STUDY PROTOCOL

The Relationship Between Exercise Frequency, Intensity, and Restoration of Cardiometabolic Health

NCT #03376685

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1.0 INTRODUCTION

1.1 Background

Involvement in regular physical activity is well established to reduce the risk of many clinically relevant risk factors, including hypertension, dyslipidemia, obesity, and hyperglycemia. Traditional physical activity recommendations suggest 150 minutes of moderate-intensity continuous endurance (END) exercise dispersed over 5 days per week is sufficient to improve physical fitness in adults (1). However, given the commonly cited barrier of “lack of time," literature has recently focused on time effective sprint interval training (SIT), obtaining equivalent increases in aerobic capacity and glycemic regulation compared to classical END exercise, particularly when protocols are volume-matched (2). However, as END is conducive to daily sessions not feasible of SIT training, current literature volume-matching these approaches have restricted END to shorter and less frequency bouts than guidelines indicate is optimal. Furthermore, improvements in many clinically relevant risk factors are transient in nature (3). Therefore, the ability of END and SIT to improve these health parameters, when performed as per general practice (i.e. high-frequency END, low-frequency SIT) remains unknown.

1.2 Objectives

The aim of this study is to determine the ability of 6-week high-frequency END or low-frequency SIT exercise training to reduce clinically relevant cardiometabolic risk factors in overweight/obese males.

1.3 Hypothesis

It is hypothesized that END of greater frequency will markedly improve cardiometabolic health, while lower frequency SIT will not.

2.0 STUDY DESIGN AND METHODS

This study is a 6-week parallel exercise intervention trial. The temporal sequence of events in this study is displayed below in *Figure 1: Experimental Timeline*. Further details are provided in the subsequent text.

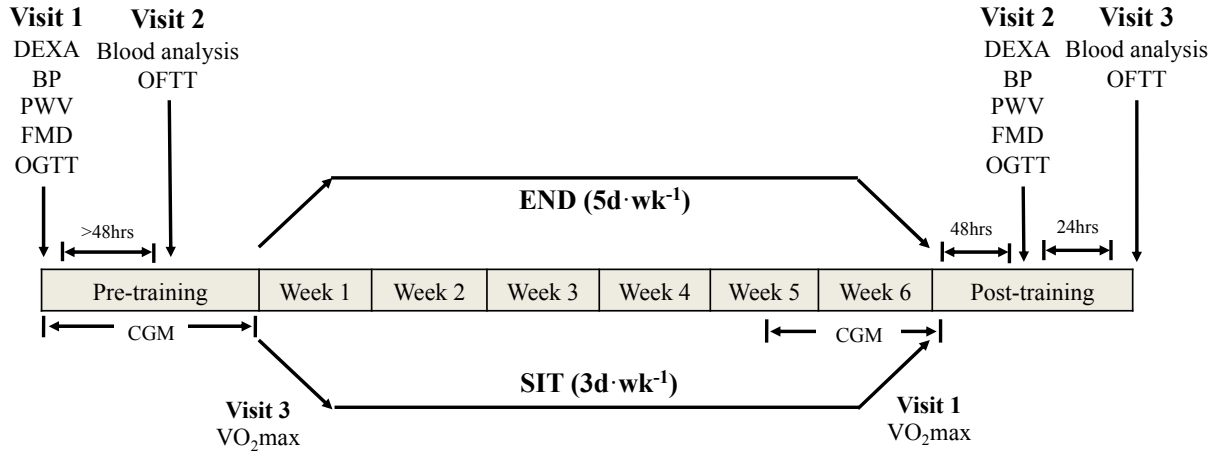

Figure 1: Experimental Timeline

2.1 Participant Characteristics

2.1.1 Inclusion Criteria

- Male
- Aged 18-70 years
- Body mass index > 25 kg/m_2 (classified as overweight or obese)
- Physically inactive (< 100 minutes of moderate physical activity per week)
- Willingness and physical ability to begin a vigorous exercise regime
- Approval for exercise via physical activity readiness questionnaire (PARQ+)

2.1.2 Exclusion Criteria

- Smoker
- Prescribed with glucose lowering medication
- Not cleared for physical activity

2.2 Pre-Screening Assessments

Participants will report to the laboratory at the University of Guelph to be informed of study details, any possible risks associated with the study, and provide written informed consent (approved by University of Guelph Human Research Ethics Board REB #17-08-008). To determine eligibility for this study, the following will be assessed:

- **Health Questionnaire/ PARQ+**
- **Resting Blood Pressure**
- **Height and Weight**

2.3 Pre-Exercise Testing

The pre-training testing will be conducted over three separate days, each of which will be following a 12-hour overnight fast, and having refrained from exercise or caffeine for 24-hours.

2.3.1 Pre-Exercise Visit 1:

- **Dual-Energy X-Ray Absorptiometry (DXA):** Lean body mass, body fat percentages (total and regional), and body mass index will be assessed via a whole-body DXA scan.
- **Pulse Wave Velocity (PWV):** Arterial stiffness will be assessed via central PWV between carotid artery and femoral artery sites.
- **Flow Mediated Dilation (FMD):** Vascular function of the brachial artery will be assessed using FMD procedures of forearm occlusion and re-perfusion.
- **Continuous Glucose Monitor (CGM) Sensor Insertion:** This device (FreeStyle Libre Pro, Abbott Diabetes) will remain inserted for 14 days in duration at the beginning of this study to assess free-living blood glucose levels at 15-minute intervals. An additional CGM period will occur during the final two weeks of exercise training (14 days in duration).
- **Accelerometer Physical Activity Monitoring:** This device will be administered to participants for 3 days at baseline, 3 days during the initial week of exercise, and 3 days during the final week of training to assess sedentary/active time during the day.
- **Oral Glucose Tolerance Test (OGTT):** The 2-hour post-prandial glucose response will be assessed via capillary finger-stick following the consumption of a 75g glucose beverage.

2.3.2 Pre-Exercise Visit 2:

- **Fasting Blood Lipid Profile:** Venous blood lipid analysis will include high-density lipoprotein (HDL), low-density lipoprotein (LDL), high-sensitivity C-reactive protein (hs-CRP), free fatty acids (FFA), total cholesterol, serum triglycerides (TAG), and non-HDL cholesterol, cholesterol/HDL ratio. HbA1C will also be assessed as an indication of glycemic homeostasis.
- **Oral Fat Tolerance Test (OFTT):** Consumption of a 90g lipid beverage will be followed by the assessment of serum TAG and free fatty acids (FFA) each subsequent hour for a total of five (5) hours in duration. Blood draws will occur through an intravenous catheter line.
- **Diet Log:** Participants will record their dietary intake for three (3) days following this visit. Three (3) additional dietary recording periods will occur throughout the study, which will additionally encompass a three (3) day recording period.

2.3.3 Pre-Exercise Visit 3:
This assessment will occur as the first exercise bout.

- **VO_2 Peak Assessment**: Maximal aerobic capacity will be assessed during an exercise test to exhaustion conducted on a cycle ergometer.

2.4 Exercise Training Protocol

Participants will be randomized to one of two training interventions in a parallel design. The total training intervention will be 6 weeks in duration with progression throughout in terms of exercise bout duration. The intervention groups are listed below.

2.4.1 Endurance (END) Training (Table 1)

END (5d/wk)				
	Week 1		Weeks 2-4	Weeks 5-6
Protocol	M, T	W, Th, F	M-F	M-F
	30 min (60% VO_{2peak})	30 min (60% VO_{2peak})	35 min (60% VO_{2peak})	40 min (60% VO_{2peak})
Daily Time Commitment	30 min	30 min	35 min	40 min

2.4.2 Sprint (SIT) Training (Table 2)

SIT (3d/wk)				
	Week 1		Weeks 2-4	Weeks 5-6
Protocol	3 min warm-up (50W); 2 min cool-down (50W)			
	M, W	F	M, W, F	M, W, F
	4 x 30 sec (170% Peak Wattage) / 2 min (50W)	4 x 30 sec (170% Peak Wattage) / 2 min (50W)	5 x 30 sec (170% Peak Wattage) / 2 min (50W)	6 x 30 sec (170% Peak Wattage) / 2 min (50W)
Daily Time Commitment	13 min	13 min	15.5 min	18 min

All training will be supervised on cycle ergometers. Before each exercise bout, blood pressure (BP) will be measured. If within a normal range, participants will begin exercising with heart rate

monitored throughout. During one exercise visit in Week 1, PWV will be conducted pre-exercise, immediately post-exercise, 15-minutes post-exercise, and 30-minutes post-exercise to assess acute vascular changes. Similarly, FMD will be conducted pre-exercise, post-exercise, and 30-minutes post-exercise.

2.5 Post-Exercise Testing

The pre-exercise tests (as explained above) will be re-assessed following the training intervention. The order in which these tests will occur is as follows:

2.5.1 Post-Training Testing Visit 1: VO_2 Peak Test
2.5.2 Post-Training Testing Visit 2: PWV, FMD, OGTT, CGM Removal, DXA
2.5.3 Post-Training Testing Visit 3: Blood Analysis, OFTT

3.0 DATA ANALYSIS

Additional information is provided in the attached statistical analysis plan (SAP).

4.0 REFERENCES

(1) Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC, Macera CA and Castaneda-Sceppa C (2007). Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Circulation.* **116,** 1094-1105.

(2) Gibala MJ, Little JP, MacDonald MJ and Hawley JA (2012). Physiological adaptations to low-volume, high-intensity interval training in health and disease. *J. Physiol.* **590,** 1077-1084.

(3) Burr JF, Rowan CP, Jamnik VK and Riddell MC (2010). The role of physical activity in type 2 diabetes prevention: physiological and practical perspectives. *Phys. Sportsmed.* **38,** 72-82.