LEG BLOOD FLOW RESTRICTION DURING ROWING EXERCISE AS A COUNTERMEASURE TO MICROGRAVITY INDUCED DECONDITIONING

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The Supervisory Committee certifies that this ***disquisition*** complies with North Dakota State University's regulations and meets the accepted standards for the degree of

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ABSTRACT

BACKGROUND: Prolonged exposure to microgravity leads to a progressive loss in muscular strength, endurance and aerobic capacity ($VO_{2)}$. Rowing exercise combined with blood flow restriction (BFR) could be a supplemental countermeasure to maintain pre-flight muscle and VO_2 function during prolonged spaceflight missions. **METHODS:** Twenty moderately trained male participants completed five sets of rowing exercise with and without BFR. Heart rate (HR), blood pressure (BP), surface muscle electromyography (sEMG), whole blood lactate ($[La^-]_b$), and rate of perceived exertion (RPE) were measured. **STATISTICAL ANALYSES:** Repeated measures ANOVAs were used to analyze HR, BP, $[La^-]_b$ and SEMG and a paired sample t-test was used to analyze RPE. **RESULTS:** HR and RPE showed significant increases during BFR compared to CON ($F(2,38) = 5.220$, $P = .010$) and ($t(19) = -5.878$, $P < .001$), respectively. **CONCLUSION:** Exercise intensity and cuff inflation pressure used was sufficient to elicit increased cardiovascular responses.

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DEDICATION

I would like to dedicate this research to my family and friends who have always supported me throughout my education. I would like to thank Nathan Dicks and Shane McCullough for greatly assisting with data collection and analysis. I would also like to thank my committee members: Dr. Katie Lyman, Dr. Bryan Christensen, and Dr. Daniel Ewert for all their support and assistance. Finally, I would like to thank my advisor, Dr. Kyle Hackney for supporting and guiding me through the entire research process.

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LIST OF ABBREVIATIONS

ANOVA……..……Analysis of Variance.

ARED…...……..……Advanced resistance exercise device.

BF…...……..Biceps Femoris.

BFR……...…….Blood flow restriction.

BP……...……...……Blood pressure.

COLBERT…….....……Combined operational load bearing external resistance treadmill.

CON/BFR……..……...Control and BFR session.

CRT……...……...……Capillary refill time.

DVT……...……....Deep venous thrombosis.

HR.....……Heart rate.

HRP……...……..Human Research Program.

IRED ……...……...……Interim resistance exercise device.

ISS…..…….…..International Space Station.

$[La^-]_b$……..…….Whole Blood Lactate.

LBNP……...…….....……..Lower body negative pressure.

NASA……...……....National Aeronautics and Space Administration.

OI...……...……Orthostatic intolerance.

PARQ+……..……...…....Physical Activity Readiness Questionnaire.

Q……...…….Cardiac output.

RPE……...……..……Rate of perceived exertion.

sEMG……...…..……Surface electromyography.

SKU……...……..……..Standard Kaatsu Units.

SV……...……...…….Stroke volume.

TVIS ……..…..……Treadmill with vibration isolation and stabilization.

VL……..…….....Vastus Lateralis.

VO_{2peak}…...……...….Peak oxygen utilization during exercise.

VO_{2max}…...……Maximum oxygen utilization during exercise.

W..……...……Watts.

1G...……...…1 unit of Gravity.

LIST OF SYMBOLS

*…… denotes significance at $p < 0.05$

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CHAPTER I. INTRODUCTION

Prolonged exposure to microgravity leads to a progressive loss in muscular strength, endurance, and aerobic capacity (Antonutto & Prampero, 2003; Bishop et al., 1999; Buckey et al., 1996; Downs, Moore, Lee & Ploutz-Snyder, 2015; Ploutz-Snyder, Ryder, English, Haddad & Baldwin, 2015; Fomina et al., 2004; Hackney, Everett, Scott & Ploutz-Snyder, 2012; Hargens & Watenpaugh, 1996; Hawkey, 2003; Moore et al., 2014; Nicgossian, Bungo & Leach-Huntoon, 1991; Tesch, Pozzo, Ainegren, Swaren & Linnehan, 2013). This microgravity-induced deconditioning is detrimental to the health and performance of crewmembers, as well as overall mission success. Countermeasures are in place on board the International Space Station (ISS) to combat in-flight deconditioning; however, these current methods do not mitigate deconditioning entirely. As much as a fifth of muscle mass is lost during the first four months in space; additionally, peak oxygen consumption (VO_{2peak}) and left ventricular mass decrease early in flight by ~17% and ~ 12% respectively (Hawkey, 2003; Moore et al., 1985; Perhonen et al., 2001). Emergency mission egress tasks may require normal ambulatory participants to work at intensities at 85% of maximum heart rate. Even a relatively small decrease in VO_{2peak} (e.g., 10%) can greatly impact an astronaut's ability to meet these high-energy demands (Bishop et al., 1999).

The National Aeronautics and Space Administration (NASA) created the Human Research Program (HRP) to investigate and mitigate high risk outcomes that impede crewmember health and performance. Two major risks identified by the HRP include the risk of reduced physical performance capabilities due to reduced aerobic capacity and the risk of impaired performance due to reduced muscle mass, strength, and endurance. Gaps of knowledge within these risks include the development of effective exercise programs for the maintenance of

muscle function and VO_2 standards, and the development of pre-flight, in-flight, and post-flight evaluations to determine if muscle function and VO_2 standards are being met during missions. Prior research and study acknowledges that VO_{2peak} and muscle function decline during spaceflight, but can be mitigated with in-flight exercise (Bishop et al., 1999; Downs et al., 2015; Ploutz-Snyder et al., 2015). However, performance decrements are still observed despite current countermeasures, and research into advanced in-flight exercise protocols is necessary to identify activity thresholds and exercise prescriptions for crewmembers.

The current exercise countermeasures on board the ISS must be completed on separate devices, increasing the time required to meet exercise prescriptions (Downs et al., 2015; Hawkey, 2003; Ploutz-Snyder et al., 2015). Two notable pieces of equipment are the Advanced Resistance Exercise Device (ARED) and the Combined Operational Load Bearing External Resistance Treadmill (COLBERT). The former allows for up to 600 lbs. of eccentric-concentric resistance strength training, while the latter provides astronauts with aerobic training by reaching up to 12 mph. Both devices help to mitigate microgravity-induced side effects, but they do not counter them entirely (Downs et al., 2015; Hawkey, 2003; Ploutz-Snyder et al., 2015). Additionally, these large pieces of equipment require preparation before use and reduce available space on board the ISS. Therefore, advanced in-flight exercise protocols and equipment are required to ensure astronauts are capable of completing exercise prescriptions efficiently.

The physiological adaptations to prolonged microgravity exposure affect crewmembers both during and after spaceflight missions. Orthostatic intolerance is one of the earliest and most consistent findings associated with microgravity induced deconditioning (Nicgossian et al., 1991). Orthostatic intolerance is caused by the headward shift of fluids in the body when exposed to microgravity. Side effects manifest upon returning to the influence of gravity, and

include: increased heart rate, decreased blood pressure, and dizziness (Hargens & Watenpaugh, 1996). Previous countermeasures for orthostatic intolerance involved pressurized cuffs and equipment that would reduce pressure around the legs and promote the flow of blood and fluid to the lower extremities. During past missions, these lower body negative pressure (LBNP) devices were used with increasing practice to prepare crewmembers for reentry into earth's gravity. However, these devices were bulky in size and restricted astronaut movement (Hackney et al., 2012; Hawkey, 2003).

Blood flow restriction (BFR) is a novel exercise intervention that involves the application of inflated tourniquet cuffs that restrict venous blood flow during exercise. Despite being a novel form of exercise intervention, BFR has been shown to elicit rapid and progressive gains in muscular strength, endurance and aerobic capacity (Abe, Kearns & Sato, 2006; Abe et al., 2010; de Oliveira, Caputo, Corvino & Denadai, 2016; Renzi, Tanaka & Sugawara, 2010; Sakamaki & Abe, 2011; Sugawara, Tomoto & Tanaka, 2015; Wernbom, Jarrebring, Andreasson & Augustsson, 2009). Two widely used forms of BFR are the Kaatsu and Delfi training cuffs. The former has been widely used in Japan and the ladder is showing increasing use in clinical populations. BFR allows participants to train at lower-submaximal (30% of one repetition maximum (1RM)) intensities yet receive the benefits as if they had trained at higher-submaximal (70% 1RM) intensities. For example, a study by de Oliveira et al. (2016) identified low-intensity interval BFR training as the only mode of training capable of simultaneously improving aerobic fitness and muscular strength when compared to low-intensity interval training without BFR, high-intensity interval training, and combined high-intensity interval training and BFR. The restriction of venous blood flow lowers heart and stroke volume thus, increasing heart rate to meet energy demands (Renzi et al., 2010). Allowing crewmembers to train at lower intensities

and still elicit a cardiac response capable of maintaining their pre-flight VO_{2peak} and muscular strength. Additionally, restricted venous blood flow has been shown to help maintain central and peripheral hemodynamics during short-term spaceflights (Fomina et al., 2004). As mentioned, previous methods to mitigate post-flight orthostatic intolerance (LBNP devices) were bulky and restricted movement. BFR exercise may prove to be a superior alternative to past endeavors as the training cuffs are smaller and less restrictive on movement.

Another novel form of instrumentation gaining popularity with NASA are rowing ergometers. The ARED and COLBERT devices offer the capabilities to complete either resistance training or cardiovascular training, but not both simultaneously (Downs et al., 2015; Hargens & Watenpaugh, 1996). Effective musculoskeletal and aerobic training can be performed on a rowing ergometer without significantly increasing hardware mass or compromising desired physiological responses (Tesch et al., 2013). The seated nature of rowing exercise appears to promote venous blood return and elicits smaller heart rate responses when compared to treadmill exercise of similar intensity (Yoshiga & Higuchi, 2002), but higher heart rate responses when compared to cycling exercise of similar intensity (Rosiello, Mahler & Ward, 1987). The heart rate response from rowing exercise is similar to the response recorded during long-term exposure to microgravity (Antonutto & Pampero, 2003). BFR combined with rowing exercise could be a supplemental countermeasure that requires minimal equipment and offers the potential to maintain pre-flight strength and VO_{2peak} during prolonged spaceflight.

The purpose of this research project was to determine the acute physiological effects of leg blood flow restriction during low-intensity rowing exercise. Our aim was to begin a new line of research which addresses current barriers and to progress by adding knowledge to the gaps identified by the HRP such as: develop the most efficient and effective exercise program for the

maintenance of VO_2 standards and muscle function; and identify and validate exploration countermeasure hardware for the maintenance of VO_2 standards and muscle function. Research findings will potentially add to current literature on exercise prescriptions to prolong human exposure during exposure to microgravity, and potentially transcend the use of BFR technology in other spinoff populations that may benefit such as: elderly sarcopenic and dynapenic, elite-athletes, and clinical recovery patients from certain conditions (Abe et al., 2010; Park et al., 2010; Tennent et al., 2016; Ohta et al., 2002).

CHAPTER II. LITERATURE REVIEW

Prolonged exposure to microgravity leads to incremental losses in cardiovascular and musculoskeletal systems (Antonutto & Pampero, 2003; Bishop et al., 1999; Buckey et al., 1996; Downs et al., 2015; Ploutz-Snyder et al., 2015; Fomina et al., 2004; Hackney et al., 2012; Hargens & Watenpaugh, 1996; Hawkey, 2003; Moore et al., 2014; Nicgossian et al., 1991; Tesch et al., 2013). These negative effects can be seen in the cardiovascular system within the first 24 hours of spaceflight (Hargens & Watenpaugh, 1996; Nicgossian et al., 1991), and in the musculoskeletal system within as little as 4 days in space (Hawkey, 2003). Exercise has been shown to help reduce the negative effects of microgravity; however, on its own, it does not negate them entirely. Deconditioning caused by microgravity is progressive and associated with the time spent in the unique envirnment (Nicgossian et al., 1991). To ensure astronaut safety and overall mission success, additional exercise protocols must be researched and implemented (Hawkey, 2003).

NASA

NASA continues to push the boundaries of space exploration by identifying and addressing the risks of human space exploration. In October 2005, the HRP was established at the Johnson Space Center, Houston, Texas. The goal of the HRP is to establish human health and performance countermeasures, knowledge, technologies, and tools to enable safe, reliable, and productive human space exploration (Human Research Roadmap). Data collected and analyzed from past and current spaceflight missions help the HRP achieve their goal.

Physiological Adaptations to Spaceflight

The human body is not capable of withstanding the harsh environment of space unassisted. However, even with assistance the body still succumbs to detrimental physiological

changes (Hackney et al., 2012). These adaptations can be the single greatest detriment to a crewmember's ability to perform mission-critical tasks while in spaceflight (Moore et al., 2014). The most notable of these changes are decreases in the cardiovascular and musculoskeletal systems (Downs et al., 2015; Ploutz-Snyder et al., 2015); with evidence suggesting that as mission length increases, so do the physiological impacts (Nicgossian et al, 1991). The *Apollo 15* mission had reports of cardiac arrhythmia, all *Gemini* and *Apollo* crewmembers experienced orthostatic intolerance (OI), and findings from *Skylab* indicate significant loss of muscle and bone mass, accompanied by a reduction in muscle strength and endurance (Hawkey, 2013).

1G Environment

Many of these adaptations are due to the removal of gravity upon the body in space. On earth the human body is constantly under the effect of Earth's gravity. This constant force is known as one unit of gravity (1G). Upon entering the microgravity of space, there is a headwards shift of bodily fluids as the mechanisms that normally act to counter the pooling of bodily fluids act unopposed. Volume sensors, located in the upper body, interpret the shift as an increase in body fluid volume; and thus, attempt to initiate increased fluid loss. Decreased thirst, increased evaporation and diuresis are all ways the body attempts to eliminate the perceived "fluid overload" (Hawkey, 2013). Astronauts adapt to these new conditions after a few days in space. However, upon returning to earth, the adaptations leave the spacefarer with less protection against orthostatic stress (i.e., dizziness, fainting) (Hawkey, 2013).

Orthostatic Intolerance

OI is quite common in returning astronauts from spaceflight and is commonly manifested by increased heart rates and decreased blood pressures (Nicgossian et al., 1991). OI is caused by the shift in bodily fluid due to the microgravity environment of space. In the early days of

spaceflight, bodily fluid in the chest, and as much as one liter from each leg, is shifted upwards in the body. The shift happens rapidly during the first day of spaceflight, concluding after six to ten hours. Increased fluids in the head and neck lead to congested sinuses, puffiness of the eyelids, and engorgement of the superficial veins (Hawkey, 2013).

Cardiovascular Deconditioning

Microgravity can cause detrimental changes to cardiovascular health. Perhonen et al. (2001) demonstrated that left ventricular mass decreased by ~12% after short-duration spaceflight. This reduction in chamber volume can be attributed to the chronically reduced preload (cardiac filling pressure) caused by microgravity (Hargens & Watenpaugh, 1996). With less blood returning to the right atrium, the left ventricle is unable to pump blood volumes consistent under normal conditions, resulting in decreased stroke volume (SV). Using data collected during U.S. manned spaceflights from 1962-1985, Nicgossian et al. (1991) found that heart rate of crewmembers in the standing position increased from pre-flight to post-flight measurements. With reduced stroke volume heart rate must increase to meet energy demands and maintain cardiac output (Q).

Musculoskeletal Deconditioning

Prolonged stays in microgravity lead to constant changes in the musculoskeletal system (Downs et al., 2015; Hawkey, 2013; LeBlanc, Rowe, Schneider, Evans & Hedrick, 1995; Ploutz-Snyder et al., 2015). *Skylab* findings and biomedical data from manned space missions have indicated a significant loss of muscle and bone mass; accompanied by decreases in lower leg circumference and muscular strength and endurance. These results are directly caused by the weightlessness of gravitational unloading while in space. Similar results can be seen in both short duration missions as well as longer duration, and it is typical for astronauts to lose as much

as a fifth of their muscle mass during a four month stay in space. As with cardiovascular detriments, this effect appears to be progressive, with no definite indication as to the outcome of missions longer than fourteen months (Hawkey, 2013).

These effects are a crucial topic when planning and enacting long term human exploration. An example being a manned mission to Mars, which using current rocket technology would take up to three years round-trip. With our current understanding of the stress expressed on the human body during spaceflight, there is no guarantee that astronauts reaching Mars would be able to complete the basic mission tasks upon arrival. Therefore, countermeasures must be developed to reduce the effects of microgravity on the human body.

Countermeasures to Microgravity Induced Deconditioning

Since the beginning of our exploration into space there have been numerous methods developed to maintain astronaut health. The major methods being: assistive devices, dietary and pharmacological supplements, and exercise.

Assistive Devices

From the beginning of *Skylab* missions, LBNP devices were used to help reduce the effect of microgravity on the cardiovascular system. LBNP suits were worn over the legs and help to reverse the headwards shift of fluid by reducing pressure around the legs. Early LBNP devices were bulky and cumbersome, however the Chibis vacuum suit, developed in the former Soviet Union, was flexible and less bulky than other devices. While preparing crews for reentry to earth's gravity, LBNP sessions were conducted regularly and with increased usage (Hawkey, 2013).

To help reduce muscle loss during space flight, cosmonauts have worn special elasticated suits known as the penguin suit. With rubber bands woven into the fabric of the suit the penguin

suit was worn throughout the day, and during appropriate exercise sessions. The suit can generate up to seventy percent of earth body weight on the musculoskeletal system – compensating for the absence of gravity. However, even these suits are uncomfortable and reduce mobility (Hawkey, 2013).

Dietary and Pharmacological Supplements

Supplements have been used to help counter bodily fluid imbalance and cardiovascular deconditioning caused by microgravity. Fluids and salts have been used to rehydrate crews, saline solutions, ingested before reentry, are used to decrease orthostatic intolerance, and mineral supplements are consumed to reduce bone loss (Hawkey, 2013). These interventions have had success in reducing the impact of microgravity on the human body, however, they are all reactive solutions and are mainly used before reentry into earth's gravitational field. Other methods must be utilized to proactively counter these negative physiological adaptations during prolonged spaceflight.

Six-Degree Head Down Tilt

Current research aiming to counter microgravity induced deconditioning through exercise primarily use bed rest with a 6-degree head down tilt as an earth-based analog to simulate the detrimental physiological effects of microgravity (Hackney et al., 2012; Hastings et al., 2012; Hawkey, 2003; Murach et al., 2018). Concurrent rowing and resistance exercise training during 5-weeks of bed rest with 6-degree head down tilt was capable of preventing the cardiac atrophy and stiffening that occurs with prolonged bed rest (Hastings et al., 2012). Additionally, aerobic and resistance exercise completed on a novel concurrent flywheel exercise device (Murach et al., 2018; Tesch et al., 2010) during 70 days of bed rest with 6-degree head down tilt was capable of maintaining key myocellular characteristics in the vastus lateralis (VL); however, further

refinement of the exercise protocol is necessary to also effect the soleus (Murach et al., 2018). These findings demonstrate that rowing exercise can maintain cardiovascular function during prolonged bed rest but requires additional exercise supplementation and equipment to simultaneously maintain muscle function.

Exercise During Spaceflight

Currently, exercise is the most widely used method for countering the negative effects of microgravity on the human body. However, during early spaceflight missions (*Mercury*, *Gemini* and *Apollo* 1961 – 72) this was not the case. During these early missions, the small size of spacecraft, combined with short mission duration, did not yield adequate conditions to perform regular exercise regimens. It was not until later *Apollo* and *Gemini* missions that an exercise device was used. This rudimentary device was primarily used to relieve astronaut discomfort caused by both weightlessness and immobilization within the small craft; and it was during the *Apollo* missions that deconditioning first became apparent (Hawkey, 2013).

With the development of *Skylab* (1973-74) and the *International Space Station* (ISS) (2001) astronauts were given more room to move freely and maneuver. With more room, astronauts were now capable of using exercise equipment similar to what can be seen on earth. Treadmills, cycle ergometers and other exercise equipment have been utilized on both shuttle missions and the *ISS* (Hawkey, 2013; Tesch et al., 2013). Some of the earliest implementations aboard the *ISS* were the treadmill with vibration isolation and stabilization (TVIS) and the interim resistive exercise device (IRED) – later replaced with the Combined Operational Load Bearing External Resistance Treadmill (COLBERT, 2010) and the Advanced Resistance Exercise Device (ARED, 2008), respectively (Downs et al., 2015). The TVIS resembled basic treadmills seen on earth. Limited to 6-7 mph, it offered the possibility of generating 1G

equivalent loads on the lower extremities while stressing and stimulating the musculoskeletal system. In 2010, the COLBERT, technically named the Treadmill 2, allows astronauts to run up to 12 mph with higher percentages of body weight loading due to improvements in the harness comfort. The IRED was used to replicate up to sixteen different exercises that under normal conditions are performed using free weights. Provisional data suggested that the IRED could prove to be as effective as free weight training (Hawkey, 2013) and in 2008 it was surpassed by the ARED. The ARED is capable of concentric loading up to 600 lbs., an eccentric ratio of ~90%, and constant force throughout the range of motion. Marked improvements when compared to its predecessor which offered only 300 lbs., an eccentric to concentric ratio of only 60-80% and no constant force throughout the range of motion. (Downs et al., 2015).

The capabilities of exercise equipment on board the ISS has grown substantially. However, while the addition of the COLBERT and ARED exercise devices has helped reduce the negative effects of microgravity on astronauts, the ability to use these apparatuses during long term shuttle missions, like a trip to Mars, can be difficult due to their size and available shuttle space (Tesch et al., 2013). Not only that, it has been shown that following the prescribed training protocol while in microgravity still does not fully counter the negative effects of weightlessness. Russian astronaut Valerie Polyakov still suffered significant deterioration during his fourteen month stay on *Mir*, despite exercising constantly (Hawkey, 2013). Therefore, future exercise countermeasures will need to both implement additional exercise protocols and exercise equipment that can fit onboard future shuttle crafts and stations.

Blood Flow Restriction

Blood flow restriction (BFR) is a novel exercise modality that is becoming increasingly more popular. BFR uses exercise cuffs or bands to restrict venous blood flow during exercise.

The restriction of venous blood flow limits stroke volume and compensatory increases in heart rate during exercise (Sugawara et al., 2015). Recent studies have shown that BFR exercise training can result in significant and rapid increases in muscle hypertrophy (Abe et al., 2006; Abe et al., 2010) and aerobic capacity (Park et al., 2010). While the exact reason for these rapid results is still unknown, the results produced are similar to the results gained through high-intensity resistance training programs. This unique characteristic of BFR training allows substantial muscle hypertrophy to occur even when training at exercise intensities as low as 20% of 1 RM (Abe et al., 2006; Abe at el., 2010). Therefore, low-intensity exercise (i.e. walking) with BFR may provide a more favorable alternative to high-intensity exercise to increase muscle size, strength and functional capacity (Staunton, May, Brandner & Warmington, 2015). Much of the research done using BFR has been acute training studies lasting up to 6 weeks as the long-term effects of BFR combined with exercise are still not established. However, BFR research has been done in a variety of populations, including: the elderly, elite-athlete, and clinical recovery patients (Abe et al., 2010; Park et al., 2010; Tennent et al., 2016; Ohta et al., 2002). Two primary exercise modalities used in combination with BFR are resistance exercise and aerobic exercise.

Safety Concerns Using BFR

Safety concerns using BFR have arisen due to the cuff inflation and restriction of venous blood flow during exercise. Numerous reviews have shown that BFR exercise has possible side effects but does not increase risk for cardiovascular disease. A nationwide review of safety of BFR practitioners reported possible side effects and prevalence during BFR exercise: bruising (mostly in arms) – 13.1%, temporary numbness – 1%, thrombosis – 0.055%, and pulmonary embolism – 0.008% (Nakajima, 2006). Another review reported: thrombosis - < 0.06%, rhabdomyolysis - < 0.01%, and pulmonary embolism - < 0.01% (Vanwye, Weatherholt &

Mikesky, 2017). Despite low reported rates of thrombosis and pulmonary embolism, the development of blood clots during BFR continues to be a concern. Recent studies looking into blood markers post-BFR exercise has shown no increase in clot formation markers (Clark et al., 2011; Madarame et al., 2010; Madarame, Kurano, Fukumura, Fukuda & Nakajima, 2013; Nakajima et al., 2007). Additionally, increased cardiovascular responses seen during low-intensity BFR exercise are lower than those seen during traditional high-intensity exercise. Therefore, low-intensity BFR exercise poses no greater threat to participant safety than traditional high-intensity exercise (Horiuchi & Okita, 2012; Hughes, Paton, Rosenblatt, Gissane & Patterson, 2017; Loenneke, Wilson, Wilson, Pujol & Bemben, 2011).

BFR Combined with Aerobic and Resistance Exercise Training

Findings demonstrate that BFR when used in combination with resistance exercise can lead to increased muscle cross-sectional area and muscle strength (Abe et al., 2006; Abe et al., 2010; Neto et al., 2016). Additionally, during a 2-week walk training study with BFR, maximal oxygen utilization (VO_{2max}) increased by 11.6% in college male athletes (Park et al., 2010). Studies have shown that the decrease in venous blood return during BFR training causes a resulting decrease in heart SV) and a compensatory increase in heart rate (HR) (Sugawara et al., 2015). This decrease in SV is likely caused by the restricted venous return of blood due to the inflated cuff. BFR exercise is also a potential countermeasure for OI. Cuffs worn on the upper thighs during space flight have been shown to help maintain central and peripheral hemodynamics and mitigate the flow of bodily fluids headwards (Hackney et al., 2012)

Blood flow restriction offers great potential to counter the negative physiological effects of microgravity. With the potential to prevent muscle loss, and minimize OI upon reentry to earth's gravity, BFR is an ideal intervention to counter two of the most common side-effects

experienced by astronauts (Hawkey, 2013). Equipment needed to complete BFR exercise are also very minimal when compared to previous methods (COLBERT, ARED), making it an ideal exercise protocol during long during space flight missions where future mission craft space will be minimal.

Rowing

NASA's strategic plan has identified the need for integrating features to allow both resistance and aerobic exercise training to be carried out on a single exercise apparatus (2014 NASA Strategic Plan). Rowing ergometers offer the capability to perform strength and aerobic exercise simultaneously. Due to the large size of the current exercise equipment on board the ISS, NASA is seeking new, innovative exercise protocols and equipment to help establish and maintain VO_2 standards during spaceflight. Future long duration spaceflight missions will require compact, lightweight equipment to capable of utilizing the small available volume on future space crafts. (Downs et al., 2015; Ploutz-Snyder et al., 2015). Effective musculoskeletal and aerobic training can be performed on a rowing ergometer without significantly increasing hardware mass or compromising desired physiological responses (Tesch et al., 2013); making rowing an ideal form of exercise to meet NASA's needs. muscle function and VO_2 standards during long duration spaceflight missions.

Physiological Responses to Rowing

The seated position and involvement of more muscles during rowing exercise facilitates venous return and is accompanied by a higher VO_2 response when compared to running at the same relative intensity. Enhanced venous return elevates central blood volume and lowers HR response due to increases in stroke volume by the Frank-Starling mechanism (Yoshiga & Higuchi, 2002). Interestingly, when compared to cycle ergometers, at the same metabolic rates,

there were no significant differences in Q when using the cycle and rowing ergometers (Rosiello et al., 1987). Additionally, Horn, Ostadal & Ostadal (2015) has shown that when compared to cycling, rowing exercise lead to a more extensive stimulation of cardiac contractility and/or decreased peripheral vascular resistance.

BFR Combined with Rowing

At this time, a study using BFR and rowing exercise has not been initiated. Our goal is to establish the cardiovascular, musculoskeletal, and metabolic differences between rowing exercise with and without BFR intervention as preliminary evidence of efficacy.

CHAPTER III. METHODS

This experimental study measured participants' heart rate (HR), blood pressure (BP), leg muscle surface electromyography (sEMG), rate of perceived exertion (RPE), whole blood lactate ($[La^-]_b$), and peak oxygen consumption (VO_{2peak}) during a maximal exercise session, a control exercise session and a blood flow restriction (BFR) intervention session. The purpose of this study was to identify the acute physiological cardiovascular, musculoskeletal, and metabolic changes when using leg BFR during low-intensity rowing exercise. **Research Question:**

1. What are the acute cardiovascular, musculoskeletal, and metabolic effects that occur when using leg blood flow restriction during low-intensity rowing exercise?
    - **a.** What differences are seen in:
        - **i.** Heart rate and blood pressure?
        - **ii.** Muscle activation via surface electromyography?
        - **iii.** Whole blood lactate?
        - **iv.** Rate of perceived exertion

Participants

Inclusion

The participants in this study were 20 males who were healthy, regularly active, and 18-40 years of age. This sample size was selected based on similar study sizes (Abe et al., 2006; Abe et al., 2010; Park et al., 2010; Rosiello et al., 1986). Participants completed a Physical Activity Readiness Questionnaire (PARQ+) to determine if they were healthy and ready to participate in the exercise. To be considered, participants were required to have participated in a minimum of 100 minutes of aerobic and/or resistance exercise training, within a seven-day period, for at least the last six months. Before acceptance into the study, participants were

informed of the research procedures that would be used and briefed on what their responsibilities during testing would be. Participants were given the opportunity to ask any questions or address any concerns that they had with the research protocol. Participants agreeing to continue with the study were presented with an informed consent form to voluntarily sign.

Exclusion

The participants' PARQ+ was reviewed to determine if they were healthy and ready for the required exercise. Participants who answered 'yes' to any of the questions on the PARQ+ were excluded from the study pending review of their answer. Any participants with, or at risk for, hypertension or hypotension, were excluded. The National Institute of Health and American Heart association have identified being "at risk for hypertension" as any blood pressure ≥120 for systolic and ≥80 for diastolic; and hypotension as any blood pressure <90 for systolic and <60 for diastolic. Furthermore, any individuals with a history of lower back, neck, or leg pain; and/or a history/family history of cardiovascular disease, had sickle cell anemia, recent surgery, a history of blood clots or exertional rhabdomyolysis (breakdown of muscle) were excluded from the study. Additional exclusions included: individuals with a calculated body mass index (weight/height^2) of 30 kg/m^2 or greater, those with prior ligamentous, bony or other soft tissue reconstruction to the lower-extremity, a history of deep venous thrombosis (DVT), peripheral vascular disease (narrowing or blockage in a blood vessel), diabetes, acute fracture, tumor, or infection, being an active smoker, a user of illegal drugs, having an implanted medical device, or the inability to consent. Screening for illicit drug use was completed on the Informed Consent Form. Accepted participants were then scheduled for two exercise trial sessions: VO_{2peak} and CON/BFR.

To assist with recruitment and reduce participant dropout, participants received monetary compensation for their participation. Participants received $10.00 after completing the first session (VO_{2peak}) and $10.00 upon completing the second session (CON/BFR) – for a total of $20.00. Any participants that dropped out of the study before completion received any compensation that they had earned up to that point. A call for participants was posted using the North Dakota State University Listserve email announcements and flyers were posted at local gyms in the Fargo/Moorhead area to help recruit participants with possible rowing experience. All procedures and instruments used during the study were approved by the North Dakota State Institutional Review Board.

Instrumentation

Before being accepted into the study, potential participants filled out the PARQ+ survey. Participants that met the study criteria voluntarily signed an informed consent form and acknowledged that they understood the study procedures, what was expected of them, and any potential risks. To measure participant height and body mass a Stadiometer (Seca 213, Chino, CA) and an Eye level scale (Detecto, Webb City, MO) were used. A Polar heart rate strap monitor and wrist watch (Polar Electro, Kempele, FIN) or a Garmin heart rate monitor (Garmin, Olathe, KS) were used to measure participant HR at rest and during exercise. Blood pressure was measured ~5 minutes before and after exercise testing using a manual sphygmomanometer cuff and stethoscope (American Diagnostic Corporation, Hauppauge, NY). Participant VO_{2peak} was determined using the TrueOne 2400 Parvo metabolic cart (Parvo Medics, Sandy, UT) and completed on the Concept2 Model E rowing ergometer (Concept2, Morrisville, VT). Rate of perceived exertion (RPE) was measured using the Borg 6-20 scale. Surface muscle electromyography (sEMG) was collected using self-adhesive monitoring electrodes and an EMG

MP150 machine (Biopac Systems, 3M Healthcare, London, Ontario, Canada). $[La^-]_b$ levels were collected using a handheld Lactate Plus (NOVA Biomedical, Waltham, MA) blood lactate analyzer. During the BFR portion of the CON/BFR session, Kaatsu brand training cuffs (Kaatsu Global, Inc., Japan) were used to restrict venous blood flow.

Obesity

Researchers used the SECA Stadiometer and Tanita Body Composition Analyzer Scale to measure height and body mass for each participant. From those measurements, Body Mass Index (BMI) was calculated (weight/height^2). Those over a BMI of 30 kg/m^2, which was classified as obese, were excluded from the study (Pescatello, Arena, Riebe & Thompson, 2014).

Muscle Surface Electromyography

Muscle sensor sEMG electrodes (Red Dot 2560 monitoring electrodes, 3M Healthcare, London, Ontario, Canada) were placed on the right leg VL and BF muscles to measure sEMG during exercise. Areas of placement were shaved with a hand razor and carefully cleaned with ethanol before electrode placement. Electrodes were placed on the medial portion of the VL and the BF muscles with a 4.0 cm interelectrode distance. Electrodes were placed approximately 10-15 cm above the proximal border of the patella. These placings are like those used by Wernbom et al. (2009) and allow for the application of the BFR training cuffs along with freedom of movement during exercise testing. Data were collected and stored using the sEMG MP150 machine (Biopac Systems Inc., Goleta, CA) and saved under the participant's number before being transferred onto an encrypted hard-drive.

Whole Blood Lactate Testing [La^-]

Whole blood lactate was measured at rest and five minutes after exercise using a handheld Lactate Plus (NOVA Biomedical, Waltham, MA) blood lactate analyzer. Participants

selected a finger to be pricked and cleaned with alcohol wipes so that a drop of blood can be collected on the analyzer stick. Researchers wore wear protective gloves and clothing to prevent any transfer of fluids. ~30 µl of blood was collected ~5 min pre- and post-exercise for all three exercise sessions (Total: 6 finger sticks, ~180 µl of blood over entire study). A Band-aid was placed on the stuck finger and all disposable materials were discarded in the biohazard bins in the research lab.

Heart Rate & Blood Pressure

Participants' HR was monitored using a Polar heart rate strap monitor (Polar Electro, Kempele, FIN) during the VO_{2peak} session and a Garmin heart rate strap monitor (Garmin, Olathe, KS). Participants' BP was measured using a manual sphygmomanometer and stethoscope (American Diagnostic Corporation, Hauppauge, NY). The sphygmomanometer was snuggly wrapped around the left arm and slowly inflated until pulse rate could be heard through the stethoscope placed on the antecubital space of the arm. The sphygmomanometer was then inflated to ~10 mm Hg above the last beat heard and then slowly deflated. Systolic and diastolic measures were recorded based on the first and last beats heard while deflating the sphygmomanometer cuff. Blood pressure measurement protocols were followed according to The Sixth Report of The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (National Institute of Health, 1997). Baseline and post-exercise HR and BP were measured after five minutes of resting and roughly five minutes post-exercise. Exercise HR was monitored throughout exercise and the peak HR was recorded.

Orthostatic Hypotension Screening

Participant's blood pressure was measured both while they were sitting and while they were standing to compare measurements. If the participant had a drop of 20 millimeters of

mercury (mmHg) in their systolic blood pressure, or a drop of 10 mmHg in their diastolic blood pressure after two minutes of standing up, or if standing caused signs and symptoms of lightheadedness or dizziness, the participant was excluded from the study.

Rate of Perceived Exertion

Perceived exercise intensity was measured using the Borg 6-20 Rating of Perceived Exertion (RPE) scale. This form of evaluation has been used in prior studies to determine participants' perceived exercise intensity (Wernbom et al., 2009). During the last 30 seconds of each exercise set, participants were shown a scale from 6 – 20 and asked to rate their level of exertion. A six on the scale equates to no exertion and a 20 on the scale equates to maximal exertion.

Kaatsu Training Cuffs

The restriction of venous blood flow was accomplished by using Kaatsu Nano exercise training cuffs (Kaatsu Global, Inc., Japan). The training cuffs were applied around the proximal portion of the legs, and during exercise were inflated according to the Kaatsu training protocol. Prior studies have identified Kaatsu brand training cuffs as a reliable method for attaining rapid gains in muscle strength, endurance and cardiovascular function (Abe et al., 2006; Abe et al., 2010; Park et al., 2010; Renziet al., 2010; Sakamaki & Abe, 2011; Wernbom et al., 2009). To familiarize participants with the feeling of BFR they were taken through a traditional Kaatsu Cycle which involves 8 rounds of cuff inflation. Each round had the cuff inflated for 20 seconds followed by five seconds of cuff deflation. The Kaatsu cycle began at an inflation of 40 Standard Kaatsu Units (SKU), which are approximately equivalent to mmHg. After the five seconds of deflation the cuff pressure increased by ~15-20 SKU for each subsequent round, ending at ~160 SKU. To find optimal SKU for exercise, researchers measured the individual's capillary refill

time (CRT), or the time in seconds taken for color to return to an external capillary bed. CRT was checked by applying pressure to the quadriceps, just above the knee, to cause blanching during cuff inflation. A CRT of ~3 seconds indicates optimal SKU pressure for exercise; pressure was continually increased by ~15-20 SKU until optimal SKU was reached. However, to ensure participant safety an individualized training cuff inflation limit was set for each participant at 1.3 x their resting systolic BP. During the BFR portion of the CON/BFR session the training cuffs remained inflated throughout the entire exercise.

Procedures

All participants completed the two exercise sessions in order: VO_{2peak} followed by Control (CON)/BFR. Each session was separated by at least 48 hours. Sessions took place on Monday through Friday in the Human Performance Lab of the Bentson Bunker Field House. Times for sessions were dictated based on participants' and researchers' schedules. Attempts were made to ensure participants completed exercise at the same time of day for each session. Data collection began November 27th, 2017 and ended March 1st, 2018.

VO_{2peak} Session

Participants reported to the research lab in the Bentson Bunker Fieldhouse. Upon arrival, they were presented with the screening forms and consent form for the study. Once participants were screened, consented to participate, and signed the consent form, their height and weight was measured to calculate BMI. Afterwards, participants remained seated for roughly five minutes so that resting HR and BP could be taken; and screening for hypertension/hypotension could be performed. Participants were then familiarized with the Concept2 Model E rowing ergometer and 2400Parvo metabolic cart that were used during exercise sessions and to measure their peak oxygen utilization. Additionally, during exercise sessions, if a participant's resting

blood pressure continually falls (after 2 measures 10 minutes apart) within the ranges of "elevated" or "hypertension" (≥120 systolic and ≥80 diastolic) or hypotension (<90 systolic and <60 diastolic), their exercise session was rescheduled for a later date. To become familiar with the equipment, the participants were given time to practice using the rowing ergometer while being coached on their technique. When the participants were comfortable using the rower, they were then shown the metabolic mask and equipment used to measure their VO_{2peak}. After completing the VO_{2peak} exercise test, participants were familiarized with the additional equipment that would be used during future testing (BFR training cuffs, muscle EMG electrodes, blood lactate analyzer) and taken through a Kaatsu cycle.

VO_{2peak} Exercise Test

Participants were tested for peak aerobic capacity and oxygen utilization using an incremental maximal exercise test with the Parvo metabolic cart and the Concept2 Model E rowing ergometer. Previous research has established the TrueOne 2400 metabolic device as a valid and reliable method for calculating participant metabolic rates (Welch, Strath & Swartz, 2015); and rowing ergometers have been established as a valid means to effectively perform both aerobic and resistance exercise simultaneously (Tesch et al., 2013). Participants were attached to the metabolic cart and seated on the rower. The rower damper setting was set to five for all exercise tests. Participants began the test by maintaining an average workload of 100W while rowing for four minutes. After four minutes, the average workload to maintain was increased by 25W. This protocol was repeated with an increased workload of 25W every minute until the participant reached exhaustion. Exhaustion was determined when the participant met two of the following criteria: 1) unable to maintain average workload (±15W) for ≥15 seconds, 2) no increase in VO_2 or HR despite increased exercise intensity, 3) respiratory exchange ratio greater

than 1.10, and 4) HR exceeds 90% of age-predicted maximum heart rate for ≥15 seconds (Park, 2010). This exercise protocol has been modified from previous studies that recruited trained rowing athletes (Beneke, Leithäuser & Hütler, 2001; Cheng, Yang, Lin, Lee & Wang, 2012). Expired gas was collected and analyzed every 15 seconds.

CON/BFR Session

During the CON/BFR session, participants completed five, three-minute exercise sets with a one-minute rest in-between sets – for a total of 19 minutes of exercise. Exercise intensity for this session was set at 30% of the maximum wattage achieved during the VO_{2peak} session. This type of protocol has been used in previous studies when using BFR. (Abe et al., 2006; Abe et al., 2010; de Oliveira et al., 2016). Baseline and post-exercise HR, BP, and $[La^-]_b$ were taken after five minutes of resting and roughly five minutes post-exercise. HR levels were also monitored throughout the entire exercise session. HR, RPE, and muscle SEMG, measured at the right leg VL and BF, were recorded simultaneously during the last 30 seconds of each exercise set. All exercise was completed on the Concept2 Model E rowing ergometer. Participants were verbally encouraged to complete exercise to the best of their ability. However, participants were told to stop the test at any time if they chose to no longer participate or experienced any extreme discomfort. Researchers were prepared to stop the test if the safety of the participant was threatened in any way. Criteria for stopping the test early included, but was not limited to: participant dizziness, light-headedness, severe loss of breath or pain/numbness in the chest, back, or legs.

BFR portion

The same protocol used in the CON portion of the CON/BFR session was used during the BFR portion. However, during this session participants had Kaatsu Nano training cuffs applied

on the proximal portion of both legs. These training cuffs were inflated during exercise sets per the Kaatsu training capillary refill protocol (~3 sec refill time). For additional safety, an upper limit on cuff inflation was set for each individual participant. This limit was equal to 1.3 x the participant's resting systolic BP. Thus, the operating range for cuff pressure during inflation was between 117-156 mmHg corresponding with subject's systolic BP between 90 mmHg and 120 mmHg (Clark et al., 2011). Training cuffs were inflated throughout the entire exercise session.

Statistics

This study was of experimental design. All participants completed the control and intervention, allowing participants to act as their own control. Statistical significance was set at the alpha ≤ 0.05 level of confidence. When a significant *F* was found, addition tests with Bonferroni adjustments were performed. All analysis was performed using SPSS (IBM, Armonk, NY). In the event of missing data, the sequence of data in correlation with the missing piece was not included in the statistics. Anthropometric measurements of participants are presented using descriptive statistics. Repeated measures ANOVAs were used to analyze HR, BP, $[La^-]_b$, and SEMG. A paired sample t-test was used to examine peak RPE. Heart rate ($F(2, 38) = 5.220$, $P = .010$; $t(19) = -4.940$, $P < .001$) and RPE ($t(19) = -5.878$, $P < .001$) showed significant increases during BFR compared to CON (**Fig. 1 & 2**). No statistical significance was found for systolic ($F(1, 19) = 1.207$, $P = .286$) and diastolic ($F(1, 19) = 3.417$, $P = .080$) BP. Additionally, there was no significant changes in $[La^-]_b$ ($F(1, 19) = .363$, $P = .554$) and sEMG for the VL ($F(4, 76) = 2.062$, $P = .094$) and BF ($F(4, 76) = 1.547$, $P = .197$).

CHAPTER IV. RESEARCH ARTICLE[1]

Abstract

BACKGROUND: Exposure to microgravity leads to a progressive loss in muscular strength, endurance, and aerobic capacity (VO_2). Blood flow restriction (BFR) has been shown to elicit rapid gains in muscular strength and aerobic capacity. Rowing exercise combined with BFR could be a supplemental countermeasure to maintain pre-flight muscle and VO_2 function. **METHODS:** Twenty moderately trained males completed rowing exercise during two sessions: VO_{2peak} and CON/BFR. VO_{2peak} was determined during an incremental maximal exercise test on a rowing ergometer. During the CON/BFR session, participants completed a 19-minute rowing protocol. Exercise intensity for the CON/BFR session was 30% of peak work achieved during the VO_{2peak} session. Kaatsu cuffs were inflated around each leg during the BFR portion of the CON/BFR session. HR was measured throughout exercise. RPE, and sEMG of the right leg vastus lateralis and biceps femoris was measured at the end of each exercise set. BP and blood lactate ($[La^-]_b$) were measured at rest and post-exercise. **RESULTS:** HR and RPE showed significant increases during BFR (120.5 ± 5.53 vs. 128.9 ± 9.86 bts·min $^{-1}$) and (9.8 ± 1.85 vs. 11.8 ± 1.88 arbitrary units), respectively. No differences were found for BP, $[La^-]_b$, and sEMG. **DISCUSSION:** These findings indicate the exercise intensity and cuff pressure used were only sufficient to elicit an increased cardiovascular response without elevating BP post-exercise. To

[1] [1] The material in this chapter was co-authored by Sean Mahoney and Dr. Kyle Hackney. Sean Mahoney had primary responsibility for protocol development and data collection. Sean Mahoney was the primary developer of the conclusions that are advanced here. Sean Mahoney also drafted and revised all versions of this chapter. Dr. Kyle Hackney served as proofreader and checked the math in the statistical analysis conducted by Sean Mahoney.

simultaneously elicit cardiovascular and musculoskeletal responses, exercise intensity and/or cuff pressure may need to be increased.

Key Words: Prolonged spaceflight, in-flight exercise protocols, cosmonaut health, mission success

Introduction

Prolonged exposure to microgravity leads to a progressive loss in muscular strength, endurance, and aerobic capacity (Antonutto & Pampero, 2003; Bishop et al., 1999; Hackney et al., 2012.) This microgravity-induced deconditioning is detrimental to crewmember health, performance and overall mission success. Exercise countermeasures are in place on board the International Space Station (ISS) to combat in-flight deconditioning; however, these current methods do not mitigate deconditioning entirely. As much as a fifth of muscle mass is lost during the first four months in space; additionally, peak oxygen consumption (VO_{2peak}) and left ventricular mass decrease early in flight by ~17% and ~ 12% respectively (Hawkey, 2003; Moore et al., 1985; Perhonen et al., 2001). Emergency mission egress tasks may require normal ambulatory participants to work at intensities at 85% of maximum heart rate. Even a relatively small decrease in VO_{2peak} (e.g., 10%) can greatly impact an astronaut's ability to meet these high-energy demands (Bishop et al., 1999).

The National Aeronautics and Space Administration (NASA) created the Human Research Program (HRP) to investigate and mitigate high risk outcomes that impede crewmember health and performance. Two major risks identified by the HRP include the risk of reduced physical performance capabilities due to reduced aerobic capacity and the risk of impaired performance due to reduced muscle mass, strength, and endurance. Gaps of knowledge within these risks include the development of effective exercise programs for the maintenance of

muscle function and VO_2 standards, and the development of pre-flight, in-flight, and post-flight evaluations to determine if muscle function and VO_2 standards are being met during missions. Prior research acknowledges that VO_{2peak} and muscle function decline during spaceflight, but can be mitigated with in-flight exercise (Bishop et al., 1999; Downs et al., 2015; Ploutz-Snyder et al., 2015). However, performance decrements are still observed despite current countermeasures. Research into advanced in-flight exercise protocols, capable of being completed on a singular device, are necessary to identify activity thresholds, exercise prescriptions, and promote in-flight exercise adherence and efficiency.

Current research aiming to counter microgravity-induced deconditioning through exercise primarily use bed rest with a 6-degree head down tilt as an earth-based analog to simulate the detrimental physiological effects of microgravity (Hackney et al., 2012; Hastings et al., 2012; Hawkey, 2003; Murach et al., 2018). Concurrent rowing and resistance exercise training during 5-weeks of bed rest with 6-degree head down tilt was capable of preventing the cardiac atrophy and stiffening that occurs with prolonged bed rest (Hastings, 2012). Additionally, aerobic and resistance exercise completed on a novel concurrent flywheel exercise device (Murach et al., 2018; Tesch et al., 2010) during 70 days of bed rest with 6-degree head down tilt was capable of maintaining key myocellular characteristics in the vastus lateralis muscle; however, further refinement of the exercise protocol is necessary to also effect the soleus (Murach et al., 2018). These findings demonstrate that rowing exercise can maintain cardiovascular function during prolonged bed rest but requires additional exercise supplementation and equipment to simultaneously maintain muscle function.

Blood flow restriction (BFR) is a novel form of exercise intervention that involves the application of inflated tourniquet cuffs that restrict venous blood flow during exercise. BFR has

been shown to elicit rapid and progressive gains in muscular strength, endurance and aerobic capacity (Abe et al., 2006; de Oliveira et al., 2016; Park et al., 2010). Low-intensity interval BFR training has been identified as the only mode of training capable of simultaneously improving aerobic fitness and muscular strength when compared to low-intensity interval training without BFR, high-intensity interval training, and combined high-intensity interval training and BFR (de Oliveira et al., 2016). The restriction of venous blood flow lowers heart stroke volume, thus, increasing heart rate to meet energy demands (Renzi et al., 2010; Hackney et al., 2012). This unique cardiovascular response may allow crewmembers to train at lower intensities and still elicit a cardiac response capable of maintaining their pre-flight VO_{2peak} (Hackney et al., 2012). Additionally, restricted venous blood flow has been shown to counter orthostatic intolerance and maintain central and peripheral hemodynamics during short-term spaceflights (Fomina et al., 2004).

Current in-flight exercise devices offer the capabilities to complete either resistance training or cardiovascular training, but not both simultaneously (Downs et al., 2015; Hargens & Watenpaugh, 1996; Loehr et al., 2011). Effective musculoskeletal and aerobic training can be performed on a rowing ergometer without significantly increasing hardware mass or compromising desired physiological responses (Tesch et al., 2013). The seated nature of rowing exercise appears to promote venous blood return and elicits smaller heart rate (HR) responses when compared to treadmill exercise of similar intensity (Yoshiga & Higuchi, 2002). Low-intensity BFR combined with rowing exercise could be a supplemental countermeasure that requires minimal equipment, physical volume, and power and offers the potential to maintain pre-flight strength and VO_{2peak} during prolonged spaceflight. The purpose of this experimental

study was to identify the acute cardiovascular, musculoskeletal, and metabolic changes when using leg BFR during low-intensity rowing exercise.

Methods

Subjects

Participants experienced both control and intervention sessions in a within subjects, cross over design. All procedures and instruments used during this study were approved by the North Dakota State University Institutional Review Board. Twenty healthy and regularly active adults (22.1 ± 1.71 years; 172.89 ± 24.49 cm; 87.26 ± 27.40 kg) volunteered and gave written informed consent to participate in the study. Any participant with, or at risk for, hypertension or hypotension, or classified as obese (BMI ≥ 30 kg/m^2) were excluded. Additionally, any participant who had recent surgery, muscle disease, or history of cardiovascular disease were excluded.

Table 1

Descriptive Statistics

Age (years)	22.1 ± 1.71
Height (cm)	172.89 ± 24.49
Body mass (kg)	87.26 ± 27.40
Thigh Size (cm)	57.55 ± 4.04
VO_{2peak} (ml/kg/min)	47.57 ± 6.95
30% work rate (W)	80.78 ± 14.15
Cuff Pressure (mmHg)	157.8 ± 5.27

Note: Data are mean ± standard deviation.

Instrumentation

Participant VO_{2peak} was determined using a TrueOne 2400 metabolic cart (Parvo Medics, Sandy, UT) and exercise was completed on a Concept2 Model E rowing ergometer (Concept2, Morrisville, VT). HR was recorded throughout exercise using a wireless heart rate strap monitor and extracted via Golden Cheetah streaming software. BP was taken using a manual sphygmomanometer cuff and stethoscope. sEMG was collected using self-adhesive Red Dot 2560 monitoring electrodes (3M Healthcare, London, Ontario, Canada) and EMG MP150 (Biopac Systems Inc., Goleta, CA). Recorded sEMG files were analyzed as root mean squared using AcqKnowledge 4.0 software and normalized to a maximal dynamic rowing stroke. Participant RPE was ranked using the Borg 6-20 rating scale and $[La^-]_b$ was measured with a handheld whole blood lactate analyzer (Lactate Plus, NOVA Biomedical, Waltham, MA). During BFR exercise, five cm wide Kaatsu Nano training cuffs (Kaatsu Global, Inc., Japan) were applied to restrict blood flow.

Procedures

All participants completed two exercise sessions in order: VO_{2peak} followed by CON/BFR. Each session was separated by at least 48 hours and attempts were made to ensure participants completed exercise at the same time of day for each session.

VO_{2peak} Session. Participants arrived for the first session and were familiarized with the procedures and instruments being used. Consent forms were provided, and inclusion/exclusion screening took place. Before exercise, baseline HR and BP were taken. VO_{2peak} was determined using an incremental exercise test on the rowing ergometer. For all exercise testing the rower damper setting was set to five. Prior to each test the metabolic cart was calibrated for known gas concentrations and flow via the manufactures recommendation. Participants began the test by

maintaining an average workload of 100W while rowing for four minutes. After four minutes, the average workload to maintain was increased by 25W. This protocol was repeated with an increased workload of 25W every minute until the participant reached exhaustion. Exhaustion was determined when the participant met two of the following criteria: 1) unable to remain within 10-15W of average workload for ≥15 seconds, 2) no increase in VO_2 or HR despite increased exercise intensity, 3) respiratory exchange ratio greater than 1.10, and 4) HR exceeds 90% of age-predicted maximum heart rate for ≥15 seconds (Park et al., 2010). This exercise protocol has been modified from previous a previous study involving trained rowing athletes (Cheng et al., 2012). Expired gas was collected and analyzed every 15 seconds. Peak work rate was determined based on the final stage reached during VO_{2peak} testing.

Fig 1. Incremental VO_{2peak} Protocol

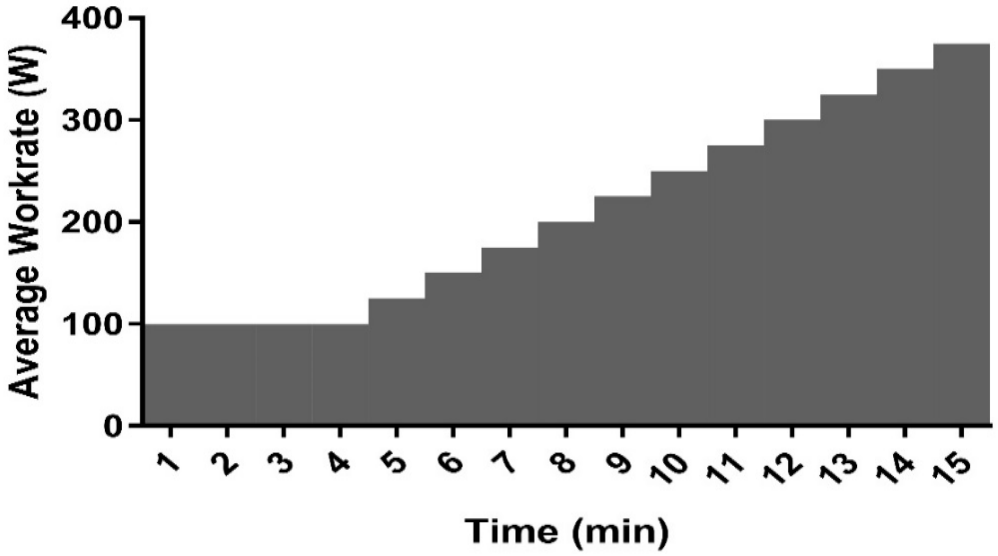

Figure 1. Incremental VO2peak Protocol
Note: Outline of exercise protocol used during VO2peak session

CON/BFR Session. This session involved two portions: exercise without limb occlusion (CON) and exercise with limb occlusion (BFR). At least 20 minutes of rest separated each portion and participants completed the portions in a randomized order.

CON Session. Before exercise, baseline HR, BP and $[La^-]_b$, were measured. Additionally, muscle sensor sEMG electrodes were placed on the right leg VL and BF muscles to measure electrical activity of the muscle membrane during exercise. Areas of placement were shaved with a hand razor and carefully cleaned with ethanol before electrode placement. Electrodes were placed on the medial portion of the VL and the BF muscles, approximately 10-15 cm above the proximal border of the patella, with a 4.0 cm interelectrode distance. These placings are like those used by Wernbom et al. (2009) and allow for the application of the BFR training cuffs without interrupting electrode placement or restricting movement. Participants completed five, three-minute exercise sets with a one-minute rest in-between sets for a total of 19 minutes. Exercise intensity was set at 30% of the peak work rate achieved during the VO_{2peak} session. This type of protocol has been used in previous studies when using BFR (Abe et al., 2006; Abe et al., 2010; de Oliveira et al., 2016). Post-exercise HR, BP, and $[La^-]_b$ measurements were taken roughly five minutes post-exercise. HR levels were also monitored throughout the entire exercise session. RPE and sEMG, measured at the right leg VL and BF, were recorded simultaneously during the last 30 seconds of each exercise set. All exercise was completed on the Concept2 Model E rowing ergometer. Participants were verbally encouraged to complete exercise to the best of their ability. However, participants were told to stop the test at any time if they chose to no longer participate or experienced any extreme discomfort. Researchers were prepared to stop the test if the safety of the participant was threatened in any way. Criteria for stopping the test

early included, but was not limited to: participant dizziness, light-headedness, severe loss of breath or pain/numbness in the chest, back, or legs.

BFR Session. The same protocol used in the CON was used during the BFR exercise. However, during this session participants had 5 cm Kaatsu Nano training cuffs applied on the proximal portion of both legs. Immediately before exercise began, participants were taken through a traditional Kaatsu Cycle which involves eight rounds of cuff inflation. Each round had the cuff inflated for 20 seconds followed by five seconds of total cuff deflation. The Kaatsu cycle began at an inflation of 40 Standard Kaatsu Units (SKU), which are approximately equivalent to mmHg. After the five seconds of deflation, the cuff pressure increased by ~15-20 SKU for each subsequent round, ending at ~160 SKU. To find optimal SKU for exercise, researchers measured individual's capillary refill time (CRT), or the time in seconds taken for color to return to an external capillary bed, during the cycle. Pressure was applied to the quadriceps, just above the knee, to cause blanching during cuff inflation. A CRT of ~3 seconds indicates optimal SKU pressure for exercise; pressure was continually increased by ~15-20 SKU until optimal SKU was reached. However, to ensure participant safety, an individualized training cuff inflation limit was set for each participant at 1.3 x their resting systolic BP (Clark et al., 2011). During the BFR portion, training cuffs remained inflated throughout the entire exercise.

Statistical Analysis

All analyses were performed using SPSS (IBM, Armonk, NY). In the event of missing data, the sequence of data in correlation with the missing piece was not included in the statistics. Anthropometric measurements of participants are presented using descriptive statistics. Repeated measures ANOVAs (exercise x time) were used to analyze HR, BP and $[La^-]_b$. Heart rate was analyzed pre-, during, and post-exercise. Blood pressure and $[La^-]_b$ was analyzed pre- and post-

exercise. Paired sample *t*-tests were used to compare peak RPE and sEMG during CON and BFR. Statistical significance was determined by $P < 0.05$. When a significant *F* was found, additional tests with Bonferroni adjustments were performed.

Results

Mean cuff pressure for participants was 157.8 ± 5.27 SKU (**Table 1**). There was a significant exercise by time effect for HR ($F(2, 38) = 5.220$, $P = .010$). Follow-up comparisons determined there was a significant elevation of HR during exercise in BFR compared to control (120.5 ± 5.53 vs. 128.9 ± 9.86 bpm; $t(19) = -4.940$, $P < .001$; **Fig. 2**). RPE ($t(19) = -5.878$, $P < .001$) showed significant increases during BFR compared to CON (**Fig. 3**). No statistically significant differences were found for systolic ($F(1, 19) = 1.207$, $P = .286$) and diastolic ($F(1, 19) = 3.417$, $P = .080$) BP (**Table 2)**. Additionally, there were no statistically significant differences observed in $[La^-]_b$ ($F(1, 19) = .363$, $P = .554$) (**Table 2)** and sEMG for the VL ($F(4, 76) = 2.062$, $P = .094$) and BF ($F(4, 76) = 1.547$, $P = .197$) (**Table 3)**.

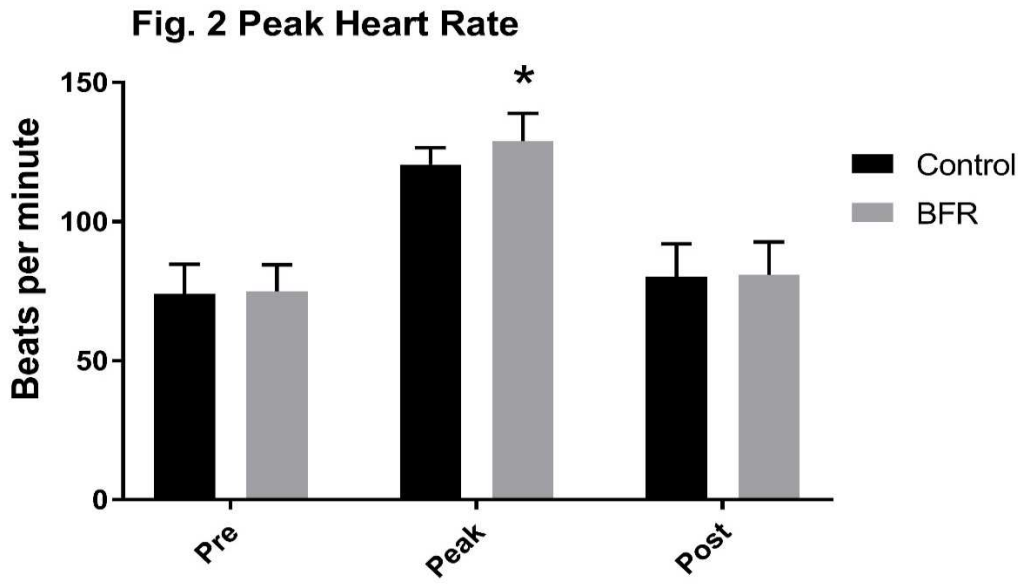

Figure 2. Peak Heart Rate
Note: Peak HR taken pre-, during, and post-exercise. * denotes significance at $p < 0.05$

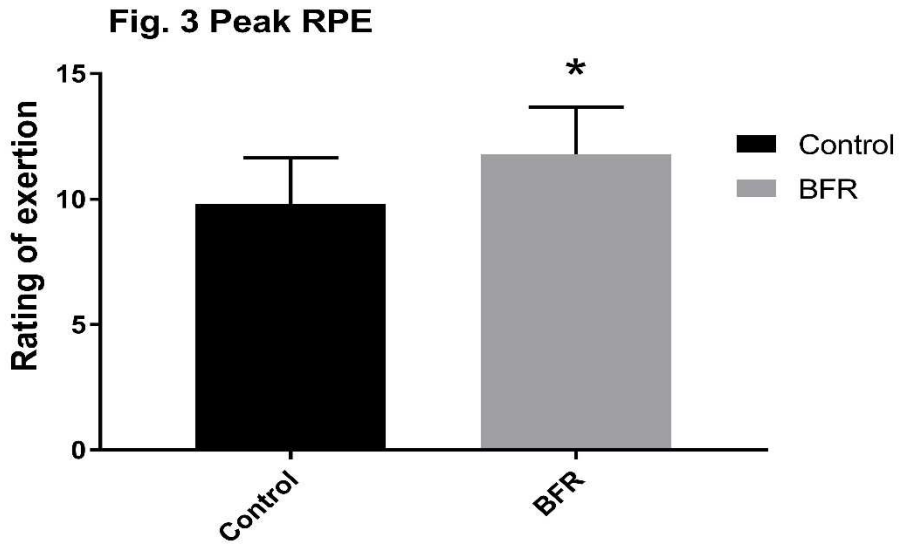

Figure 3. Peak RPE
Note: Peak RPE recorded during the last 30 seconds of each exercise set. * denotes significance at $p < 0.05$

Discussion

This is the first study evaluating the effects of BFR during rowing exercise in a 1G environment. As such, the goal of this study was to establish the acute physiological responses of leg BFR during rowing exercise to guide future research design during bed rest or spaceflight. The major findings of this study were the exercise intensity and cuff inflation pressure used were sufficient to elicit an increased cardiovascular response with exercise, without elevating BP post-exercise. However, this exercise protocol was insufficient to increase musculoskeletal, and metabolic responses (e.g., $[La^-]_b$).

Rowing

Due to its partially supine nature, rowing exercise promotes venous blood return, thus increasing stroke volume and cardiac output to a greater extent than other upright exercises (e.g. cycling, walking) (Horn et al., 2015). Additionally, for the same relative exercise intensity, HR response is lower during ergometer rowing than during treadmill running (Yoshiga & Higuchi,

2002). Consequently, the application of BFR cuffs works to restrict venous blood flow, therefore reducing stroke volume and increasing HR to maintain cardiac output. The interaction of these conflicting mechanics was not the focus of this study, but this interaction could play an important role in prescribing exercise intensity and cuff inflation pressure during BFR rowing exercise.

Table 2

Blood Pressure and Whole Blood Lactate

	CON		BFR	
Variable	Pre	Post	Pre	Post
Systolic BP	120.6 ± 6.59	122.05 ± 7.23	121.5 ± 5.65	117.6 ± 22.63
Diastolic BP	77.8 ± 5.73	79.9 ± 3.14	79 ± 4.47	78.6 ± 4.45
$[La^-]_b$ (mmol/L)	1.21 ± 0.66	1.19 ± 0.56	1.12 ± 0.50	1.20 ± 0.43

Note: Data are mean ± standard deviation.

Heart Rate & Blood Pressure

Significant increases in HR were observed between CON and BFR (~7%). This result is similar to the HR increases observed during previous studies using BFR exercise (de Oliveira et al., 2016; Renzi et al., 2010). Renzi et al. (2010) completed a similar protocol using BFR during walking exercise with the same cuff pressure used in this study. However, Renzi et al. (2010) reported an almost 20% increase in HR between CON and BFR during walking. These findings indicate that while rowing exercise is capable of eliciting an increased cardiovascular response with BFR, it is not as potent an exercise as upright walking. Additionally, BFR during walking exercise has shown significant increases in both systolic and diastolic BP when compared to non-BFR exercise (Renzi et al., 2010; Staunton et al., 2015). However, the exercise protocol completed in this study showed no significant increases in either systolic or diastolic BP from

pre- to post-exercise (**Table 2**). Cuff inflation and exercise modality could be factors influencing blood pressure responses. It is also important to note, systemic reviews of BFR exercise have shown that the increased cardiovascular responses witnessed during low-intensity BFR exercise are all well below increases that occur during high-intensity resistance training (Loenneke et al., 2011).

Rate of Perceived Exertion

In this study, RPE was shown to be higher during BFR than CON. It has previously been reported to be significantly higher during high-intensity (80%) resistance exercise compared with low-intensity (20%) BFR exercise (Neto et al., 2016). Hackney et al. (2016) showed that low-intensity (20%) BFR resistance exercise at 140 mmHg was insufficient to elicit differences in RPE between exercise with and without BFR. Additionally, reported RPE in young and older adults was shown to be lower during BFR treadmill exercise compared to leg press exercise (Staunton et al., 2015).

Table 3

Surface Muscle Electromyography of the Vastus Lateralis and Biceps Femoris

Control Session	**Set 1**	**Set 2**	**Set 3**	**Set 4**	**Set 5**
Vastus Lateralis (%)	60 ± 109	36 ± 30	41 ± 57	34 ± 22	32 ± 24
Biceps Femoris (%)	17 ± 10	35 ± 65	17 ± 15	23 ± 21	16 ± 11
BFR Session	**Set 1**	**Set 2**	**Set 3**	**Set4**	**Set5**
Vastus Lateralis (%)	25 ± 11	47 ± 58	28 ± 20	41 ± 43	39 ± 41
Biceps Femoris (%)	25 ± 38	26 ± 40	12 ± 8	13 ± 9	17 ±14

Note: Data are in percent (%) of peak sEMG during maximal rowing strokes and mean ± standard deviation.

sEMG & Lactate

Surface electromyography of the right leg VL and BF were not significantly different between CON and BFR (**Table 3**). Wernbom et al. (2009) reported similar findings and showed that BFR during low-intensity dynamic knee extension at 30% of 1RM decreased endurance but did not increase muscle activity (Wernbom et al., 2009). Additionally, increased relative integrated sEMG of the VL during low-intensity BFR knee extension was shown to be related to the production and accumulation of $[La^-]_b$ during a hypoxic intramuscular environment (Takarada et al., 2000). The relationship between muscle activation and $[La^-]_b$ accumulation appears to be linear as more glycolytic muscle fibers are recruited (Takarada et al., 2000). Elevations in $[La^-]_b$ concentrations occur following BFR exercise due to increased rates of fast glycolysis in the ischemic muscle (Hackney et al., 2016; Takarada et al., 2000). In our study, no significant differences were seen in $[La^-]_b$ from pre- to post-exercise for both CON and BFR (**Table 2**). There are two possible explanations for this event. First, the lack of elevated $[La^-]_b$ during BFR indicates a possibility the prescribed cuff size (5 cm) and pressure (150 – 160 mmHg) were not sufficient enough to significantly challenge metabolic stress. Similar results when using lower cuff size (5 cm) and pressure (140 mmHg) during resistance exercise have been previously reported (Hackney et al., 2016). Additionally, it is worth noting that during prolonged aerobic exercise, $[La^-]_b$ can be used to fuel oxidative metabolism (Brooks, 1998). Due to the exercise length (19-minutes), it is possible that elevated $[La^-]_b$ was not seen due to increased aerobic metabolism specifically given the arms were also active during the rowing exercise. Staunton et al. (2015) also demonstrated that $[La^-]_b$ measures remained unchanged from baseline after treadmill walking in both young and old adults. It has been previously suggested cuff inflation pressures required to elicit resistance training adaptations are between 160-230

mmHg (Burgomaster et al., 2003; Park et al., 2010; Takarada et al., 2000). The inflation pressures used in this study were between 150-160 SKU (i.e., 150-160 mmHg). This pressure was determined using the standard Kaatsu protocol for prescribing cuff pressure. However, to ensure participant safety during this novel study, an upper limit of 1.3 x resting systolic BP was set for total inflation. Therefore, it is possible that the cuff inflation pressures used in the current study were not high enough to elicit additional motor unit recruitment.

Finally, it is important to state limitations for this study. Participants recruited were not elite-trained rowing athlete nor astronauts. Any inexperience with the rowing ergometer could have impacted exercise efficiency. Additionally, the VO_2peak exercise protocol was adapted from prior research using elite-rowing athletes (Cheng et al., 2012). The adapted protocol may have been insufficient in determining rowing VO_2peak. Many participants were highly aerobically trained, and this may have impacted cardiovascular and metabolic responses. All participants recruited were young, healthy males, making it difficult to generalize the findings to other populations. Lastly, the study was not completed in a microgravity environment.

Conclusion

Short-term low-intensity interval BFR training has been previously shown to simultaneously improve aerobic fitness and muscular strength (de Oliveira, 2016). Additionally, two-week BFR walk training simultaneously improved VO_{2max} (11.6%) and anaerobic capacity (2.5%) (Park et al., 2010). The final cuff inflation pressures used in the previous studies were between 200-220 mmHg. The findings of this study were novel in they indicate that low-intensity (30% 1RM) leg BFR (150 – 160 mmHg) during rowing exercise was sufficient in elevating HR and RPE during exercise without impacting BP from pre- to post-exercise. However, this protocol was insufficient to elevate more motor unit recruitment and metabolic

muscle perturbation. Due to the partially supine nature of rowing, increased exercise intensity or cuff pressure may be required to simultaneously elicit cardiovascular and musculoskeletal responses in bed rest or spaceflight models.

Leg BFR during rowing exercise could prove to be a useful exercise countermeasure for microgravity deconditioning; however, further studies should focus on evaluating different ranges of exercise intensity (40%, 50%, etc.) or increased inflation pressure (>160 mmHg) to elicit elevated muscular and metabolic stress and mimic increased aerobic and anaerobic responses during one method of exercise. One exercise device with multiple capabilities or adjuncts performing at minimal external power within a small amount of volumetric space would be efficacious for future long duration space missions beyond low earth orbit.

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APPENDIX A. PRESCRIBING WORKLOAD

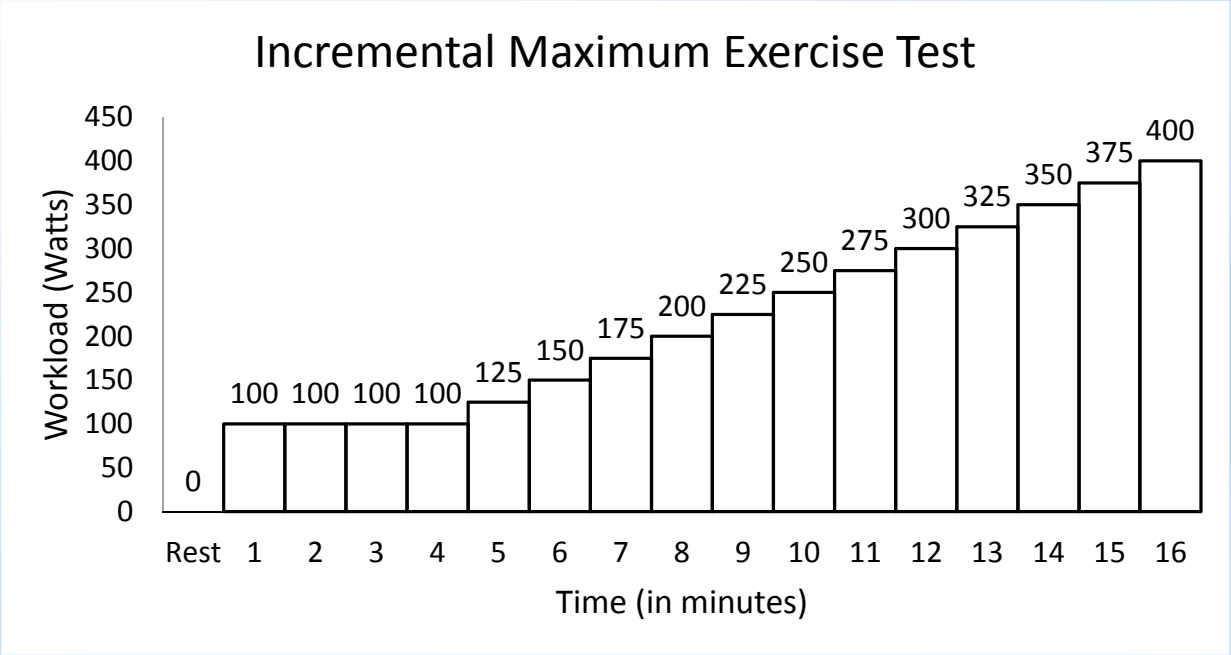

Figure A1. Incremental Maximum Exercise Test.
Note: Used to determine 30% workload for CON & BFR session.

Peak Workload during Max Test:	30% of Peak Workload (rounded up)
100W	30W
125W	37.5W
150W	45W
175W	52.5W
200W	60W
225W	67.5W
250W	75W
275W	82.5W
300W	90W
325W	97.5W
350W	105W
375W	112.5W
400W	120

Figure A2. 30% of Peak Workload.
Note: Used to find 30% of peak work rate achieved during the VO2peak session.

APPENDIX B. IRB APPROVAL LETTER

NDSU NORTH DAKOTA STATE UNIVERSITY

May 24, 2017

Dr. Kyle Hackney
Department of Health, Nutrition & Exercise Science

IRB Approval of Protocol #HE17225, "Leg blood flow restriction during rowing exercise as a countermeasure for microgravity induced deconditioning"
Co-investigator(s) and research team: Sean Mahoney, Nathan Dicks, Bryan Christensen, Katie Lyman

Approval period: 5/24/2017 to 5/23/2018 Continuing Review Report Due: 4/1/2018

Research site(s): NDSU Funding agency: Northland ACSM
Review Type: Full Board, meeting date – 5/12/2017
Risk Level: A minor increase over minimal risk
IRB approval is based on the revised protocol submission (received 5/23/2017).

Additional approval is required:
o prior to implementation of any proposed changes to the protocol (Protocol Amendment Request Form).
o for continuation of the project beyond the approval period (Continuing Review/Completion Report Form). A reminder is typically sent two months prior to the expiration date; timely submission of the report is your responsibility. To avoid a lapse in approval, suspension of recruitment, and/or data collection, a report must be received, and the protocol reviewed and approved prior to the expiration date.

A report is required for:
o any research-related injuries, adverse events, or other unanticipated problems involving risks to participants or others within 72 hours of known occurrence (Report of Unanticipated Problem or Serious Adverse Event Form).
o any significant new findings that may affect risks to participants.
o closure of the project (Continuing Review/Completion Report Form).

Research records are subject to random or directed audits at any time to verify compliance with IRB regulations and NDSU policies.

Thank you for cooperating with NDSU IRB procedures, and best wishes for a successful study.

Sincerely,
Kristy Shirley
Digitally signed by Kristy Shirley
DN: cn=Kristy Shirley, o=NDSU, ou=Institutional Review Board, email=kristy.shirley@ndsu.edu, c=US
Date: 2017.05.24 08:47:37 -05'00'

Kristy Shirley, CIP
Research Compliance Administrator

For more information regarding IRB Office submissions and guidelines, please consult www.ndsu.edu/irb. This Institution has an approved FederalWide Assurance with the Department of Health and Human Services: FWA00002439.

INSTITUTIONAL REVIEW BOARD
NDSU Dept 4000 | PO Box 6050 | Fargo ND 58108-6050 | 701.231.8995 | Fax 701.231.8098 | ndsu.edu/irb
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APPENDIX C. INFORMED CONSENT FORM

NDSU North Dakota State University
Health, Nutrition, and Exercise Science
1301 Centennial Blvd
Fargo, ND 58108-6050
701-231-6706

Title of Research Study: Leg blood flow restriction during rowing exercise as a countermeasure for microgravity induced deconditioning.

This study is being conducted by:
Sean Mahoney phone: (651)-249-9151 email: sean.mahoney@ndsu.edu;
Kyle Hackney: email: kyle.hackney@ndsu.edu

Why am I being asked to take part in this research study? You are being asked to participate in this study, because we are seeking 20 males, between the ages of 18 – 40 and considered to be "regularly active" and healthy, to complete rowing exercise during three exercise sessions.

What is it about the individual that makes them of interest to the research team?

Inclusions: You have been asked to participate, because you are "regularly active" and healthy enough for exercise. For the purposes of this study, you will be considered "regularly active" if you have completed at least 100 minutes of physical activity each week for the last six months. These 100 minutes can be any combination of cardiovascular and resistance training. You will be asked to complete several health-related questionnaires to help the researchers assess if you have any condition which would preclude you from participating in the study.

Exclusions: You may be excluded from the study if you have: had any previous injuries in your neck, back or legs, you are taking any medications for high blood pressure/hypertension or have uncontrolled hypertension, you have any previous history of cardiovascular disease, have sickle cell anemia/trait, have recently had surgery, have a history of blood clots, or a history of muscle breakdown due to extreme exertion.

Additional exclusions include: individuals with a calculated body mass index (weight/height^2) of 30 kg/m^2 or greater, those with abnormal blood pressure, those with prior ligamentous, bony, or other soft tissue reconstruction to the lower-extremity, a history of deep venous thrombosis (blood clots), peripheral vascular disease (narrowing or blockage in a blood vessel), diabetes, acute fracture, tumor, or infection, are an active smoker, a user of illegal drug use, have an implanted medical device, or the inability to consent. You will also be excluded from the study if you have a fever before any of the exercise sessions or the sessions will need to be rescheduled.

What is the reason for doing the study? The purpose of this study is to determine the short-term effects that leg blood flow restriction have on the body during rowing exercise. The results from this study will have an impact on the future research and the creation of new innovative exercise methods for clinical patients, elite-athletes, and spaceflight crewmembers.

What will I be asked to do? You will be asked to attend an information session and two exercise sessions using a rowing machine. The order for the CON and BFR sessions will be random. A description of each is below:

Information Session: You will first attend an informational session to become familiar with the equipment being used in the study. During this session, you will complete the 2017 Physical Activity Readiness Questionnaire (PAR-Q)+ to determine if you are healthy enough to participate in the exercise required. During this session, your weight and height will be measured to calculate your body mass index. Last, a test will be performed to screen for abnormally low blood pressure. Your blood pressure will be measured while sitting and two minutes after standing up. Abnormal drops in blood pressure between positions may be grounds for exclusion from the study.

VO_{2peak} Session: During this session, you will complete a test to find your peak oxygen use (VO_{2peak}) during exercise. To begin, your height and weight will be measured, and your resting heart rate and blood pressure will be measured before testing. A Polar heart rate monitor and blood pressure cuff and stethoscope will be used to measure these values. The test protocol will have you doing rowing exercise until you become exhausted (physically unable to complete any more exercise). During testing your peak oxygen use will be tracked using a PARVO metabolic cart. This will involve you wearing a mask to record the oxygen that you intake and expire. The mask will be attached to a tube that will connect to the metabolic cart. You will wear a nose plug during testing to make sure all breath measures are collected.

Control (CON) & Blood Flow Restriction (BFR) Session: During this session, you will complete the following portions in random order.

CON session: During the CON session, you will complete rowing exercise at a set workload of 30% of the peak workload you achieved during the previous session. Around five minutes pre- and post- exercise, your resting and recovery heart rate, blood pressure, and blood lactate will be measured. Blood lactate will be measured from a by collecting a few drops of blood from a small finger stick on a finger of your choice. There will be a total of 4 finger sticks across the entire session, and a Band-aid will be provided after each one.

The rowing exercise for this study is a full body exercise that will consist of five, three-minute stages with a one-minute rest interval between each stage for a total of 19 minutes. During the last 30 seconds of exercise sets, your heart rate, surface muscle electromyography (EMG) and rate of perceived exertion (RPE) will be collected. EMG will be measured by applying muscle sensor electrodes to two of your leg muscles on

your right leg. A muscle oxygen sensor will also be placed on your left leg. Before applying the sensors, your upper legs will need to be shaved with a handheld razor and cleaned with alcohol wipes. Your RPE is a personal rating of the intensity of the exercise you are participating in. To collect this measure, a clipboard with a range of numbers from 6-20 will be shown to you during rest intervals. You will point to the number that equals your perceived level of exhaustion (6 being the lowest possible and a 20 being the highest).

BFRsession: The exercise protocol for the BFR session will remain the same as the control session; however, during this session you will have Kaatsu brand training cuffs on the upper portion of both of your legs. The cuffs will be worn and inflated for the entire 19-minute exercise session. Wearing the training cuff will feel very similar to what it feels like to wear a blood pressure cuff.

Where is the study going to take place, and how long will it take? This study will take place in the North Dakota State University Human Performance Lab, room 15 and room 14. Each session will be between 30 - 60 minutes long, and sessions will take place at least 48 hours apart from each other. The total time commitment for the study is approximately ≤ 120 minutes.

What are the risks and discomforts? It is not possible to identify all risks in research procedures, but the researcher(s) have taken reasonable actions to reduce any known risks. Some of the most common risks and discomforts include: muscle soreness/cramping following exercise, lightheadedness, difficulty breathing, and increased heart rate and blood pressure. During exercise, if your heart rate exceeds your age-predicted heart rate maximum for 15 seconds, or you report an RPE of 17 or greater, the test will end immediately. If new findings develop during this research which may change your willingness to participate, we will tell you about these findings. Due to the small risk of blood clotting during exercise and the use of BFR, you will leave the final session with a hand out of possible symptoms, and researchers will contact you by phone within 24 hours of your last exercise session to monitor for signs and symptoms you may have developed after the testing sessions.

What are the benefits to me? You are not expected to get any benefit from being in this research study.

What are the benefits to other people? Possible benefits to others will include new exercise routines to assist in crewmember safety during long duration spaceflight missions and the creation of exercise routines for clinical patients and elite-athletes.

Do I have to take part in the study? Your participation in this research is your choice. If you decide to participate in the study, you may change your mind and stop participating at any time.

What are the alternatives to being in this research study? Instead of being in this research study, you can choose not to participate.

Who will see the information that I give? We will keep all research records that identify you private. Your information will be combined with information from other people taking part in the study and stored on a password protected data file. You will be assigned a participant number and that number will be associated with all your information. When we write about the study, we will write about the combined information that we have gathered. We may publish the results of the study; however, we will keep your name and other identifying information private.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. For example, your name will be kept separate from your research records and these two things will be stored in different places under lock and key. If you withdraw before the research is over, your information will be retained in the research record OR removed at your request, and we will not collect additional information about you.

Can my taking part in the study end early? Your participation in the study may end whenever you wish. If you choose to end your participation early, you will receive any money that you have gained up to that point (see below). If you fail to attend any of the designated session, researcher(s) may remove you from the study and you will receive any money that you have gained up to that point.

Will I receive any compensation for taking part in this study? You will receive $10.00 after completing the VO_{2peak} session and $10.00 after completing the CON and BFR combined Session - for a total of $20.00. If you drop out of the study before completing both sessions you will only earn money for the session that you completed.

What happens if I am injured because of this research? If you receive an injury when taking part in the research, you should contact Sean Mahoney (651-249-9151) or Kyle Hackney (701-231-6706). If injury occurs during testing, treatment for the injury will be available including first aid, emergency treatment and follow-up care as needed. Payment for this treatment must be provided by you and your third-party payer (such as health insurance). This does not mean that you are releasing or waiving any legal right you might have against the researcher or NDSU as a result of your participation in this research.

What if I have questions? Before you decide whether to accept this invitation to take part in the research study, please ask any questions that you have. Later, if you have any questions about the study, you can contact the researcher, Sean Mahoney at (651-249-9151) or sean.mahoney@ndsu.edu or Dr. Kyle Hackney at 701-231-6706 or kyle.hackney@ndsu.edu.

What are my rights as a research participant? You have rights as a participant in research. If you have questions about your rights, or complaints about this research, you may talk to the researcher or contact the NDSU Human Research Protection Program by:

- Telephone: 701.231.8995 or toll-free 1-855-800-6717
- Email: ndsu.irb@ndsu.edu

- Mail: NDSU HRPP Office, NDSU Dept. 4000, PO Box 6050, Fargo, ND 58108-6050.

The role of the Human Research Protection Program is to see that your rights are protected in this research; more information about your rights can be found at: www.ndsu.edu/irb .

Documentation of Informed Consent:

You are freely making a decision whether to be in this research study. Signing this form means that

1. you have read and understood this consent form
2. you have had your questions answered, and
3. you have decided to be in the study.

You will be given a copy of this consent form to keep.

Your signature	Date
Your printed name	
Signature of researcher explaining study	Date
Printed name of researcher explaining study	

APPENDIX D. RECRUITMENT EMAIL

EMAIL PROMPT:

NASA Sponsored Research Study

Greetings Students and Faculty!

You are being invited to participate in a research study supported through the North Dakota Space Grant Consortium and Northland ACSM. This research study will be looking at the short-term effects of leg blood flow restriction during rowing exercise. Participants who complete the entire study will receive $20.00 cash to compensate them for their time. To receive full compensation, individuals must attend all sessions listed below:

> ***Information Session*** – Participants will become familiarized with equipment and procedures used during testing.
>
> ***Exercise Session #1*** – Participants will have their maximum aerobic capacity and peak work rate measured by completing rowing exercise to fatigue.
>
> ***Exercise Session #2*** – Participants will complete five, three-minute sets of rowing exercise *without* leg blood flow restriction. After a ~20-minute rest, the same exercise protocol will be repeated *with* leg blood flow restriction.

Data Collected: Heart rate, blood pressure, rate of perceived exertion, surface muscle electromyography, blood lactate, and leg muscle oxygen levels.

Participant Exclusion and Risks: Due to the physical requirements of the study, individuals with any history or neck, leg, or back pain will be excluded from participation. Individuals who are diagnosed with any cardiovascular disease and females taking any form of contraception will also be excluded. Participants who complete this study may experience regular exercise side effects (shortness of breath, sore muscles, etc.). All precautions will be taken to ensure participant safety during testing.

Participant Benefits: Individuals who complete this study will be compensated $20.00 for their time. Data collected from participants will be analyzed to determine the short-term effects of leg blood flow restriction and its place as a future exercise intervention.

Those interested in participating or seeking more information should contact Sean Mahoney (sean.mahoney@ndsu.edu) or Dr. Kyle Hackney (kyle.hackney@ndsu.edu) for more information.

Thank you for your time, and have a wonderful day!

Sean J. Mahoney
Graduate Assistant
Health, Nutrition, and Exercise Science
North Dakota State University

APPENDIX E. PARTICIPANT DATA COLLECTION SHEET

Participant # **Data Collection Sheet**

VO_2peak Session												**Anthropometric**
	Resting		< 5 min post			**Hypotension Test**						Age:
HR						Seated BP:						Height:
BP						Standing BP:						Weight:
						BFR Settings						Limb Size:
VO_2peak (ml/kg/min):						Base SKU:						Cuff Size:
Peak Work Rate:						Optimal SKU:						**Notes:**
30% Peak Work Rate:						1.3(SBP):						
Notes:												

Control Session						**BFR Session**					
	HR	BP	La	EMG	RPE		HR	BP	La	EMG	RPE
Pre				xxxxx	xxxxx	Pre				xxxxx	xxxxx
1st		xxxxx	xxxxx			1st		xxxxx	xxxxx		
2nd		xxxxx	xxxxx			2nd		xxxxx	xxxxx		
3rd		xxxxx	xxxxx			3rd		xxxxx	xxxxx		
4th		xxxxx	xxxxx			4th		xxxxx	xxxxx		
5th		xxxxx	xxxxx			5th		xxxxx	xxxxx		
Post				xxxxx	xxxxx	Post				xxxxx	xxxxx