SWACSM Abstract

Differential Cardiovascular Responses to Acute Exercise in Adults with Cerebral Palsy

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ABSTRACT

Cerebral palsy (CP) is a non-progressive and permanent neurological disorder leading to musculoskeletal dysfunction and immobility. A major clinical problem with CP is early development of cardiovascular diseases with increased rates of mortality. Due to the inevitability of motor dysfunction adults with CP can develop health risk factors, such as obesity and hypertension, at a higher rate compared to the general population. To date, the physiological basis for CP has not been established; how cardiovascular dynamics, such as heart rate (HR), blood pressure (BP), and blood flow (BF), are controlled in individuals with CP has never been identified. **PURPOSE:** To determine differential cardiovascular responses to acute dynamic exercise in adults with CP. **METHODS:** Total of eighteen adults with and without CP participated in the study. HR from ECG, beat-to-beat arterial BP from Finapres and brachial BP, and respiration via pneumobelt were continuously measured before, during and after 2 minutes of dynamic handgrip exercise at 35% and 50% of maximal voluntary contraction. In addition, diameter, blood velocity, and flow of the brachial artery were measured using Doppler ultrasound on the contracting arm throughout the experiment. **RESULTS:** At rest, both control and CP groups had similar resting HR (60.7±1.9 control and 63.0±7.5 CP, bpm). While resting respiratory rate was lower in CP group compared to the control, resting mean arterial pressure (MAP) and brachial blood flow tended to be higher in CP ($p=0.08$). MAP and HR were significantly increased to exercise from rest in both groups with no group differences (MAP, Δ 9.3±2.2 control and Δ11.2±3.3 CP, mmHg; HR, Δ8.4±1.5 control and Δ12.1±4.1 CP, bpm). Respiratory rate was significantly increased to exercise from rest in only the CP group. The delta changes of blood flow from rest to exercise was slightly smaller in the CP group. **CONCLUSIONS:** While HR and MAP increased to exercise from rest in similar fashion in both groups, increase in BF to exercise was blunted in adults with CP. Our preliminary data suggest that there are differential neural control mechanisms to regulate BP in the CP population. Other mechanisms, possibly vascular contribution from non-contracting limbs or chemoreceptor activity, may contribute to BP response during exercise in the CP population.

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EXPANDED ABSTRACT

INTRODUCTION

Cerebral palsy (CP) is a non-progressive and permanent neurological disorder leading to musculoskeletal dysfunction and immobility (1, 2). A major clinical problem with CP is early development of chronic diseases with increased rates of mortality (3, 4). Previous studies have identified that health conditions, such as health-related risk factors (e.g., obesity, hypertension, dyslipidemia) that are known to increase chances of developing chronic cardio-metabolic disease (e.g., type 2 diabetes, cardiovascular disease), are concurrent with individuals with CP at significantly higher rate compared to populations without CP (4, 5, 6). Such health-related problems further burden the CP population and their caretakers; thus, it is worthy to study physiological basis to gain a better understanding of the state of CP.

Individuals with CP experience higher rates of cardiovascular issues starting early in adulthood and worsening with age (6, 7). Cardiovascular function appears to be compromised in the general population with cardiovascular and metabolic diseases; vascular dysfunction is an indicative of atherosclerotic cardiovascular disease risk (8). Although it lacks enough scientific evidence, the vascular health of children and adolescents with CP seems to match that of the typically developing peers (9). However, recent evidence suggests that endothelial function driven from the flow mediated dilation was significantly lower in the adult CP population compared to controls (10). Individuals with CP exhibit different pathophysiology stemming from unique neurological disturbances. However, the early aging effect in the adults with CP may be one of the contributing factors to facilitate the cardiovascular dysfunction.

During an acute bout of dynamic exercise, the human physiological system is altered to meet the metabolic demands of contracting skeletal muscles (11). Such physiological alterations to exercise are harmonized by neural, cardiovascular, and musculoskeletal systems. Arterial blood pressure (BP) is elevated with acute exercise to adjust to a new homeostatic condition derived from exercise (11, 12). Elevated BP during exercise is accomplished by any increases in heart rate (HR), stroke volume (SV), and total peripheral resistance (11, 12). It is well recognized that such adjustments are under the strong influence of both central neural activity and local contracting skeletal muscles during an acute bout of exercise (11, 12). An exaggerated BP response to acute exercise is typically seen in individuals with hypertension and cardiovascular disease, and such changes in BP are also associated with an increased risk of future stroke and cardiovascular mortality (13,14). To date, the physiological basis for CP during acute exercise has not been established; how cardiovascular dynamics, such as HR, SV, BP, and peripheral blood flow (BF), are controlled in adults with CP has never been identified. Understanding overall physiological mechanisms by which acute exercise may alter the cardiovascular system in the CP population may uncover insights into CP pathophysiology.

Thus, the purpose of our study is to determine differential cardiovascular responses to acute dynamic exercise in adults with CP who have already progressed into early aging characterized by muscle atrophy and low bone mineral density.

METHODS

Total of eighteen adults with and without CP (24±1 control vs. 39±7 CP, years) participated in the study. All CP participants had muscle atrophy and low bone mineral density (data not included in this

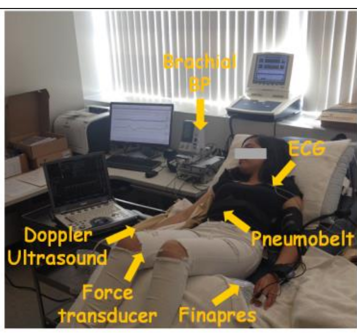

Figure 1A. Experimental set-up for overall cardiovascular measurements.

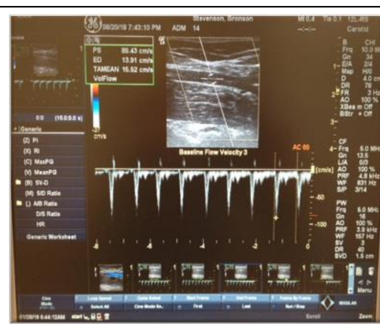

Figure 1B. Image of blood flow diameter and velocity recordings from a brachial artery using Doppler Ultrasound.

Figure 1C. A force transducer setting for a rhythmic handgrip exercise.

abstract). HR from electrocardiogram, beat-to-beat arterial BP from Finapres and brachial BP, and respiration via pneumobelt were continuously measured before, during and after 2 minutes of dynamic handgrip exercise at 35% and 50% of maximal voluntary contraction. Experimental setting is shown in Figure 1A. In addition, diameter, blood velocity, and flow of the brachial artery were measured using Doppler ultrasound (flow images shown in Figure 1B) on the contracting arm throughout the experiment.

In addition, diameter, blood flow velocity, and flow of the brachial artery were measured using Doppler ultrasound (flow images shown in Figure 1B), and a force transducer setting for a rhythmic handgrip exercise (Figure 1C) on the contracting arm throughout the experiment.

RESULTS

At rest, both control and CP groups had similar resting HR (60.7±1.9 control and 63.0±7.5 CP, bpm, Figure 2A). While resting respiratory rate was lower in CP group compared to the control, resting mean arterial pressure (MAP) and brachial blood flow (BF) tended to be higher in CP ($p=0.08$).

MAP and HR were significantly increased to exercise from rest in both groups with no group differences (MAP, Δ 9.3±2.2 control and Δ11.2±3.3 CP, mmHg; HR, Δ8.4±1.5 control and Δ12.1±4.1 CP, bpm, Figure 2A and 2B). Respiratory rate was significantly increased to exercise from rest in only the CP group (Figure 2C).

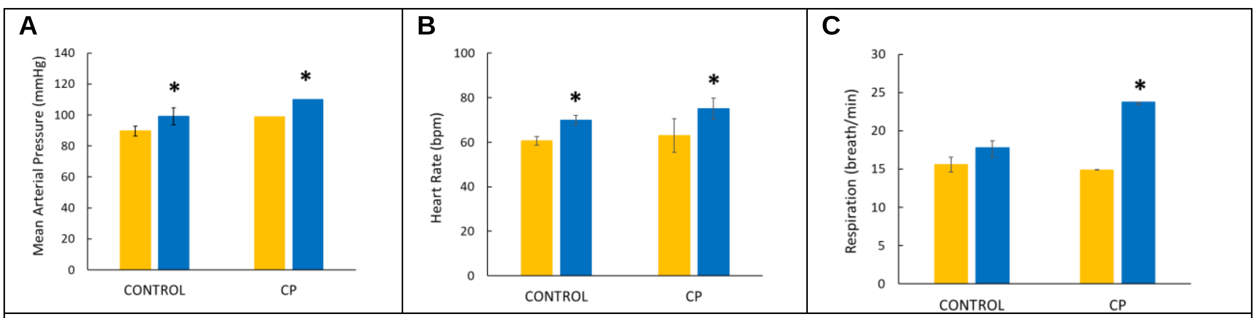

Figure 2. Summary data showing mean arteria pressure (panel A), heart rate (panel B), and respiration (panel C) responses at rest (yellow) and during dynamic handgrip exercise at 50% Maximal Voluntary Contraction (blue) in adults with and without CP. * represents $p<0.05$ vs. rest.

The diameters of the brachial artery were similar at baseline and during exercise when compared to control (Figure 3A). The changes in brachial diameter resting to exercise are minimal in both groups. As noted, the diameter during exercise indicates the average values of diameters during muscular contraction (constricted) and relaxation (dilated) phases. As a result of both diameter and velocity changes, brachial blood flow was increased from rest to exercise in both groups in qualitatively similar fashion (Figure 3C). The delta changes of blood flow from rest to exercise was slightly smaller in the CP group.

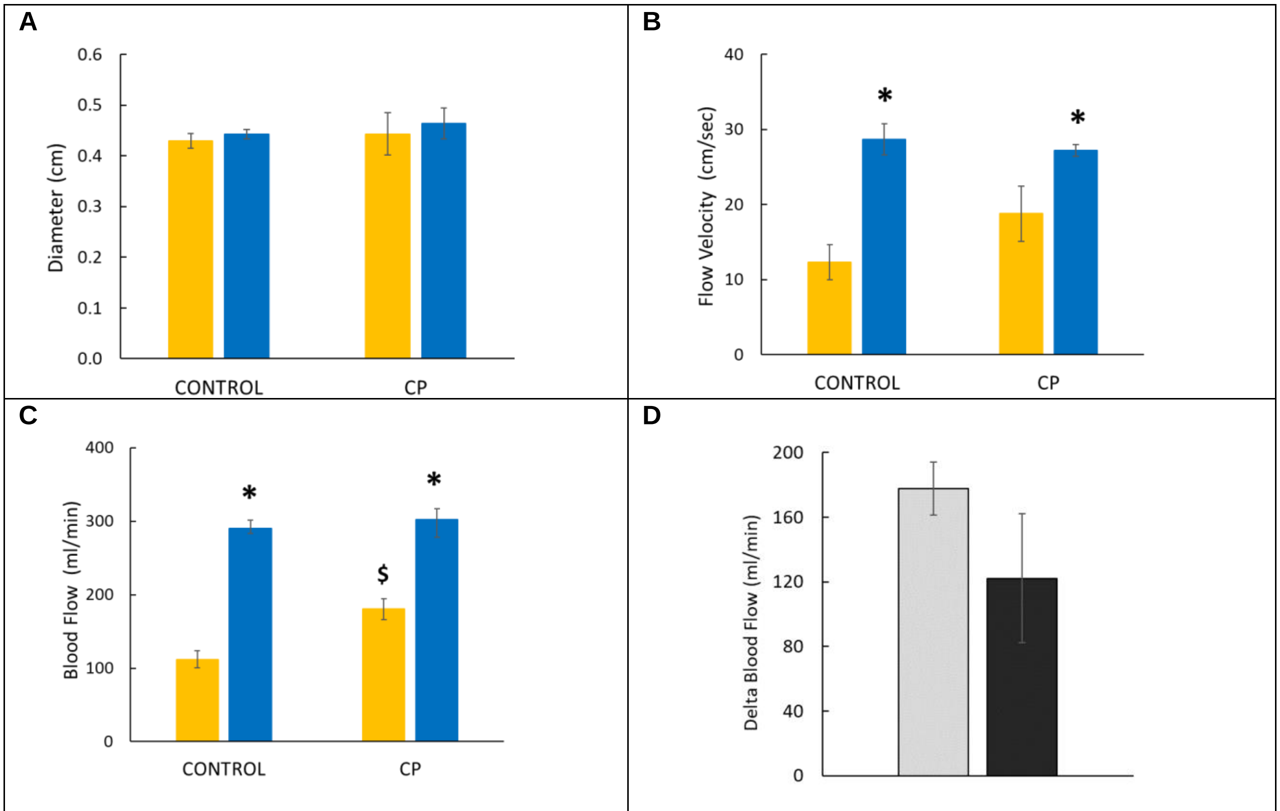

Figure 3. Summary data showing diameters (panel A), blood flow velocity (panel B), and brachial blood flow (panel C) responses at rest and during dynamic handgrip exercise at 50% Maximal Voluntary Contraction (blue) in adults with and without CP. Changes in blood flow from rest to exercise (panel D) in control (gray) and CP (black) groups. * represents p<0.05 vs. rest. $ represents p<0.05 vs. control.

CONCLUSION

While HR and MAP increased to exercise from rest in similar fashion, increase in BF to exercise was blunted in adults with CP. Interestingly, resting BF was higher in adults with CP compared to controls which made us speculate that CP participants may have a higher demand of flow to resting skeletal muscles due to general spasticity which all our CP participants have as a main characteristic of CP. Nonetheless, BF response to exercise appears to be blunted in CP groups which may indicate impaired vascular function. Increase in MAP to exercise is a result from higher cardiac output (a product of HR and stroke volume) and total peripheral resistance. Similar increase in MAP to exercise may be due to both higher HR (Figure 2A, 2B) with differential changes in BF (attenuated vasodilation) to contracting muscles (Figure 3C and 3D) in the CP population.

To conclude, our preliminary data suggest that there are differential neural control mechanisms to regulate BP in the CP population. Other mechanisms, possibly vascular contribution from non-contracting limbs or chemoreceptor activity, may contribute to BP response during exercise in the CP population.

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The Effects of Exercise on Hunger and Satiety Hormone Concentrations Over a 36-Hour Fast: A Randomized Crossover Study

1. Introduction

Food intake and metabolism are often key indicators for the onset of chronic diseases such as diabetes, heart disease and cancer (1). Food intake is largely regulated by hormones that signal satiety and hunger (2). Numerous studies have evaluated how exercise and fasting influence the secretion of these hormones (3,4). Ghrelin is a well know gut hormone that signals a state of hunger to the brain. GLP-1, Leptin, PP, and PYY are known hormones that increase satiation and reduce hunger in humans (5).

It has been found that both an acute bout of exercise, and chronic exercise increases circulating levels of satiety hormones. These changes in satiety hormones influence feelings of satisfaction and decrease food seeking behavior (6). In addition, research in this realm has indicated that intermittent fasting can lead to faster weight loss in obese men and women, but also increases hunger hormones such as ghrelin and reduces satiety hormones such as GLP-1 throughout the fast (7). This hormonal change can influence food consumption, making it difficult to endure the fast.

Currently, there are no studies that we are aware of that couple exercise and fasting to measure the influence on hunger and satiety hormones. Understanding the connection between fasting, exercise and the secretion of these hormones would help determine if and how exercise and fasting should be used together. We aimed to answer this question by measuring hunger (ghrelin, GLP-1, leptin, PP, and PYY) and satiety hormones every 12 hours during a 36-hour fast with and without an initial bout of intense exercise. An additional aim of this study was to measure how subjective ratings of hunger and mood change, and if these ratings are consistent with the expectations gathered from hormonal changes.

2. Materials and Methods

A randomized crossover design with counterbalanced treatment conditions was used to compare the influence of fasting alone to fasting combined with vigorous exercise on the concentration curves of the hormones ghrelin, GLP-1, leptin, PP, and PYY. These two conditions included a 36-hour water-only fast. The outcome variables were hunger, thirst, stomach discomfort, mood, plasma hormone levels of ghrelin, leptin, glp-1, PP, and PYY.

Participants arrived at the lab having not eaten for four hours. Only water was allowed leading up to the visit. After screenings and assessments, a standardized meal was provided, and a 36-hour fast initiated. Participants were instructed to stay hydrated throughout the fast with water only. Noncaloric, electrolyte, or caffeinated additives were not allowed. Gum chewing was also prohibited.

Based on random assignment, participants either proceeded with a fasting-only regimen or participated in the exercise regimen 30 minutes following the initiation of the fasting period. During the testing period, participants were required to complete hunger and mood assessments every two hours, except during sleeping hours. Additionally, they returned to the lab for venous blood draws every 12 hours beginning at 8:00 pm following the standardized meal.

Body weight and height were measured and participants were asked to rate their mood and energy levels using the Brunel Mood Scale (BRUMS), every two hours. The 24-item BRUMS measures six identifiable mood states (Tension, Depression, Anger, Vigor, Fatigue, and Confusion) through a self-report inventory on a 5-point Likert (8).

Two 4 ml tubes of blood were taken from each participant every 12 hours (time 0, 12, 24, and 36 hours). Hunger and satiety hormone levels were quantified using standard 96-well microplate ELISA kits according to the manufacturer’s instructions.

The energy needs for each participant were estimated using equations validated by Hall et al. (2011). This equation uses height (cm), weight (kg), age (years) and gender to predict basal metabolic rates (BMR). Standardized meals were based on macronutrient content (60% CHO, 25% fat, 15% protein). Participants were given 25% (BMR x 1.55 x 0.25) of their daily caloric requirements in the standardized meal. The same foods were given on both test days and participants were instructed to consume all the food provided for each meal.

Participants exercised on a treadmill at a grade and speed that brought their estimated heart rate reserve (HRR) to 70%. Exercise at this intensity is classified as intense (9) and was used because it has been shown to maximize glucose oxidation during aerobic exercise as compared to lower-intensity training (10). Participants exercised in this manner until an equivalent number of calories was expended as given in the standardized meal. The length of exercise was calculated based on the standard ACSM-established metabolic calculation converting oxygen to kcal by multiplying liters of oxygen by 5 (11). All calculations were performed in a preset, protected spreadsheet to ensure accuracy. Energy expenditure was verified using indirect calorimetry.

Area under the curve was calculated using the trapezoidal method. Mixed ANOVAs were used to evaluate differences between conditions and changes in variables over time. Responses from the visual analog scales for hunger, thirst and stomach discomfort were evaluated independently. Significance was set at 0.05. All analyzes were completed using PC-SAS 9.4.

3. Results

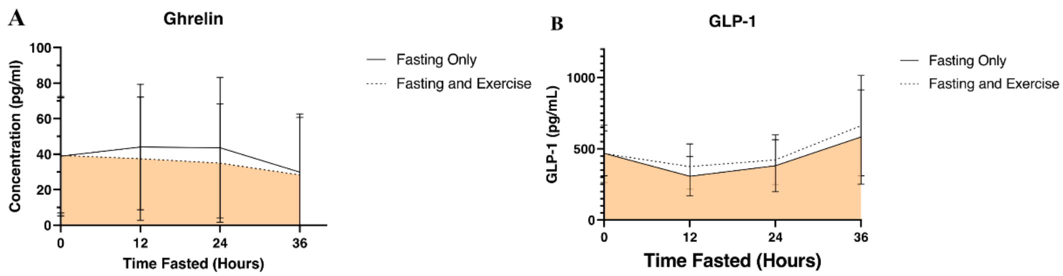
Eleven men and nine women were recruited, and all participants completed all aspects of the study. The standardized meal fed to participants prior to each fast was 614.84 ± 85.18 kcal. Measured energy expenditure during the exercise bout on the fast and exercise day was 587.55 ± 120.13 kcal. The average METs during the prescribed exercise was 9.14 ± 1.37. The average respiratory quotient (R) throughout the prescribed exercise was 0.95 (± 0.14), indicating that the major fuel source for the exercise was glucose.(13)

Plasma ghrelin concentrations remained constant for the first 24 hours of the fast and then decreased from 24 to 36 hours. In addition, area under the curve for ghrelin was higher during the fasting only condition compared to the fasting and exercise condition (1456.12 ± 111.10 pg/ml and 1244.31pg/ml ± 111.10 pg/ml ($p=0.01$), respectively).(see Figure 1A) Plasma GLP-1 concentrations was lower than baseline at hours 12 ($p<0.01$) and 24 ($p=0.04$), then rebounded above baseline levels at 36 hours ($p<0.01$). The area under the curve for GLP-1 was lower in the non-exercise condition compared to the exercise condition (14495 ± 837.58 pg/ml and 16363 ± 837.58 pg/ml ($p=0.04$), respectfully)(see Figure 1B).

In contrast, plasma leptin concentration was progressively lower at each measurement time point over the 36-hour fast ($p<0.01$) but area under the curve was not different between conditions ($p=0.43$). Similarly, both PP ($p=0.11$) and PYY ($p=0.29$) were not different between conditions. Plasma PP concentration was lower than baseline at 12, 24 and 36 hours (p’s<0.01). However, at 24 and the 36 hours PP concentrations were higher compared to hour 12 but remained lower than baseline (p's<0.01). Concentrations of PYY progressively decreased for the first 24 hours and then stayed constant ($p<0.01$).

Subjective feelings of hunger, thirst, and stomach discomfort were measured using a Visual Analog Scale. While hunger increased over course of the study in both conditions ($p<0.01$), there was no main effect of condition on hunger, thirst, or stomach discomfort.

Figure 1 Change in Ghrelin and GLP-1 over a 36-hour fast beginning with or without exercise



4. Discussion

The results of this study suggest that initiating a period of fasting with a bout of exercise resulted in lower ghrelin and higher GLP-1 concentrations compared to fasting alone. Since, higher levels of circulating ghrelin has a powerful impact on hunger, these results indicate that starting a fast with exercise does not make fasting more challenging but may actually make it easier. This finding is strengthened when combined with the results of GLP-1, which was higher in the exercise condition. GLP-1 has been shown to signal fullness and has a satiating property that can reduce food seeking behavior.

Results from our lab have recently demonstrated that initiating a period of fasting with a bout of exercise significantly accelerates the metabolic changes associated fasting. Specifically, we demonstrated that ketosis was achieved about 3.5 hours faster when a fast was initiated with exercise. Additionally, plasma glucagon concentrations were higher. Taken together, these results with the results of the current study suggest that the metabolic changes associated with fasting can be achieved quicker with exercise and without any negative impact on hunger. In fact, exercise may reduce the biological drive to consume food.

Our results also indicate that objectively measured markers of hunger and satiety do not necessarily match subjective ratings of the same feelings. We observed that perceptions of hunger increase over the course of a fast but there was no difference between conditions. This leads to an interesting discussion regarding the ability of our sample to accurately assess their subjective feelings of hunger and satiety during an acute fast. The drive to consume food is complex and involves biological drive and a number of cognitive and environmental factors.

5. Conclusion

Combining exercise with fasting has a positive impact on ghrelin and GLP-1 during a 36-hour fast. Not only does exercise accelerate metabolic changes during a fast, the results from this study show that biological markers of hunger are decreased. The results may inform individuals participating in a variety of approaches to fasting (alternate day fasting, intermittent fasting or time restricted feeding may), possibly making the behaviors more sustainable over time.

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SWACSM Abstract

Do it for the gram: results from the physical activity and social media support (PASS) study

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BACKGROUND: Sedentary lifestyles and physical inactivity are prevalent global public health issues [1]. These issues have been further perpetuated by the current COVID-19 pandemic. Researchers have enlisted different modes to deliver interventions to promote physical activity. Physical activity promotion interventions provide education and motivational strategies which have been shown to produce positive effects on physical activity [1]. Internet-based interventions may offer the most potential due to the opportunity for widespread community outreach, large-scale physical activity promotion, and active user engagement [2]. Active user engagement is particularly of interest as intervention engagement influences change in physical activity, which can improve the efficacy of future interventions [3]. Social media-based interventions are becoming increasingly common as a mode of delivery for physical activity promotion interventions as they can produce moderate improvements in physical activity, but this is still an understudied area [4]. While Facebook has been utilized by researchers to deliver interventions [5], its sister platform, Instagram, is an understudied social media platform [6]. Instagram is of particular interest because of the various methods of interaction with options including sharing photos, videos, hashtags, temporary stories, and commenting on other posts. Its wide reach and potential for increased user engagement make it a promising platform for physical activity promotion interventions. Alongside the increased use of social media as an educational modality is the staggering prevalence of physical activity related misinformation on the platform as perpetuated by various sources. This misinformation can become increasingly problematic if users accept content at face value and do not consider if the source is credible [7]. The impact of misinformation spread throughout the social media platform could be harmful

to the effectiveness of social media as a physical activity education modality. With the potential reach of Instagram as a physical activity promotion intervention, research is needed to determine if the Instagram profile and content play a role in the user's trust in the information and their level of engagement with the platform.

PURPOSE: The primary purpose of the current study is to determine the level of trust that participants place in account holders and if users do further verification regarding provided educational content. The current study also aims to fill the current literature gaps and understanding of the possible role of Instagram as a social media platform for physical activity promotion and content delivery.

METHODS: This study was designed based upon the input from a sample of eight stakeholders. Participants took part in focus groups in Fall 2020 to understand their current use of social media and their preferences in social media interventions and account holders. At the time of the focus group, stakeholders did not use social media as their primary source of physical activity education but were interested in shifting towards such programming. Stakeholders mostly emphasized a desire for personalized feedback from account owners and intervention leaders. Overall, participants stated interest in using social media for receiving physical activity education due to potential support and community with others.

Stakeholder feedback was utilized to design the Physical Activity and Social media Support (PASS) study. The PASS study was approved by the Institutional Review Board (IRB-21-8) and registered on clinicaltrials.gov (NCT04744077). The PASS study took place from January to June 2021 and all study activities were completed virtually. Participants were recruited on a rolling basis from February to March 2021. Eligibility criteria required participants to be 18 years or older, engage in 150 minutes of moderate-to-vigorous exercise per week, and must have a personal Instagram account.

The PASS study was a three-arm randomized intervention that took place through Instagram. Once eligibility was determined, participants were randomized to one of three groups and corresponding Instagram accounts. The three accounts consisted of the control group, student group, and scientist group. Participants randomized to the control group were asked to follow a public account, @itschloeting, a popular fitness influencer that has amassed 749,000 followers. This account was selected as the control as this page accurately represents exercise content that users are commonly exposed to. The two intervention groups were led by a student and a scientist to determine if account holder had an impact on user trust and acceptance of educational and motivational content. The first intervention group was managed by a Kinesiology student and health care worker (SD). SD did not disclose this information and presented herself as a general college student. By withholding area of study and career aspirations, a baseline level of trust could be studied when users are not influenced by academic qualifications and large following. The scientist account was managed by a Kinesiology professor and certified exercise physiologist (ZHL). ZHL disclosed this information on the account and was considered the gold standard as participants could expect reliable information. Both intervention groups, student-led and scientist-led posted identical educational and informative content daily for thirteen weeks. All delivered content was evidence-based and sourced from reputable organizations such as the American College of Sports Medicine, American Heart Association, Center for Disease Control, and World Health Organization. To determine whether participants had confidence in the presented information, source references were not available for participants. Participants were asked to complete weekly questionnaires for a period of four weeks and complete follow-up questionnaires at two and three months through Qualtrics (Qualtrics XM, Qualtrics, Drive Provo, UT USA). As an incentive to complete the study surveys, participants were entered into a raffle where 30% of participants received a free wearable activity monitor, valued at $150. Participants rated their trust in the content presented by the Instagram account and their enjoyment of the Instagram account on a scale of 1 to 10, with 1 being the lower boundary and 10 being the upper boundary. Participants also answered if they learned something new, did any further research, and satisfaction by rating on a 5-point scale from extremely disagree to extremely agree.

The Statistical Package for the Social Sciences (SPSS, version 26, IBM, Chicago, IL USA) were used to perform the analysis. The α-level was set at 0.05. Descriptive statistics were calculated by means and frequencies. Comparisons between groups at 4-weeks were analyzed using non-parametric method through Kruskal-Wallis and Fisher's exact tests for continuous or categorical variables, respectfully. Non-parametric methods were used as the data was not normally distributed. Post comparisons within groups were analyzed using Wilcox Signed Rank test. Outcomes were assessed using the intent-to-treat principle carrying the last measurements forward.

RESULTS: Participants were not statistically different by study groups. Overall, participants were young adult (18-25 years of age), White, and female. Most participants resided within the United States outside of California in states including Arizona, Colorado, Georgia, Illinois, Maryland, Missouri, New Jersey, New York, Ohio, Oregon, Pennsylvania, Rhode Island, Texas, and Utah. Nearly all participants received at least some college education and were regular Instagram users that have used the platform for two years or more and check the app 7 or more times per day. Most participants were categorized as high physical activity based on the IPAQ. Participants were excluded for being active based on a single-item questions that asked the individual to report how many minutes of planned exercise they complete each week.

A summary of baseline and 4-week values is displayed in **Table 1.** There were no group differences on the study outcomes from baseline to 4-weeks using the intent-to-treat principle. With the exception of enjoyment which was different between the control and student group. There was also no difference in pre-post values within study groups with the exception of “learning something” in the student group.

Table 1. Baseline and 4-week ITT values of study variable

		Control (n=13)		**Student (n=17)**		**Scientist (n=16)**	
		Baseline	**4-weeks**	**Baseline**	**4-weeks**	**Baseline**	**4-weeks**
Trust Median (range)		**6.00**	**5.00**	**5.00**	**5.00**	**5.00**	**7.00**
Enjoyment Median (range)˚		**7.00**	**2.50**	**6.00**	**7.00**	**6.00**	**7.00**
Learning something (%) †	Strongly Agree	**7.7**	**0.0**	**20.0**	**17.6**	**13.3**	**25.0**
	Somewhat Agree	**61.5**	**23.1**	**26.7**	**47.1**	**40.0**	**25.0**
	Neither Agree nor Disagree	**23.1**	**23.1**	**33.3**	**29.4**	**26.7**	**25.0**
	Somewhat Disagree	**7.7**	**23.1**	**13.3**	**5.9**	**20.0**	**18.8**
	Strongly Disagree	**0.0**	**30.8**	**6.7**	**0.0**	**0.0**	**6.3**
Further research (%)	Strongly Agree	**0.0**	**0.0**	**6.7**	**0.0**	**6.7**	**0.0**
	Somewhat Agree	**69.2**	**30.8**	**80.0**	**29.4**	**46.7**	**25.0**
	Neither Agree nor Disagree	**23.1**	**30.8**	**6.7**	**23.5**	**20.0**	**6.3**
	Somewhat Disagree	**0.0**	**15.4**	**6.7**	**31.3**	**20.0**	**31.3**
	Strongly Disagree	**7.7**	**23.1**	**0.0**	**37.5**	**6.7**	**37.5**
	Extremely Satisfaction		**0.0**		**15.4**		**10.0**

Overall satisfaction (%)	Somewhat Satisfied		**20.0**		**61.5**		**40.0**
	Neither Satisfied nor Dissatisfied		**20.0**		**15.4**		**30.0**
	Somewhat Dissatisfied		**30.0**		**7.7**		**20.0**
	Extremely Dissatisfied		**30.0**		**0.0**		**0.0**
˚Statistically different between control and student group (<0.05) †Statistically different pre-post in student group (<0.05)							

DISCUSSION: The present study is novel as the results of different Instagram accounts were compared, while most other research does not compare intervention structure. Supplementing the limited research regarding comparative social media-based intervention structures is essential to consider for future use. As most of the results were null, we can conclude that account owner qualifications and identity do not have a meaningful influence on participant trust levels, learning, and overall satisfaction. However, enjoyment significantly differed from the control and student group at 4 weeks. Possible reasoning for this difference in enjoyment could be explained by posting frequency. At the 4-week mark, the student-led group had been consistently posting daily for 4 weeks. In contrast, the control account had decreased posting frequency and new content population. This suggests that interventions are more enjoyable to participants with regular posting frequency. Additionally, only the student-led group reported learning something new over 4 weeks. This could result from relatability as the student account was managed by a white, young adult female, similar to much of the participant demographic. More research is needed to determine whether identity homogeneity plays is meaningful in participant receptiveness to new information.

CONCLUSION: The present study investigated the level of trust that participants place in Instagram account holders and if users do further verification regarding provided educational physical activity content. These factors were not statistically significant amongst groups. However, level of enjoyment differed when comparing the control and student groups. Further research should be done on the impact of posting schedule and account holders identity on intervention enjoyment to be used in future study implementation.

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SWACSM Abstract

The Effects of Meditative and Mindful Walking on Mental and Cardiovascular Health

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ABSTRACT

BACKGROUND: Global health is threatened by the double burden of mental and cardiovascular diseases. One-fifth of adults have a diagnosable mental disorder in one year, and one-third of adults have such a disorder in their lifetimes[1]. More adults live with a disability and die prematurely because of cardiovascular diseases (CVDs) than any other non-communicable disease[2,3]. Treating diseases with exercise as medicine is a major goal of the American College of Sports Medicine (ACSM). The ACSM is in the vanguard of identifying non-pharmacological treatments for mental and cardiovascular diseases. A related novel treatment is mindful exercise. Mindful exercise is "physical exercise executed with a profound inwardly directed contemplative focus[4,5]." Popular modalities are tai chi, qigong, and yoga. These modalities improve mental and cardiovascular health in some healthy and clinical populations, sometimes more than traditional (i.e., non-mindful) exercise modalities[6–14]. However, there is no consensus on the efficacy of two other mindful exercise modalities, meditative and mindful walking. This is because there is not a published synthesis of the relevant literature. Traditional walking is walking without cultivating a profound inwardly directed contemplative focus, thus letting the mind wander. Meditative and mindful walking are walking while applying an accepting, non-judgmental, and present-moment awareness to the bodily sensations, emotions, and thoughts and the walking environment. A person who is walking meditatively or mindfully watches and acknowledges the contents of the mind as they come and go. This practice is called noting, which is not an inherent feature of mind-wandering. Meditative and mindful walking are similar practices, but meditative walking typically involves repeating a word or sound, called a mantra, in the mind or aloud. Determining the

effects of meditative and mindful walking on mental and cardiovascular health is important. First, walking is an accessible exercise modality because it is a natural human behavior that most people can do without intense effort or specialized training. Second, traditional walking without applying mindfulness reduces symptoms of depression and anxiety[15,16], increases aerobic capacity[17], and decreases CVD risk factors[17] and all-cause mortality[18]. A natural question is whether meditative and mindful walking improve mental and cardiovascular health more than traditional walking. **PURPOSE**: We conducted the present study to synthesize the primary literature on meditative and mindful walking to determine their efficacy relative to traditional walking. Our purpose was also to assess the quality of the relevant published research studies. **METHODS**: To achieve our purpose, we conducted a replicable and methodologically rigorous systematic review, as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The full protocol is registered in the international prospective register of systematic reviews called PROSPERO (Registration #: CRD42021241180) and will soon be in press (we submitted minor revisions). The full protocol explains our populations, interventions, comparators, outcomes, and study designs (PICOS criteria); eligibility criteria; search strategy; eligibility screening; data extraction; and risk of bias assessment. Briefly, a five-member review team searched five online databases for primary research articles published in peer-reviewed journals. The five databases were Academic Search Premier, APA PsycInfo, Google Scholar, PubMed, and SPORTDiscus. The risk of bias in parallel and crossover randomized controlled trials (RCTs) was assessed via the corresponding versions of the Cochrane Risk of Bias 2 (RoB 2) tool[19]. The risk of bias in non-randomized controlled studies was assessed via the Cochrane Risk of Bias in Non-randomized Studies - of Interventions (ROBINS-I) tool[20,21]. Our protocol did not include a meta-analysis because the studies included in the systematic review were not homogeneous. The included studies were clinically heterogeneous, meaning they reported diverse populations, interventions, comparators, outcomes, and settings. This heterogeneity prevented a valid meta-analysis, as per published guidance on conducting systematic reviews and meta-analyses[22]. **RESULTS**: To our knowledge, our systematic review is the first synthesis of the meditative and mindful walking literature. Using our search combination in the five databases returned 2,800 hits. Of these hits, 158 sources were included by title. These sources were narrowed to the 14 peer-reviewed journal articles included in the systematic review (Figure 1). Searching the references of the included articles did not lead us to any more relevant articles. The included articles were published between 2013 and 2021 and described studies conducted in Brazil, Germany, the Netherlands, South Korea, Taiwan, Thailand, and the United States. Each study recruited adults who were at least 18 years of age from apparently healthy and clinical populations. Six studies used an intervention called meditative walking/walking meditation. The other eight studies used an intervention called mindful walking/walking while practicing mindfulness/breathing-based walking. Eight studies had participants walk only alone, one study had participants walk only in groups, and one study had participants do both. Another study had participants walk alone or in groups, depending on the study phase. Whether participants walked alone or in groups was unclear in three studies, but participants likely walked alone in two of the studies and in groups in the other. Meditative and mindful walking took place indoors in six studies, outdoors in five studies, and both indoors and outdoors in two studies. The setting was not specified in one study. Nine studies reported only mental health outcomes, and one study reported only cardiovascular health outcomes. The other four studies reported both mental and cardiovascular health outcomes. Four studies provided a short-term intervention (called short-term studies; provided up to two sessions of meditative or mindful within one week; three of the four studies were RCTs). The other 10 studies provided long-term interventions (called long-term studies; provided up to 40 sessions over eight weeks; eight of the 10 studies were RCTs). In 13 of the 14 studies (93%), the interventions significantly improved at least one mental or cardiovascular health outcome. Four short-term studies reported significant improvements in affect, anxiety, attentional focus, distress, enjoyment of physical activity, happiness, perceived activation, self-esteem, overall state mindfulness, and state mindfulness of the body. Eight short-term studies reported significant improvements in affect, anxiety, depression, distress, emotional awareness, perceived stress, post-traumatic thoughts, quality of life, ruminative thoughts, self-worth, overall state mindfulness, and stress. One study showed that one bout of meditative walking in South Korean young-adult females significantly decreased anxiety pre- to post-walk by 25-32% ($p < 0.05$)[20]. A separate study showed that 12 weeks of mindful walking in adults with chronic obstructive pulmonary disease (COPD) significantly decreased anxiety and depression by 57% and 62%, respectively ($p < 0.05$)[23]. No short-term study reported effects on cardiovascular health, but four long-term studies reported significant improvements in aerobic capacity, C-reactive protein, total and low-density lipoprotein cholesterol, cortisol, fasting blood glucose, glycated hemoglobin, flow-mediated dilation of the brachial artery, interleukin-6, nitric oxide, percent body fat, pulse-wave velocity, self-reported physical activity, six-minute walk distance, systolic and diastolic blood pressure (SBP and DBP), and triglycerides. One study showed that 12 weeks of meditative walking in adults with type 2 diabetes significantly decreased SBP and DBP by 12% and 8%, respectively ($p < 0.05$)[24]. A separate study showed that 12 weeks of mindful walking in adults with COPD significantly increased the six-minute walk distance (meters) in as little as eight weeks ($\beta = 32.7$ [95% CI: 12.7, 52.8], $p = 0.002$)[21]. Across all the short- and long-term studies, eight of the nine parallel RCTs and both crossover RCTs had some concerns or a high risk of bias. The two non-randomized studies included in the systematic review had a serious risk of bias. **DISCUSSION:** The primary purpose of the present systematic review was to synthesize the primary literature on meditative and mindful walking and determine their efficacy relative to traditional walking. Meditative and mindful walking consistently and significantly improve mental and cardiovascular health outcomes. Often, the improvements are better than those caused by non-mindful walking or not walking. This finding is consistent with a meta-analysis that shows yoga reduces anxiety more than non-mindful exercises (small significant effect)[9]. The findings of the present systematic review must be interpreted cautiously for three reasons. First, few of the included studies required meditative or mindful walking as an independent intervention: Many of the studies also required group discussions, physical exercises, or seated meditation that could have confounded the relationship between walking and the outcomes. Second, nearly every study that shows significant improvements in at least one outcome has a high or serious risk of bias and notable methodological limitations. The risk of bias was most commonly high in the randomization process, measurement of the outcomes, and selection of the reported results. Third, the meaningfulness of the improvements to the participants is unclear. This is because population-specific minimal clinically important differences (MCIDs) have not been established for most of the outcomes measured in the studies of meditative and mindful walking. Population-specific MCIDs for these outcomes should be established so researchers can determine if improvements by meditative or mindful walking are clinically meaningful for participants' societal function, morbidity, and mortality. The present systematic review should also be interpreted cautiously because of its limitations. A meta-analysis was not conducted because the included studies were clinically heterogeneous. Relevant studies not written in English or indexed in the five selected databases may have been missed. Relevant unpublished data were also possibly missed. Finally, studies of labyrinth walking were not included. Labyrinth walking is a unique form of meditative walking that should be considered separately. The first author reviewed the relevant literature recently in a separate narrative review[23]. **CONCLUSION:** The present systematic review is a comprehensive and rigorous synthesis of the primary literature on meditative and mindful walking. Collectively, published studies of meditative and mindful walking show that both mindful exercise modalities significantly improve mental and cardiovascular health outcomes better than non-mindful walking and non-walking control interventions. The accuracy of this conclusion should be determined by new RCTs that are methodologically rigorous, minimize bias, and require meditative or mindful walking as an independent intervention without added physical or mental exercises.

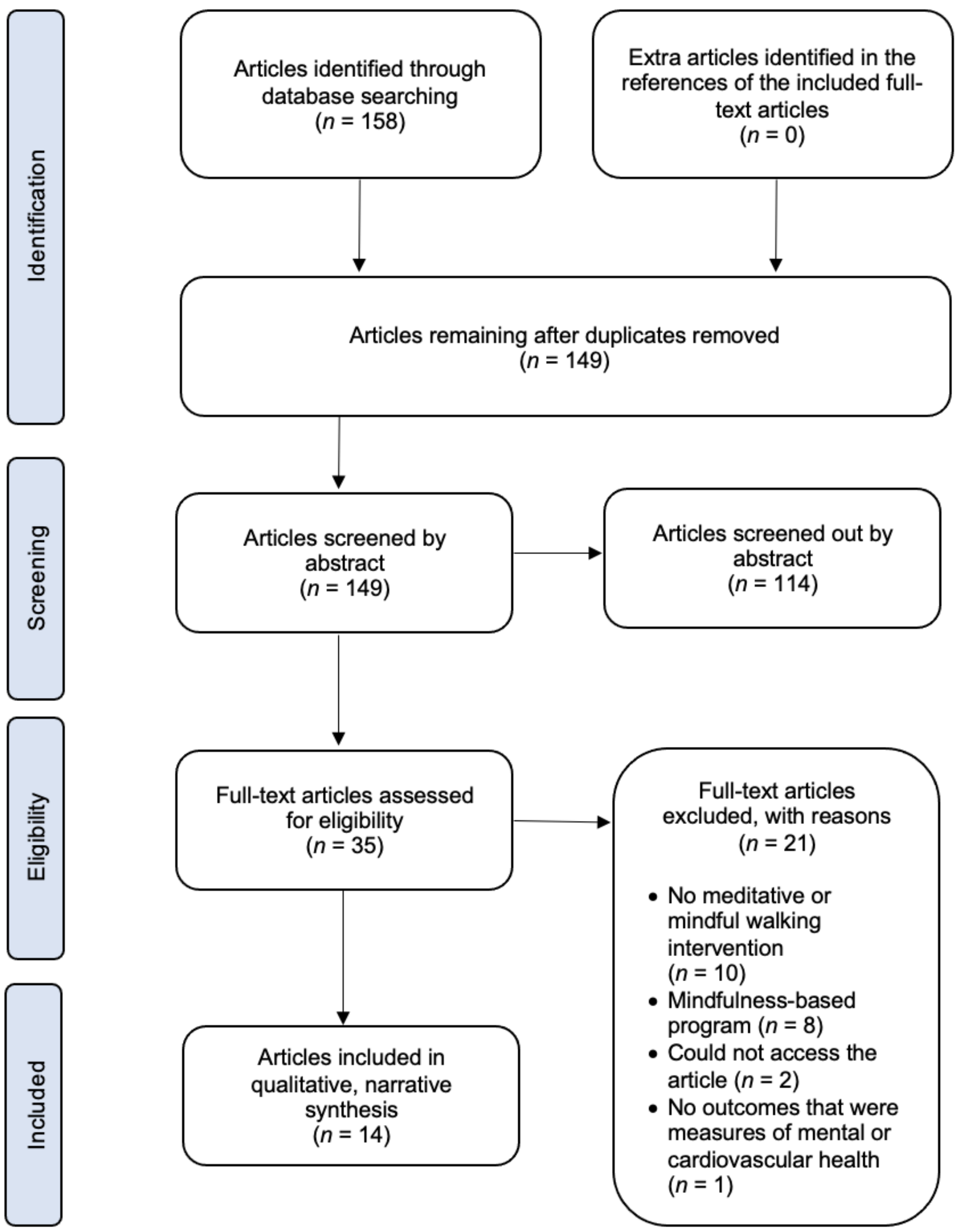

Figure 1. Flow diagram that illustrates how articles were screened for inclusion.

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SWACSM Abstract

Efficacy of a Regression Method to Confirm VO_2max in Middle-Aged and Older Adults: A Pilot Study

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ABSTRACT

Verification testing following a maximal graded exercise test (GXT) has been shown to be effective at indicating whether VO_2max was attained for middle-aged and older adults but performing two maximal efforts in a single day may not be practical or possible for certain individuals. **PURPOSE**: To evaluate the efficacy of a regression method for identifying a VO_2 plateau in order to confirm the attainment of VO_2max. **METHODS**: Twenty-one recreationally active (VO_2max: 21.8-50.3 ml/kg/min) middle-aged and older (46-76 yrs.) men (n=11) and women (n=10) completed an individualized ramp GXT on the cycle ergometer, and one hour later, a verification protocol at 105% of their maximal work rate (WR) achieved during the GXT. Verification criterion was met if the difference between the highest VO_2 during the verification was ≤2% greater than the VO_2max achieved during the GXT. VO_2 plateau was identified by least-squares regression analysis of the 4 minutes immediately prior to the last 2 minutes of the VO_2-WR curve. Modelled VO_2max was extrapolated using the VO_2-WR regression equation and the maximum WR achieved during the GXT. If the difference between modelled and actual VO_2max was >50% of the slope for the linear portion of the VO_2-WR relationship relative to the assigned protocol, then a plateau was observed. McNemar's test of marginal homogeneity was used to detect differences in the proportion of paired data of individuals' attainment of VO_2max criteria. **RESULTS**: Of the 21 participants,15 (71.4%) met the verification criterion while 6 (28.6%) did not, compared to the regression method where 16 (76.2%) achieved the regression criterion while 5 (23.8%) did not. McNemar's test revealed no significant difference between participants' ability to achieve the regression and verification criteria ($X^2(1)=0$, p=.999). **CONCLUSION**: The regression method used in this study may be an effective strategy for determining VO_2 plateau and confirming that VO_2max was attained during a GXT with middle-aged and older adults on a cycle ergometer. This time-efficient regression method is comparable with the verification criterion but does not require a second maximal test, which may be advantageous for those where the verification trial may not be practical.

Introduction

The identification and confirmation of 'true' maximal oxygen uptake (VO_2max) achieved during a graded exercise test (GXT) has been the source of debate since the seminal works of A.V. Hill and colleagues (7). The most common indicator of VO_2max is a plateau in VO_2 despite an increase in exercise intensity (1). Despite its prevalence in research, there is no agreed upon 'gold standard' for what constitutes a plateau (8,11). The most cited VO_2 plateau criterion was proposed by Taylor et al. (16) and is a difference in VO_2 of ≤2.1 ml/kg/min or approximately ≤150 ml/min as a participant nears exhaustion (11). Achieving this criterion is highly variable (2) and has been demonstrated to be influenced by age, protocol, modality, and the methodology used in data analysis (3). The inclusion of a verification bout following a GXT that requires participants to exercise at a greater absolute work rate than that achieved during the GXT helps to avoid issues concerning the 150 ml/min VO_2 plateau criterion (10). A higher VO_2 observed when exercising at a greater work rate (WR), indicates that the highest VO_2 during the GXT was not a 'true' maximal value (12). While this method has been demonstrated to be an effective assessment to indicate that VO_2max was attained with middle-aged and older adults (5,6), performing two maximal efforts in a single day may not be comfortable, practical, or possible for certain populations.

A technique to confirm VO_2max that does not require a second maximal test is a least-squares linear regression analysis of the slope of the VO_2-WR relationship (9,13). By modelling the rate at which VO_2 increases during the linear portion of an individual's VO_2-WR relationship relative to the protocol used during the GXT and assessing the difference between a modeled and predicted VO_2max values, a plateau can be identified that is individualized to each participant's VO_2 kinetics (9,12). This regression method has only been used in young (27 ± 4 yrs.) adult males (13) or a cohort of very fit male cyclists and runners with an average age of 37 yrs. (9). Importantly, previous researchers have demonstrated that advancing age alters VO_2 kinetics during exercise (15). Therefore, the efficacy of this criterion to confirm attainment of VO_2max for middle-aged and older adults is unknown. Accordingly, expanding on the work of Poole et al. (13) and Midgley et al. (9), the present study seeks to evaluate the efficacy of a regression strategy for identifying a VO_2 plateau and therefore confirming that VO_2max was attained in a sample of middle-aged and older adults on the cycle ergometer compared to the verification criterion.

Methods

Participants

Twenty-four recreationally active (≥150 minutes of moderate to vigorous intensity aerobic activity per week for one or more years) middle-aged and older men (n=12) and women (n=12) participated in the parent study in which the maximal exertion data were recorded (6). The study was conducted in Albuquerque, NM at an altitude of 1,585 m and at which participants had resided for at least 6 months prior to testing. All participants provided written informed consent before enrolling in the study and all procedures were approved by the local Institutional Review Board for human subjects research.

Experimental Design

Participants completed a maximal GXT and a verification bout on an electronically braked cycle ergometer (Excalibur Sport, Corval Lode B. V., Lode Medical Technology, Groningen, Netherlands). Testing was completed in a single day and tests were separated by 60 minutes of seated recovery. Participants were asked to refrain from caffeine (12 hours), heavy exercise and alcohol (24 hours) prior to testing. Participants performed a 5-minute warm-up on the cycle ergometer at a self-selected exercise intensity. After the warm-up, subjects donned a mouthpiece (Hans Rudolph Inc., Kansas City, MO) and nose clip. Gas exchange data were analyzed using a metabolic cart (Parvomedics TrueOne 2400, Sandy, UT). The metabolic cart was calibrated prior to each test according to the manufacturer's instructions. Participants began an individualized GXT designed to elicit volitional exhaustion within 8-12 min (17). Individualized ramp protocols (10-30 watts/min) were selected based on sex, body mass, and activity level. Expired gases were collected for the verification protocol in the same manner as was done during the GXT. The verification protocol consisted of exercising for 2 minutes at 50%, 1 minute at 70%, and until volitional exhaustion at 105% of the maximal work rate achieved during the GXT (10). Upon verification trial termination, participants engaged in an active recovery for five minutes.

Data Processing

Data were time-averaged using retrograde 30s intervals; the highest averaged 30s value for VO_2 was classified as VO_2max (10). VO_2max was confirmed using a verification trial. A 2% criterion for measurement error between VO_2max and the highest VO_2 during the verification trial (VO_2verfi) was used. This criterion was based on the measurement error claimed by the manufacturer (ParvoMedics) when assessing flow via a pneumotachometer (Hans Rudolph Inc., Kansas City, MO) (4). The verification criterion was met if the difference between the VO_2verfi was ≤2% greater than the VO_2max achieved during the GXT (10). A VO_2 plateau was identified by least-squares regression analysis of the 4 minutes immediately prior to the last 2 minutes of the VO_2-WR (30s average values) curve as this was determined to best represent the linear portion of the VO_2-WR relationship (Figure 1) (9). The strength of this linear relationship was assessed using the coefficient of determination (R^2). A modelled VO_2max (mVO_2max) was extrapolated using the VO_2-WR regression equation and the maximum WR achieved during the GXT. To account for the influence of the protocol used during maximal testing on VO_2 kinetics, the slope was multiplied by the WR of the protocol. If the difference between the modelled and actual VO_2max was >50% of the slope for linear portion of the VO_2-WR relationship relative to the assigned protocol, then a plateau was observed (9). Furthermore, individual VO_2-WR responses were assessed using the 95% confidence interval (CI) of the regression slope at mVO_2max, so that if VO_2max was above the 95%CI, then this was evidence of an accelerated or nonlinear VO_2 response. If VO_2max was within the 95%CI this was a linear VO_2 response, and if VO_2max was below the 95%CI, then this confirmed that a plateau in VO_2 occurred (12,13).

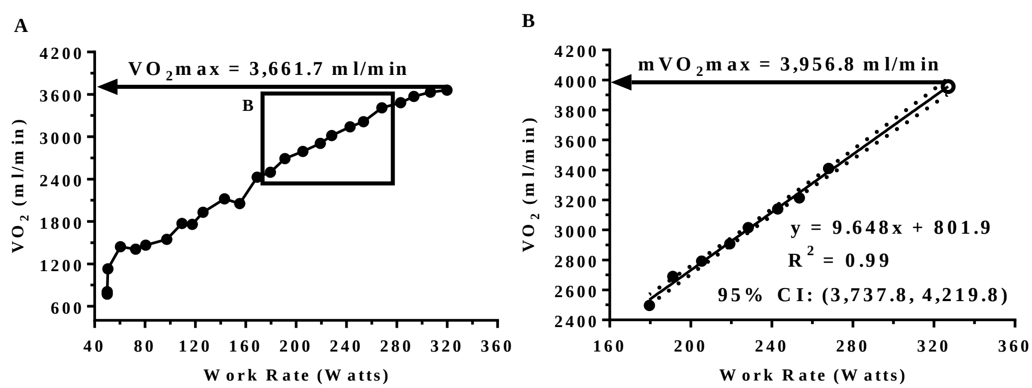

Figure 1. Example of a plateau in VO_2 identified through least-squares regression analysis of the linear VO_2 kinetics during a 25 watts/min ramp protocol (n=1). A) Raw data of the VO_2-WR relationship using 30s retrograde values during a graded exercise test. B) Least-squares regression of the linear VO_2 kinetics and modeled VO_2max (mVO_2max) extrapolated from maximum work rate achieved during the graded exercise test (open circle). VO_2 kinetics relative to the protocol used during maximal testing was determined to be 241.2 ml/min for every 25 watts increase as calculated by the product of the slope (9.648 ml/min) and protocol (25 watts/min). The difference between the modelled and actual VO_2max was 295.1 ml/min, which is >50% of 241.2 ml/min, therefore, a plateau was observed. VO_2max also fell below the 95%CI of mVO_2max confirming that a plateau in VO_2 occurred.

Statistical Analysis

Individual responses for the verification and regression methods were compared to confirm VO_2max attainment. McNemar's tests of marginal homogeneity was used to detect differences in the proportion of paired data of individuals' attainment of VO_2max criteria via R version 4.0.2 (R Core Team, 2021). The least-squares regression technique was performed via Prism version 6 (GraphPad Software Inc., La Jolla, CA).

Results

Due to technical difficulties with the metabolic cart, data from two of the women could not be used. Additionally, case diagnostics identified a 47-year-old man with a VO_2max of 47.1 ml/kg/min as an influential outlier by having a large Cook's D relative to the rest of the data set. The analysis after the removal of this participant will be presented. Table 1 shows the participant demographics and physiological data for the remaining men (n=11) and women (n=10) that were included in data analysis. The slopes of the linear VO_2-WR relationship during the GXT ranged from 69.2 to 331.2 ml/watt/min with an average of 178.7 ± 63.3 ml/watt/min. The R^2 for the regression models ranged from .85 to .99 with an average of .96 ± .04. The average upper and lower bounds of the 95%CI of mVO_2max were 2,351.9 ± 842.7 and 2,704.5 ± 961.4 ml/min, respectively.

Table 1. Participant characteristics (n=21)

	Mean ± SD	**Range**
Age (yrs.)	61.0 ± 8.1	46.0 – 76.0
Height (cm)	168.3 ± 9.8	145.7 – 184.0
Body mass (kg)	67.7 ± 14.0	49.7 – 103.2
VO_2max (ml//min)	2,371.4 ± 839.2	1,205.0 – 4,038.7
VO_2max (ml/kg/min)	34.7 ± 9.2	21.8 – 50.3
Work rate max (watts)	217.9 ± 74.1	86.0 – 364.0

The results of McNemar's test revealed no significant difference between participants' ability to achieve the regression and verification criteria ($X^2(1) = 0$, p =.999). Of the 21 participants included in the analysis, 15 (71.4%) met the verification criterion while 6 (28.6%) did not; compared to the regression method where 16 (76.2%) achieved the regression criterion while 5 (23.8%) did not. Individual VO_2 responses during the GXT revealed that; 9 participants (42.8%) had additional evidence of a plateau since their VO_2max fell below the 95%CI of the mVO_2max, 12 participants (57.1%) demonstrated linear VO_2 kinetics as they were within the 95%CI, and no participants were above the 95%CI.

Discussion

The purpose of this study was to evaluate the efficacy of a regression strategy for identifying a VO_2 plateau that does not require a second bout of maximal exercise in a sample of middle-aged and older adults on the cycle ergometer. No significant difference was observed in the achievement rate between the regression model for assessing VO_2 plateau and the verification criterion for our sample, 76.2% vs 71.4%, respectively. Previous researchers have concluded that the regression method is comparable to the verification criterion with young adults (13) and the current study builds upon this finding by demonstrating its effectiveness in a sample of middle-aged and older adults of both sexes.

In this study, the verification bout was used as the reference method due to the wide variability in older adults exhibiting the ≤150 ml/min criteria for a plateau in VO_2 at the end of a GXT (14). Additionally, the verification criterion avoids relying on arbitrary cut-off values to indicate a physiological maximum has been achieved (13). In theory, those interpreting VO_2 data from a GXT could use the VO_2-WR relationship regression method to identify if a VO_2 plateau was achieved using the steps described above (Figure 1). A participant that meets both the regression and 95%CI criteria does not require a verification bout, thereby, not necessitating a second maximal test. On the other hand, if an individual met the regression criterion but their VO_2max was not below the 95%CI of the mVO_2max, then a verification bout is recommended to confirm VO_2max was attained during the GXT.

Conclusion

The results of this study suggest that using a regression method is an effective strategy for determining a VO_2 plateau in a sample of middle-aged and older adults exercising on a cycle ergometer. Furthermore, this method of confirming VO_2max is comparable with the verification criterion but does not require a second maximal test, which may be advantageous for those where the verification trial may not be comfortable, practical, or possible. We recommend that exercise physiologists and other health professionals consider using the regression method combined with the 95%CI of the modeled VO_2max criterion to confirm VO_2max during a GXT.

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A Comparison of Heat Treatment-Induced Skeletal Muscle Adaptations Relative to Exercise Training

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ABSTRACT

In vitro and animal studies indicate that the response to heat stress is associated with beneficial adaptations that promote cell health and survival. Few studies to date have examined this finding in human subjects, and it is unclear how the adaptation compares in magnitude to exercise training. **PURPOSE**: To investigate the skeletal muscle adaptations (namely mitochondrial biogenesis and capillarization) of 6 weeks of deep-muscle heat treatment relative to exercise training. We hypothesized that heat treatment (HT), applied through pulsed shortwave diathermy (2 hr, 3 days/week) over a 6-week intervention period would lead to increased mitochondrial content and capillarity within skeletal muscle, though to a lesser extent than single-leg knee extension exercise training (EX; 40 min, 3 days/week). **METHODS**: We randomized 28 sedentary but otherwise healthy, young adults (ages 18–36; n = 13 female, n = 15 male) to receive either HT, EX, or sham heating sessions (CON; 2 hr, 3 days/week) over 6 weeks. Diathermy increased muscle temperature by 3.2 ± 0.33 °C ($P < 0.0001$) within 20 minutes. Muscle biopsies were taken from the vastus lateralis at baseline, after 3 weeks of intervention and again after 6 weeks of intervention. **RESULTS**: Following 3 and 6 weeks of heat treatment, we did not observe significant changes in mitochondrial biogenesis or capillarization. However, exercise training was sufficient to elicit an increase in individual capillary-to-fiber ratio ($P = 0.0003$), capillary density ($P = 0.0428$), and the Capillary to Fiber Perimeter Exchange Index ($P = 0.0089$). Significant increases in the expression of mitochondrial protein Complexes I ($P = 0.0073$) and IV ($P = 0.0015$), were observed in the exercise group, but not the heat or control groups. **CONCLUSIONS**: 6 weeks of localized HT, when applied to young healthy individuals, is insufficient to induce mitochondrial biogenesis or capillarization in skeletal muscle. Additionally, our findings provide support for the extensive body of literature that connects exercise training to beneficial skeletal muscle adaptations.

A Comparison of Heat Treatment-Induced Skeletal Muscle Adaptations Relative to Exercise Training

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BACKGROUND: Skeletal muscle is a dynamic and adaptable tissue that contributes to mobility, exercise capability, and the performance of activities of daily living[1].It is recognized that endurance training elicits robust adaptations in skeletal muscle[2], two of the primary underlying and most well-characterized of these adaptations being increased microvascular density[3] and mitochondrial biogenesis[4,5,6]. It is understood that these adaptations arise from the variety of stresses imposed on the muscle by exercise, including oxidative, metabolic, mechanical, and heat stresses[7,8]. A limited number of studies suggest that repeated exposure to mild heat treatment (HT) stimulates mitochondrial biogenesis[9] and pro-angiogenic[10] microvascular remodeling in human skeletal muscle. However, it is currently unknown how the magnitude of these adaptations compare to those observed via exercise training. The **PURPOSE** of this study was to examine the effect of 6 weeks of deep muscle heating on skeletal muscle mitochondrial biogenesis and microvascular remodeling, relative to the adaptations observed through exercise training. I hypothesized that 6 weeks of heat treatment would increase mitochondrial content and capillarity within skeletal muscle relative to a sham heat treatment, but to a lesser extent than what would be observed through the exercise training intervention.

METHODS

Subjects: Twenty-eight untrained adults (15 male, 13 female; 18-36 years) completed this study. Inclusion criteria included participation in no structured physical activity (PA) for the preceding 3 months and passing a health screening questionnaire. Exclusion criteria included known cardiovascular/metabolic diseases, pregnancy, or taking any prescription medication excluding birth control. The study was approved by the Brigham Young University Institutional Review Board.

Study Design: Subjects were randomly assigned to a control (CON), passive heat treatment (HT), or exercise (EX) group. One week after the initial muscle biopsy, subjects began reporting to the laboratory 3 days a week for a 120-min HT or CON session, or 40-min EX session on the right leg. HT was administered using pulsed shortwave diathermy. Two diathermy drums were placed directly on the vastus lateralis (VL) and turned on at 27.12 MHz and 800 bursts per second. In order to heat muscles of the quadricep group evenly, the drums were alternated from a more proximal to a more distal position every 20 min over each 2-hr HT bout. CON subjects had nearly identical visits to those in the HT group. The same settings that were used for HT were programmed for the CON group, however, the diathermy was not turned on. The EX subjects performed 40 min of knee extension (KE) exercise 3 days per week. The intensity of exercise during each visit alternated from light intensity to 4-min bouts of high-intensity exercise. Six minutes of light-intensity exercise was performed at the start and end of each session to allow the subject to adequately warm up and cool down. Subjects were also randomly selected from each group to have thermocouple temperature probes inserted into the VL during their first intervention visit to assess intramuscular temperature. Midpoint and post-training biopsies were obtained from the right VL at 3 and 6 weeks, respectively. Tissue samples were stored at −80 °C. All biopsies were taken from the right VL and moved proximally from the first incision ~1 cm for each subsequent biopsy. For analyses, all samples from each subject were measured on the same plate to account for any variability between plates.

Immunohistochemistry: Eight-micrometer cross-sections of muscle tissue samples were cut using a cryostat at −25°C, mounted on Superfrost slides, and air-dried for 10 min. After fixation and blocking steps, the samples were incubated in the appropriate primary antibodies (CD31 and Dystrophin) in a humidified chamber overnight at 4 °C. Following several washes, sections were incubated in the appropriate secondary antibodies (Alexa Fluor 488 and Cy3) for 30 min at 37 °C.

Protein Analyses: Frozen samples were weighed and homogenized in T-PER buffer at a ratio of 9 µL per mg of tissue with an added protease and phosphatase inhibitor cocktail. Homogenates were centrifuged and then stored at –80 °C. To quantify biomarkers of microvascular remodeling, homogenates were measured with a Luminex Magpix multiplexing system using a 17-plex Human Angiogenesis/Growth Factor Magnetic Bead Panel. Mitochondrial protein Complexes I-V and PGC-1α protein expression were analyzed using an automated capillary electrophoresis system Wes (ProteinSimple). The following primary antibodies were used: Total OXPHOS Human WB Antibody Cocktail and Anti-PGC-1.

Statistics: A mixed model ANOVA was used to examine the main effects of time (pre vs. mid vs. post) and intervention (control vs. heat vs. exercise) in conjunction with the interaction of group × time. A Tukey-Kramer HSD test was performed post hoc when appropriate. Alpha was set at $P < 0.05$. Data are expressed as means ± SD.

RESULTS

Intramuscular Temperature: VL temperature in the HT group increased 3.2 ± 0.33 °C ($P < 0.0001$) within 20 min of application of shortwave diathermy, where it remained elevated for the remaining 1.5-hr session. In the EX group, temperatures increased by 1.8 ± 0.42 °C ($P < 0.0001$) by 10 min and remained elevated for the following 30 min. In the CON group, temperatures did not change significantly over the 2 hour session.

Muscle Capillarization: No significant main effect of group ($P = 0.2014$) was detected for the individual capillary-to-fiber ratio (C/F_i) following 6 weeks of intervention. A significant main effect of time ($P < .0001$) was observed, and post hoc analysis revealed this difference to be in the EX group from pre to post ($P = 0.0003$). Post hoc analysis on our group × time interaction ($P = .0408$) revealed a significant difference between EX and CON groups following 6 weeks of intervention. There were no significant changes in C/F_i at 3 or 6 weeks in either the HT or CON groups. When data were analyzed per volume (capillary density (CD)), no significant main effect of group ($P = 0.2445$) was detected following 6 weeks. A significant main effect of time ($P = 0.0028$) was observed, and post hoc analysis revealed this difference to be in the EX group from pre to post ($P = 0.0428$). There were no significant changes in CD at 3 or 6 weeks in either HT or CON groups. Similarly, analysis of the Capillary to Fiber Perimeter Exchange Index (CFPE Index) revealed no significant main effect of group ($P = 0.4182$) following 6 weeks of intervention. A significant main effect of time ($P = 0.0006$) was observed, and post hoc analysis revealed this difference to be in in the EX group from pre to post (P = 0.0089). There were no significant changes in the CFPE Index at 3 or 6 weeks in either the HT or CON groups.

Molecular Indicators of Angiogenesis: In total, 14 of the 17 analytes were detected within skeletal muscle. Overall, HT had little effect on expression of these markers, but EX elicited significant changes in several of the markers. Angiopoietin-2 (ANG-2), Fibroblast Growth Factor (FGF-1), Hepatocyte Growth Factor (HGF) and Vascular Endothelial Growth Factor A (VEGF-A) increased significantly from baseline following 6 weeks of EX training.

Mitochondrial Biogenesis: We measured the concentrations of 3 mitochondrial respiratory chain subunits (Complex I, II, and IV), as well as protein expression of PGC-1α, an upstream regulator of mitochondrial biogenesis. Following 6 weeks of intervention, no significant main effect of group (P = 0.1305) was observed in the expression of Complex I. A significant main effect of time (P = 0.0307) was observed, and post hoc analyses revealed these differences to be in the EX group following 3 weeks (P = 0.0129) and 6 weeks (P = 0.0073) of intervention. No significant main effect of group (P = 0.4773) or main effect of time (P = 0.4608) was detected in Complex II protein expression. No significant main effect of group (P = 0.0982) was observed in the expression of Complex IV following 6 weeks of intervention. A significant main effect of time (P = 0.0005) was observed, and post hoc analyses revealed these differences to be in the EX group following 3 weeks (P = 0.0133) and 6 weeks (P = 0.0015) of exercise training. There were no changes in the protein expression of mitochondrial Complexes I, II, and IV in HT or CON groups. Finally, no significant main effect of group (P = 0.7614) or main effect of time (P = 0.6678) was observed for PGC-1α protein expression.

DISCUSSION

The purpose of this study was to examine the skeletal muscle adaptations induced by HT, namely microvascular remodeling and mitochondrial biogenesis, relative to EX training. Contrary to our hypotheses, we found that 6 weeks of HT administered to the knee extensor muscle group using shortwave diathermy, did not elicit significant increases in either skeletal muscle capillarization or mitochondrial content. We also report that 6 weeks of high-intensity interval single-leg KE exercise was sufficient to induce both mitochondrial biogenesis and microvascular remodeling in the VL.

Kuhlenhoelter et al. (2016) first reported that after an acute bout of lower body heating or unilateral thigh heating, the mRNA expression of angiogenic regulators in young adults increased significantly. Subsequently, Kim et al. (2020) reported that the expression of pro-angiogenic factor VEGF was enhanced after a single session, as well as after 5 days of repeated HT. These studies suggested that a long-term application of HT may induce angiogenesis in skeletal muscle. Hesketh et al. (2019) reported improvements in skeletal muscle capillarization similar to those induced by moderate intensity continuous training (MICT) following 6 weeks of whole body HT in healthy, untrained adults. In contrast to their findings, we did not observe increases in any index of capillarity or the expression of pro-angiogenic factors after our 6-week intervention of localized deep-muscle HT. This can potentially be explained by the differing time courses, subject characteristics, and HT modalities used by the prior studies. For example, the higher level of PA that was accepted by Hesketh et al. (2019) among their participants may have contributed to the angiogenic benefits that they observed following HT intervention. This is evidenced through the increased maximal rate of oxygen consumption observed in the HT and MICT groups alike. Whereas their exclusion criteria included exercising more than 150 min/week, we did not allow any structured PA. Additionally, most of the recent heat studies (Hesketh et al., 2019; Kim et al., 2020) have used heating modalities that heated a greater portion of muscle mass and/or likely elicited some systemic effects in addition to those observed within the skeletal muscle specifically. For example, Hesketh et al. (2019), who reported increased capillary density following a similar 6 weeks of intervention, utilized a protocol in which their participants sat in a heat chamber, a systemic form of HT. On the other hand, Kim et al. (2020), whose form of HT was more localized, elicited no significant improvements in VEGF, ANG1, or capillary contacts. It is therefore reasonable to question whether or not our localized HT did not promote greater systemic effects that may contribute to skeletal muscle adaptations. For instance, existing literature associates sauna bathing, a form of systemic passive HT, with better cardiovascular and circulatory function in humans[10,13]. Perhaps skeletal muscle adaptations are more likely to be elicited through systemic, rather than localized HT, and this raises an interesting question for future research.

Consistent with existing literature, 6 weeks of EX training led to improvements in skeletal muscle capillarization. Expression of CD31, as well as the expression of pro-angiogenic factors such as VEGF-A, HGF, and ANG-2 all increased significantly with EX training. This finding provides further support to previous studies that have reported beneficial microvascular skeletal muscle adaptations following at least 6 weeks of EX training[10, 14, 15].

Contrary to our hypothesis, no changes were observed that would be consistent with mitochondrial biogenesis after 6 weeks of HT intervention. Our hypothesis was primarily based on the results of Hafen et al. (2018), who used the same HT modality and reported increases in both PGC-1α and mitochondrial respiratory protein Complexes I and V. However, increases in mitochondrial function in response to HT has not necessarily been a universal finding in the literature. Both Kim et al. (2020) and Hesketh et al. (2019) reported that local HT had no effect on respiratory chain protein content. Like us, both of these studies implemented extended heating protocols (6–8 weeks). Together, the findings of our study and those recently conducted by Kim et al. (2020) and Hesketh et al. (2019), indicate that 6 weeks of repeated bouts of HT may be insufficient to increase long-term mitochondrial content in healthy, untrained adults. It is worth noting that Hafen et al. (2018) did not see an increase in maximal enzymatic activity of citrate synthase, a common surrogate marker of mitochondrial content. However, Hafen et al. (2018) reported significant augmentation of maximal coupled and uncoupled respiratory capacity using high-resolution respirometry. This finding may indicate that HT, rather than signaling for increased mitochondrial content, could possibly lead to improved efficiency of existing mitochondria.

In contrast to the findings of HT, 6 weeks of our EX intervention was sufficient to induce increased mitochondrial content. Significant increases were observed in Complexes I and IV, at both 3 and 6 weeks of EX. These results add to the extensive body of literature that supports exercise training as a means of improving skeletal muscle mitochondrial biogenesis[16, 17, 18]. A recent study by MacInnis et al. (2017) reported that following 6 sessions of single-leg cycling, Complex IV protein content increased by 24% post-training. This is in line with our finding that 6 weeks of single leg KE led to a significant increase in Complex IV protein expression post-training (P = 0.0015).

We chose to apply local HT for 120 minutes, as this dose has previously been shown, when applied over a shorter time course (6–14 consecutive days), to increase mitochondrial biogenesis and PGC-1α expression, attenuate the reduction in angiogenic signaling associated with limb disuse (unpublished data), and increase the expression of heat shock proteins[9, 20, 21]. One unintended consequence of this protocol was that some participants reported the inability to maintain their habitual levels of PA throughout the study. The additional 2 hr of sitting, 3 days/week, could have decreased the amount of time that participants may have spent on PA such as walking to campus, grocery shopping, etc. The results of existing step reduction studies demonstrate the potency of decreased ambulation as a means of skeletal muscle deconditioning[22, 23, 24]. While our protocol likely did not lead to such a drastic step reduction, it was perhaps ample enough to overshadow any potential benefits of the HT. Perhaps the additional sedentary time was not enough to elicit maladaptation below baseline (hence the lack of significant decreases in HT and CON groups), but it may have been sufficient to prevent any potential mitochondrial or pro-angiogenic remodeling following 6 weeks of HT.

In conclusion, 6 weeks of localized HT, applied to the knee extensor muscles through pulsed shortwave diathermy, appears to be insufficient to induce skeletal microvascular remodeling and increased mitochondrial biogenesis in healthy, untrained adults. Further research is necessary to determine if HT may illicit beneficial skeletal muscle adaptations in other populations (i.e., elderly, injured, or bedridden adults), serving as more of a protective mechanism against muscle maladaptation. Additionally, our findings among the EX group align with existing literature, in that 6 weeks of EX training is sufficient to induce skeletal muscle mitochondrial biogenesis, as well as increased capillarization.

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Kinematics and Motor Responses of Law Enforcement Officers in a Spontaneous Lethal Threat Scenario

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ABSTRACT

When law enforcement officers (LEOs) face the spontaneous acts lethal force, there is no “warning or foreperiod;” as in typical assessments of motor response, which rapidly evokes a startle response. The Firearms draw in controlled settings is; however, such an analysis when under duress has not been examined for motor response. **PURPOSE**: The purpose of the present study was to evaluate LEOs firearm draw and motor response following a spontaneous presentation of lethal force in a training scenario. **METHODS**: A total of 22 active duty LEOs engaged in training scenario under the ruse of a “communication experiment.” The officers were instructed to take the report from a woman that was struck by her husband. The first trial was terminated with a whistle below at approximately 1 min. In the second trial, a door in the back of the room slams and a husband enters the room yelling. When the husband entered the visual field of the LEO (~20 ft away), he drew and fired a training pistol armed with training ammunition at the LEO. The LEOs were video recorded (Go Pro) and their kinematics were measured using wearable sensors (OPAL). A third gun draw trial, not under duress, was recorded to act as a control. **RESULTS**: The threat of lethal force evoked a startle response of 0.78 ± 0.44 s with the most common startle responses characterized by shielding of the body with the non-shooting arm and flexion of the neck and/or back to “dodge” the gun shot. Initiation of the tactical response, i.e., moving to draw their weapon to return gun fire, occurred during the startle suggesting the startle is an open-loop motor program and the tactical responses is a close loop motor program. Draw times were 0.35 ± 0.29 s slower under duress vs. the control trial ($t=3.40$, $p=0.003$, $d=1.05$). The elbow kinematic profiles of the practice draw were observed being more efficient and faster, whereas the ambush draw displayed characteristics of over emphasizing each phase of the gun draw kinematic profile, causing the gun draw to take longer ($r= -0.111$, $p=0.622$). **CONCLUSION**: More dynamic environment training in ambush type situations is needed based on our findings that suggest no performance or kinematic efficiency carry over to the ambush trial compared to the practice draw, due to the novel observation of the startle response and firearm draw overlapping.

BACKGROUND

The examination of human performance movements in law enforcement officers (LEOs) under life-threatening scenarios are pivotal concepts to understand, educate, and to better train those who protect society against crime. LEOs can develop firearm skills in different environments, whether in a control and stable environment (Closed Skills), or in an uncontrolled and changing environment (Open Skills) (Schmidt et al., 2018). Also, motor skill can be performed within these two environments as either Open looped system, which are pre-programmed, previously learned skills, that are executed rapidly with insufficient time for feedback from the nervous system. The other system, Closed-loop systems contain the neurological processing of feedback against a reference of correctness for a skill during the execution (Schmidt et al., 2018). *Bona fide* assessment of reaction time includes a warning and foreperiod, as demonstrated in the Reaction Time Paradigm (Schmidt et al., 2018). When LEOs are facing a spontaneous threat of lethal force, there is no warning nor foreperiod. Indeed, when faced with an ambush-type situation, it takes approximately 0.46-0.70 seconds for LEOs to identify and process a threat to begin a physical response (Lewinski et al., 2015; Ripoll et al., 1995; Vickers, 2007). It has been observed that it can take LEOs between 1.68 to 1.94 seconds to draw from a holster and discharge a pistol when provided a warning and visual signal (Campbell et al., 2013). How fast LEOs can respond when facing a spontaneous and unanticipated threat of lethal force is unknown.

PURPOSE

In a previous study involving simulated threat of lethal force, many subjects exhibited a “startle response” (Dysterheft Robb et al., 2013). Hypothetically, a startle is reflexive (i.e., an open-loop motor program) and not part of the tactical response. Thus, with differences between a laboratory reaction time experiment, we sought to evaluate active duty LEOs motor response and firearm draw kinematics in the present study and how they respond to the simulated spontaneous threat of lethal force.

METHODS

A total of 22 male LEOs (Age = 34 ± 7.3 y; Body Mass = 91.5 ± 12.2 kg; Height = 180.9 ± 9.3 cm) volunteered to participate in the study. All subjects were recruited from a local police department located in Utah. The LEOs were asked to remove all gear from their duty belt and person, and were only provided with a practice pistol in their current holster. All subjects provided informed consent, and all procedures were approved by the host's University's Institutional Review Board prior to data collection. A classroom in the Police Department's training center was arranged to simulate the dining area of a house. To ensure measurement of authentic responses, we did not disclose the true intention of the study in advance; rather, the officers were told the study was a "communication exercise." The LEOs we informed to take the report of a women who had called and complained that her husband hit her and left the property. The first trial was terminated with a whistle below at approximately 1 min. In the second trial, a door in the back of the room slams and a confederate enters the room yelling. When the confederate entered the visual field of the LEO (~20 ft away), he drew and fired a training pistol armed with training ammunition toward the LEO. A final session of data collection was done by having the LEO remove the training pistol from their holster and fire at a stationary target ~6 m away as fast as possible to act as a control trial.

A tripod-mounted video camera (GoPro, California) was placed in the corner and used to time-stamp the appearance of the threat. Kinematic data was collected using a 15-sensor, wearable motion capture system (ADPM Wearable Technologies, Portland, OR), sampling at a rate of 128 Hz. The (OPAL) sensors were strapped to each subject according to the manufacturer's guidelines. Data were retrieved using the manufacturer's software (Moveo, ADPM Wearable Technology, Portland, OR). Time points for the initiation of the motion and the firing of the weapon were made by viewing joint angular-time plots by the initiation of the movement indicated by the start of elbow flexion, and the termination of the firing was indicated by peak elbow flexion.

Descriptive statistics for experimental trial, and control trial where initiation of the motion, termination, kinematics profiles of the shooting arm were examined, and startle response times of the motions were reported in mean ± SD. A paired sample t-test and Pearson product correlation test were completed to compare times between the practice draw and room draw. Statistical significance was set at the $p<0.05$ level.

RESULTS

When faced with the threat of lethal force, during the experimental condition, the reaction time to initiate motion was 0.20 ± 0.21 s. The startle response was observed subsequent to the confederate's behavior, i.e., either the action of him drawing his weapon or the noise of the pistol being discharged. The startle response was 0.78 ± 0.44 s in duration, and was observed as shoulder shrugs, arm shielding body, jumping, etc. The mean times for the LEOs (n=22) to draw and extend their firearm during the control (0.91 ± 0.11 s) trial exceeded the times for the experimental trial (1.27 ± 0.47). Total draw time performance was 0.35 ± 0.29 s slower when under duress ($t_{21} = 3.42$, $p = 0.003$, $d = 1.05$) and observed poor correlation between the two conditions (r = -0.111, $p = 0.62$).

When examining kinematics of the gun draws, majority demonstrated a double hump kinematic profile, depicting each phase of the gun draw, reaching for gun (first hump), gun pulled out of holster (second hump), and gun extension (time to shoot) towards the target/confederate. In the experimental trial, the gun-draw kinematics observed higher levels of elbow flexion and extension (Figure 2, Right Panel) compared to the control trial.

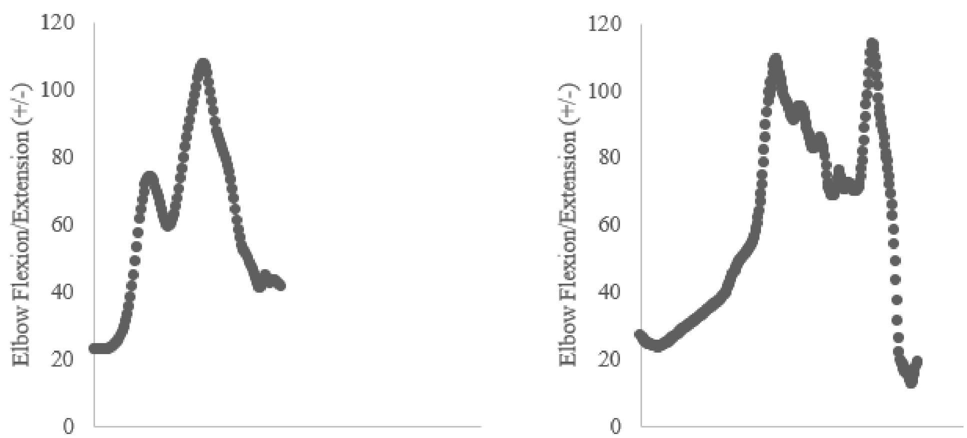

FIGURE 2. Kinematic Profile of practice draw (Left Figure) and Room draw (Right Figure). The X-axis represents the amount of data points that were collected at the rate of 128 Hz per second, and Y-axis is the degrees of the elbow joint.

DISCUSSION

What was observed in the current study was how the startle response directly affected draw time, and gun draw kinematic profiles quality. LEOs are likely experiencing a startle response that impairs their ability to begin a proper physical response as fast and efficiently as in closed skill environments under no duress. What was novel in majority of the subjects regardless of the duration of the startle, was this continuation of the startle response movement while the LEO was beginning to draw their weapon in experimental trial, different from the current Reaction Time Paradigm (Schmidt et al., 2018). The overlap, which has never been observed, is what is potentially causing the increase time to draw their weapon and simultaneously negatively impacting firearm draw motion kinematics. Many of the startle responses were of the opposite arm used for their gun draw, which makes it possible, yet challenging to draw their weapon while the startle response was occurring. This increase in limb movement is one of the factors that could have caused the draw time to be extended in the experimental trial. Our findings support the recommendations to train motor patterns in realistic levels of occupational stress to train out the perceptual and movement strategies (i.e., startle response movements) that put a LEO at risk for assaults, and minimizing incorrect responses when spontaneous stimulus' are presented in open skill environments (Di Nota & Huhta, 2019).

Furthermore, total draw time performance in the experimental trial was 0.35 ± 0.29 s slower, demonstrating the lack of performance consistency in the experimental trial. The current study's results are informative for law enforcement leaders who train LEOs to understand that the recommendations of open skill training to develop a higher capacity to process environmental cues to efficiently respond to lethal threats with fast gun draws and better manage a startle responses.

CONCLUSION

The current study provides the first understanding of performance times and motion kinematics comparisons of a LEO firearm draw in both a closed and open skill environment. In addition, LEOs who performed fast in the closed skill environment in the case of a control trial, had no carry over affect into the experimental trial which represents an open skill environment. There may be a lack of open-skill training, causing the LEO to be unable to process the high levels of environmental feedback being sent to the brain in dynamic environments. This may cause a startle response that can negatively impacts a LEO's firearm draw time and efficient motion kinematics that may put LEOs and civilians' life at risk if unable to respond appropriately when lethal force is spontaneously presented while on duty.

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SWACSM Abstract

COVID-19 Induced Changes in Physical Activity at Public Parks in Los Angeles County

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ABSTRACT

There are many health benefits to outdoor physical activity (PA). However, the ability of public parks to provide PA options for those most vulnerable during pandemic-related public health restrictions is unknown. **PURPOSE**: To examine how COVID-19 has affected the use of public parks in Los Angeles and the resulting PA of park goers. **METHODS:** A total of 8 public parks (4 low income (LI), 2 medium income (MI), 2 high income (HI)) (N= 5864) were observed using the System for Observing Play and Recreation in Communities (SOPARC) tool between October 2020 and July 2021. Activity zones were assigned an activity score based on the number of park goers engaged in sedentary, moderate, or vigorous PA. Park goers were also surveyed about their PA habits (n=84). Data was combined with similar data collected during 2009 prior to analysis in SPSS to determine the impacts of pandemic stages on PA behaviors across demographics. **RESULTS**: Parks were visited more frequently in 2009 (3.2±0.15 visits/week) and 2021 (3.2±0.21) compared to 2020 (2.5±0.23), $p<.05$. More children and teens were observed in larger and greener MI and HI compared to LI parks which were overrun by homeless encampments. An interaction effect between income, COVID-19 restrictions, and age-group was discovered for activity score ($p<.05$). Activity scores for all age-groups in MI and HI and for children in LI parks were highest during the peak of the pandemic. In LI parks, activity scores for adult and elderly park goers were not affected by changing restriction levels and were generally lower (adults: 1.5±.03; elderly: 1.4±.04) compared to MI (adults: 1.5±.03; elderly: 1.5±.08) and HI (adults:1.6±.04; elderly: 1.8± .08) parks. In 2020, a higher percentage of MI (38.1%) and HI (29.2%) survey respondents reported meeting the ACSM PA guidelines than LI (13.9%) participants but were less reliant on public parks for accumulation of all daily MVPA minutes (LI: 77.8%, MI: 41.5%, HI: 14.9%). **CONCLUSION**: The results of this study support previous conclusions about income-based PA disparities. Results suggest that public parks in higher income neighborhoods continually provide residents with safe, health-promoting PA opportunities. However, during a public health crisis, PA inactivity levels are exacerbated in low income neighborhoods due, in-part, to park shortfalls.

EXPANDED ABSTRACT

Background

With the advent of COVID-19, and its associated restrictions, physical activity (PA) options for many have been largely limited (5,11). The closure of schools and restriction of activities outside of the home have particularly affected children. Increased screen time and reduced access to PA opportunities such as physical education classes or after school sport programs has been associated with an increase in sedentary behaviors (8). Physical inactivity is associated with obesity and poor cognitive development in children as well as an increased risk of high blood pressure, type 2 diabetes, depression, and even COVID-19 mortality in adults (2, 5, 11).

In parallel to a general decrease in PA, research shows that there is a higher COVID-19 infection rate in more racially diverse areas and a higher death rate in low-income areas (1,6). Prior to the pandemic, it was shown that outdoor exercise is associated with numerous health benefits including: stress reduction, mental fatigue restoration, and improvement of mood, self-esteem and perceived health (4). In the past several months, it has also been shown that PA in outdoor spaces helps to decrease the spread of the virus to vulnerable populations due to better air flow and dispersion of respiratory droplets that lead to infection (13). Additionally, simply spending time outdoors, also known as nature therapy, has been correlated with health-promoting responses of the nervous, endocrine, respiratory, and immune systems (7, 12).

There are significant disparities in access to safe outdoor spaces conducive to PA in Los Angeles (9). Parks located in low income and minority neighborhoods typically are smaller in size, lack well-maintained green open spaces, contain fewer park amenities, are located a greater distance from resident homes, and are for all these reasons more likely to be used for sedentary activity compared to parks located in high income neighborhoods (3, 9, 14, 15). We are not aware of any study that has examined the relative impact of public park resource inequities combined with social distancing and masking requirements and closures of schools during COVID-19 on PA behaviors. It is not clear if public health guidelines related to the utilization of public parks have exacerbated PA and health disparities in Los Angeles neighborhoods.

Purpose

Therefore, the purpose of this project was to examine the effects of the SARS-CoV-2 pandemic and subsequent public safety measures on the reliance and utilization of public parks for PA in Los Angeles.

The influence of public park access, amenities present in these recreational spaces as well as the socioeconomic and demographics of surrounding neighborhoods were considered independent variables during data analysis. By examining the alterations people have made in their park behaviors, it may be possible to provide evidence-based recommendations for future park design and amenity modifications.

Design/Methods

All methods received institutional IRB approval before study initiation (FA20-009=RAN). A multimethod longitudinal study was conducted in Los Angeles County. A total of 8 parks, 4 low income (LI: median household income = <$60,000/year), 2 medium income (MI: median household income = $60,000-$100,000/year), and 2 high income (HI: median household income = >$100,000/year), based on US Census data were divided into activity zones and observed using the validated System for Observing Play and Recreation in Communities (SOPARC) tool 1-4 different times between October 2020 and July 2021 (10). A total of 5864 (children: n=1443; teens: n=578; adults: n=3419; elderly: n=424) park goers were observed throughout the study.

SOPARC records park amenities, park user demographics, activity modes, and activity levels (sedentary, moderate, vigorous). An activity score was calculated for each activity zone at each park during each observation period by summing the number of park-goers engaged in sedentary, moderate, or vigorous activity multiplied by a code value and dividing by the total number of people in the zone [S*1+M*2+V*3/(S+W+V)]. The highest activity score possible is a value of 3. The data collected during the pandemic was combined with similar observation data (N =1084) collected during summer 2009 at the LI parks.

Adult and elderly park goers at each location were also surveyed about their own and their family's PA habits during COVID and more recently as restrictions have been lifted (N=84; women: n=56, men: n=28). In the survey, respondents were asked a series of questions about their weekly PA, their usage of public parks, and how their PA habits and comfort at parks has been impacted by COVID restrictions and closures.

Linear mixed model analysis, ANOVA, and nonparametric McNemar analyses at an alpha level of .05 was performed using SPSS to analyze the impacts of the stages of the pandemic on activity behaviors across demographics.

Results

Survey analysis showed that people visited parks more frequently during summer 2009 (3.2 +/- 0.15 visits/week) and 2021 (3.2 +/- 0.21 visits/week) compared to summer 2020 (2.5 +/- 0.23 visits/week), $p < .05$. It was also discovered that people were more likely to visit the park for picnicking, a sedentary activity, in May-June 2021 than May-June 2020 ($p < .05$). In 2021, 68.3% of survey respondents indicated that they felt more comfortable utilizing public parks after being vaccinated.

The closure of indoor gyms and other exercise locations during the pandemic was less likely to increase PA at public parks for LI and MI compared to HI park goers (Figure 1) as demonstrated by the % who disagree or strongly disagree to the Likert prompt. Additionally, the closure of schools was more likely to increase family use of public parks for HI park goers (Figure 2). In 2020, only 13.9% and in 2021, only 12.1% of adults surveyed in LI parks reported meeting ACSM PA guidelines (150 minutes moderate intensity aerobic activity/week + 2X per week muscle strengthening activity) and of those who did, 77.8% (2020) and 68.9% (2021) accumulated all MVPA minutes at public parks. In contrast, in 2020, 38.1% and 29.2% of individuals surveyed in MI and HI parks respectively reported meeting the PA guidelines. In 2021, these percentages were 50.0% (MI) and 26.1% (HI). In 2020, 41.5% of MI and 14.9% of HI participants met these guidelines through PA in public parks. In 2021, the percentages were 66.7% and 16.7% respectively.

Although park visits were lower during the most restrictive public health guidelines, in general, the activity score of MI and HI parks was highest during the peak of the pandemic (figure 3). While this pattern holds for children across income levels, changing restriction levels had no effect on the activity score of adults and elderly subjects in parks located in low-income neighborhoods (interaction effect: $F_{(12,1542)} = 2.757$, $p < .05$, figure 3). Activity scores for adults and elderly at LI parks were also consistently lower at all time periods compared to activity scores at MI and HI parks (figure 3). Across all observation periods, the percentage of sedentary park goers was lower at HI (42.7 +/- 2.1%) compared to both LI (56.1 +/- 1.7%) and MI (51.6 +/- 1.7%) parks and the percentage of park goers engaged in vigorous activity was lower at LI (9.6 +/- 0.9%) compared to both MI (14.9 +/- 1.2%) and HI (18.0 +/- 1.6%) parks, $p < .05$. Lastly, the biggest difference in activity scores across income levels was discovered in green space (e.g., open grass fields, grassy areas with tree coverage) activity zones.

Figure 1: Closure of indoor gyms and other exercise locations (due to COVID-19 restrictions) increased my physical activity levels at public parks.

Figure 2: Likert Breakdown - Closure of my child's school (due to COVID-19 restrictions) increased our family's use of public parks.

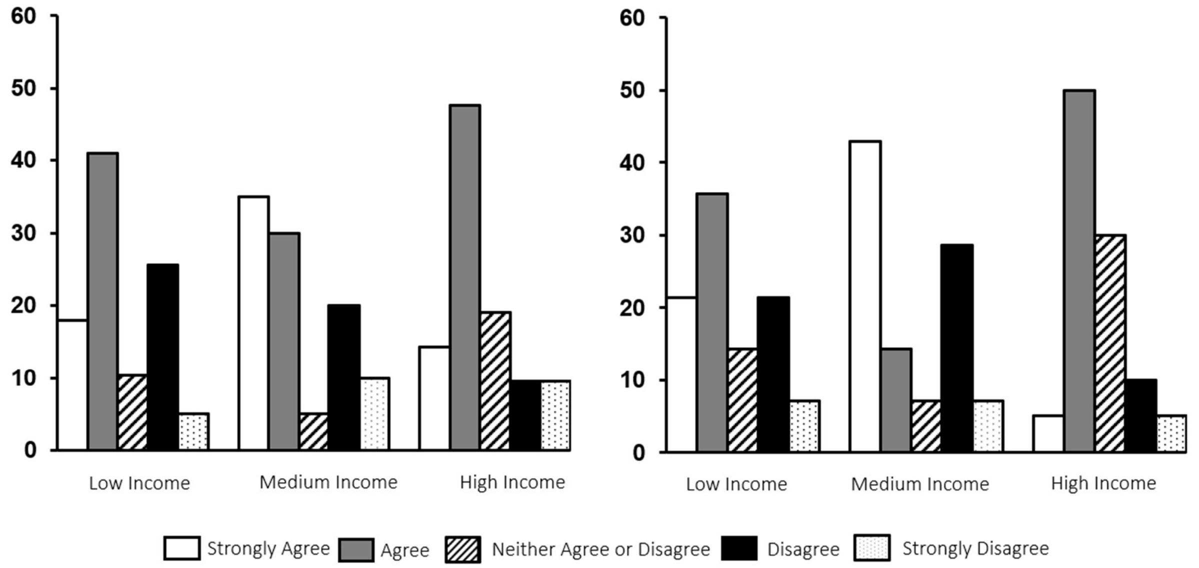
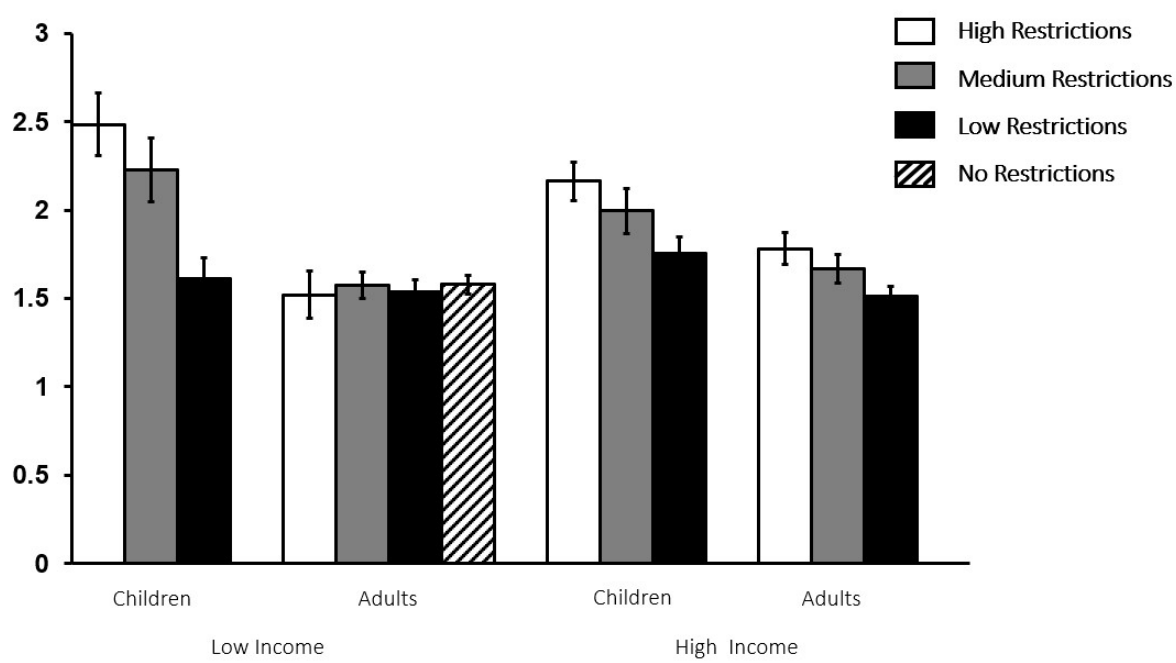


Figure 3: Effect of COVID-19 Restrictions on Public Park Activity

Score



Note: The summer 2009 (no COVID-19 restrictions) data only includes adult and elderly park goers in low income parks.

Discussion

Overall, the results suggest that the pandemic exacerbated pre-existing PA disparities between families in predominantly Latino/Hispanic and Black low-income and predominately non-Hispanic White high-income neighborhoods. In this study, LI parks included fewer amenities, were not well maintained, and had poor lighting. Specific to the pandemic, an increased number of homeless encampments were observed in LI parks. Homeless encampments acted as an additional deterrent to public park usage. Furthermore, low income individuals are less likely to belong to indoor gyms and in low income households, both parents are more likely to work jobs with less flexibility and thus may have had less time during the pandemic to increase park visits. Indeed, the average number of children and teens at HI parks was consistently greater than the number at LI parks. As a result, although child activity scores in LI parks were not different from MI and HI, fewer total children were accumulating MVPA minutes in LI neighborhoods. In addition to more diverse, well-maintained, and highly popular PA zones including walking paths and play structures in MI and HI parks which were lacking in LI parks in this study, MI and HI parks also had large well-maintained grassy areas well suited for PA. As noted by researchers, many of the above-mentioned park amenities in MI and HI parks were better suited for family-based PA. For instance, walking and biking paths were not located next to busy streets and playgrounds were gated to allow children to engage safely in PA.

Conclusion

While public parks have the ability to serve high income individuals even during a public health crisis when other PA spaces are inaccessible, results from this study show that public parks in low income areas do not provide a viable option for increasing PA and improving immune system health despite the heavy reliance of individuals living in low income neighborhoods to use public parks for PA. As a result, opportunities to decrease income-based health inequities are lost. Given the research related to the value of outdoor PA, it is recommended that activity zones better suited to family-based PA should be introduced into parks located in low-income neighborhoods. Furthermore, in conjunction with many other social and public health campaigns, this study emphasizes the importance of contributing resources to the homeless crisis. Lastly, it is recommended that efforts are made to increase accessibility to green space in public parks and/or other public spaces and awareness of the benefits of outdoor exercise in low-income areas.

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SWACSM Abstract

Evaluation of Skipping in College Students With and Without Autism Spectrum Disorder

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ABSTRACT
Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that affects social interactions and behaviors. Previous research has shown that children with ASD demonstrate motor skill deficits in comparison to their neurotypically developing peers. However, it is unknown whether these motor skill deficits translate into adulthood. **PURPOSE**: The study intended to evaluate skipping performance and kinematics in college students with and without ASD to identify potential deficits. **METHODS**: A total of 20 college students, 10 with ASD and 10 without, participated in this study. Following a skipping demonstration, each participant completed three skipping trials. Data was collected using a three-dimensional (3-D), 12-camera motion capture system at 120Hz using reflective markers that were placed on participants' upper and lower extremities. Developmental scoring of skipping performance was performed using a combination of Everyone Can! and the Halverson Developmental Sequences for Skipping. Data were processed using Cortex, Visual 3D, Matlab, and SPSS software. Center of mass excursion, the peak velocity of joint extension during the stance phase, and peak joint angles of the hip, knee, and ankle of the dominant leg were extracted and compared between both groups. Independent t-tests were used to compare normally distributed kinematic variables and Mann-Whitney U test were used to examine the center of mass excursion as well as the difference in developmental scores between both groups with an alpha level of ≤ 0.5. **RESULTS**: Individuals with ASD performed less proficiently in skipping than individuals without ASD as assessed by the developmental scoring. However, there were no statistically significant differences for the peak joint angles, velocities, or vertical center of mass excursion. The ASD group demonstrated an increased medial-lateral center of mass displacement ($p= 0.026$). **CONCLUSION**: Participants with ASD were less proficient in their skip performance in comparison to participants without ASD. Given that skipping is a motor skill used in many common sports and leisure activities, interventions addressing the ability to skip proficiently may promote participation in these activities and help individuals with ASD lead more physically active lives.

BACKGROUND: Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that affects social interactions and behaviors (American Psychiatric Association, 2013); individuals with ASD may demonstrate a deficit in gross motor skills which include reduced balance and posture stability, walking and running gait deficits, and impaired gross and fine motor skills. Extensive research has shown that children with ASD display motor skill deficits in comparison to their neurotypically developing peers. It is predicted that motor skill deficits may contribute to lower levels of physical activity in ASD, which can then lead to a sedentary lifestyle or obesity. It is unknown whether these motor skill deficits carry over into adulthood. Few studies have focused on observing the kinematics of fundamental motor skills in adults with ASD, but not enough evidence exists to conclude how motor skill performance is affected into adulthood. Studying advanced gross motor skill performance might give us a better understanding of motor development in individuals with ASD. **PURPOSE**: The study aimed to evaluate skipping performance in college students with and without ASD. We hypothesized that young adults with ASD would demonstrate lower developmental scores and deficient skipping kinematics compared to young adults without ASD. **METHODS**: A total of 20 college students, 10 with ASD and 10 without, provided consent to participate in this study. Participants were eligible to participate in the study if they were participating in a minimum of 100 minutes of physical activity per week. Individuals in the ASD group also were required to self-disclose a formal diagnosis of ASD. Participants were excluded from this study if they (a) had experienced seizures, stroke, or traumatic brain injury, (b) had a severe visual impairment preventing independent navigation, (c) had a gross sensory defect, (d) required the use of an assistive ambulatory device, and/or (e) displayed significant physical impairments that would limit participation in fundamental motor skills. All participants were asked to provide written informed consent. This protocol was approved by the University Institutional Review Board. Following a skipping demonstration, each participant completed three skipping trials. Data was collected using a three-dimensional (3-D), 12-camera motion capture system at 120Hz using reflective markers that were placed on participants' upper and lower extremities. Developmental scoring of skipping performance was performed using a combination of Everyone Can! and the Halverson Developmental Sequences for Skipping. Two participants with ASD were identified as not performing a skipping movement and were excluded from further analysis. Kinematic data were processed using Cortex (Motion Analysis), Visual 3D (C-Motion, Inc.), MATLAB (Mathworks), and SPSS software. Marker trajectory data were filtered using a low-pass fourth-order Butterworth filter with a cutoff frequency of 12 Hz. The kinematics of the model were measured by determining the shift from each segment's triad of reflective markers to the position and orientation of each segment assessed from the standing calibration trial. Center of mass excursion, the peak velocity of joint extension during the stance phase, and peak joint angles of the hip, knee, and ankle of the dominant leg were extracted and compared between both groups. The Shapiro-Wilk test was used to assess data distribution. Independent t-tests were used to compare normally distributed kinematic variables and Mann-Whitney U test were used to examine the center of mass excursion as well as the difference in developmental scores between both groups with an alpha level of ≤ 0.5. **RESULTS**: Individuals with ASD performed less proficiently in skipping than individuals without ASD as assessed by the developmental scoring (Table 1). The Everyone Can developmental sequence for skipping displayed a lower proficiency in skip performance, specifically in the hop and smooth integration components, as well as the composite score among individuals with ASD. The Halverson Developmental Sequences for Skipping also revealed significant differences in arm (U = 21, p = 0.015) and leg (U = 35, p = 0.045) movements during skipping performance among young adults with ASD. There were no statistically significant differences in the peak joint angles of the hip, knee, or ankle, and no statistically significant differences were found in the vertical center of mass excursion (Table 2). The ASD group demonstrated an increased medial-lateral center of mass displacement (*p*= 0.026). **DISCUSSION**: Children with ASD tend to acquire and mature in their motor skill performance later than typically developing children. Although skipping is one of the least common motor skills to be used after grade school, it is nonetheless the most complex gross motor skill that is developed in childhood. Skipping requires coordination between the legs and arms to move in opposition to one another, as well as sufficient lower extremity muscle strength. Given that skipping is a motor skill used in many common sports and leisure activities, the ability to skip proficiently may promote participation in these activities and help individuals with ASD lead more physically active lives. The purpose of this study was to evaluate skipping performance in college students with and without ASD. Participants with ASD were less proficient in their skip performance in comparison to participants without ASD, as indicated by the lower composite scores on the Everyone Can! criteria, and the lower scores on the Halverson Developmental Sequence leg action and arm action (Table 1). Additionally, specific deficits were identified in criteria b and d of the Everyone

Can! Criteria which identify key mechanical components of skipping, and in criteria e which assesses the smoothness of movement. Individuals with ASD were not as successful in performing the skipping action. However, these results overall were not reflected in the biomechanical variables chosen for analysis. Peak lower extremity joint flexion and extension, peak lower extremity joint extension velocity, and vertical center of mass excursion were similar between groups (Table 2). Many participants performed the skipping in a leisurely manner and there was a high degree of variability in the kinematic results; it is possible that greater kinematic differences may have been seen if participants had been asked to power skip with a more explosive movement pattern. Although we did not identify statistical significance, large effect sizes with greater peak ankle dorsiflexion, peak ankle plantar flexion, and peak ankle plantar flexion velocity in the individuals with ASD. Potentially, individuals with ASD exhibited decreased ankle stability, contributing to a less coordinated performance. In terms of kinematics, the only statistically significant difference identified was increased medial-lateral center of mass excursion in individuals with ASD (Table 2). A large effect size ($r = 1.06$) associated with the medial-lateral center of mass excursion supports this significance. The increased center of mass excursion indicates that individuals with ASD may have trouble coordinating and may not have sufficient strength and stability to propel themselves forward, therefore compensating by moving in a side-to-side motion. Given the evidence of difficulties in movement coordination among children and adults with ASD, this finding does not come as a surprise (Fournier et al., 2010; Isenhower et al., 2012; Travers et al., 2013). Although more analysis of various motor skills is needed, this evidence implies that issues with movement coordination may persist into adulthood. Limitations: Although some important results were found in our study, there were a few limitations. Only 8 out of 10 ASD participants were able to perform what was determined to be a skipping movement, so two participants were excluded from our kinematic analysis. This further reduced our already fairly small sample size. It is possible that more deficits in skipping could be identified with a larger sample. Another limitation may have been that skipping was performed indoors in a laboratory which may have placed individual constraints of the laboratory where the skill took place. Finally, our ASD participants were high functioning as all our ASD participants were college students. According to the literature, individuals with ASD will be largely free from symptoms of the disorder by adulthood (Lancet, 2018). This is especially true for individuals with high-functioning autism, so looking at moderate to low functioning ASD participants may be something to consider in further studies. **CONCLUSION**: Individuals with ASD exhibited kinematic and developmental differences in skipping performance compared to individuals without ASD. Lack of instruction and participation in activities that involve skipping movements may have been a factor in the skipping performance of college students with ASD. The results of this study provide evidence that young adults with ASD perform a less developmentally mature version of a skip compared to their peers without ASD. Deficits observed in skipping may be barriers to participating in sports and physically active leisure activities. Given the severe health consequences related to sedentary behavior, it is important to attend to these barriers to lead a physically active lifestyle. Considering these results, practitioners should implement motor skill interventions for children with ASD as increased confidence in performing complex motor skills may aid in promoting healthy behaviors in this population.

Table 1. Developmental scoring of skipping.

Variable	Control	ASD	*p*	Effect Size
Everyone Can! Composite Score	15.0 (0)	10.5 (8)	0.008*	1.344
a. Facing and looking forward	3.0 (0)	3.0 (0)	1	0
b. Steps forward and then hops on the same leg, repeating cycle while alternating legs	3.0 (0)	2.0 (2)	0.018*	1.002
c. Arms move in opposition to legs, slightly flexed at waist level	3.0 (0)	3.0 (2)	0.241	0.432
d. Period of nonsupport during the hop phase before weight transfer to opposite foot	3.0 (0)	2.5 (2)	0.044*	0.78
e. Smooth integration (not mechanical or jerky)	3.0 (0)	1.0 (3)	0.014*	1.099
Halverson Leg Action	3.0 (0)	2.5 (2)	0.045*	0.524
Halverson Arm Action	3.0 (0)	2.0 (2)	0.015*	1.125

Note. Data presented as median (interquartile range).
* indicates statistical significance, $p \leq 0.05$

Table 2. Center of mass and lower extremity kinematics during skipping.

Variable	Control	ASD	*p*	Effect Size
Medial-Lateral COM Displacement (m)	0.03 (0.03)	0.08 (0.1)	0.026*	1.06
Vertical COM Displacement (m)	0.25 (0.08)	0.27 (0.04)	0.155	0.805
Peak Hip Flexion (°)	50.77 ± 9.79	54.60 ± 7.74	0.368	0.434
Peak Knee Flexion (°)	43.34 ± 8.96	44.79 ± 8.69	0.734	0.164
Peak Ankle Dorsiflexion (°)	26.39 ± 4.18	30.65 ± 7.75	0.155	0.684
Peak Hip Extension (°)	-11.04 ± 6.90	-12.87 ± 14.84	0.733	0.158
Peak Knee Extension (°)	3.69 ± 6.98	6.37 ± 8.42	0.471	0.347
Peak Ankle Plantar Flexion (°)	-19.56 ± 8.33	-25.76 ± 9.50	0.160	0.694
Peak Hip Extension Velocity (°/s)	-329.22 ± 67.39	-349.76 ± 89.30	0.585	0.26
Peak Knee Extension Velocity (°/s)	-297.78 ± 50.08	-302.75 ± 72.43	0.866	0.08
Peak Ankle Plantar Flexion Velocity (°/s)	-516.15 ± 81.00	-576.86 ± 127.92	0.237	0.567

Note. Data presented as median (interquartile range) or mean ± standard deviation.

* indicates statistical significance, $p \leq 0.05$

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SWACSM Abstract

Genetic drivers of cardiac remodeling in health and disease in female mice

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ABSTRACT
PURPOSE: Sex differences in cardiac metabolism and cardiometabolic disease susceptibility are well documented. However, the mechanisms underlying sexual dimorphism and the role estrogens play in cardiac physiology aren't well understood, especially in aging women when cardiometabolic disease susceptibility is heightened. The purpose of the current study was to determine key genetic drivers of healthy vs. pathogenic cardiac remodeling and determine the impact of estrogen action on cardiomyocellular function.
METHODS: The UCLA Exercise Hybrid Mouse Diversity Panel (ExcHMDP), comprised of ~100 strains of inbred mice, was leveraged to interrogate genetic drivers of cardiac remodeling in response to exercise training. Female mice from the ExcHMDP remained sedentary (SED) or preformed volitional exercise (TRN) by in cage wheel running (30d). Heart samples (4 SED and 4 TRN mice per strain) harvested following a 6h fast, 30h after the last bout of exercise, were subjected to RNA sequencing. A similar analysis was performed on hearts from 91 strains of female mice treated with the cardiac remodeling drug isoproterenol (ISO). Estrogen action related to cardiac remodeling was studied in female mice with a conditional cardiac-specific deletion of estrogen receptor alpha (encoded by Esr1). Integrated informatic assessment of these transcriptomic data sets identified pathways driving healthy versus pathogenic cardiac remodeling.
RESULTS: Heart weight was increased following exercise training in 85 of 100 strains studied. Cardiac enrichment analysis of differentially expressed transcripts and candidate gene identification analyses revealed 5 potential regulatory genes associated with healthy cardiac remodeling in response to exercise training. We contrasted these findings with the genetic architecture of two mouse models of cardiac hypertrophy-associated heart failure, the ISO-HMDP and cardiac-specific Esr1 knockout. Mitochondrial function and calcium homeostasis emerged as key pathways of regulation related to cardiac hypertrophy.
CONCLUSION: Our studies provide important insight into the genetic architecture and key genetic drivers of cardiac remodeling in females. The goal of our research is to identify cardiac-specific transcripts and pathways that can be targeted therapeutically to preserve cardiac function during aging in women.

Genetic Drivers of Cardiac Remodeling in Health and Disease in Female Mice

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BACKGROUND

Cardiovascular Disease (CVDs) impacts more than 17 million deaths annually, making CVDs the number one cause of mortality in both men and women worldwide[1]. Evidence suggests sex biasing of cardiac disease risk and outcomes, and estrogens are shown to play a role in protection against cardiac pathology. Importantly the incidence of cardiometabolic disease increases in post-menopausal women however the mechanisms underlying this loss of cardioprotection remain inadequately understood[2,3]. Estradiol exerts its effects through both genomic and non-genomic actions regulating cardiovascular physiology primarily by binding and activating estrogen receptor alpha (ERα)[4]. ERα binds to chromatin as dimers at specific [5]DNA sequences known as estrogen response elements (EREs); or may activate other transcription factors to regulate downstream gene expression. Although the protective effects of E_2 in regulating cardiac fibrosis, oxidative stress, mitochondrial function and hypertrophy, the selective effects of ERα in the regulation of E_2 mediated outcomes are unknown. We find in other metabolic tissues that Esr1 exerts strong regulatory control over mitochondrial function and indeed mitochondrial dynamics and function are implicated in the pathobiology of cardiomyopathies including fibrosis, diabetic cardiomyopathy, and ischemic reperfusion injury.[14-16] The heart is a high energy demand organ that consumes ATP derived from the mitochondria and to meet the demand of cardiomyocytes, mitochondria are shown to occupy more than one-third of myocytes by volume.[10] Similar to estradiol, exercise is shown to exert cardioprotective effects however the molecular drivers of this protection are unknown.

PURPOSE

Sex differences in cardiac metabolism and cardiometabolic disease susceptibility are documented. The mechanisms underlying sexual dimorphism and the role estrogens play in cardiac physiology aren't well understood, especially in aging women when cardiometabolic disease susceptibility is heightened. The purpose of the current study was to identify key genetic drivers of healthy vs pathogenic cardiac remodeling and determine the impact of estrogen action on cardiomyocellular function.

DESIGN and METHODS

Animals

ExcHMDP and ISO-HMDP. All studies were approved by the Institutional Animal Care and Use Committee (IACUC) and the Animal Research Committee (ARC) at the University of California, Los Angeles (UCLA). Female mouse strains of the ExcHMDP were acquired from The Jackson Laboratory (Bar Harbor, ME, USA) or through the University of Tennessee Health Science Center. Mice were maintained on a strict 12h light/dark cycle with *ad libitum* access to standard rodent chow (Teklad 8604, Envigo, Indianapolis, IN, USA) and water. Sedentary mice were housed 1-4 animals per cage. Exercised mice were individually housed with access to an in cage running wheel monitored by VitalView® Activity Software (Starr Life Sciences, Oakmont, PA, USA). Mice were given access to the running wheel for about 30 days. After the 30 days, running wheels were locked between 6-9am local time. 24-hours post, cages were replaced, and chow removed from all animals for six hours. Animals were sacrificed between 12-4pm local time.

Daily running distance was calculated as the average running distance per day over the experiment timeframe. Average running speed was calculated by normalizing all 15 second intervals with values > 0 relative to 1 second. Percent of time running was calculated by dividing the sum of 15 second intervals > 0 by the sum of all 15 second intervals.

To interrogate the genetic architecture of isoproterenol (ISO)-induced heart failure, female mice (age 10 weeks) of a second HMDP cohort were treated with ISO for 21 days (30mg/kg per day) by ALZET osmotic mini-pump as previously described (Rau et al. 2015b). Animals will euthanized and hearts excised and prepared for RNAsequencing as described below.

Genetically engineered mice. Control f/f animals were bred with a transgenic line expressing Cre recombinase driven by a tamoxifen-inducible alpha-MHC-MerCreMer (Jackson: 005657) promoter to generate animals with a cardiomyocyte- and time-specific deletion of *Esr1*. Animals were aged to 12 weeks and then injected with a single dose of tamoxifen to induce ERα deletion. Animals were studied 4-6 weeks after tamoxifen washout. All animal experiments were conducted following the guidelines and protocols approved by the University of California, Los Angeles Institutional Animal Care and Use Committee (IACUC).

RNA Isolation, Library Preparation, and Sequencing

ExcHMDP. Whole heart was pulverized in liquid nitrogen. Tissue was homogenized in Trizol (Invitrogen, Carlsbad, CA, USA), RNA was isolated using the RNeasy Isolation Kit (Qiagen, Hilden, Germany), and then tested for concentration and quality with samples where RIN > 7.0 used in downstream applications. Libraries were prepared using KAPA mRNA HyperPrep Kits and KAPA Dual Index Adapters (Roche, Basel, Switzerland) per manufacturer's instructions. A total of 800-1000 ng of RNA was used for library preparation with settings 200-300 bp and 12 PCR cycles. The resultant libraries were tested for quality. Individual libraries were pooled and sequenced using a HiSeq 3000 or NovaSeq 6000 S4 UCLA Technology Center for Genomics and Bioinformatics (TCGB) following in house established protocols.

ExcHMDP Genome Wide Association Analyses

Genome wide association analyses were conducted as described previously (Norheim *et al.*, 2019). Quantitative trait loci (QTLs) were considered distinct between groups if the significant locus was more than 20 Mb from a locus in the other group below the suggestive significant threshold ($P<4.1x10^{-5}$).

ExcHMDP Trait by Trait Correlations

Biweight midcorrelation was calculated for pairwise trait correlations within each group using the WGCNA package in R. The sedentary and exercised trait correlation matrix was visualized using the 'ComplexHeatmap' package (Gu et al., 2016) in R. For trait by trait correlations involving a group difference (sedentary value subtracted from trained value for each strain, or trait delta), a random pairing method was used.

Candidate Gene Identification

Candidate genes in GWAS loci were prioritized based on known biologic function or correlation in co-expression with a specific trait. In particular, genes whose *cis*- regulation was correlated with the trait were considered as highly likely candidate genes. Calculations were computed as described previously (Gusev et al., 2016). Briefly, when only exercise trained animals were used, SNPs within 1 Mb (*cis*-acting) of a gene with a *cis*-eQTL ($p < 1E^{-4}$) were identified. The median of the allele specific expression for each SNP of that gene was calculated and those values were then correlated with a particular trait. For candidate genes identified using both sedentary and exercised animals, sedentary gene expression was subtracted from trained gene expression giving the exercise induced change in gene expression.

RESULTS

Molecular Response to Exercise Training in Heart

Exercise is reproducibly shown to improve cardiovascular function (Ades et al., 1996; Hellsten and Nyberg, 2015). Because heart weight was increased in TRN vs. SED animals (increased in 85% of strains), we conducted cardiac transcriptomics. Enrichment analysis of DEG displayed mitochondrial function, inflammatory and immune processes (leukocyte regulation, macrophage activation, and *TNFα* and other cytokine products), calcium signaling and regulation, muscle growth and development, and angiogenesis (FDR<0.05). These biological processes overlap with those identified in skeletal muscle. Candidate gene identification analysis of exercise-induced cardiac hypertrophy identified five potential regulatory genes associated with healthy cardiac remodeling: *IL31ra*, *Fam167b*, *Tafa5*, *Crip3*, and *Nanos1* (P<0.01). We have identified two of these targets as E_2-responsive with EREs in their proximal promoters.

***ER*α is required for normal cardiac function and protection against fibrosis.**

Female mice showed a significant increase in heart weight (10% increase; p<0.02) 4 weeks after *Esr1* gene deletion compared with f/f control. To assess the cardioprotective impact of ERα we performed echocardiography on the hERαKO model as described[20]. hERαKO and f/f control (n=5) were subjected to three echo evaluations: baseline prior to gene deletion, and 2 and 4-weeks after gene deletion. hERαKO mice presented with a reduced left ventricular ejection fraction (LVEF) reaching significance by four weeks when compared controls. A similar finding was observed for left ventricular fractional shortening (LVFS) and heart rate. Each of these functional changes are indicative of cardiomyopathy further solidifying the significance of ERα in overall heart functional capacity. Collectively, these structural and functional changes in ejection fraction, fractional shortening, heart rate and left ventricular end-systolic diameter in hERαKO mice substantiate the cardioprotective effects of ERα/E2 in rodents and human subjects. Previous studies have shown that E_2 supplementation in ovariectomized (OVX) rodents reduces cardiac fibrosis after transverse aortic contrition (TAC)[23-25]. Hearts from hERαKO and f/f control were harvested from 4-month-old mice, four weeks after conditional *Esr1* gene deletion. Masson's trichrome staining showed a marked increase in fibrotic area in hERαKO compared to control.

DISCUSSION

Postmenopausal women with low circulating E_2 have a substantially increased risk of cardiometabolic dysfunction. Interventions to prevent morbidity and delay mortality as a consequence of cardiometabolic decline are needed. We leveraged large transcriptomics data sets to better understand the pathobiology of heart failure and the healthy vs. pathogenic underpinnings of cardiac hypertrophy. Using transcriptomic analyses to mine for gene drivers of these biological processes allowed us to formulate and test new hypotheses related to cardiac function. We used mouse genetics to test hypotheses related to gene targets of interest controlled by Esr1. The cardiomyocyte-specific estrogen receptor alpha knockout model allowed us to illustrate the importance of ERα expression selectively in cardiomyocytes in the regulation of mitochondrial metabolism, fibrosis, and cardiac function.

CONCLUSIONS Our studies provide important insight into the genetic architecture and key genetic drivers of cardiac remodeling in females with the overarching goal to identify cardiac-specific transcripts and pathways that can be targeted therapeutically to preserve cardiac function during aging in women.

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SWACSM Brief Abstract

Self-Generated Lower Body Negative Pressure as a No-Power Countermeasure for Deep Space

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ABSTRACT

The absence of gravitational forces experienced during spaceflight produces headward fluid shifts which probably cause Spaceflight Associated Neuro-Ocular Syndrome (SANS). In order to counteract these fluid shifts and prevent SANS, especially when power is limited and a human centrifuge is unavailable, other strategies are needed. One possible strategy is the use of self-generated, lower body negative pressure (LBNP) which meets the low power and safety requirements of deep-space missions. **PURPOSE:** In this study we explored acute physiologic responses to self-generated LBNP in a horizontal model of simulated microgravity. **METHODS:** Participants of the study were tested during static 25 mmHg LBNP and compared dynamic self-generating 25 mmHg LBNP chamber as well as upright and supine postures without LBNP. After informed, written consent was obtained, five female and six male subjects' heart rates and blood pressures were recorded along with cross sectional areas (CSA) of left and right internal jugular veins (IJV) by quantitative ultrasound. **RESULTS:** Upright IJV CSAs increased significantly when compared to both static and dynamic LBNP. There was a large standard error in the supine posture and no significant differences when comparing the supine posture to the upright posture or either LBNP condition. However, static LBNP reduced IJV CSA by 70% when compared to the supine posture, while dynamic LBNP reduced IJV cross sectional area by 62% compared to supine posture. **CONCLUSION:** The administered self-generated LBNP and supine LBNP tests and analyses demonstrated that the dynamic, self-generated LBNP may have a similar impact on reducing IJV CSA when compared to traditional static LBNP, thus warranting longer-term tests of self-generated LBNP. In summary, our results suggest that self-generated LBNP at 25 mmHg is as a low-mass, low-volume, unpowered replacement for traditional LBNP hardware (for example, Chibis Suit) during deep-space missions.

SWACSM Expanded Abstract

Self-Generated Lower Body Negative Pressure as a No-Power Countermeasure for Deep Space

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EXPANDED ABSTRACT

BACKGROUND/PURPOSE:

Body fluids shift headward in a microgravity environment. The cephalad fluid shift may contribute to the development of Spaceflight Associated Neuro-ocular Syndrome (SANS) and other spaceflight-related adaptations [1]. While on Earth, postural changes generate hydrostatic forces which alter intracranial pressure (ICP). In microgravity, astronauts experience a headward fluid shift because there is no gravitational vector to produce a hydrostatic gradient [2]. This leads to a mild, but chronically elevated ICP which generates a gradient between ICP and intraocular pressure (IOP) [3]. The pressure gradient may at least partially underlie the pathogenesis of SANS [4]. In 2011, Mader et al. published a landmark paper that identified ocular pathologies in astronauts after long-duration spaceflight [10]. Mader et al. were the first to hypothesize that cephalad fluid shifts and venous congestion may be the mechanism behind ocular structural and functional changes. The cephalad fluid shift may also affect venous flow, specifically affecting volume and outflow in the internal jugular vein (IJV) which is responsible for venous outflow from the head [11]. LBNP offers a potential countermeasure to reverse cephalad fluid shifts in microgravity. Researchers explored this concept and found LBNP effectively reduced ICP, IOP, and internal jugular vein cross-sectional area in simulated microgravity [4], [12]– [14]. More recent publications indicate daily LBNP exposure reduces choroid thickening observed in HDT [15]. However, in 2021, Marshall-Goebel et al. found LBNP reduced IOP in astronauts during spaceflight but did not reduce choroidal thickening [16]. While LBNP did not reduce choroid thickening in astronauts, Marshall-Goebel et al. found LBNP reduced internal jugular vein cross-sectional area and restored stagnant or reversed flow in the IJV [17]. While LBNP does not address all associated pathologies, it may be an integral countermeasure to protect against SANS.

However, LBNP chambers are large, heavy, and electrically powered. Volume, mass, and electrical power are limited resources in spaceflight. A low mass, collapsible, unpowered LBNP device can minimize the impact on resources [18]. The purpose of this study is to evaluate a self-generated LBNP device and to compare acute physiological responses between a traditional, static LBNP chamber and a self-generated LBNP chamber. We hypothesize that self-generated LBNP will produce similar physiological responses when compared to a traditional static LBNP chamber.

METHODS:

<u>Subjects</u>

Eleven healthy subjects (6 males, 5 females; avg. weight 142.8 lbs.; avg. height 67.2 inches; and avg. waist circumference 31.4 inches) participated in self-generated LBNP exercise along with static trials of LBNP. As a group, subjects were of average fitness based on their average height and weight. Participants were selected for the trial based on height and BMI. Subjects were between 5'1" and 6'4" with a BMI of less than 30 kg/m^2. Subjects gave informed, voluntary consent to participate in the study.

<u>Device Descriptions</u>

SELF Device

The self-generating lower body negative pressure device (SELF) consists of a collapsible cylindrical chamber that covers the user's lower limbs and a neoprene skirt fitted around the waist to provide a seal (Figure 1). A belt is used to ensure an adequate seal around the subject. Air leakage is minimized using gaskets and vinyl cement. 24" metal rings maintain the structure of the chamber, allowing it to expand and contract lengthwise.

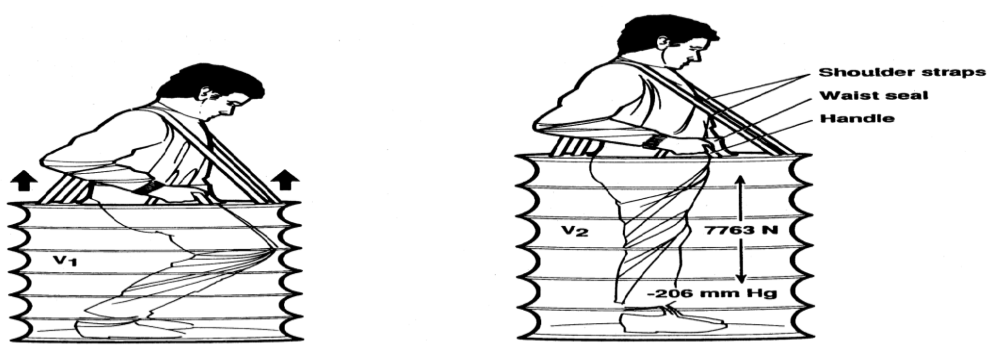

Figure 1: Diagram of the SELF. The user operates adjustable valves near the handles to adjust airflow. The user closes the valves while pushing the bottom plate with their feet to expand the chamber (left). Volume within the sealed chamber increases and pressure consequently decreases to effectively generate negative pressures (right). Opening the valves equalizes the pressure. Subjects can then pull both legs back before closing the valves and repeating the procedure.

Subjects use the SELF device while in a supine posture. The upper body is supported by a stationary, raised platform. The bottom metal plate of the chamber is positioned over a rollable platform, allowing the chamber to expand and collapse in the supine posture. The top plate of the chamber is attached to a vest which distributes loads evenly across subjects' shoulders.

Static LBNP Chamber

The static LBNP chamber consists of a stationary, rigid chamber (Figure 2). A neoprene skirt maintains a seal around the waist. A belt and shoulder straps were used to ensure a tight seal. Subjects were in the supine posture with their lower body within the chamber and their upper body and head supported by a padded platform. A vacuum attached to the chamber generated the negative pressure.

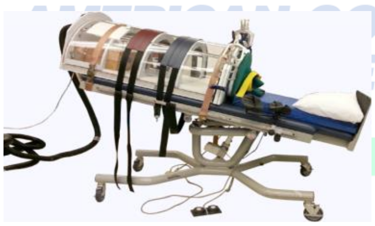

Figure 2: The static LBNP chamber. Subjects place their lower body within the chamber. A powered vacuum attaches to the chamber to generate negative pressure. The chamber is positioned horizontally (not tilted) with the subject in a supine posture.*

<u>Data Acquisition</u>

Cross-sectional images of both the left and right internal jugular vein were obtained via ultrasonography (Phillips, Amsterdam, Netherlands). Images were taken in triplicate just caudal to the bifurcation of the common carotid artery. Measurements of the IJV CSA were manually delineated using an image computing software (3D Slicer) by two independent sonographers. For each set of images, sonographers identified and analyzed the smallest IJV CSA just before a carotid pulse. The Finometer system (Finapres, Enschede, Netherlands) monitored and recorded subjects' heart rate and blood pressure throughout the experiment.

Protocol

Baseline measurements of heart rate, blood pressure, and IJV CSA were recorded after the subject gave informed consent. Trial conditions included 10 minutes of seated posture, 10 minutes of supine posture, 15 minutes of static LBNP in supine posture, and 15 minutes of dynamic SELF LBNP in supine posture. Negative pressure conditions were carried out at 25 mmHg. The horizontal supine posture was used as an analog for microgravity. The order of conditions was randomly assigned for each subject and all trials were completed during a 1.5-hour, single day study. During the 10-minute supine and seated upright conditions, subjects remained stationary in each respective posture without negative pressure. During static LBNP, subjects were positioned supine with their lower extremities inside the LBNP chamber and remained stationary while constant negative pressure was generated by a vacuum. Dynamic SELF exercise was also performed in supine posture. Subjects performed repetitive leg press movements in the SELF device, generating negative pressure when the adjustable valves were closed during leg extension. Subjects were instructed to maintain extension for as long as possible, until leaks caused negative pressure to drop to approximately -23 mmHg. At this point, subjects opened the adjustable valves of the chamber to equilibrate pressure inside the device. Subjects returned both legs into a flexed position and began the dynamic process again. This procedure was repeated for the duration of the trial. Subjects practiced the dynamic motions before the trial to ensure pressure consistently reached -25 mmHg.

Statistical Analysis

Statistical analyses were performed using SPSS version 27 (IBM, Chicago, IL). Statistically significant results were determined with $\alpha = 0.05$. The longitudinal study was analyzed using repeated measures ANOVA. Our data violated the assumption of sphericity and were corrected using the most conservative lower bound. We utilized Bonferroni correction to account for multiple comparisons. P-values less than 0.05 were considered significant.

RESULTS:

IJV CSA measurements at different time points were not significantly different. Our data suggest IJV CSA does not change over the course of 15 minutes of static or dynamic LBNP. Similarly, we did not observe trends or significant differences when comparing IJV CSA responses between the left and right sides, or between men and women. Because there were no trends or significant differences based on time, gender, or side, data were combined into 4 conditions: Upright, supine, static LBNP, and SELF LBNP. Data are presented in Table 1.

Condition	Mean	Std. Error
Upright	7.415	1.115
Supine	56.264	15.214
Static LBNP	16.933	2.720
SELF LBNP	21.570	3.934

Table 1

Pairwise comparisons indicate significant differences between upright posture and static LBNP as well as upright posture and SELF LBNP (Figure 3). The supine condition was not significantly different when compared to any other condition. Static and SELF LBNP were not significantly different.

DISCUSSIONCONCLUSION:

Our results indicate there is a significant difference between the upright posture and static LBNP conditions. These findings are in accordance with previous studies in which LBNP reduced ICP in a supine posture, but not to upright levels [3]. The IJV CSA was slightly larger in SELF LBNP when compared to static LBNP, but the difference was not significant. Our data suggest that both static and SELF LBNP have similar effects on IJV CSA. Despite the established efficacy of LBNP at reducing IJV CSA, our data do not indicate either LBNP condition significantly reduced IJV CSA when compared to the supine condition. Additionally, the supine condition was not significantly different when compared to the upright condition. There are several factors which may have reduced significance. We had a small number of subjects with N=11. Variances were not equal, requiring large correction factors. Shorter subjects could not expand the chamber as much as taller subjects and struggled to reach 25 mmHg. Finally, there was a very large variability in IJV CSA in the supine posture between subjects. These factors increased the standard error, and in turn reduced power and significance. While neither LBNP condition reached statistical significance, both conditions demonstrated trends toward reducing IJV CSA when compared to supine posture. Previous studies established the efficacy of static LBNP at reducing IJV CSA and ICP. Because both the static and SELF LBNP conditions reduced IJV CSA to a similar extent, our results suggest dynamic, self-generated LBNP may have a similar effect of reducing IJV CSA, and potentially ICP, when compared to traditional static LBNP. These results warrant further investigation into self-generated LBNP as it may be a low-mass, low-volume, unpowered replacement for traditional LBNP chambers in long-duration spaceflight.

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