Table 6 and Figure 8. The difference between conditions and the variability of that difference is found in Table 6 and Figure 9. Since there is not a readily available Bayesian non-parametric omnibus test, we included the p value for the Frequentist Friedman test. The Friedman test was not statistically significant (p=0.73) which agrees with our Bayesian Wilcoxon pair-wise comparisons. Our results indicate that there was no change with this variable with any of the exercise conditions.

Figure 7. Model Averaged Q-Q Plot for the Stroop Score. This plot was generated on the comparison of change scores using the Bayesian Repeated Measures ANOVA analysis. Since this plot illustrates that the data is not normally distributed, we elected to use non-parametric analysis which is an analysis that does not require a normal distribution.

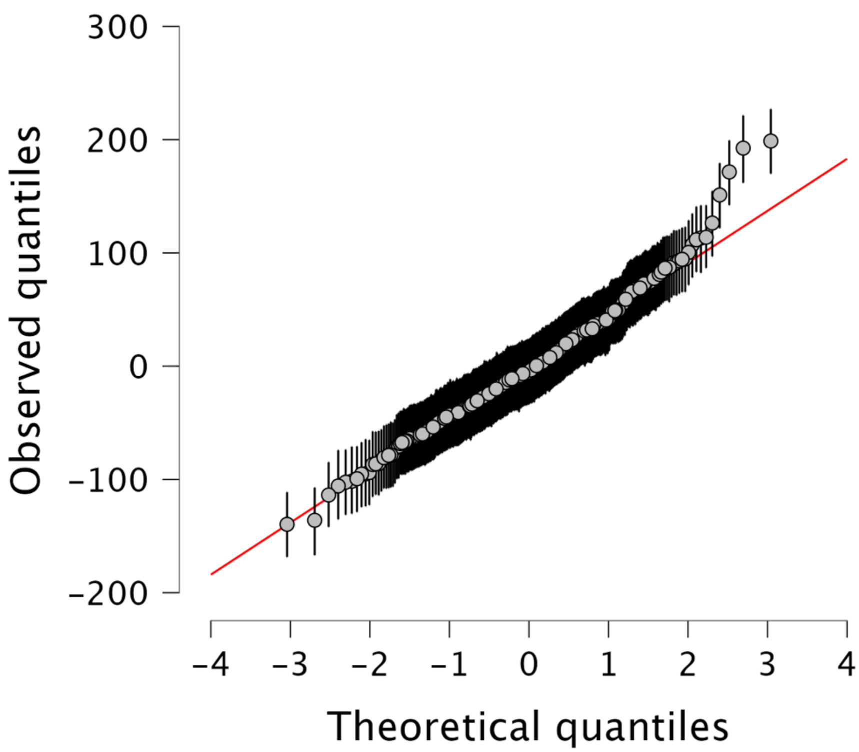


Table 6**.** Stroop Score (n=85) separated by condition. Pre, Post, and within condition change scores are provided for each of the five conditions. The inferential statistics are provided in the bottom half of the table. Each condition is compared head to head and the difference values and the variability of that difference is provided as a 95% credible interval. The Bayes Factor provides evidence for or against the null hypothesis. Anything below 0.33 is evidence for the null hypothesis (medians do not differ) and anything above 3 is evidence for the alternative hypothesis (medians differ). Importantly, Bayes Factors should be interpreted as a continuous

variable. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.

Condition	**Pre (ms)**	**Post (ms)**	**Change Score (SD)**
Ex	63.35	73.81	10.45 (58.58)
ExB	77.32	79.42	2.10 (52.93)
ExC	74.76	75.82	1.06 (53.42)
ExBC	72.90	72.67	-0.23 (46.55)
Con	74.83	77.24	2.42 (47.74)
Comparison	*Difference (ms)*	*95% credible interval*	*Bayes Factor*
Ex vs. ExB	7.98	-8.07, 23.53	0.198
Ex vs. ExC	9.12	-8.28, 26.31	0.202
Ex vs. ExBC	10.33	-5.64, 26.41	0.266
Ex vs Con	7.69	-7.37, 22.73	0.198
ExB vs. ExC	0.89	-14.30, 16.52	0.121
ExB vs. ExBC	2.03	-11.57, 16.50	0.126
ExB vs. Con	-0.35	-14.94, 13.86	0.120
ExC vs. ExBC	1.26	-12.82, 15.30	0.122
Ex C vs. Con	-1.36	-16.08, 13.04	0.122
ExBC vs. Con	-2.56	-15.98, 11.17	0.128

Figure 8. Within condition changes (n=85) in the Stroop Score (ms). This is provided as a visual representation for the change and this is meant only to provide descriptive information. The difference between conditions and the variability of that difference is provided in Table 6 and Figure 9. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.

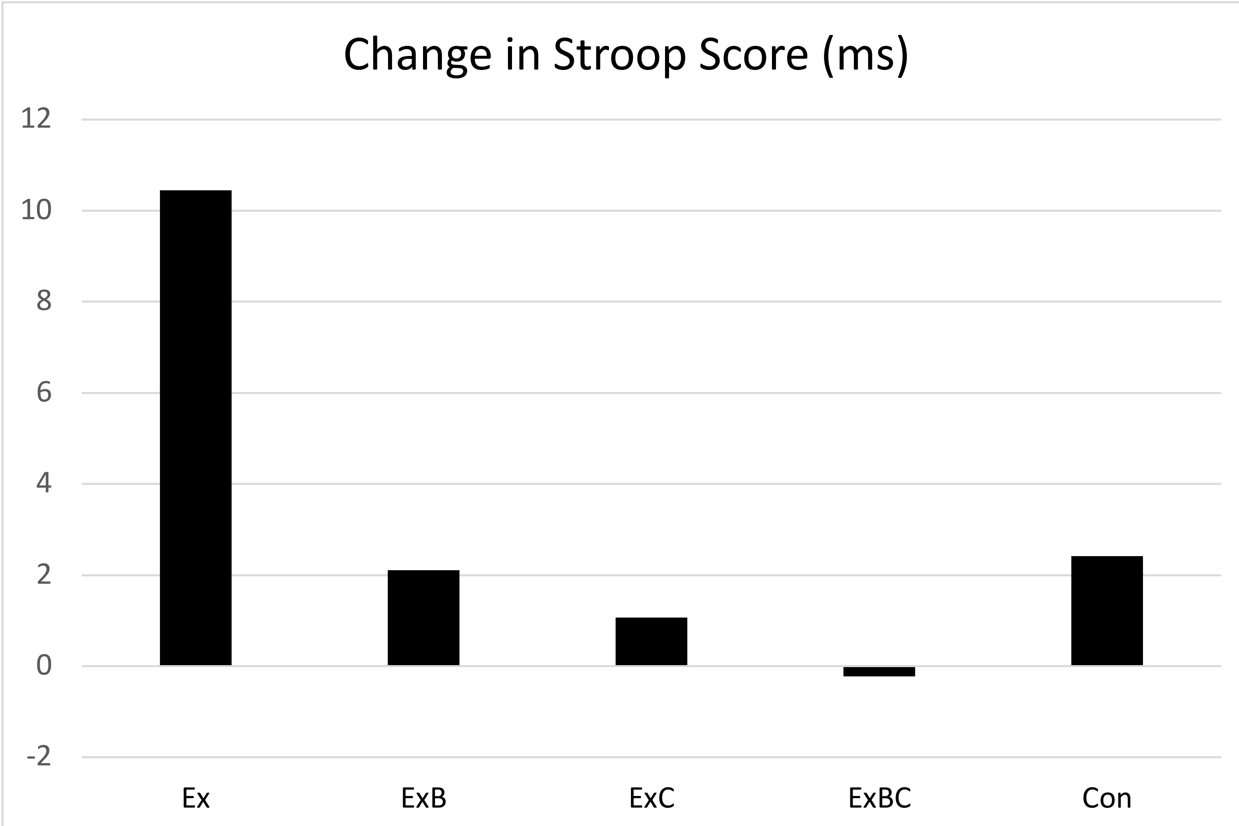
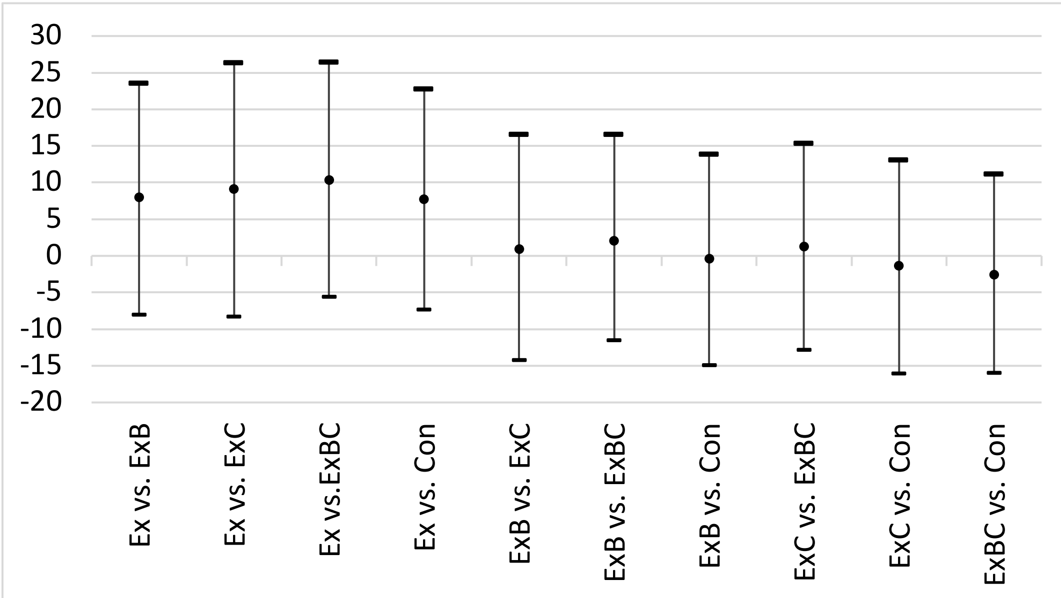


Figure 9. Differences in the Stroop Score between each condition. The x-axis indicates the comparison being made. The first variable listed is being subtracted from the second variable. Thus, a positive value indicates that the first condition in the comparison has a higher score and a negative value indicates that the second condition in the comparison has a higher score. The Bayes Factors associated with each comparison are found in Table 6. The middle dot represents the median difference surrounded by the 95% credible interval of the posterior distribution. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.



INCONGRUENT ERROR RATE

Changes in incongruent error rate are found in Table 7 and Figure 10. The difference between conditions and the variability of that difference is found in Table 7 and Figure 11. Given the nature of the data (difference in % correct), we elected to compare changes with a non-parametric Wilcoxon signed-rank test (results based on data augmentation algorithm with 5 chains of 10000 iterations). Since there is not a readily available Bayesian non-parametric omnibus test, we included the p value for the Frequentist Friedman test. The Friedman test was not statistically significant (p=0.748) which agrees with our Bayesian Wilcoxon pair-wise comparisons. Our results indicate that there was no change with this variable with any of the exercise conditions.

Table 7. Incongruent error rates (n=85 except for Exercise + Cooling which had a missing data point (n=84)). Pre, Post, and within condition change scores are provided for each of the five conditions. The inferential statistics are provided in the bottom half of the table. Each condition is compared head-to-head and the difference values, and the variability of that difference is

provided as a 95% credible interval. The Bayes Factor provides evidence for or against the null hypothesis. Anything below 0.33 is evidence for the null hypothesis (medians do not differ) and anything above 3 is evidence for the alternative hypothesis (medians differ). Importantly, Bayes Factors should be interpreted as a continuous variable. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control. All comparisons including Exercise + Cooling include 84 due to the missing data point.

Condition	**Pre (%)**	**Post (%)**	**Change Score (SD)**
Ex	3.37	4.27	0.89 (3.14)
ExB	3.31	3.84	0.52 (3.16)
ExC (n=84)	3.22	3.57	0.34 (3.33)
ExBC	3.20	3.58	0.38 (3.00)
Con	3.07	3.64	0.77 (3.08)
Comparison	*Difference (%)*	*95% credible interval*	*Bayes Factor*
Ex vs. ExB	0.34	-0.54,1.26	0.179
Ex vs. ExC	0.55	-0.40, 1.52	0.287
Ex vs. ExBC	0.48	-0.40, 1.37	0.151
Ex vs Con	0.31	-0.70, 1.31	0.136
ExB vs. ExC	0.20	-0.69, 1.08	0.144
ExB vs. ExBC	0.13	-0.77, 1.06	0.123
ExB vs. Con	-0.04	-0.98, 0.87	0.120
ExC vs. ExBC	0.016	-1.03, 1.09	0.124
Ex C vs. Con	-0.13	-1.05, 0.79	0.129
ExBC vs. Con	-0.16	-1.06, 0.72	0.152

Figure 10. Within condition changes (n=85 except for Exercise + Cooling which had a missing data point (n=84)) in the incongruent error rates (%). This is provided as a visual representation for the change, and this is meant only to provide descriptive information. The difference between conditions and the variability of that difference is provided in Table 7 and Figure 11. Ex:

Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.

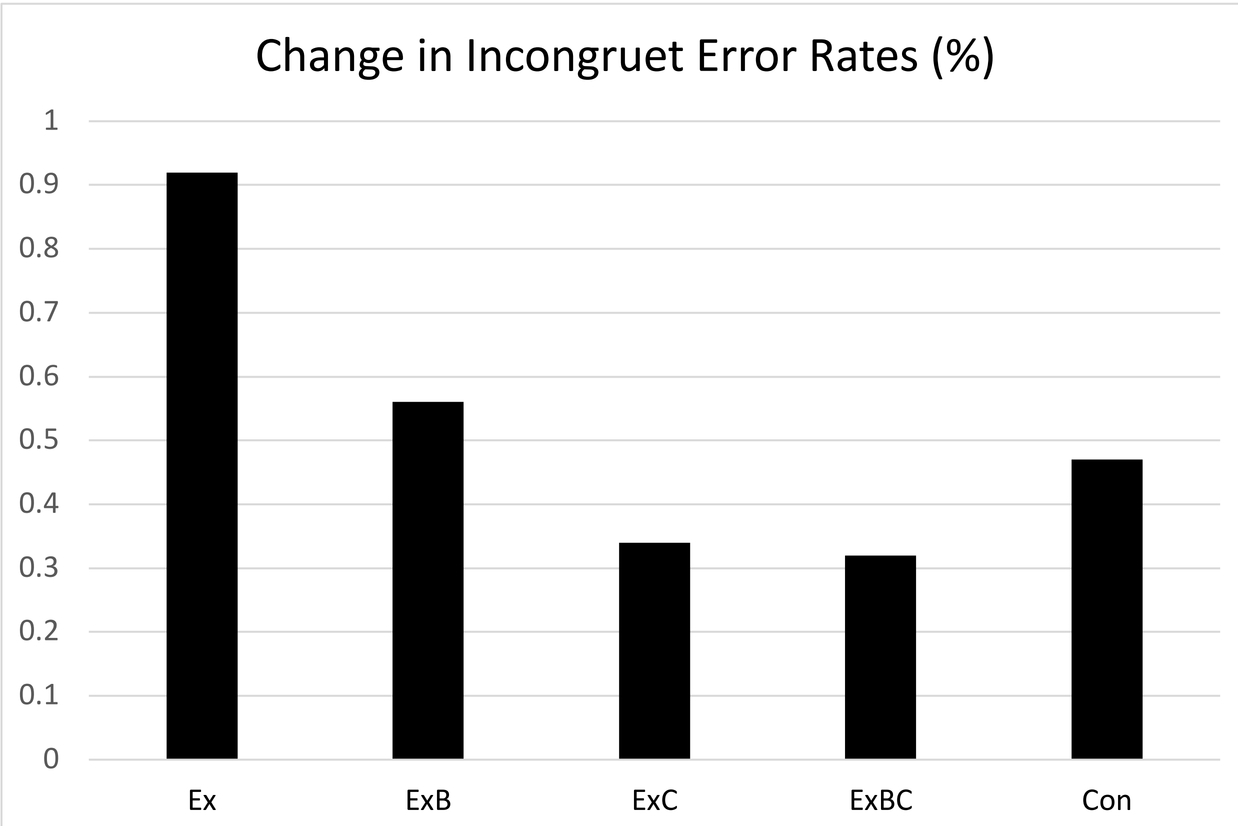
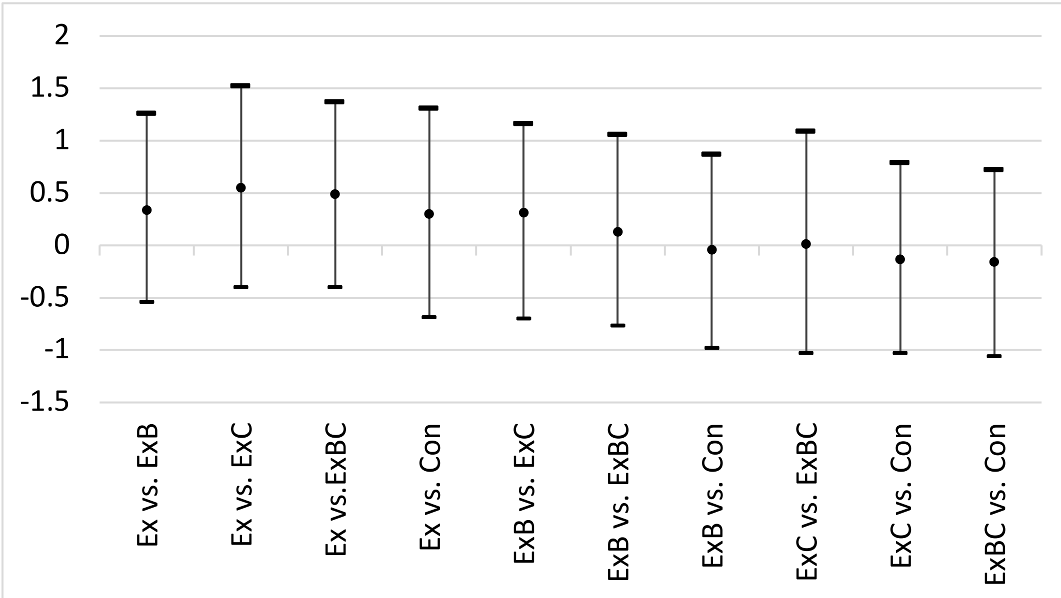


Figure 11. Differences in the incongruent error rates between each condition. The x-axis indicates the comparison being made. The first variable listed is being subtracted from the second variable. Thus, a positive value indicates that the first condition in the comparison has a higher score and a negative value indicates that the second condition in the comparison has a higher score. The Bayes Factors associated with each comparison are found in Table 7. The middle dot represents the median difference surrounded by the 95% credible interval of the posterior distribution. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.



CONGRUENT ERROR

Changes in congruent error are found in Table 8 and Figure 12. The difference between conditions and the variability of that difference is found in Table 8 and Figure 13. Given the nature of the data (difference in % correct), we elected to compare changes with a non-parametric Wilcoxon signed-rank test (results based on data augmentation algorithm with 5 chains of 10000 iterations). Since there is not a readily available Bayesian non-parametric omnibus test, we included the p value for the Frequentist Friedman test. The Friedman test was not statistically significant (p=0.151) which agrees with our Bayesian Wilcoxon pair-wise comparisons. Our results indicate that there was no change with this variable with any of the exercise conditions.

Table 8. Congruent error rates (n=85 except for Exercise + Cooling which had a missing data point (n=84) separated by condition. Pre, Post, and within condition change scores are provided for each of the five conditions. The inferential statistics are provided in the bottom half of the table. Each condition is compared head-to-head and the difference values, and the variability of

that difference is provided as a 95% credible interval. The Bayes Factor provides evidence for or against the null hypothesis. Anything below 0.33 is evidence for the null hypothesis (medians do not differ) and anything above 3 is evidence for the alternative hypothesis (medians differ). Importantly, Bayes Factors should be interpreted as a continuous variable. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control. All comparisons including Exercise + Cooling include 84 due to the missing data point.

Condition	**Pre (%)**	**Post (%)**	**Change Score (SD)**
Ex	1.41	1.45	0.04 (3.88)
ExB	1.89	1.67	-0.22 (3.74)
ExC (n=84)	0.85	1.78	0.92 (2.95)
ExBC	1.20	1.24	0.04 (3.11)
Con	1.47	1.48	0.01 (3.60)
Comparison	*Difference (%)*	*95% credible interval*	*Bayes Factor*
Ex vs. ExB	0.25	-0.89, 1.41	0.134
Ex vs. ExC	-0.78	-1.83, 0.23	0.445
Ex vs. ExBC	0.0088	-1.05, 1.05	0.130
Ex vs Con	0.04	-1.07, 1.15	0.146
ExB vs. ExC	-1.10	-2.16, -0.07	0.715
ExB vs. ExBC	-0.25	-1.33, 0.83	0.133
ExB vs. Con	-0.22	-1.29, 0.81	0.127
ExC vs. ExBC	0.78	-0.10, 1.69	0.633
Ex C vs. Con	0.73	-0.17, 1.65	0.855
ExBC vs. Con	0.04	-0.93, 0.95	0.126

Figure 12. Within condition changes (n=85 except for Exercise + Cooling which had a missing data point (n=84)) in the congruent error rates (%). This is provided as a visual representation for the change, and this is meant only to provide descriptive information. The difference between conditions and the variability of that difference is provided in Table 8 and Figure 13. Ex:

Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.

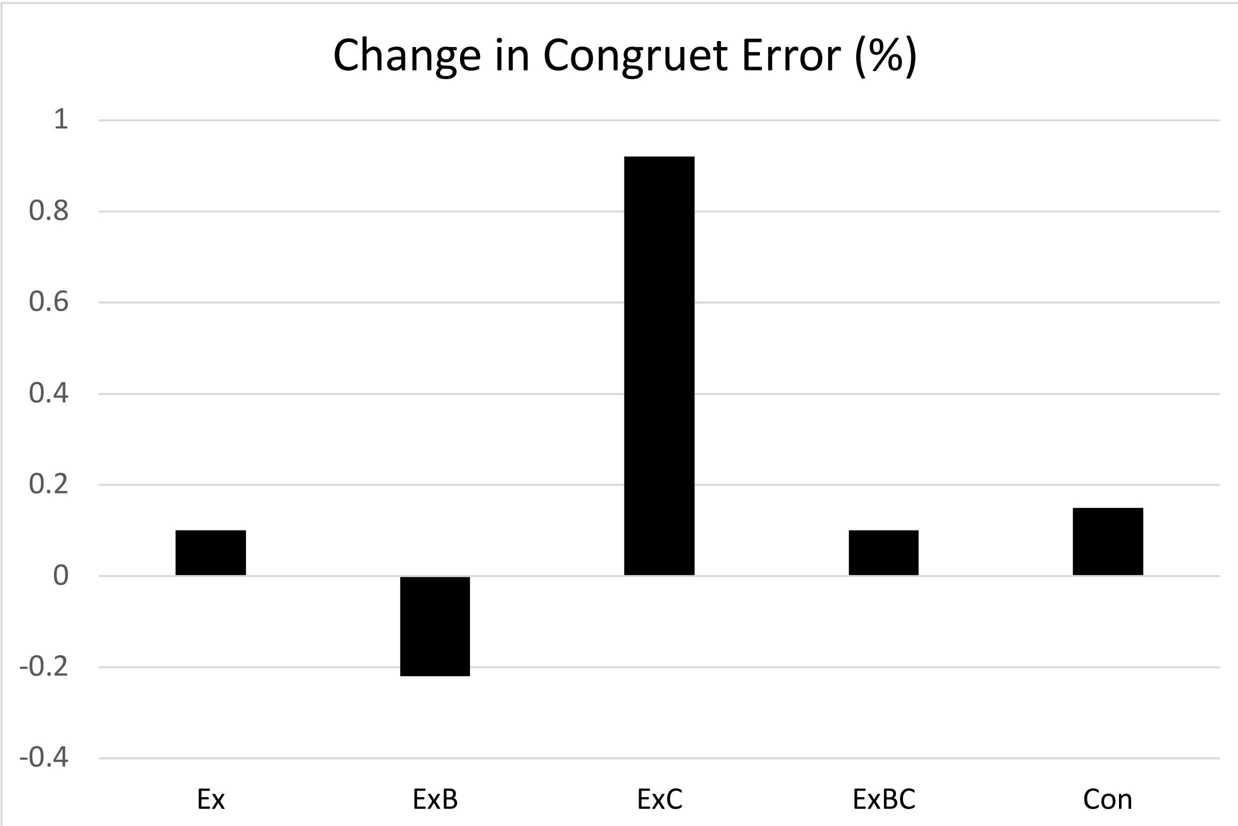
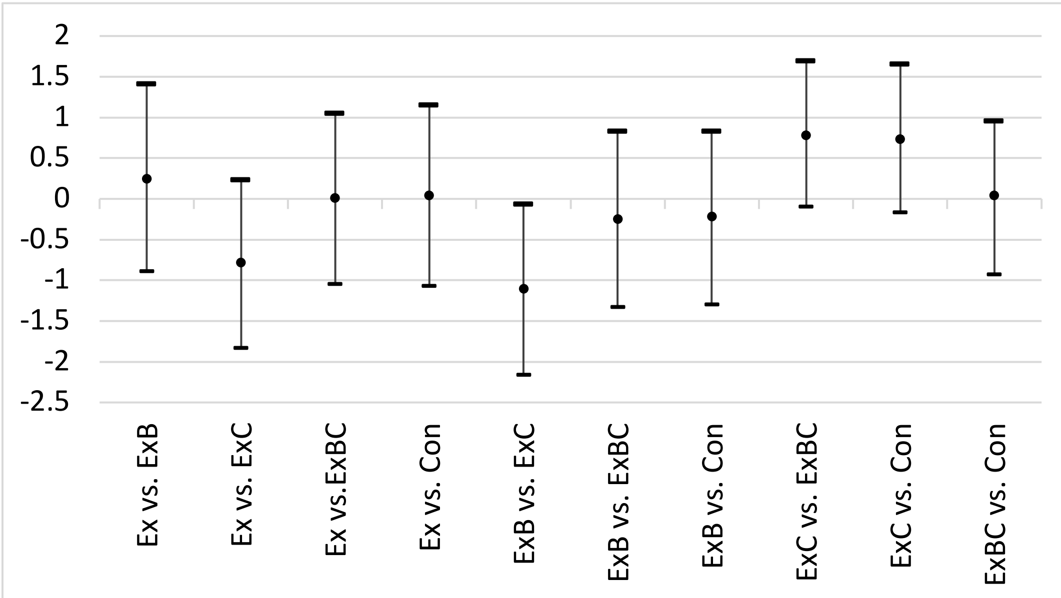


Figure 13. Differences in the congruent error rates between each condition. The x-axis indicates the comparison being made. The first variable listed is being subtracted from the second variable. Thus, a positive value indicates that the first condition in the comparison has a higher score, and a negative value indicates that the second condition in the comparison has a higher score. The middle dot represents the median difference surrounded by the 95% credible interval of the posterior distribution. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.



LACTATE

Changes in blood lactate are found in Table 9 and Figure 15. The difference between conditions and the variability of that difference is found in Table 9 and Figure 16. Changes in blood lactate were normally distributed (visually confirmed by QQ-plot, in Figure 14), therefore, we elected to compare changes with Bayesian repeated measured ANOVA (r scale fixed effect = 0.5, r scale random effects = 1, r scale covariates = 0.354). Since this analysis found that inclusion the effect of condition (inclusion Bayes factor = 3.946e+93), we followed up with Bayesian paired sample t-tests (default prior = 0.707 centered on zero, Cauchy distribution). The post hoc tests determined that Exercise [σ: 2.10 (1.72, 2.50)], Exercise with Blood Flow Restriction [σ: 2.28 (-1.87, 2.7)], Exercise with Cooling [σ: 2.18 (1.79, 2.59)], and Exercise with Blood Flow Restriction and Cooling [σ: 2.14 (1.76, 2.54)] produce changes in blood lactate different from that of the non-exercise control condition. There was no evidence that any of the exercise conditions differed from each other.

Figure 14. Model Averaged Q-Q Plot for the blood lactate concentration. This plot was generated on the comparison of change scores using the Bayesian Repeated Measures ANOVA analysis. Since this plot illustrates that the data is normally distributed, we elected to use parametric analysis.

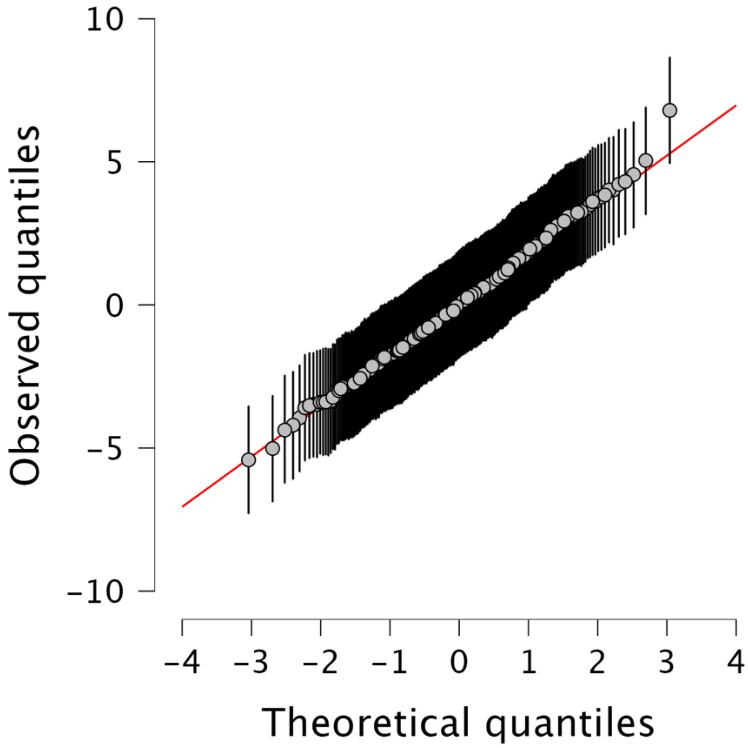


Table 9. Blood lactate concentrations (n=85) separated by condition. Pre, Post, and within condition change scores are provided for each of the five conditions. The inferential statistics are provided in the bottom half of the table. Each condition is compared head-to-head and the difference values, and the variability of that difference is provided as a 95% credible interval. The Bayes Factor provides evidence for or against the null hypothesis. Anything below 0.33 is evidence for the null hypothesis (medians do not differ) and anything above 3 is evidence for the alternative hypothesis (medians differ). Importantly, Bayes Factors should be interpreted as a continuous variable. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise

+ Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.

Condition	**Pre (mmol/L)**	**Post (mmol/L)**	**Change Score (SD)**
Ex	1.12	8.83	7.71 (3.63)
ExB	1.20	8.55	7.35 (3.18)
ExC	1.20	8.53	7.32 (3.28)
ExBC	1.20	8.47	7.27 (3.32)
Con	1.16	1.05	-0.10 (0.56)
Comparison	*Difference mmol/L*	*95% credible interval*	*Bayes Factor*
Ex vs. ExB	0.34	-0.12, 0.82	0.351
Ex vs. ExC	0.37	-0.13, 0.88	0.338
Ex vs. ExBC	0.43	-0.12, 0.98	0.382
Ex vs Con	7.78	6.98, 8.58	8.653e+29
ExB vs. ExC	0.02	-0.47, 0.51	0.120
ExB vs. ExBC	0.08	-0.40, 0.57	0.126
ExB vs. Con	7.43	6.72, 8.12	1.907e+32
ExC vs. ExBC	0.04	-0.41, 0.53	0.123
Ex C vs. Con	7.39	6.67, 8.12	1.088e+31
ExBC vs. Con	7.34	6.59, 8.06	2.992e+30

Figure 15. Within condition changes (n=85) in the blood lactate concentration (mmol/L). This is provided as a visual representation for the change, and this is meant only to provide descriptive information. The difference between conditions and the variability of that difference is provided in Table 9 and Figure 17. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.

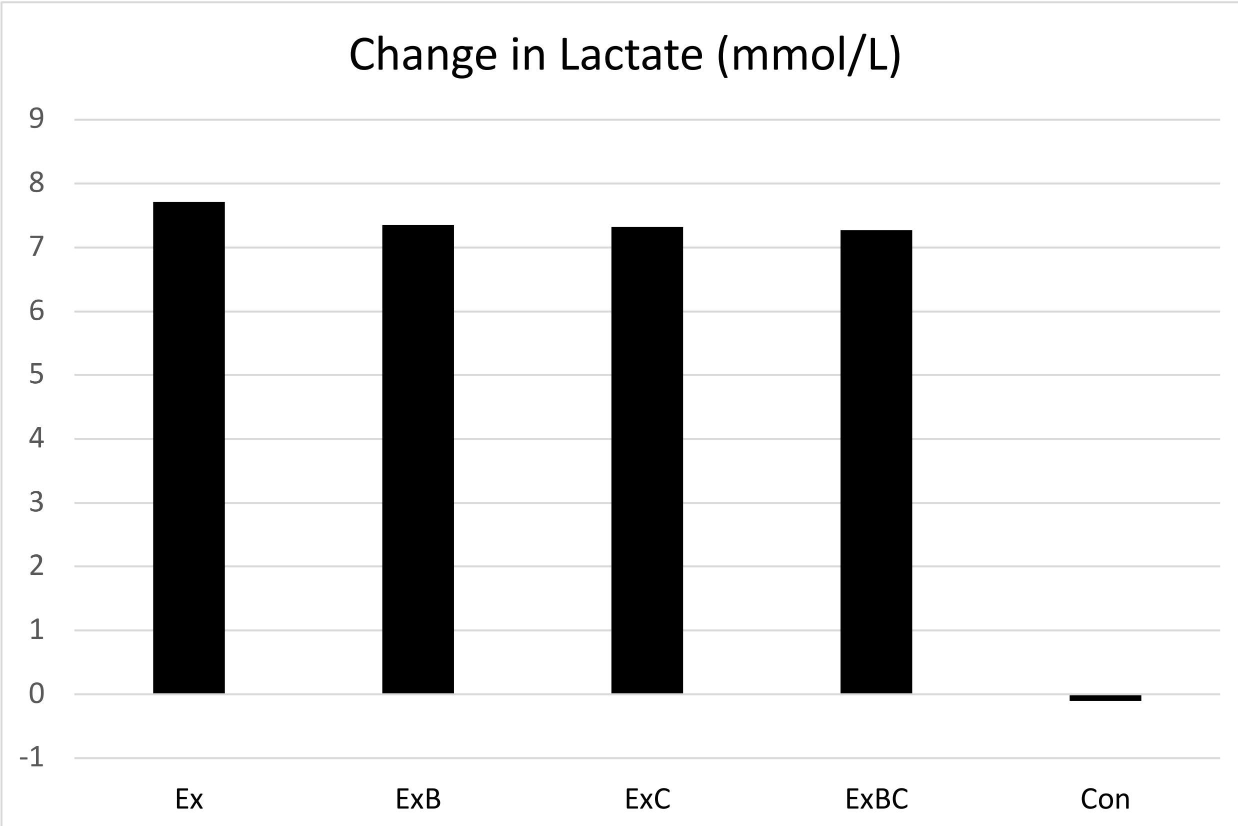
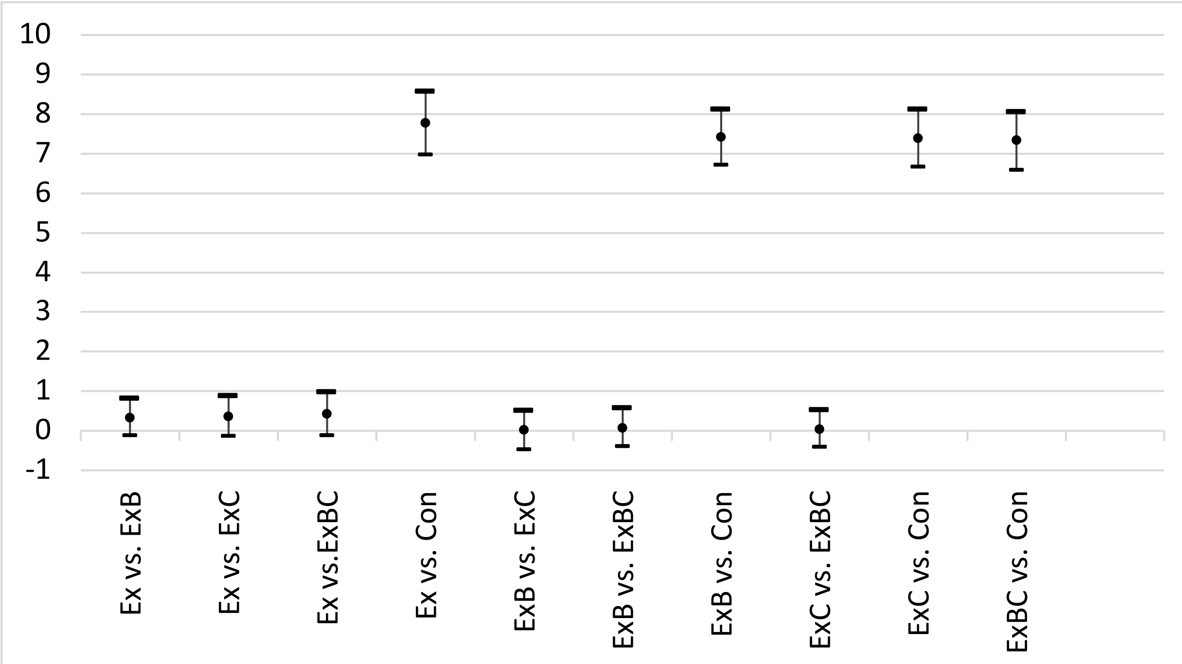


Figure 16. Differences in the blood lactate concentrations between each condition. The x-axis indicates the comparison being made. The first variable listed is being subtracted from the second variable. Thus, a positive value indicates that the first condition in the comparison has a higher change, and a negative value indicates that the second condition in the comparison has a higher change. The middle dot represents the median difference surrounded by the 95% credible interval of the posterior distribution. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.



DOES LACTATE MEDIATE CHANGES IN INCONGRUENT REACTION TIME?

We compared each exercise condition to the non-exercise control condition in order to test whether changes in lactate mediated changes in incongruent reaction time (Figure 18). We used the MEMORE macro in SPSS which produces bootstrapped estimates of the indirect effects (Table 10). If the 95% confidence interval was all negative, that would provide evidence for a mediating effect on incongruent reaction time. Conceptually, the model provides a total effect (c path) which is just a difference (y diff) in reaction time between exercise and control (exercise – control). Statistically, the p value provided from MEMORE for this step is equivalent to a one-sample t-test on the difference score. Next, Mdiff was calculated which is the difference in lactate change scores between conditions (exercise – control). This is the a path and the p value provided is statistically equivalent to a one-sample t-test on the difference score. The direct effect (c' path) and b path can be calculated by running a regression on the difference in incongruent reaction time (y diff) as the dependent variable with Mdiff and Maverage [0.5 * (lactate from exercise + lactate from control)] as the independent variables. The B coefficient for

Mdiff represents the b path. The intercept represents the direct effect. Importantly, this value needs to be centered. MEMORE function then multiples a*b to estimate the indirect effects. Notably, none of our models found a mediating effect of changes in lactate for changes in incongruent reaction time.

Figure 17. Conceptual model of our within-subject mediation. Notably, for our hypothesis the coefficient for "a" would need to be positive and the coefficient for "b" would need to be negative

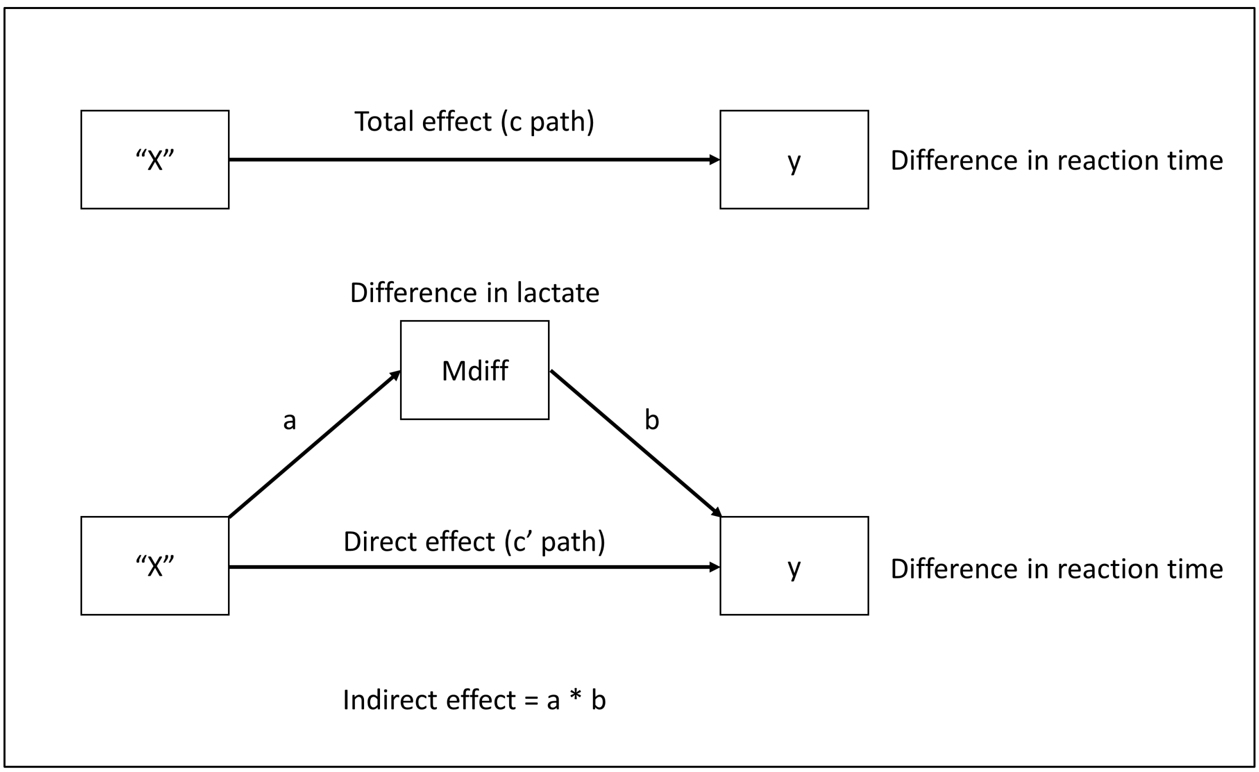


Table 10. Coefficients from our within subject mediation. Ex: Exercise only; ExB: Exercise + Blood Flow Restriction; ExC: Exercise + Cooling; ExBC: Exercise + Blood Flow Restriction + Cooling; and Con: Non-exercise time matched control.

	Ex vs. Con		
	Coefficient	**P value**	**95% CI**
Total effect of "x" on y (ms)	-13.2	.0507	-26.6, 0.04
a path (Mdiff, mmol/L)	7.8	<0.001	7.0, 8.6
Direct effect of "x" on y (ms)	-39.2	0.414	-134.2, 55.8
b path (ms)	3.3	0.585	-8.7, 15.3
Indirect effect (a*b)			
Lactate (ms)	25.9		-51.3, 114.9
	ExB vs. Con		
	Coefficient	**P value**	**95% CI**
Total effect of "x" on y (ms)	-18	0.03	-34.6, -1.3
a path (Mdiff, mmol/L)	7.4	<0.001	6.7, 8.1
Direct effect of "x" on y (ms)	19.3	0.73	-91.9, 130.6
b path (ms)	-5.0	0.50	-19.7, 9.7
Indirect effect (a*b)			
Lactate (ms)	-37.3		-140.6, 64.7
	ExC vs. Con		
	Coefficient	**P value**	**95% CI**
Total effect of "x" on y (ms)	-20.2	0.004	-33., -6.4
a path (Mdiff, mmol/L)	7.4	<0.001	6.7, 8.1
Direct effect of "x" on y (ms)	-70.3	0.13	-161.8, 21.2
b path (ms)	6.7	0.27	-5.4, 18.9
Indirect effect (a*b)			
Lactate (ms)	50.1		-24.6, 138.3
	ExBC vs. Con		
	Coefficient	**P value**	**95% CI**
Total effect of "x" on y (ms)	-19.4	0.008	-33.6, -5.1
a path (Mdiff, mmol/L)	7.3	<0.001	6.6, 8.1
Direct effect of "x" on y (ms)	34.8	0.467	-59.9, 129.5
b path (ms)	-7.3	0.253	-20, 5.3
Indirect effect (a*b)			
Lactate (ms)	-54.2		-122.9, 35.8

CHAPTER V: DISCUSSION

MAIN FINDINGS

The main findings from this thesis are as follows: 1) the improvement of incongruent reaction time was evident when cooling was concomitantly applied during the exercise, 2) all exercise conditions enhanced congruent reaction time, 3) the change in Stroop score did not differ among conditions, 4) whole blood lactate concentration was similarly elevated in all exercise conditions, and 5) there was no mediating effect of lactate on changes in interference control.

THE EFFECT OF EXERCISE ON INTERFERENCE CONTROL

We were unable to provide evidence to support the contention that exercise itself can improve incongruent reaction time. This finding is in disagreement with the previously reported benefit of exercise on high-order cognitive performance (Chang et al., 2012; Etnier et al., 1997; Lambourne & Tomporowski, 2010; Oberste et al., 2019). Our exercise protocol consisted of moderate continuous aerobic exercise (10 minutes) and all-out sprint intervals (5 sets of 20 seconds with 40 seconds rest interval between sets). Both moderate aerobic exercise and high intensity interval exercise has shown to produce beneficial effects on interference control (Oberste et al., 2019). Although exercise intensity is an important moderating factor, the effects of acute exercise on interference control are also impacted by other factors, including the timing of posttest assessment, participants (i.e., age, aerobic fitness level, training status, and cognitive disorder) and methodological quality of the study (e.g., sample size, familiarization, study design, and type of control conditions) (Pontifex et al., 2019). Considering the findings and suggestion from previous studies, we administrated the post-exercise cognitive test 11-minutes after exercise (Chang et al., 2012), familiarized participants to the cognitive tasks in the first visit and each experimental visit, used a within-subject design, and included a non-exercise control condition that accounted for social interaction during the exercise conditions (Oberste et al., 2019). Nevertheless, some moderating factors that we did not account for, such as aerobic fitness level and training status, might mask the true effect. Importantly, the classification scheme of Bayes Factor (i.e., above 3 for supporting alternative, below 0.33 for supporting null hypothesis) was adopted to facilitate communication and interpretation of evidential strength and should not be interpreted as an absolute rule for all-or-nothing conclusions (van Doorn et al., 2021). Since a lack of confidence to support null or alternative hypothesis, more data might need to be collected to find stronger evidence regarding the effect of exercise itself on interference control.

COOLING DURING EXERCISE AND INTERFERENCE CONTROL

Although the effect of exercise itself on interference control was uncertain, there was strong evidence (BF_{10} = 33.41) showing the improvement of incongruent reaction time (~20 millisecond) was observed when the exercise protocol was performed with cooling. Interestingly, the improvement of incongruent reaction time was also moderately evident after exercise with blood flow restriction and cooling (BF_{10} = 6.7), but evidence was not as strong for exercise with only blood flow restriction (BF_{10} = 2.24). Collectively, the results indicate that cooling during the exercise, not blood flow restriction, facilitated the post-exercise interference control performance. However, given the findings from the ExB condition, it is also possible that blood flow restriction could have been playing a small role too. Particularly given the numerically lower volume of work completed in these conditions.

A previous study found a benefit of cooling during exercise on cognitive performance when compared to exercise itself, despite the different location of cooling from the present study (Lee et al., 2014). For example, that study utilized a neck-cooling collar during treadmill exercise to exhaustion (70% of maximal oxygen consumption) and found improvement in a complex cognitive task (Lee et al., 2014). Since the neck-cooling did not affect the core temperature but lowered neck temperature substantially, the authors suggested that the reduction in skin temperature may mask the cognitive load to regulate heat and save more cognitive resources (e.g., neurotransmitter and ions) for activating the brain area needed during the later cognitive task (Lee et al., 2014). Therefore, the potential aid of cooling for post-exercise interference control performance in the present study may be not due to reducing increases in core temperature but due to the reduced cognitive load for thermoregulation. In other words, rather than using resources to regulate temperature, those resources can be used for other cognitive function. However, caution is needed since we did not measure the interaction of skin/core temperature and neural activity (by electroencephalogram or functional magnetic resonance). A mechanistical approach in future studies would be necessary to know whether cooling reduced the neural activity of the brain region that regulates temperature (i.e., hypothalamus).

BLOOD FLOW RESTRICTED EXERCISE AND INTERFERENCE CONTROL

The potential efficacy of blood flow restriction on post-exercise cognitive performance was suggested based on several physiological mechanisms (Törpel et al., 2018; Yamada, Frith, et al., 2021). One of the suggested mechanisms was the key role of lactate for neural energy production in brain. More details of the lactate-related mechanism will be discussed in a later section, but in short, the increase in systemic lactate circulation can play an important role in post-exercise cognitive enhancement (Hashimoto et al., 2021). We hypothesized that the increased systemic blood lactate concentration by blood flow restricted exercise would lead to further improvement in interference control performance (Yamada, Frith, et al., 2021). The finding in the present study suggested that there was not sufficient evidence ($BF_{10} = 2.24$) supporting that blood flow restriction foster the effect of the exercise on interference control performance although exercise with blood flow restriction produced numerically greater reduction in incongruent reaction time compared to control (-17.2 milliseconds (95% credible interval; -33.3, -1.1)).

A previous study from our group found interference control was not improved after isometric handgrip exercise with or without blood flow restriction when compared to time-matched non-exercise control (Yamada, Song, et al., 2021). In that study, we speculated that since isometric handgrip exercise only requires contraction of the smaller muscle group relative to pectoralis muscles and quadriceps/hamstring muscles, the exercise might not provide sufficient systemic metabolic responses (e.g., lactate) even when blood flow restriction is added (Yamada, Song, et al., 2021). The speculation does not apply to the present study because the exercise on recumbent cross trainers involved whole-body movement as well as exercise by itself elicited the systemic metabolic response (i.e., 7.78 mmol/L increase in blood lactate concentration, relative to control). The increase in blood lactate was not different between exercise and exercise with blood flow restriction. In the case of this thesis, the exercise may have been of sufficient intensity that applying blood flow restriction would be unlikely to lead to a further increase in the systemic blood lactate. In contrast, Sugimoto et al. (2021) observed the walking with blood flow restriction improved interference control when compared to walking by itself. Greater metabolic response (i.e., capillary blood lactate) was also observed in walking with blood flow restriction compared to walking by itself (Sugimoto et al., 2021). Therefore, the effect of blood flow restriction may depend on the combined exercise characteristics (e.g., constriction, type, intensity, duration of exercise).

Another potential explanation of our results could be the method of blood flow restriction. In the present study, the default absolute pressure (i.e., 40 mmHg for arm and 65 mmHg for leg) was applied due to the incapability of measuring arterial occlusion pressure with the liquid compression system. Because the amount of pressure required to occlude blood flow (i.e., arterial occlusion pressure) is related to tourniquet shape, width and length, and the size of the limb, the use of relative pressure (i.e., % of arterial occlusion pressure) has been recommended not only to limit adverse cardiovascular response and discomfort but also to support an efficacy of the procedure (Jessee et al., 2016; Loenneke, Fahs, et al., 2012; Patterson et al., 2019). For example, the applied pressure could be more restrictive as participant's limb circumference is smaller. Therefore, the heterogeneity of the degree of blood flow restriction between individuals might affect our result.

MEDIATING EFFECT OF LACTATE ON CHANGES IN CONGITIVE PERFORMANCE

There is an increasingly amount of literature supporting the potential role of lactate for improving cognitive function in animal (El Hayek et al., 2019; Holloway et al., 2007; Rice et al., 2002) and human (Hashimoto et al., 2018; Kujach et al., 2020; Sugimoto et al., 2021) studies. Although glucose is a main fuel source for the brain at rest and low intensity exercise, the brain lactate metabolism increases as exercise intensity increases (Kemppainen et al., 2005). The lactate in blood circulation can readily cross the blood-brain barrier by the lactate transporter (i.e., monocarboxylate transporters), and is used by neurons to meet the increased energy requirements associated with neuronal activation during intense exercise (Brooks et al., 2022; Hashimoto et al., 2021; Magistretti & Allaman, 2015). Therefore, lactate is the key energy substrate to sustain the heightened neural activity during and after exercise. The improvement of interference control after exercise may be due to the heightened neural activation sustained by energy supply from lactate (Hashimoto et al., 2021). Considering the collective evidence from previous literature, we chose to use the change in fingertip capillary blood lactate as a third variable for the mediation analysis. The fingertip capillary blood lactate represents arterial/systemic blood lactate (Williams et al., 1992). The changes in arterial lactate circulation were associated with the changes in brain lactate uptake (Hashimoto et al., 2018).

However, our mediation analysis found that none of our models found a mediating effect of changes in systemic blood lactate for changes in interference control performance, indicated by the change in incongruent reaction time The result from the mediation analysis brings up the concern in current literature. The evidence supporting the potential role of lactate as a mediator in human studies come from correlational analyses (Hashimoto et al., 2018; Kujach et al., 2020) or parallel increase in interference control performance and blood lactate (Sugimoto et al., 2021). Although the present study also observed both improvement on interference control and increased systemic blood lactate together in exercise with cooling and exercise with cooling and blood flow restriction, two variables changing in parallel does not necessarily mean that lactate contributes to changes in interference control. The improvement of the interference control in exercise with cooling and exercise with cooling and blood flow restriction might be driven by different physiological mechanisms, such as increased norepinephrine-mediated neurophysiological activity and increased neurotrophic factors (i.e., BDNF (brain-derived neurotrophic factor), IGF-1 (insulin-like growth factor 1), and VEGF (vascular endothelial growth factor)) (Pontifex et al., 2019). Further study may want to consider using the mediation analysis to assess these mediating factors that may explain causal relationship between exercise and interference control, instead of correlational analyses.

CHAPTER VI: CONCLUSION

The purpose of this study was to evaluate the effects of exercise alone, exercise with cooling, exercise with blood flow restriction, and exercise with blood flow restriction and cooling on interference control assessed by Stroop Color Word Test. Secondly, we aimed to assess whether the changes in systemic blood lactate mediated the changes in interference control.

RESERCH QUESTIONS

1) **What was the impact of the exercise on interference control?**

We were unable to find sufficient evidence that the exercise by itself (which consisted of 5 minutes of warm up, 10 minutes of moderate continuous exercise and 5 minutes of sprint interval exercise) altered interference control when compared to time-matched non-exercise control.

2) **Is the change in the cognitive marker affected by cooling, blood flow restriction, or cooling and blood flow restriction?**

Yes, exercise with cooling and exercise with cooling and blood flow restriction were shown to improve interference control when compared to a time-matched non-exercise control.

3) **If there is a change in the cognitive marker, is it related to the change in lactate?**

No, the mediation analysis suggested that none of our models found a mediating effect of changes in lactate for changes in incongruent reaction time.

SIGNIFICANCE

From our knowledge, this study was the first to compare the effect of exercise with cooling and blood flow restriction together or with each component individually affect interference control to time-matched non-exercise control. Interference control is one of the core executive functions, which is required in everyday life to avoid impulsive reactions and remain focused on tasks relevant to present goals. Our study found that exercise with cooling and exercise with blood flow restriction and cooling resulted in a favorable treatment effect (i.e., improved interference control). This result suggests that the exercise modality could be used to enhance brain health, which could be beneficial for those in business and school settings.

FUTURE RESEARCH

Based on the findings of the present study, future work should consider measuring cognitive flexibility and working memory (the other two domains of executive function). Given that both favorable conditions included cooling, it would be worth further exploring the cooling aspect of VASPER technology. Future work could also potentially investigate the use of relative pressure for the blood flow restriction. It is possible that applying a more uniform pressure to each individual might further improve this marker of executive function. It would also be of interest to investigate effects that might occur in the hours following an exercise bout (sleep quality, overall vitality).

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Yamada, Y., Song, J. S., Bell, Z. W., Wong, V., Spitz, R. W., Abe, T., & Loenneke, J. P. (2021). Effects of isometric handgrip exercise with or without blood flow restriction on interference control and feelings. *Clinical Physiology and Functional Imaging*, *41*(6), 480–487. https://doi.org/10.1111/cpf.12723

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CURRICULUM VITAE

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EDUCATION

University of Mississippi 2022
Master of Science in Exercise Science

Thesis: The cognitive inhibitory response to acute exercise with and without blood flow restriction and full body cooling.
Committee Members: Dr. Loenneke, Dr. Loprinzi, and Dr. Del Arco

Ohio Dominican University 2019
Bachelor of Science in Exercise Science

Senior Research Thesis: Effects of practical Blood Flow Restriction on Knee Joint Proprioception and Muscle Coactivation during Low Intensity Aerobic Exercise
Mentor: Dr. Thistlethwaite

RESEARCH POSITIONS HELD

Keywords/Research Interests: Blood Flow Restriction (BFR) Exercise, Skeletal Muscle Physiology, Exercise-Cognition Interaction, Joint Proprioception and Muscle Coactivation

Graduate Research Assistant, University of Mississippi 2019-present
Department of Health, Exercise Science, and Recreation Management
Advisor/Mentor: Dr. Loenneke
→Recruit participants
→Conduct experiments (e.g. instruct resistance/aerobic exercises, operate blood flow restriction exercise, measure arterial occlusion pressure, utilize ultrasound for muscle thickness measurements, and maneuver Biodex dynamometer, and etc.)
→Write/review manuscripts

Principal Research Investigator, Ohio Dominican University 2017-2019
Department of Exercise Science
Advisor/Mentor: Dr. Cayot and Dr. Thistlethwaite
→Create a study design and the research proposal
→Recruit subjects and conduct experiments (ex. practical blood flow restriction exercise, measurement of joint proprioception and muscle coactivation, and etc.)
→Perform data analysis and write a manuscript

PUBLICATIONS

PEER-REVIEWED JOURNAL ARTICLES

1. Wong, V., Bell, ZW., Sptiz, RW., Song, J., Song, J., **Yamada, Y.**, Abe, T., & Loenneke, JP. (2022). Blood flow restriction maintains blood pressure upon head-up tilt. *Physiology International*. Advance online publication. https://doi.org/10.1556/2060.2022.00051

2. **Yamada, Y.,** Spitz, RW., Wong, V., Bell, ZW., Song, J., Abe, T., & Loenneke, JP. (2022). The Impact of Isometric Handgrip Exercise and Training on Health-Related Factors: A Systematic Review. *Clinical Physiology and Functional Imaging.* 42(2): 57-87. http://dx.doi.org/10.1111/cpf.12741

3. Wong, V., Song, J., Abe, T., Spitz, RW., **Yamada, Y**., Bell, ZW., Kataoka, R., Kang, M., & Loenneke, JP. (2022). Muscle Thickness Assessment via Ultrasonography: Is experience level important? *Biomedical Physics & Engineering Express*. 8: 027003. https://doi.org/10.1088/2057-1976/ac4d42

4. Song JS, **Yamada Y**, Wong V, Bell ZW, Spitz RW, Abe T, Loenneke JP. Hypoalgesia following isometric handgrip exercise with and without blood flow restriction is not mediated by discomfort nor changes in systolic blood pressure. 2021. *Journal of Sports Science*. https://doi.org/10.1080/02640414.2021.2003569

5. Bell, ZW., Spitz, RW., Wong, V., **Yamada, Y**., Song, J., Abe, T., & Loenneke, JP. (2021). Can Individuals Be Taught to Sense the Degree of Vascular Occlusion? A Comparison of Methods and Implications for Practical Blood Flow Restriction. *Journal of Strength and Conditioning Research*. http://dx.doi.org/10.1519/JSC.0000000000004151.

6. **Yamada, Y**., Kasprizak, R., Shotten, S., Brown, AM., Mathew, A., Loenneke, JP., & Thistlethwaite, J. (2021). Brisk walking with practical blood flow restriction did not induce impairment of knee proprioception and fatigue. *Journal of Trainology.*10(2): 16-19. https://doi.org/10.17338/trainology.10.2_16.

7. **Yamada, Y**., Song, J., Bell, ZW., Wong, V., Spitz, RW., Abe, T., & Loenneke, JP. (2021). Effects of Isometric Handgrip Exercise with or without Blood Flow Restriction on Interference Control and Feelings. *Clinical Physiology and Functional Imaging*. https://doi-org.umiss.idm.oclc.org/10.1111/cpf.12723.

8. Wong, V., Song, J., Bell, ZW., **Yamada, Y**., Spitz, RW., Abe, T., and Loenneke, JP. (2021). Blood flow restriction training on resting blood pressure and heart rate: a meta-analysis of the available literature. *Journal of Human Hypertension.* https://doi.org/10.1038/s41371-021-00561-0.

9. Abe, T., Song, J., Bell, ZW., Wong, V., Spitz, RW., **Yamada, Y**., and Loenneke, JP. (2021). Comparisons of calorie restriction and structured exercise on reductions in visceral and abdominal subcutaneous adipose tissue: a systematic review. *European Journal of Clinical Nutrition*. https://doi.org/10.1038/s41430-021-00942-1

10. Song, J., Spitz, RW., **Yamada, Y**., Bell, ZW., Wong, V., Abe, T., and Loenneke, JP. (2021). Exercise-induced hypoalgesia and pain reduction following blood flow restriction: a brief review. *Physical Therapy in Sport*. https://doi.org/10.1016/j.ptsp.2021.04.005

11. **Yamada, Y.,** Frith, EM., Wong, Vickie., Spitz, RW., Bell, ZW., Chatakondi, RN., Abe, T., and Loenneke, JP. (2021). Acute Exercise and Cognition: A Review with Testable Questions for Future Research into Cognitive Enhancement with Blood Flow Restriction. *Medical Hypotheses*. https://doi.org/10.1016/j.mehy.2021.110586

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PEER-REVIEWED MANUSCRIPTS (UNDER REVIEW)

1. Spitz, RW., Ryo, K., Dankel, SJ., Bell, ZW., Song, J., Wong, V., **Yamada, Y**., & Loenneke, JP. (Under review). Quantifying the Generality of Strength Adaptation: A Meta-Analysis.

2. Song, J., **Yamada**, **Y**., Kataoka, R., Wong, V., Spitz, RW., Bell, ZW., & Loenneke, JP. (Under review). Training-induced hypoalgesia and its underlying mechanisms.

3. Loenneke, JP., Matthew, J., Wong, V., Bell, ZW., **Yamada, Y**., Song, J., Spitz, RW., Buckner, S., Mouser, J., & Abe, T. (Under review). Limb Blood Flow and Changes in Muscle Thickness with Different Types of Resistance Exercise.

PEER-REVIEWED MANUSCRIPTS (IN PREPARATION/PROGRESS)

1. Cayot, TE., Barnette, JD., Scott, B., **Yamada, Y**., Sunday, R., Baldwin, N., & Thistlethwaite, JR. (in progress). Effects of Practical Blood Flow Restriction Resistance Exercise on Sagittal Joint Kinematics and Proprioception.

GRANTS AND CONTRACTS

Loenneke JP. Principal Investigator (2022). "An efficient and effective way to mitigate the rise in anxiety." John W. Brick Mental Health Foundation. $438,328 (Pre-Application, Under Review).

- Co-Investigator (Dr. Matthew B. Jessee)
- Consultant (Dr. Paul Loprinzi)
- Zachary Bell, Robert Spitz, Vickie Wong, Ryo Kataoka, Jun Seob Song, and **Yujiro Yamada** intellectually contributed to this grant.

Loenneke JP. Principal Investigator (2022). "A Novel Strategy for Improving Anxiety and Blood Pressure Simultaneously." National Institutes of Mental Health. $275,000 (Not Awarded).

- Co-Investigator (Dr. Matthew B. Jessee)
- Consultant (Dr. Paul Loprinzi)
- Zachary Bell, Robert Spitz, Vickie Wong, Ryo Kataoka, Jun Seob Song, and **Yujiro Yamada** intellectually contributed to this grant.

Loenneke JP **(**Principal Investigator); Jessee MB (Co-Investigator); Dankel SJ (Co-Investigator); Owens J (Consultant); and JG Mouser (Consultant). (2021). "The Impact of Blood Flow Restriction Training on Vascular Function and Blood Pressure: Does the effect depend on race and sex?" Department of Defense (PRMRP Clinical Trial) $1,208,862 (Not Awarded).

- Zachary W. Bell, Robert W. Spitz, Vickie Wong, **Yujiro Yamada**, and Jun Seob Song intellectually contributed to this grant.

Loenneke JP. Principal Investigator (2021). "The influence of Blood Flow Restriction Training on Resting Blood Pressure in Women: Adaptive or Maladaptive?" Foundation for Women's Wellness $25,000 (Not Awarded).

- Robert W. Spitz, Zachary W. Bell, Vickie Wong, **Yujiro Yamada**, and Jun Seob Song intellectually contributed to this grant.

Loenneke JP. Principal Investigator (2020). "The effect of blood flow restriction on preventing orthostatic intolerance." Mississippi Space Grant Consortium $12,000 (**Awarded**)

- Vickie Wong, Zachary W. Bell, Robert W. Spitz, **Yujiro Yamada**, and Jun Seob Song intellectually contributed to this grant.

Loenneke JP. Principal Investigator (2019). "The cognitive effects of acute exercise with and without blood flow restriction and full body cooling (VASPERTM exercise)." VASPER $30,953 (**Awarded**)

- Zachary W. Bell, Vickie Wong, Robert W. Spitz, and **Yujiro Yamada** intellectually contributed to this grant.

Loenneke JP. Principal Investigator (2020). "The role of lactate in the cognitive inhibitory response to acute exercise." American College of Sports Medicine $5400 (Not Awarded).

- Zachary W. Bell, Vickie Wong, Robert W. Spitz, and **Yujiro Yamada** intellectually contributed to this grant.

POSTER PRESENTATIONS

1. **Yamada, Y**., Song, J., Bell, ZW., Wong, V., Spitz, RW., Abe, T., Loenneke, JP. Impact of Isometric Handgrip Exercise with Blood Flow Restriction on Interference Control and Affect. Poster Presentation In: Proceedings of the Annual American College of Sports Medicine. Virtual Experience. 2021.

2. Bell, ZW., Spitz, RW., Wong, V., **Yamada, Y.,** Song, J., Abe, T., Loenneke, JP. Comparing Condition Methods: Implications For Practical Blood Flow Restriction Exercise. Poster Presentation In: Proceedings of the Annual American College of Sports Medicine. Virtual Experience. 2021.

3. Spitz, RW., Song, J., Wong, V., Bell, ZW., **Yamada, Y.,** Abe, T., Loenneke, JP. The Effect of Blood Flow Restricted Isometric Forearm Exercise On Discomfort And Force Production. Poster Presentation In: Proceedings of the Annual American College of Sports Medicine. Virtual Experience. 2021.

4. Song, J., Bell, ZW., Wong, V., Spitz, RW., **Yamada, Y**., Abe, T., Loenneke, JP. Effect of Blood Flow Restricted Handgrip Exercise On Exercise-induced Hypoalgesia At Local And Non-Local Muscles. Poster Presentation In: Proceedings of the Annual American College of Sports Medicine. Virtual Experience. 2021.

5. Wong, V., Jessee, MB., Bell, ZW**., Yamada, Y**., Song, J., Spitz, RW., Buckner, S., Mouser, G., Abe, T., Loenneke, JP. The Influence Of Limb Blood Flow On Muscle Growth With Different Resistance Training Protocols. Poster Presentation In: Proceedings of the Annual American College of Sports Medicine. Virtual Experience. 2021.

6. **Yamada, Y**., Kasprizak, R., Shotten, S., Brown, AM., Mathew, A., Cayot, TE., Thistlethwaite, J. Acute Effects of Practical Blood Flow Restriction on Knee Proprioception During Low-Intensity Aerobic Exercise. Poster Presentation In: Proceedings of the Annual American College of Sports Medicine. Virtual Experience. 2020.

7. Wong, V., **Yamada, Y.,** Bell, ZW., Spitz, RW., Viana, R., Chatakondi, R., Abe, T., Loenneke, JP. Is There A Cross Over Effect In Post Activation Potentiation? Poster Presentation In: Proceedings of the Annual American College of Sports Medicine. Virtual Experience. 2020.

8. Spitz, RW., Chatakondi, R., Bell, ZW., Wong, V., Viana, R., Dankel, S., Abe, T., **Yamada, Y.,** Loenneke, JP. The Influence Of Sex And Cuff Width On Discomfort To Blood Flow Restriction In The Lower Body. Poster Presentation In: Proceedings of the Annual American College of Sports Medicine. Virtual Experience. 2020.

9. Bell, ZW., Abe, T., Wong, V., Spitz, RW., Viana, R., Chatakondi, R., Dankel, S., **Yamada, Y.**, Loenneke, JP. Muscle Swelling Following Low Load Blood Flow Restriction Exercise Does Not Differ Between Cuff Widths In The Lower Body. Poster Presentation In: Proceedings of the Annual American College of Sports Medicine. Virtual Experience. 2020.

10. Sunday R, **Yamada Y**, Barnette J, Thistlethwaite J, Cayot TE. Effects of fatiguing practical blood flow restriction exercise on muscle coactivation. Poster Presentation In: Proceedings of the 41st Annual National Strength and Conditioning Association National Conference. Indianapolis, Indiana, 2018.

11. Barnette J, Sunday R, **Yamada Y**, Thistlethwaite J, Cayot TE. Effects of practical blood flow restriction exercise on joint proprioception and muscle fatigue. Poster Presentation In: Proceedings of the 40th Annual National Strength and Conditioning Association National Conference. Las Vegas, Nevada, 2017.

12. Sunday R, **Yamada Y**, Barnette J, Thistlethwaite J, Cayot TE. Effects of fatiguing practical blood flow restriction exercise on muscle coactivation. Poster Presentation In: Proceedings of the Annual Midwest American College of Sports Medicine Conference. Grand Rapids, Michigan, 2017.

CONFERENCE PRESENTATION

GSC (Graduate Student Council) Research and Creative Achievement Symposium Podium Presentation 2022: gave a 7-minute presentation for a panel of judges from one's own or a relevantly similar discipline.
Title: Does Acute Exercise with Blood Flow Restriction and Cooling Affect Interference Control?

Trainology 5th Conference: gave 15 minutes talk to exercise scientists
Presentation Title: Effects of Isometric Handgrip Exercise with and without Blood Flow Restriction on Interference Control and Feelings

GSC (Graduate Student Council) Research and Creative Achievement Symposium Podium Presentation 2021: gave a 15-20-minute presentation for a panel of judges from one's own or a relevantly similar discipline.
Title: Effects of Isometric Handgrip Exercise with and without Blood Flow Restriction on Interference Control and Feelings

Trainology 4th Conference: gave 20 minutes talk to exercise scientists
Presentation Title: Does Acute Exercise with Blood Flow Restriction and Cooling Affect Interference Control?

GUEST SPEAKER

ES 614 Cardiovascular Physiology: gave the overview of our lab related to blood flow restriction to the classmates and the professor.

NTD 239 Sports Nutrition - Service Learning: gave sport nutrition advice and strategy to the Lafayette High School Men's Soccer Team

Damien Moore Memorial Lecture: gave 3-minute presentation for a panel of three judges. Presentation Title: Does Lactate Mediate the Exercise-induced Changes in Interference Control?
First place in master's graduate student category

TEACHING EXPERIENCE

Keywords: Exercise Physiology, Exercise Testing & Prescription, Kinesiology, First Aid/CPR/AED, Athletic Injury Prevention/Care, Motor Learning

Graduate Teaching Assistant, University of Mississippi
Department of Health, Exercise Science, and Recreation Management 2019–present

EL 156 Jogging (class size: 6-17 students)
→a warm-up and cool-down when jogging and a proper jogging/running pace; familiarize with goal setting, nutrition, hydration, and injury prevention when jogging

EL 147 Tennis (class size: 20-24 students)
→design to teach the rules and fundamentals of the game.

ES 347 Kinesiology Laboratory (class size: ~20 students)
→movement basics and analysis, measure of range of motion by using goniometry, postural analysis, gait analysis, functional movement screening.

ES 349 Physiology of Exercise Laboratory (class size: ~30 students)
→assess components of fitness and exercise physiology. Students demonstrate the ability to use and understand the reasons for using such equipment and what they are measuring physiologically.

HP 203 First Aid And CPR- WEB (class size: ~20 students)
→provide the citizen responder with the knowledge and skills necessary in an emergency to help sustain life and minimize the consequences of injury or sudden illness until advanced medical help arrives.

ES 457 Exercise Testing & Prescription Laboratory (class size ~25 students)
→students will learn the methods of exercise testing and prescription following the newest edition of American College of Sports Medicine guideline.

SERVICE

C19 Ambassadors (Spring 2020)
· serve as visible representatives of the University to assist in the implementation of a successful Public Health Education and Awareness Campaign.

AWARD

J. Robert Blackburn Graduate Award in Exercise Science 2022

- This award was given to a graduate student who made the unprecedent record in research and teaching

PROFESSIONAL AFFILIATIONS/MEMBERSHIPS

American College of Sports Medicine (ACSM)
National Member (10/17 – Present)

National Strength and Conditioning Association (NSCA)
National Member (10/16- 10/19)

American Heart Association
Heartsaver CPR AED (05/17 – 05/19)

American Red Cross
Adult, Child, and Baby First Aid/CPR/AED (07/20–07/22)
First Aid/CPR/AED Certified Instructor (08/20–08/22)

SPECIAL SKILLS/PROFICIENCES

Microsoft Office (Word/PowerPoint/Excel)
Google Docs/Slide/Sheet
PeriPedal Software & Near-infrared spectroscopy (NIRS)
ADINSTRUMENTS & Surface-Electrography (sEMG)
Kinovea (Two-dimensional video analysis software)
Tendo Unit (Linear position transducer & software)
Goniometer
Monarch Software & Bike
Hydrostatic Weighing
Anthropometric Measurements [skinfold, circumference measurements, bioelectrical impedance analysis (BIA)]
Blood Lactate Test
Statistical Analysis (SPSS, JASP, and RStudio)
Hokanson Device (Cuffs, Hand-held Doppler probe, Rapid Cuff Inflator)
B-mode Ultrasound
Isokinetic Dynamometer
Handgrip Dynamometer

REFERENCES

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