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Original Research Article

Can reduced-exertion, high-intensity interval training combat the deleterious cardiometabolic effects of a sedentary lifestyle?

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ABSTRACT

Purpose: Reduced-exertion high-intensity interval training (REHIT) has been shown to have positive benefits on health that are comparable to benefits induced by high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT), but with significant less training time. Mechanisms behind this are thought to include increased mitochondrial activity (leading to improved cardiorespiratory fitness) and glycogen depletion and elevated GLUT-4 levels, leading to improved glucose levels. This low-effort, time-saving exercise recommendation could prove useful in attenuating the risk factors of the Metabolic Syndrome (MetS) in sedentary populations. **Methods:** In a randomized crossover design, ten sedentary subjects (7 F, 3 M) who possessed at least two risk factors for MetS underwent three weeks of thrice-weekly REHIT training (10 min/session) on the High Octane Ride bike and three weeks of a control period. Before, mid-way, and after the study, VO_2 max, blood pressure (SBP and DBP), heart rate, body composition, waist circumference (WC), fasting insulin, fasting glucose, HbA1c, fasting blood lipids, and physical activity were measured. After weeks 1, 2, 4, and 5, fasting blood lipids and glucose and vitals were measured. **Results:** Two subjects did not complete more than six rides and were not included in the statistical analysis, in addition to one individual that was considered a statistical outlier. No adverse responses to the intervention were reported, and the subjects reported feeling energized after and enjoying most of the rides. HbA1c (-0.47 ± 0.18%; p=0.023) and glucose (-8.0 ± 2.88 mg/dL; p=0.017) were significantly reduced in the REHIT group when compared to the control group. Additionally, the MetS z-score was reduced in 5 of the 7 subjects and, on average, was reduced by 0.69±1.06 in the REHIT group. No significant change was found in VO_2 max, fasting insulin, or body fat. **Conclusions:** Three weeks of thrice-weekly REHIT significantly improved HbA1c and glucose measures, and SBP and WC were notably reduced. REHIT was also effective at reducing the MetS z-score in 5 of the 7 subjects. Workplace-based, unsupervised REHIT exercise is a useful and well-tolerated tool to reduce cardiometabolic risk in a sedentary population.

KEYWORDS: Cardiometabolic Health, HbA1c, Insulin, Metabolic Syndrome, Sprint Interval Training

Introduction

Cardiometabolic disease has reached crisis proportions across the globe. Over 422 million people worldwide currently suffer from type 2 diabetes (T2D), and 592 million are expected to be affected by T2D come 2035[1]. As of 2017, the Centers for Disease

Control and Prevention estimated that 30.3 million people in the US alone had T2D[2]. Physical inactivity, while not the main cause, plays a large role in the development of T2D and other health-related diseases, like the metabolic syndrome (MetS) and cardiovascular disease (CVD)[1]. As lack of time is the most commonly cited barrier to exercise in our society, exercise physiologists are working to develop ways to achieve the benefits of exercise in shorter periods of time[3].

High-intensity interval training (HIIT) is a popular, time-saving alternative to traditional moderate-intensity, aerobic exercise. HIIT consists of four to six, 30-second sprints with a three to five-minute recovery between sprints and takes approximately 30 minutes to complete[4]. At the cellular level, HIIT increases mitochondrial activity, leading to increased muscle oxidative capacity[5]. High exercise intensity initiates the activation and nuclear translocation of peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), a regulator of mitochondrial biogenesis[6]. More mitochondrial activity can lead to better endurance and improved VO_2 max values, a strong predictor of mortality in both diseased and healthy individuals[7-8]. While HIIT has been shown to have many of the same benefits as moderate, longer aerobic exercise (like improved cardiorespiratory fitness and enhanced endothelial function), the sessions still last 30 minutes and are associated with a high rate of perceived exertion, so adherence to HIIT may be difficult for sedentary or diseased populations[4].

Recent studies have focused on the minimum amount of exercise needed to see change in cardiometabolic health and performance outcomes. This newer approach is called reduced-exertion high intensity interval training (REHIT) and consists of 2-3, 10-20 second sprints within a 10-minute session. According to Metcalfe and colleagues[3], significant glycogen depletion occurs within 10-20 seconds of a supramaximal sprint. Glycogen depletion leads to an increase in 5' AMP-activated protein kinase (AMPK) activity which has been shown to have a positive effect on several health parameters, including insulin sensitivity[3]. This implies that multiple sprints (longer than 15-20 seconds) may not elicit additional effects and may contribute to excessive fatigue. Studies have found REHIT to be associated with a lower perceived exertion as well as cardiovascular and insulin sensitivity improvements, similar to moderate-intensity continuous training and HIIT[9]. The mechanisms behind the effects of REHIT include: increased mitochondrial biogenesis as indicated by an upregulation of PGC-1α, improved buffering capacity, and increased resting glycogen levels[3]. This shorter, less-intense alternative provides sedentary populations a way to easily incorporate exercise into their daily routine, reap health benefits, and develop habits that may eventually lead to adhering to a longer exercise program. This has implications for not only national, but global, health.

However, there have only been a handful of studies investigating the benefits of, and mechanisms behind, REHIT.

Ruffino and colleagues demonstrated a five-fold increase in VO_2 max (consistent with other studies) in a group of T2D subjects performing 8 weeks of REHIT when compared to a group performing 8 weeks moderate-intensity walking, but failed to see improvements in body composition, blood lipids, blood pressure, and insulin sensitivity values both over time and between groups[1]. Various factors could influence these results, such as: medication suppressing the effects of exercise, a clinical population needing a higher exercise dosage, and a disproportionate number of responders to non-responders. This study implies that REHIT may not be a potent enough exercise dosage for a diseased population.

Metcalfe and colleagues compared the effects of REHIT (3 sessions/week for 6 weeks) with sedentary behavior and found that insulin sensitivity increased by 28% in males, but not in females[9]. A follow-up study found that there were no sex differences with regards to changes in insulin sensitivity[10]. Both groups experienced a trend towards reduced plasma insulin, by -9.5% and -7.4% for women and men, respectively. They confirmed that there was a disproportionate number of responders to non-responders in the groups and individual variability contributed to this difference[10]. It has been suggested that the glycogen depletion during supramaximal sprints improves insulin sensitivity; however, this topic needs further analysis to understand exactly how REHIT may improve insulin sensitivity. There has been minimal research outside of these studies on the effects of REHIT on blood lipids, body composition, and blood pressure in sedentary people. The purpose of this randomized, cross-over study was to examine the effects of REHIT on cardiometabolic outcomes in sedentary individuals. We hypothesized three weeks of REHIT training should elicit positive effects in cardiometabolic health that counteract the deleterious effects of excessive sedentary time.

Methods

Participants

Ten (7 female, 3 male) sedentary employees of Gunnison Valley Health (GVH) and Western Colorado University (WCU) volunteered for this study. In order to participate in this study, subjects had to identify as being sedentary for eight or more hours a day (by the measure of the PACE (patient-centered assessment and counseling for exercise)) questionnaire, possess at least two cardiometabolic risk factors using MetS guidelines (refer to Table 1), and be able to exercise on a treadmill and stationary bike. If subjects were pregnant, under the age of 18 or over the age of 64, unable to exercise, not sedentary, or did not possess two or more risk factors, they were not allowed to participate in the study. Please refer to Table 2 for subject characteristics.

Table 1. Cardiometabolic Inclusion Criteria Values

Characteristic	Males	Females
HDL (mg/dL)	<40	<50
Triglycerides (mg/dL)	>150	>150
Glucose (mg/dL)	>100	>100
Waist Circumference (cm)	>102	>88
SBP (mmHg)	>130	>130
DBP (mmHg)	>85	>85

Table 2. Baseline Subject Characteristics

Characteristic	Females (n=7)	Males (n=3)	Both (n=10)
Age (yrs)	44.4 (13.4)	52.0 (17.8)	46.7 (14.3)
Height (cm)	166.2 (6.8)	174.7 (4.9)	168.8 (7.2)
Weight (kg)	81.4 (10.5)	93.1 (16.4)	84.9 (12.8)
SedBeh Wkdy (hrs/day)	10.8 (2.1)	10.3 (2.0)	10.6 (2.0)
SedBeh Wknd (hrs/day)	8.5 (1.5)	9.1 (1.6)	8.7 (1.5)
HDL (mg/dL)	57.9 (15.4)	30.7 (13.7)	49.7 (19.3)
TC (mg/dL)	201.1 (20.3)	214.5 (46.7)	205.2 (28.3)
Triglycerides (mg/dL)	103.1 (44.3)	312.3 (282.3)	165.9 (171.0)
Glucose (mg/dL)	90 (5.3)	165.7 (112.1)	112.7 (64.4)
SBP (mmHg)	114.6 (11.0)	140.0 (9.2)	122.2 (15.8)
DBP (mmHg)	80.6 (8.8)	82.7 (8.1)	81.2 (8.2)
WC (cm)	92.3 (7.5)	106.1 (9.2)	96.5 (10.1)

Note. Data are presented as Mean (SD). WC=waist circumference. SedBeh=sedentary behavior.

The subjects filled out an informed consent and were given time to ask questions during a screening appointment. After determining if they qualified for the study, the subjects were given 72 hours to decide if they would like to participate in the study. Screening took place at the High Altitude Performance Lab (HAPLab) at WCU. Testing took place at both the HAPLab and GVH, and the exercise protocol took place in the Physical Capacity Profile room at GVH and the Paul Wright Gym at WCU. This study was reviewed and approved by the Institutional Review Board at Western Colorado University [HRC2018-01-03-R35].

Experimental Design

In this randomized, experimental crossover design, subjects were assigned to either the REHIT or control group for the first three weeks of the study. After the first three weeks, the subjects switched groups. No washout period was utilized. The REHIT group rode the High Octane Ride bike three times/week for approximately 10 minutes per session with 2, 10-20 second sprints per session and were asked to maintain normal diet and activity levels outside of the intervention. Subjects in the control group were asked to maintain their normal diet and activity levels. Before participating in the study, potential subjects were screened to determine if they met the inclusion criteria by measuring: sedentary behavior (PACE), resting blood pressure, waist circumference, fasted blood lipids, and fasted glucose. Subjects that met the criteria underwent their first comprehensive testing (International Physical Activity Questionnaire (IPAQ, VO_2 max, resting blood pressure and heart rate, waist circumference, body weight, DEXA, fasted insulin, fasted glycated hemoglobin (HbA1c), fasted blood lipids, and fasted glucose) over the course of two days at both the HAPLab and GVH. Every subject underwent comprehensive testing two more times: after week 3 and at the end of the study (week 6). Subjects were given a food diary to record the food they ate 24 hours before this first comprehensive appointment and were asked to replicate that diet 24 hours before the two subsequent comprehensive testing appointments. Subjects in the treatment group were asked to complete their last HOR bike ride at least 48 hours prior to their VO_2 max test.

Subjects underwent weekly testing after weeks 1, 2, 4, and 5 at the HAPLab. Weekly testing consisted of measurements of: physical activity levels (IPAQ), resting blood pressure and heart rate, waist circumference, weight, fasted blood lipids, and fasted blood glucose. Please refer to the experimental flow chart (Figure 1) for a schematic representation of the study design.

Procedures

Screening

A recruitment email was sent out to all WCU and GVH employees. Individuals interested in participating in the study were instructed to email the PI to set up a screening appointment. Potential subjects arrived at the HAPLab in the morning on a predetermined date in that timeframe, signed an informed consent, filled out a medical history form, and underwent several tests to determine if they qualified for the study. The tests included: resting blood pressure, answering the PACE questionnaire, blood lipid and glucose testing, and waist circumference measurements. Those tests are described in detail below. Screening took approximately 30 minutes.

Resting Blood Pressure

Upon arriving at the HAPLab, the subject was asked to sit and fill out the PACE questionnaire (approximately 5 minutes). After being seated for 5 minutes, a blood pressure cuff (Mabis Healthcare Inc., Lake Forest, IL) was placed approximately 1 inch above the antecubital fossa of the subject's left arm and inflated to 220 mmHg. The pressure was released, and the researcher listened for the first and last Korotkoff sounds with a stethoscope (Mabis Healthcare Inc., Lake Forest, IL). This process took place in the HAPLab and lasted approximately 6-7 minutes, including resting time.

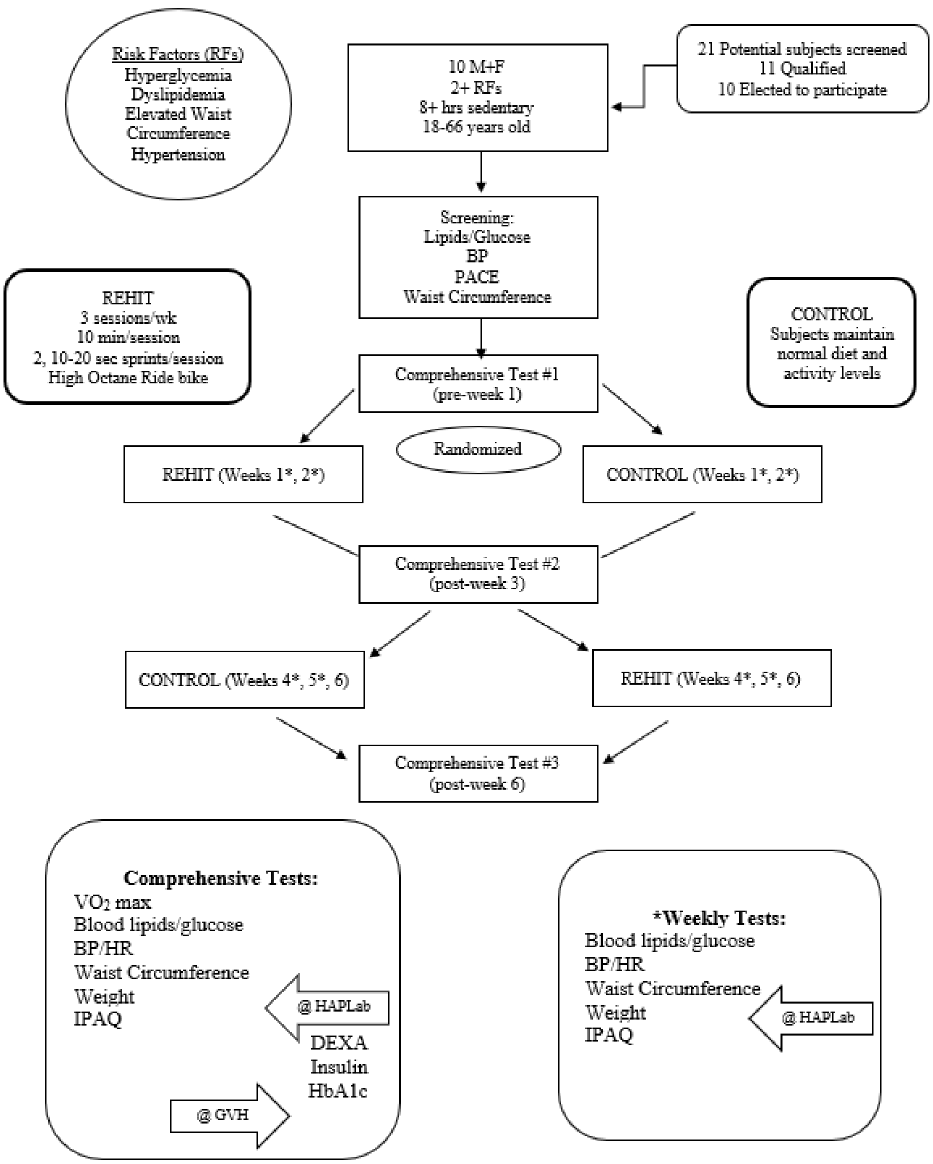

Figure 1. Experimental Flow Chart.

Blood Lipid and Glucose Testing

Subjects were asked to fast for at least 12 hours and to refrain from exercise, ingesting caffeine, and smoking during that time period. After filling out the questionnaire and getting their blood pressure taken, subjects were asked to wash their hands with soap and rinse thoroughly with warm water. Their hands were then cleaned with alcohol swabs and allowed to dry. The tip of their preferred finger was punctured using a lancet (Medipurpose, Brussels, Belgium), and a finger stick sample was collected into heparin-coated 40 µl capillary tube (Abbott, Abbott Park, IL). Samples were dispensed immediately onto commercially available test cassettes (Abbott, Abbott Park, IL) for analysis in a LDX Cholestech analyzer (Abbott, Abbott Park, IL). The LDX Cholestech measured total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides, and blood glucose. A daily optics check was performed on the LDX Cholestech analyzer used for the study. This process took 5-10 minutes and took place in the HAPLab. Subjects were not allowed to eat any food they brought to the lab until all screening tests were completed.

Waist Circumference

A measuring tape (DJO Global, Vista, CA) was wrapped around the subject's torso at the narrowest point between the umbilicus and the xiphoid process. Three measurements of waist circumference were taken and averaged. The subject was instructed to inhale, then exhale as the measurement was being taken to ensure he/she was not sucking in his/her stomach. This process took place in the HAPLab and lasted approximately 1 minute. The results of these tests were recorded on a data collection sheet. Since the results were immediate, the potential subjects were informed of whether or not they qualified for the study. If they qualified, they were given 72 hours from their screening appointment date to decide if they wanted to participate in the study. The PI sent a follow-up email to the qualifying individuals, and if the individual was interested in participating in the study, the PI arranged a time over email for the subject's first comprehensive tests and tentative times for the subsequent tests.

Comprehensive Testing

Subjects underwent comprehensive tests before week 1, after week 3, and after week 6. Comprehensive testing consisted of: answering the IPAQ, VO_2 max, resting blood pressure and heart rate, waist circumference (see above), weight, DEXA, fasted insulin, fasted HbA1c, fasted blood lipids (see above), and fasted blood glucose (see above). These tests took place over the course of two days and were performed in the same sequence for each of the three testing periods for each subject.

IPAQ

Once subjects arrived at the HAPLab for their lipid drawing appointment, they were asked to sit and fill out the IPAQ. The PI instructed them to ask questions if needed and asked the subjects to clarify any values if they did not make sense. This process took approximately 5 minutes.

Resting Heart Rate

After 5 minutes of filling out the IPAQ during the lipid drawing appointment in the morning, the subject's heart rate was taken by placing a pulse oximeter (Concord Health Supply, Skokie, IL) on the index or ring finger of the right hand. This process took approximately 6 minutes and took place at the HAPLab. After this process, the PI took the subject's blood pressure and measured blood lipids, glucose, and waist circumference (methodology mentioned previously) before measuring height and weight (see below).

Height and Weight

The measuring stick built into the scale (Tanita, Arlington Heights, IL) was used to measure the height of the subject without shoes or voluminous hair styles. Subjects were weighed without shoes or bulky jackets on a scale in the HAPLab. This took 30 seconds.

VO_2max

At a separate appointment in the evening (either on the day of the lipid testing appointment or one of the adjacent days), subjects were fitted with a mask, attached to the falconia tubing, and attached to the metabolic cart (TrueOne 2400, PARVOMedics, Sandy, UT) to collect expired gases. Subjects were asked to warm up for approximately 3-4 minutes by walking on the treadmill at 0% grade (Trackmaster, Newton, KS) at a self-selected pace. Subjects were asked to select a pace they could maintain for ~15 minutes, and the treadmill grade increased by 1% each minute. The subject was fitted with a chest strap (Polar, Lake Success, NY) to monitor heart rate. Heart rate and the rate of perceived exertion (RPE, 1-10) were recorded each minute. The subject terminated the test if he/she was unable to go any further. After the test, the subject cooled down at a self-selected pace. If the subject did not hit a plateau, the subject was asked to come back 24-72 hours later. If the subject did not plateau during the second test, it was noted in the data. This test took place in the HAPLab lasting approximately 20 minutes.

DEXA

At a separately-scheduled time during the day, subjects were instructed by an X-ray technician at GVH to change into a hospital gown if he/she had any metal in their clothing and remove any jewelry or other objects in a private setting. The technician inputted the subject's height and weight into the machine before instructing the subject to lie supine on the DEXA machine (Lunar Prodigy, GE Healthcare, Boston, MA). After the scan, the subject changed back into his/her clothing and technician printed off the results of the test to give to the PI. Subjects were informed of their results by the PI. This took place in the Radiology department at GVH and lasted approximately 15-20 minutes.

Fasted Insulin and HbA1c

Subjects were asked to fast for at least 12 hours and to refrain from exercise, ingesting caffeine, and smoking during that time period. At a time scheduled separately from all other tests, subjects checked in at the registration desk at the main lobby at GVH and were directed to head to the laboratory and sit in a chair. A trained phlebotomist applied a tourniquet above the elbow, sterilized the blood draw site, and asked the subject to make a fist. The phlebotomist drew approximately 10 ml of blood from the subject's median cubital, cephalic, or basilic vein into a collection tube (BD, Franklin Lakes, NJ). HbA1c levels were analyzed at GVH. The blood samples were sent to the Mayo Clinic to be analyzed for insulin levels and available to the PI on the secure hospital database (CPSI, Mobile, AL). This lasted approximately 10-20 minutes.

Weekly Testing

After weeks 1, 2, 4, and 5, subjects reported to the HAPLab for weekly testing on the same day and time to maintain consistency. These appointments consisted of: answering the IPAQ questionnaire, blood lipid and glucose testing, resting blood pressure and heart rate, weight, and waist circumference measurements. These tests are described in detail in the previous sections.

Intervention

Subjects were randomly assigned to the treatment or control group. Subjects in the treatment group partook in 3 REHIT sessions/week for the first three weeks. These sessions took place on the High Octane Ride (HOR) bike (CAROL, Kensington, London) at GVH in the Physical Capacity Profile room or on the HOR bike at WCU in the Paul Wright Gymnasium. Each subject had his/her own login information for the HOR bike that calculated the ideal resistance for the sprint based on the subject's weight. The researcher input this data after the subject's first comprehensive test. Sessions lasted 9 minutes 40 seconds and consisted of a 2-3-minute warm-up, 20 second all-out sprint, 3-minute recovery, a 10-20 second all-out sprint, and a 3-minute cool-down. For the first three rides, subjects sprinted for 10 seconds during the sprint bouts and warmed up for 3 minutes, and for the second three rides, subjects sprinted for 15 seconds. For the last three rides, subjects sprinted for 20 seconds during the sprint bouts and warmed up for 2 minutes. The HOR bike software coached each workout with written and verbal (if the subject listened with his/her headphones) cues of when/how long to sprint and proper breathing and recovery techniques. Because of this, these sessions were not supervised by the research team; however, the researchers could access workout data for each individual to ensure the rides were being completed properly. The treatment group was asked to maintain their normal activity and diet patterns while partaking in the intervention. The control group was asked to maintain normal activity and diet patterns during the first three weeks of the study. After three weeks, the subjects originally assigned to the treatment group were assigned to the control group and vice versa, and the intervention was repeated. The PI had access to the login information for the subjects in order to monitor progress and adherence.

Statistical Analyses

The data were analyzed for normality with a Shapiro-Wilk test. If $p<0.05$, the data were considered to be not normally-distributed. A paired samples t-test was performed to determine if pre- and post- values for blood lipids, fasted glucose, HbA1c, fasted insulin, cardiorespiratory fitness, body composition, resting HR, resting BP, weight, and waist circumference differed significantly within the individual groups ($p<0.05$). An independent samples t-test was performed to determine if the change from post- to pre-values was significant between both groups ($p<0.05$). SPSS version 25 (IBM-SPSS, Boston, MA) was used to perform these statistical analyses.

Results

Subject Recruitment

Twenty-one individuals were screened for potential participation in this study. Eleven individuals met inclusion criteria (sedentary for 8+ hours per day on average and possessed two or more cardiometabolic risk factors, outlined in Table 1). Ten of those individuals elected to participate in the study. Refer to Table 3 for the values obtained through the screening process for the subjects that elected to participate.

Table 3. Subject Screening Values.

Characteristic	Females (n=7)	Males (n=3)	Both (n=10)
Age (yrs)	44.4 (13.4)	52.0 (17.8)	46.7 (14.3)
Weight (kg)	80.7 (10.9)	93.6 (15.1)	84.6 (13.0)
SedBeh Wkdy (hrs/day)	10.8 (2.1)	10.3 (2.0)	10.6 (2.0)
SedBeh Wknd (hrs/day)	8.5 (1.5)	9.1 (1.6)	8.7 (1.5)
HDL (mg/dL)	64.0 (15.0)	31.3 (17.6)	54.2 (21.6)
TC (mg/dL)	211.3 (25.6)	224.3 (27.0)	215.2 (25.3)
Triglycerides (mg/dL)	98.0 (41.1)	254.3 (185.5)	144.9 (120.3)
Glucose (mg/dL)	95.7 (5.3)	158.0 (102.4)	114.4 (57.0)
SBP (mmHg)	119.6 (5.4)	139.3 (12.2)	125.5 (12.0)
DBP (mmHg)	85.1 (4.3)	92.0 (9.2)	87.2 (6.5)
WC (cm)	112.0 (49.1)	106.6 (8.4)	110.4 (40.4)

Note. Data are presented as Mean (SD).

Adherence to Intervention and Data Collection Attendance

Each subject was tasked with completing nine bike rides over the course of the three-week intervention. Four of the subjects did not complete all nine rides due to illness, injury not related to the intervention, or logistical issues. They completed eight, seven, six, and three rides, respectively. This was noted when calculating the exercise data presented in Table 4. All other subjects completed all the rides prescribed. The subjects that completed less than seven rides were excluded from calculations.

All subjects completed their three comprehensive tests. One subject missed a weekly testing session during the control period of the study. Two subjects missed a weekly testing session during the intervention period of the study, but they did complete the intervention. One subject completed the post-intervention comprehensive tests and the weekly test the week before but did not complete the intervention during those two weeks due to injury not related to the intervention.

Safety and Enjoyment

Subjects tolerated the intervention and testing well. No injuries due to the intervention or testing were reported during the study period. Additionally, while no subjective questionnaires about exertion or enjoyment were distributed, all subjects reported that they enjoyed the time-efficient bike workouts and, most of the time, felt energized afterwards.

Exercise Training Data

Average weekly power output and heart rate during the sprint portion of each ride for each subject is reported in Table 4. Some of the rides did not record data due to technological difficulties even if the subject completed the ride. Unless otherwise noted, the calculations for each week are an average of three rides.

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Table 4. Individual Mean Exercise Training Data.

Subject	Variables	Week 1	Week 2	Week 3
1	Power	491.5 (2)*	486.3	490.7
	HR	175 (2)*	146.7	154.7
2	Power	434.5 (2)*	428.7	492 (2)*
	HR	161 (2)*	147	138 (2)*
3	Power	691.7	700.5 (2)*	N/A*
	HR	164.3	140.5 (2)*	N/A*
4	Power	425.5 (2)**	402.7	450.7
	HR	137.5 (2)**	157.3	153
5	Power	901.3	864	908.3
	HR	134	151.3	144.3
6	Power	374.3	398	318.3
	HR	142.7	147	150.3
7	Power	413.7	391 (1)**	467.5 (2)*
	HR	133.3	135 (1)**	130.7
8	Power	306.3	336.7	N/A**
	HR	146	152	N/A**
9	Power	548.3	N/A**	N/A**
	HR	122.7	N/A**	N/A**
10	Power	625.0	611.0	596.0
	HR	161.3	168.0	169.3

Note. *Data incomplete because of technical difficulty; **Data incomplete because subject did not complete ride; Power was measured in watts and HR (heart rate) was measured in beats per minute; (2)only two rides in calculation; (1)only one ride in calculation

Main Outcomes

When analyzed for normality with the Shapiro-Wilk test, the pre- and post-data for all outcome measures were normal ($p>0.05$) with the exception of: pre-IPAQ scores
($p=0.024$), pre-body fat (legs) ($p=0.027$), and post-SBP ($p=0.017$). The results of the paired and independent samples t-tests are depicted in Table 5.

Metabolic Syndrome Variables

Measurement Issues

We obtained readings for one subject (HDL, LDL, triglycerides, HbA1c, and MetS-Z score) that we could not use. During three of the weekly tests (one during the intervention and two during the control), HDL read as N/A, <15 mg/dL, and <15 mg/dL, respectively. HDL read as <15 mg/dL and N/A during the intervention comprehensive pre-test and the control comprehensive post-test, respectively. Readings that came out as <15 mg/dL were analyzed in the data with a value of 15 mg/dL. This same subject also had several values for LDL that came out as N/A during one weekly intervention test, one weekly control test, the intervention comprehensive pre-test, and the control comprehensive post-test. During the control comprehensive post-test and one of the intervention weekly test, the values obtained for triglycerides came out as >650 mg/dL. These were noted in the data as 650 mg/dL. This subject also had HbA1c values that came out as >14.5% in the intervention comprehensive pre- and post-tests and the control comprehensive pre-test. These values were noted in the data as 14.5%. Lastly, for

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this subject, because HDL could not be computed for the control comprehensive post-test, the MetS z-score could not be calculated. This subject was a mathematical outlier and was excluded from all calculations.

MetS Results

Within the REHIT group, changes in HbA1c content (6.21 ± 0.25 % to 5.9 ± 0.47 %) and SBP (128.57 ± 21.35 mmHg to 119.14 ± 14.87 mmHg) were approaching significant with p-values of 0.064 and 0.08, respectively. Within the CON group, changes in fasting blood glucose were significant (p=0.007) and increased from 93.42 ± 7.59 mg/dL to 100.28 ± 4.46 mg/dL from pre- to post-testing. Graphs depicting changes in MetS z-scores, HbA1c, and fasting insulin between the REHIT and CON groups are represented in Figures 2 through 4. Changes in glucose (-8.0 ± 2.88 mg/dL) and HbA1c (-0.47 ± 0.18%) in the REHIT group were significant when compared to the CON group with p-values of 0.017 and 0.023, respectively. Changes in insulin were not what we had expected, and they were not significant. Changes in SBP approached significant (p=0.074) with a mean difference of -12.86 ± 6.58 mmHg in the REHIT group. While changes to the MetS z-score between groups were not significant, scores in the REHIT group decreased (by -0.69±1.06) and scores in the CON group increased (by 0.10±1.03).

Cardiorespiratory Fitness Results

A graph depicting individual and group mean changes in VO_2 max is illustrated below (Figure 5). VO_2 max increased by 0.88 ± 3.39 ml/kg/min in the REHIT group and decreased by 1.07 ± 2.08 ml/kg/min in the CON group. These changes were not statistically significant.

Table 5

Physiological Characteristics Pre- and Post- in CON and REHIT Groups

	Control		REHIT	
Measure	*Pre (n=7)*	*Post (n=7)*	*Pre (n=7)*	*Post (n=7)*
MetS z-score	-1.73 (3.03)	-1.63 (3.88)	-1.13 (3.03)	-1.82 (3.22)
HDL	50.43 (12.63)	56.29 (16.6)	51.43 (16.07)	51.71 (15.76)
LDL	126.57 (27.98)	118.86 (25.26)	124.86 (26.92)	121.86 (24.84)
Triglycerides	119 (53.00)	125 (48.35)	115.71 (39.79)	124.71 (52.00)
TC	201.86 (32.57)	200 (23.64)	199.29 (23.14)	199.57 (29.80)
Glucose	93.43 (7.59)	100.29 (4.46) *	97.71 (7.06)	96.57 (8.02) +
Insulin	12.31 (8.04)	11.84 (5.78)	10.71 (5.38)	13.31 (7.80)
HbA1c	5.99 (0.51)	6.14 (0.30)	6.21 (0.25)	5.90 (0.47) +
SedBeh	6.71 (2.93)	5.64 (2.43)	6.07 (2.13)	6.36 (2.39)
IPAQ	1936.29 (1721.31)	1726.43 (2176.62)	1989.57 (2068.52)	2541.14 (1716.27)
SBP	125.14 (14.87)	128.57 (21.72)	128.57 (21.35)	119.14 (14.87)
DBP	80.57 (7.89)	82.00 (7.89)	85.43 (8.77)	82.00 (8.56)
WC	94.57 (12.07)	94.49 (11.21)	94.91 (11.12)	92.81 (11.68)
Weight	85.86 (16.01)	85.96 (15.93)	85.46 (15.25)	86.36 (16.11)
BF	39.51 (7.70)	39.54 (7.70)	39.90 (7.94)	39.29 (7.53)
BF trunk	41.79 (6.83)	42.03 (6.49)	42.53 (6.83)	41.70 (6.64)
BF legs	39.41 (12.42)	39.27 (12.41)	39.41 (12.47)	39.19 (12.37)
BF arms	35.3 (8.62)	35 (9.05)	35.27 (9.29)	34.16 (9.24) *
And:Gyn	1.10 (0.27)	1.10 (0.24)	1.10 (0.24)	1.09 (0.24)
VO_2 max	26.88 (5.07)	25.81 (3.98)	26.36 (4.69)	27.25 (5.81)
RER max	1.04 (0.05)	1.07 (0.08)	1.08 (0.67)	1.04 (0.05) *
Resting HR	75.14 (13.97)	71.14 (11.26)	72.00 (10.61)	72.86 (8.15)

Note. Data are presented as mean (SD); *within group change is significantly different from baseline; + change from baseline is significantly different than CON group Units: MetS z-score (metabolic syndrome severity score, no units); HDL, LDL, Triglycerides, TC, Glucose (mg/dL); Insulin (uIU/mL); HbA1c (%); SedBeh (sedentary behavior, hrs/day); IPAQ (MET min/wk); SBP/DBP (mmHg); WC (waist circumference, cm); Weight (kg); BF (body fat, %); And:Gyn (android:gynoid ratio); VO_2 max (ml/kg/min); RER (respiratory exchange ratio) max (no units); Resting HR (bpm)

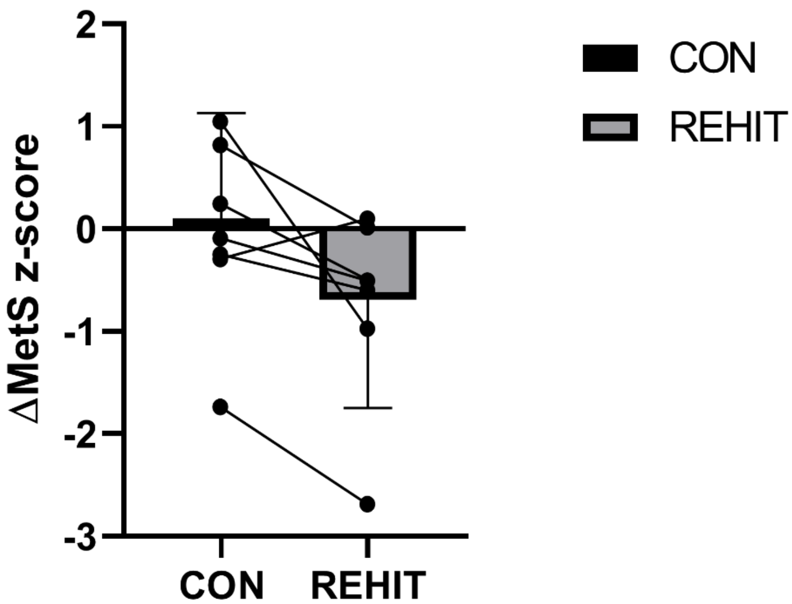

Figure 2. Individual and Group Changes in MetS Z-Score.

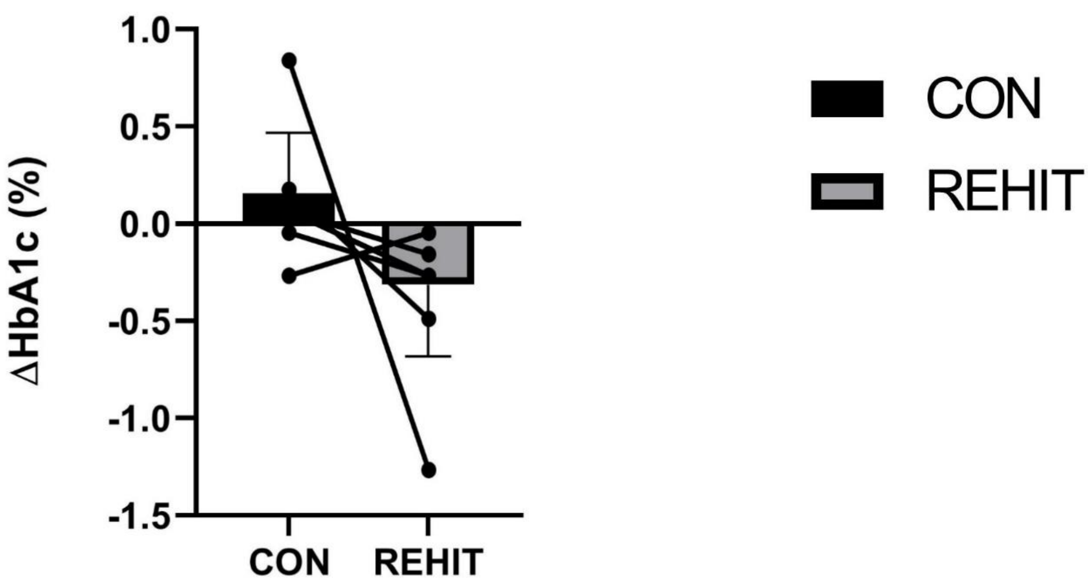

Figure 3. Individual and Group Changes in HbA1c.

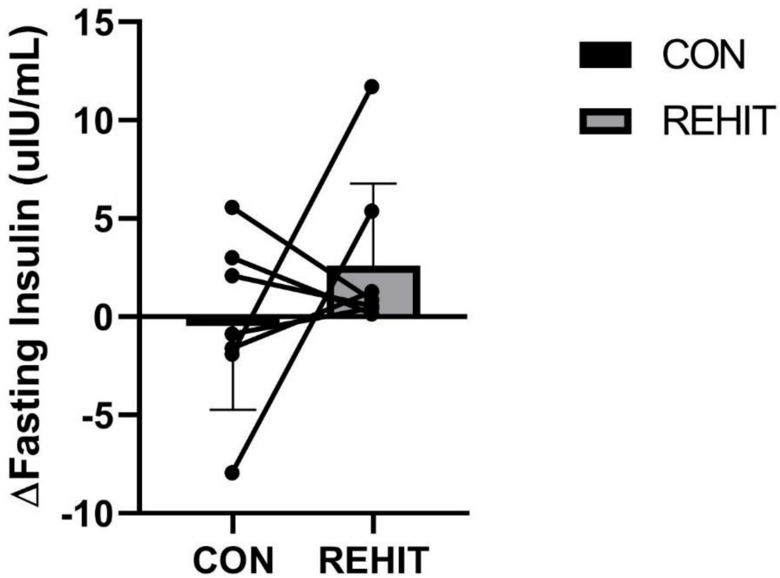

Figure 4. Individual and Group Changes in Fasting Insulin.

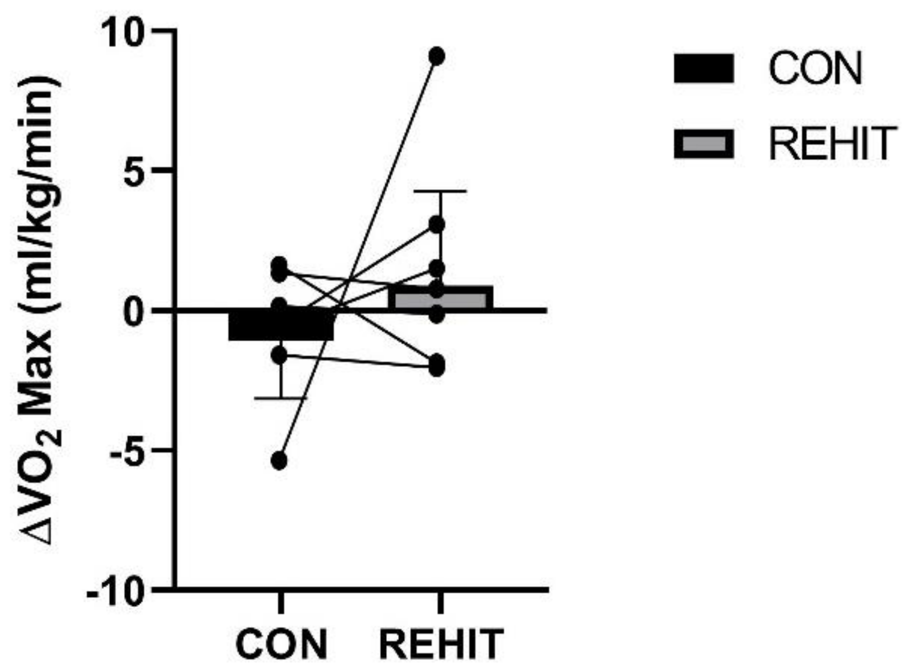

Figure 5. Individual and Group Changes in VO_2max.

Discussion

Main Findings

This study found that after three weeks of three, 10-minute REHIT sessions per week, fasting blood glucose (-8 ± 2.88 mg/dL) and HbA1c (-0.47 ± 0.18%) decreased significantly when compared to the control group in a sedentary, MetS-affected population. MetS z-scores (MetS severity), SBP, and waist circumference were notably decreased but were not statistically significant. While the mean change in the MetS z-score (which accounts for: fasting blood glucose, mean arterial pressure (MAP), WC, HDL, and triglycerides) was not statistically significant, the score improved in 5 of the 7 subjects analyzed. Additionally, this study utilized a simple, time-efficient exercise modality. The HOR bike was placed near the workplace of the subjects, allowing them convenient access to exercise and a way to break up their sedentary behavior. The software enabled them to be coached, but not supervised by any member of the research team. The mean reduction of the MetS z-score by 0.69 after three weeks of time-efficient, workplace-based training provides promising evidence for the usefulness of REHIT as an exercise recommendation in MetS-affected populations.

MetS Variables

We observed a significant decrease in fasting glucose and HbA1c values during three weeks of REHIT training when compared with the control group, in addition to decreases in SBP and WC that were approaching significant. Glucose, SBP, and WC contribute to the overall MetS z-score, which we observed a reduction of in 5 of 7 subjects. Interestingly, insulin increased in the REHIT group when compared with the control group.

HbA1c

This is the first study to our knowledge to observe a significant reduction in HbA1c during just three weeks of REHIT training. Haines[11] observed no change in HbA1c after 15 REHIT sessions in patients with non-diabetic hyperglycemia, suggesting that the small study sample size (n=5) contributed to this lack of effect. Another study observed a significant decline in fasting glucose values in men with T2D and hypothesized that this could lead to improvements in HbA1c[12]. The significant improvements in glucose that we observed in the REHIT group are not in line with results found in some studies[1,10], but align with the results found in a study performed by Metcalfe et al.[12] looking at postprandial glycemic control in the 24 hours after one bout of REHIT (and HIIT and MICT). Since high-intensity exercise relies on muscle glycogen as an energy source, the subsequent cycles of muscle glycogen depletion and post-exercise glycogen resynthesis leads to improvements in glucose tolerance. It follows that the improvements in fasting glucose would lead to the improvements observed in HbA1c. This is in line with previous research done on the effects of HIIT training on individuals with T2D[13]. Incredibly, the improvements in HbA1c came after just three weeks of thrice-weekly REHIT sessions, whereas other studies have measured improvements after over a month[13].

MetS Z-Score

While not statistically significant, our 0.69 reduction of the MetS z-score in the REHIT group is clinically significant. It has been suggested that reducing the MetS z-score by 0.15 confers approximately a 10% improvement in one of the MetS components, leading to a reduction in CVD risk[14]. The z-score paints a robust picture of someone's cardiometabolic health. It accounts for the effects of several different outcomes (fasting blood glucose, mean arterial pressure (MAP), WC, HDL, and triglycerides), meaning that unexpected values for one variable, like the HDL values we observed for the second subject mentioned in the "Unusual Cases" subsection, do not paint a skewed picture of someone's health.

A pilot-study comparing the effects of MICT, HIIT, and low-volume HIIT in sedentary men and women also found a trend towards improved MetS z-scores in the low-volume (non-all-out) HIIT group, but the values were not significant when compared with the other groups[14]. A different study comparing the effects of REHIT and MICT found a 1.5-fold greater number of cardiometabolic responders when compared to the MICT group[15]. The authors attributed this to a reduction in MAP and the potential subsequent improvements in vascular function, which contributes to the MetS z-score calculation[15].

It is possible that we could have observed a greater improvement of the MetS z-score had our intervention been more frequent. Research has identified lipoprotein lipase as a regulator of HDL metabolism[16]. It is negatively affected when an individual is sedentary, thus performing more bouts of a sedentary behavior-interrupting program could mitigate the effects of sedentary behavior on lipid metabolism[16]. Additionally, more physical activity has been shown in some studies to improve glucose metabolism by increasing glucose uptake by GLUT4 in skeletal muscle and decreasing glucose levels in the blood[16]. Higher levels of HDL and lower levels of glucose would contribute to a lower MetS z-score.

Insulin

We observed an insignificant increase in fasting insulin values in the REHIT group when compared with the CON group. The effects of REHIT on insulin resistance/sensitivity have been varied in the literature. Metcalfe and colleagues[10] found that values of insulin sensitivity were insignificantly changed following six weeks of REHIT training, but those values were subject to individual variability (-54% to 70%). A study examining six sessions of HIIT found increased resting muscle glycogen and GLUT4 expression following training, both of which are linked with improved insulin sensitivity[17]. One concept that might explain this is that mice that lack PGC-1α have a hard time resynthesizing muscle glycogen, part of that glycogen depletion-resynthesis cycle mentioned earlier that improves glucose tolerance[17]. Thus, if someone is not exercising hard/frequently enough to elicit increased PGC-1α activity, it is possible that he/she would not obtain improvements in insulin sensitivity and therefore glucose tolerance.

We observed an increase in fasting insulin values in 4 of our 7 participants, but could we say that our subjects adversely responded to exercise? One study suggested that adverse responses to exercise could possibly be due to the interaction between medication and exercise, although they had little to no experimental data to back up this idea[18]. It is highly unlikely that this phenomenon affected our study though as individuals that were on medications known to interact with the effects of exercise were excluded from the study. Others have reported impaired responses to exercise in diseased (MetS) populations[19]. Moreover, those individuals that have been afflicted longer, specifically with T2D, tend to have poorer improvements in insulin sensitivity[20].

Cardiorespiratory Fitness

Our study did not find any significant difference between VO_2 max in the REHIT and CON groups, although we observed a trend towards improved VO_2 max values in the REHIT group. This is incongruent with other study findings. A study performed in 2016 found a significant 15% (men) and 12% (women) improvement in VO_2 peak following a six-week (3 sessions/week) REHIT training regime similar to the one used in our study[9]. This study, however, examined 29 healthy, but sedentary individuals. Our study examined a population with factors associated with the MetS. As mentioned previously, it is possible that clinical, unhealthy populations require a larger dose of exercise in order to see an effect[1].

Another study compared the effects of eight weeks of REHIT and MICT training and found a 12% increase in cardiorespiratory fitness (CRF) in the REHIT group and a 7% increase in the MICT group[15]. Our lack of a significant change in CRF could be due to the length of the study. At least six weeks of REHIT training may be necessary to significantly improve CRF. The duration of the sprint could have also had an effect on CRF outcomes. One study looked at decreasing the sprint duration from 20 to 10 seconds during six weeks of REHIT training and found a significant 10% increase in VO_2max in the 20 second sprint group when compared to the 4% increase in the 10 second sprint group[21]. It is unclear as to why different numbers of sprint repetitions and durations lead to improvements in VO_2max[21]. Because the sprint time in our protocol started at 10 seconds and increased to 15 seconds and 20 seconds by the end of the sessions, it is possible that there was not enough of a stimulus to affect cardiorespiratory fitness significantly.

Practical Application

This study found that a workplace-based, time-efficient REHIT program was well-tolerated by sedentary individuals possessing MetS risk factors. Companies that want to invest in their employee's wellness could purchase a bike similar to the one utilized in this study to provide employees with a time-efficient way to interrupt their sedentary behavior during the work day. REHIT could also provide sedentary populations a way to "get moving" and develop an enjoyment for exercise, which could potentially lead to adherence to a longer and more frequent exercise regime.

Limitations

Some might consider our lack of a washout period a limitation as there could be a slight chance of the effects of REHIT carrying over to the control period. We chose not to include a washout period because of time constraints. Additionally, the minimal exercise stimulus would not carry over as previous studies have found that improvements in cardiometabolic health after 13 weeks of exercise training went back to baseline values after one week of detraining[22]. Thus, a washout period was unnecessary. Another potential limitation to our study was the lack of diet control. Our subjects' diet could have affected certain measures, like blood lipids, and skewed certain values; however, this could have made it difficult to differentiate between the effects of REHIT and the effects of diet.

Another potential limitation was that we did not track physical activity and inactivity with a precise device, like an accelerometer. It is possible that the subjects that experienced improvements in CRF started skiing more (as our study coincided with ski season) and reaped some benefit from that. However, it is worth noting that the improvements that we did see in HbA1c, glucose, and the MetS z-score happened without us controlling for these variables. It is quite incredible that we saw these benefits when our subjects were instructed to simply go about their lives as normal and only incorporate 30 minutes of exercise a week for three weeks.

A final limitation was the lack of supervision to control the power output of each subject during the sprint. If the subject chose to not give enough effort, they could have potentially not sustained a workload high enough to activate mitochondrial biogenesis. However, our goal was not to induce improvements in CRF. We wanted to reduce cardiometabolic risk and mitigate the negative effects of sedentary behavior, thus these results are not unexpected.

Conclusions

Our findings suggest that just three weeks of thrice-weekly, 10-minute REHIT sessions can significantly lower HbA1c and fasting blood glucose and start to improve the MetS z-score in MetS-affected individuals. In contrast, three weeks of thrice-weekly REHIT is not adequate to induce significant improvements in CRF. REHIT was also well-tolerated and no adverse responses were reported in this population. As lack of time is the most commonly-reported barrier to exercise, REHIT provides a promising avenue to lower cardiometabolic risk and potentially increase exercise adherence in a sedentary, MetS-affected population. Future studies should continue to examine the effect of REHIT on insulin resistance and glycemic control. Additionally, the shortened length of our intervention proved effective in some parameters. Future studies should also look at shortened REHIT interventions with larger sample sizes and/or more frequent rides in a real-world setting. Additionally, the precise mechanisms by which REHIT affects insulin resistance and CRF should continue to be examined to further our understanding of the intervention.

Competing interests

This investigation was supported financially by the American Council on Exercise (ACE). The American Council on Exercise (ACE) was not involved in development of the study design, data collection and analysis, or preparation of the manuscript. There are no other potential conflicts of interest related to this article.

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