Effects of a high-intensity interval training (HIIT) exercise intervention on sleep quality in women exposed to trauma: A randomized controlled trial

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Methods

C.2 Research design. A randomized control trial design will be used. Participants will be randomly assigned to one of the two treatment arms in blocks of two to optimize statistical power and minimize potential bias (Spieth et al., 2016). Sequentially numbered sealed envelopes created by a third-party using research randomizer (www.randomizer.org) will be used to allocate participants to treatments.

C.3 Participants. Seventy-two women who meet the inclusion criteria will be invited to participate. The seven inclusion criteria are: (i) exposure to a traumatic event, (ii) persistent PTSD-related symptoms adequate to screen positive for PTSD (Posttraumatic Diagnostic Scale-5 total scores > 27), (iii) poor sleep quality (Pittsburgh Sleep Quality Index >5), (iv) failure to meet recommended level of physical activity for U.S. adults (<150-mins of moderate or 75-mins of vigorous physical activity [or a combination] per week), (v) able to safely perform high intensity exercise (no contraindications based on the Physical Activity Readiness Questionnaire), (vi) aged 18-39 years,(vii) a non-smoker, (iix) willing to avoid alcohol and vigorous physical activity 24 hours before visiting the lab, and (ix) willing to avoid caffeine for 12 hours before visiting the lab.

C.4 Recruitment.

Several recruitment approaches will be implemented to ensure the required sample size is obtained. These approaches included: (i) e-mails sent to selected campus listservs, (ii) recruitment announcements in college classrooms, (iii) flyers placed in the University Health Center and around town, (iv) public service announcement made over the radio, and (v) by word of mouth.

C.5 Online Screening. Individuals interested in volunteering will be screened for eligibility by completing online surveys presented using Qualtrics. Eligible individuals will be invited to visit the Exercise Psychology Laboratory.

C.6 Baseline and Post-intervention. Prior to the testing, individuals will be asked to avoid alcohol consumption and moderate to vigorous physical activity 24 hours prior. Following the informed consent process, individuals will complete a brief menstrual history, 24-hour health status recall, and provide a saliva sample. Information about potential confounders and psychological symptoms also will be obtained using standardized methods supported by evidence of their validity (i.e., measures of symptoms of depression and anxiety, anxiety sensitivity, and physical activity history). These assessments will be repeated every 2 weeks and at the end of the six-week experiment. A body composition assessment via a duel-energy x-ray absorptiometry (DXA) will be completed. In a private room, the participants will fasten a wireless Zephyr™ BioHarness™ (Zephyr Technology, Auckland, New Zealand) below the sternum, (see figure 3). The Zephyr™ BioHarness™ will assess autonomic function via variability in heart rate. A baseline heart rate variability will involve adopting a seated position and measuring ECG while the participants rest for 5 minutes. Participants will complete the state portion of the State-Trait Anxiety Inventory (STAI), followed by a mental arithmetic task in which the participant will subtract by 13 from a 4-digit number for 10 minutes. Immediately after the mental arithmetic, participants will complete the state portion of the STAI. Participants will then complete a seated recovery for 5 minutes. Next, peak oxygen uptake (VO_{2Peak}) and peak power output (PPO) will be measured via a ramped bicycle protocol (Lode Excalibur Sport). Power output will be increased by 15 watts every minute until volitional exhaustion. Expired gases will be continuously measured via indirect calorimetry (Parvo Medics TrueOne 2400;

Parvo Medics, Salt Lake City, UT), and heart rate will be continuously monitored throughout the exercise test via a chest heart monitor (Polar; Polar Electro Inc., Lake Success, NY). The VO_{2peak} test will be administered so that participants can be prescribed the same exercise intensity, relative to their PPO, during exercise training. Saliva, DXA, vagal tone, peak oxygen uptake (VO_{2peak}), and sleep will be measured at baseline and after the six-week intervention.

C. 7 <u>High-Intensity Interval Training (HIIT).</u> HIIT participants will complete three leg cycle ergometer bouts weekly. During the first two weeks, the participants will complete 13, 30-seconds high intensity exercise intervals at a wattage prescribed to elicit 67% of PPO. Each 30-second exercise interval will be followed by a 1-minute active recovery interval at 30% of PPO. Each week, prescribed wattage will be increased by 4% of PPO. Thus, in the final week, the training intensity will be at 87% of PPO (See table 1 for training example). At the start of the third week, the exercise duration will be increased. Specifically, the 13, 30-second-high intensity intervals will increase to 10, 60-second high intensity intervals. All sessions will start will a three-minute warm-up and end with a two-minute cool-down on the cycle ergometer. In sedentary panic disorder patients, a 12 day HIIT training intervention of similar initial exercise intensity was well tolerated and showed rapid reductions in symptoms (Plag, Ergec, Fydrich, & Strohle, 2019). During the exercise sessions, ratings of perceived exertion, quadriceps pain, and heart rate during the exercise sessions will be assessed 0, 5, 10, 15, 20 minutes into the HIIT.

C.7 <u>Waitlist Control (WL).</u> Participants randomly assigned to the waitlist will visit the laboratory in order to complete the baseline, bi-monthly assessments and post-assessments. They will be asked to maintain their current lifestyle. They will be given the option to receive a six-week supervised HIIT training program after the waitlist participation.

D. Primary Outcome Measures for the Specific Aim

D.1 Specific Aim 1. Evaluate the impact of six-weeks of high intensity interval training on sleep quality and whether the effect is accounted for by the change in vagal tone.

Pittsburgh Sleep Quality Index-(PSQI): The PSQI is the gold standard measure of self-reported sleep quality. It consists of 19 items. Scores range from 0-21, higher scores indicate poorer sleep quality. A global score ≥5 indicates poor sleep quality with a sensitivity of 0.90 and specificity of 0.87 compared to polysomnographically determined poor sleep (Buysse et al., 1989). The PSQI instructions will be modified to better assess rapid changes in usual sleep habits (last two weeks rather than the past month).

Cardiac Vagal Tone: Each participant will place a bioharness monitor on in a private room. The R-R waveform will be sampled at 1000 hertz. Fast Fourier transformation will be applied, spectral power will be determined, and the average of the frequency domain will be calculated using Kubios analysis software (Tarvainen, Niskanen, Lipponen, Ranta-aho, & Karjalainen, 2014). After the frequency units from the heart cycles are converted to hertz, the vagal tone (high frequency band; 0.15-0.5 Hz), sympathetic tone (low frequency band; 0.05-0.15 Hz) and total power (0.017-0.5 Hz) will be calculated. The *apriori* focus is on changes in vagal tone.

Arithmetic Stress Task: Vagal tone will be measured at rest and during a stressor involving math calculations. Serial subtraction will be administered by a research team member dressed in white lab coat, with a clip board and pen for making notes. The team member will correct participants every time an incorrect answer is given and prompt participants to increase their pace every 15 seconds. Serial subtraction will involve sequentially subtracting 13 from a 4-digit number, and if an incorrect response is given, they will be asked to start over. The subtraction task will last a total of 10 minutes.

D.1.1 Expected Results. Based on our review of exercise training studies (McGranahan & O'Connor, 2021), we hypothesize HIIT to result in a clinically meaningful, moderate-sized or greater improvement in sleep quality. It is hypothesized that exercise-training induced changes in vagal tone will mediate the improvements in sleep quality. We do not expect improvements for sleep quality or vagal tone in the control group.

D.1.2 Statistical Power. A sample of 60 total participants will provide statistical power of 80%, at an alpha of 0.05. Assuming a moderate-sized interaction effect of 0.47 on sleep quality and a correlation of 0.85 between repeated measurements, the calculated sample size is 30 per group. Meta-analyses of participant drop out in exercise training trials shows that an average of 20% in the exercise groups and 15% in the control groups drop out (Kelley & Kelley, 2013). Using 20% attrition, recruiting 36 per group will result in 30 completers per group. The short-term (six-week) training duration should result in less than 20% compared to the meta-analysis which included primarily longer-term trials.

D.1.3 Statistical Analysis. ANOVA will examine the effect of exercise training on sleep quality. Mediation of the effect by the change in vagal tone will be tested by adding the variable as a covariate to the model. A change in the significance of the f-value would indicate significant mediation (Baron & Kenny, 1986; Fiske, Kenny, & Taylor, 1982). To quantify the effect size exercise training has on sleep quality at weeks 2, 4, and 6 and vagal tone at baseline and post, Hedges' d will be calculated.

D. 2.0 Specific Aim 2. Evaluate the impact of six-weeks of high intensity interval training on sleep quality, statistically testing for the effect of the change in trait anxiety and hyperarousal symptoms.

State and Trait Anxiety Inventory: Trait anxiety will be used and is reduced after exercise training (J. W. Whitworth et al., 2019a).

The Posttraumatic Diagnostic Scale-5 (PDS-5): Hyperarousal symptoms will be measured using the hyperarousal subscale of the Posttraumatic Diagnostic Scale-5 (PDS-5). The full 24-item scale also will be used as part of the inclusion criteria to assess PTSD symptoms in the past month based on the diagnostic criteria for the DMS-5. The full PDS-5 assesses trauma history, symptom onset, and index of trauma. Internal consistency of the full PDS-5 and the hyperarousal subscale ≥ 0.90.

D.2.1 Expected Results. Hyperarousal and anxiety symptoms are expected to decrease after HIIT and be correlated with improvements in sleep quality.

D.2.2 Statistical Analysis. A time-varying covariate analysis will determine if sleep quality changes are explained by the change in trait anxiety or hyperarousal at weeks 2-, 4-, or 6- of the intervention (Winer, 1991). To quantify the effect size exercise training has on PTSD symptoms and anxiety at weeks 2, 4, and 6, Hedges' d will be calculated.