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Original Research Article

The Effects of Cold vs. Hot Water Immersion on Exercise Recovery: Which Strategy is Best?

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Abstract

Introduction: Hot and cold water immersion (HWI and CWI respectively) are both options for recovery from intense and exhaustive exercise. The current research shows mixed results with some studies indicating that HWI and CWI have no effect on subsequent exercise performances while some point to improvements and/or decrements. The purpose of this research was to further the direct comparisons between HWI and CWI as methods of recovery for lower body exercise. **Methods:** Subjects (n=9) were moderately active healthy individuals aged 16-31. To analyze recovery effectiveness, an exhaustive lower body workout was performed followed immediately by one of the recovery modalities and followed again 24 hours later by the same exhaustive workout. The workout included a 70% VO₂max running trial to fatigue, a Wingate (30 second cycling test), and an 80% of leg press 1 rep max (1RM) repetitions to fatigue test. HWI was performed for 12 minutes at 40°C while CWI was performed for 12 minutes at 12°C. **Results:** A Chi-square test for independence indicated a significant association between recovery method (CON vs. HWI vs. CWI) and overall individual exercise performance, $\chi^2 (1, n = 81) = 7.264, p < .05, \phi = .299$. The proportion of individuals who exhibited a positive change in exercise performance following either HWI or CWI was significantly greater from the proportion of CON individuals ($p < 0.05$). Following HWI and CWI recovery methods, there were 63.0% and 66.7%, respectively, of individuals that exhibited maintained or increased exercise performance. In comparison, in the CON recovery condition, there were 33.3% of individuals who exhibited maintained or increased exercise performance. The Phi coefficient value ($\phi = .299$) indicates a medium-to-large effect size. **Conclusion:** The main finding of this study was that there is a higher likelihood of maintained or improved overall lower body performance with either HWI or CWI post-exercise compared to control with a recovery period of about 24 hours. This preliminary finding is a step forward in furthering the research into how HWI and CWI can benefit recovery.

Keywords: cardiorespiratory exercise, hydrotherapy, ice baths, performance, and resistance exercise.

Introduction

Successful training programs require balancing training duration, and frequency with appropriate rest to progress these variables¹⁻³. An imbalance in the training to rest equilibrium can lead to decreased performance in subsequent workouts and competitions, with a prolonged imbalance leading to the chronic fatigue and other physiological and psychological symptoms associated with overtraining syndrome^{2,4}. Recently, it has been suggested that overtraining and the resulting decline in performance may be more related to under-recovery rather than the workload of training sessions⁵. Many strategies have been suggested to enhance recovery between training sessions including stretching, massage, hydrotherapy, compression, sleep, nutrition, and active recovery^{4,6-8}.

Heat and cold applications are additional recovery options and have been studied previously⁹⁻¹¹. Hot water immersion (HWI), also referred to as thermotherapy, is one of the main forms of heat application used and is typically performed by submerging, at a minimum, the exercised muscles into water that is hot, but not to the point of causing serious burns, which is roughly 49 degrees Celsius¹². Cold water immersion (CWI), also called cryotherapy, is even more prevalent and

is typically the more scientific term used to describe ice baths.

There are have been previous head-to-head comparison studies on the effectiveness of HWI and CWI for exercise recovery. For example, Solsona and colleagues¹³ reported that sprint performance was similar between the HWI and active recovery groups and both were higher than the CWI group. Twelve national team speed skaters were recruited for that study. Each participant performed each recovery modality in a random order, one after each of three identical training sessions. Fifteen minutes after the training session, the skater either got in a hot tub (~41° C) for 20 minutes, got in an ice bath (~12° C) for 15 minutes, or participated in an active recovery (cycling at 40% of their max aerobic power) for 15 minutes. Ninety minutes after the recovery modality, participants performed a repeated sprint ability session on a stationary bike to determine performance recovery. This repeated sprint ability test consisted of a warmup (4 minutes at ventilatory threshold 1 and two six-second ~80% max speed sprints) and 10 all out 10-second sprints each separated by 30 seconds of passive rest. Mean power output during this test was significantly higher for active recovery (767 W) and HWI (766 W) relative to CWI (738 W).

In another study¹⁴, consisting of 38 strength-trained men, it was found that HWI (14 minutes at 38° C) was superior to passive recovery and CWI (14 minutes at 15° C) at isometric strength recovery. Isometric squat peak force was measured by placing subjects under a smith machine with an immovable amount of weight and having them stand on a force plate. The subjects had 3 attempts with a 3-minute rest in between each attempt where their highest peak force was determined to be their isometric strength. The fatiguing exercise bout consisted of 5 sets of 10 maximal eccentric leg press contractions followed by 2 sets of full repetition maximal contractions. The different recovery conditions (HWI vs. CWI vs. passive recovery) were applied and then isometric peak force was measured again.

Overall, research on the effectiveness of HWI and CWI as recovery strategies remain relatively sparse, especially in non-athletic populations, and therefore additional scientific inquiry is warranted. The purpose of this research was to further the direct comparisons between HWI and CWI as methods of recovery for lower body exercise, specifically in the ~24 hours post-exercise time span. Accordingly, the research question posed was do HWI and CWI as methods of recovery enhance cardiorespiratory performance, lower body muscular power output, and

muscular strength performance on next-day exercise bouts?

Methods

Participants

12 healthy, recreationally active men and women (16 to 50 years of age) were initially recruited. Study procedures were explained to subjects prior to any data collection. Recruitment occurred via word of mouth, posters, and university email. Subjects were considered active per the *Physical Activity Guidelines for Americans 2nd Edition*¹⁵ of 150 to 300 minutes of moderate-intensity cardiorespiratory exercise per week. A health history questionnaire and physical activity readiness questionnaire (PAR-Q) were filled out to ensure they met the study criteria and exercise would be safe. Subjects were excluded from the study if they were categorized as high risk, pregnant or may become pregnant, injured or disabled. Data was collected in the High Altitude Performance Lab (HAPLab) as well as the NCAA Weight Room, both within the Mountaineer Field House (MFH). This study was approved by the Human Research Committee at Western Colorado University.

Experimental Design

Each subject came into the lab eight times. The first visit the subject was able to ask any questions about the study, before they signed the informed

consent. Then they filled out the health and activity questionnaires and surveys. Then the researchers took anthropometric measures of the subjects. Finally, the subjects performed the Wingate test, maximal oxygen uptake ($VO_2\max$), leg press 1RM, 70% $VO_2\max$ running trial to fatigue, and 80% leg press trial to fatigue. With at least 3 days of rest before the second visit, subjects performed a $VO_2\max$ as well as a 1RM for the leg press. On visits three and four, ~24 hours apart, subjects performed the standard exercise session protocol consisting of a Wingate, an 80% leg press to fatigue test, and a 70% running trial to fatigue test. For visits five and seven, subjects were randomly assigned either HWI for visit five and CWI for visit seven or vice versa. During the visits, the subjects performed the standard exercise session followed by the assigned recovery method. Visits six and eight, ~24 hours after visits five and seven respectively, just included the exercise session.

Procedures

Screening Questionnaires

After obtaining informed consent, subjects were screened using the Western Colorado University's Screening Questionnaire for Research Involving Exercise and IPAQ to confirm that all subjects were rated as low risk before any exercise testing.

Resting Heart Rate

Subjects were instructed to sit quietly for five minutes. After five minutes, resting heart rate was measured using a pulse oximeter and recorded.

Height and Weight

After measuring resting heart rate, the subjects' height (in.) and weight (kg) were measured using a digital scale. Subjects were instructed to remove their shoes and step onto the scale. Height and weight were recorded.

Body Composition

After measuring height and weight, the subjects' body fat percentage was measured using a body fat analyzer. The average of three measurements was recorded.

Exercise Testing

Wingate

Next, subjects sat on the Wingate bike (Ergopedic 894E, Monark, Sweden) and adjusted it to their body. Subjects were instructed that they would pedal up to 60 rpm then the researcher would countdown from three, and on "go" they would pedal as hard as they could. Upon their rpms reaching 120, the weight would automatically drop, therefore applying the resistance. They were constantly encouraged to keep giving it their all throughout the entire 30 seconds. At the conclusion of the 30 seconds, they did a brief cooldown.

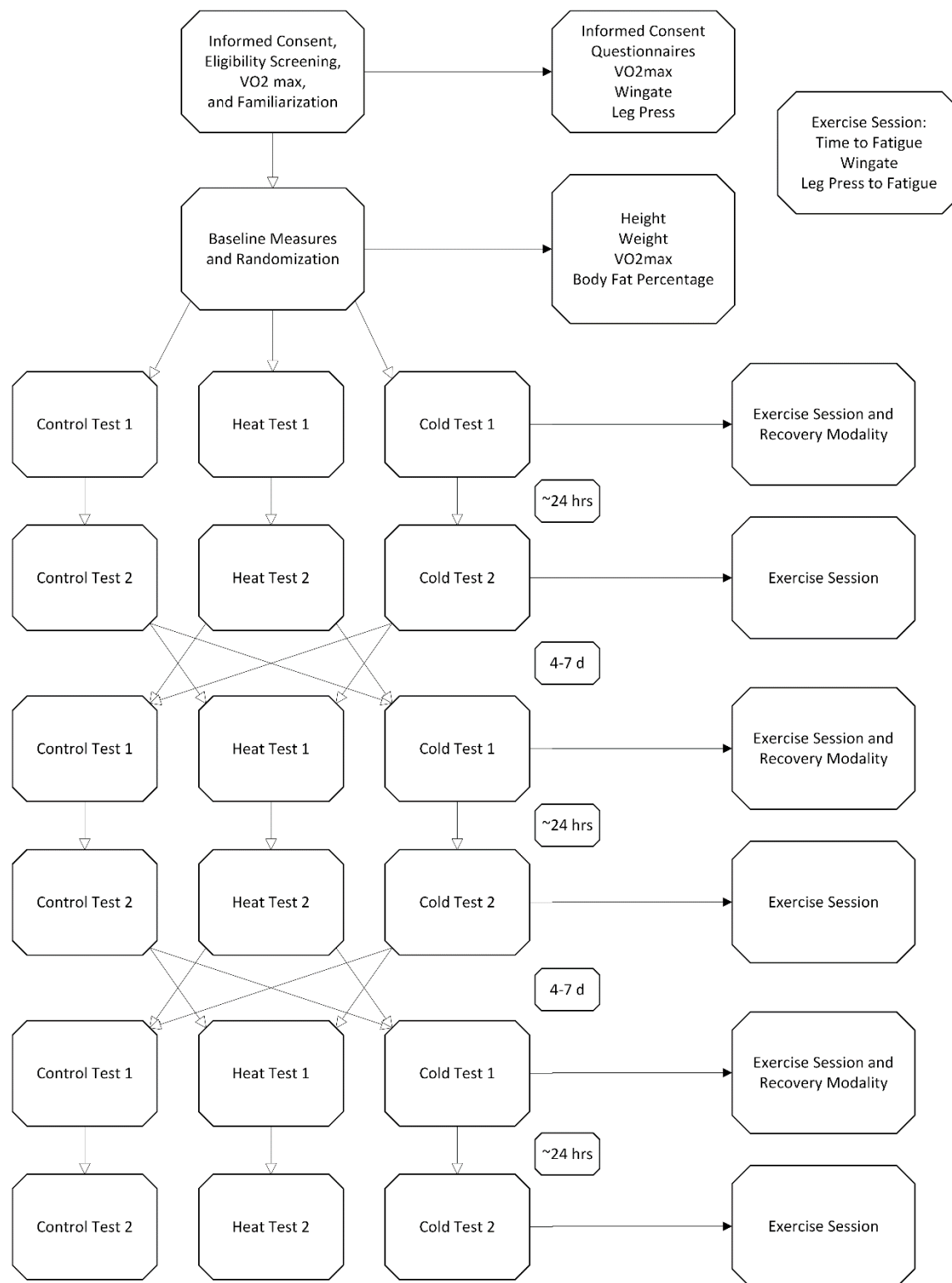


Figure 1. Experimental flowchart.

VO₂Max

Prior to the VO₂max test, subjects performed an exercise warm-up period of a few minutes. Then subjects were instructed to put on a mask with a breathing valve to collect expired gases. The gases traveled through a tube and through a metabolic cart (Parvo Medics, Sandy, UT) to be analyzed. Subjects were instructed to use hand signals to notify researchers about the need to stop the test.

Subjects were asked to jog/run on a treadmill at different combinations of speed and grade (incline) at progressively harder workloads. The test continued until the subject became fatigued and decided to stop or other symptoms prohibited further exercise.

During the VO₂max test, a subject's heart rate was monitored through a chest strap attached to a heart rate monitor. Subjects were asked to rate their perceived exertion during the test. After testing, subjects went through an exercise cool-down.

Leg Press 1RM

Next, was the leg press 1RM on the leg press (Hammer Strength, Model HSLLP, Schiller Park, IL, Serial No. HSLLP 0214001) in the NCAA weight room. The following protocol was used for 1RM testing:

1. 10 repetitions of a weight the participant felt comfortable lifting (40-60% 1RM) were performed to warm up muscles
2. RPE was recorded followed by 1 minute rest period
3. 5 repetitions of weight 60-80% 1RM was performed as a further warm up, RPE recorded followed by a 2-minute rest period
4. First 1RM attempt at weight of 2.5-20kg greater than warm up, weight was dependent on RPE of warm up
 - a. If first 1RM lift was deemed successful by the researcher (appropriate lifting form) weight was increased until maximum weight participant can lift was established with 3 minutes between each attempt.
 - b. If first 1RM lift deemed unsuccessful by the researcher, weight was decreased until participant successfully lifted the heaviest weight possible

There were 3 minutes rest between 1-RM attempts and a maximum of 5 x 1RM attempts. There were 5 minutes of rest between the 1-RM testing of each resistance exercise. Following the test participants completed a five-minute walking cool down.

TTF

Next was the 70% VO₂max treadmill running bout to fatigue. Subjects stepped onto the treadmill and had a 3-minute warmup at a self-selected intensity. Then the researcher adjusted

the treadmill's speed and incline to 70% of the subject's VO_2max intensity. It remained here until the subject signaled they were done with the test by putting their hands on the side bars and hopping off the treadmill. The researcher then decreased the speed and grade to a cooldown pace for the subject to cooldown on.

RTF

Finally, the subject sat down into the leg press machine and the researcher loaded the appropriate warmup weight onto the bars. Subjects performed one set of 12 repetitions to warmup. Then 80% of their 1RM was loaded onto the bars by the researcher. The subject pressed the weight as many times as they were physically able to with proper form. Once they were finished, they signaled to the researcher by either re-engaging the safety or tapping the side bars so the researcher could assist.

Hot Water Immersion

After the completion of an exercise session consisting of a running TTF, a Wingate, and a leg press RTF the subject had a couple minutes to transition into suitable attire. Then the subject was instructed to submerge themselves into the hot tub to at least the waist level. Every 3 minutes, the water temperature was recorded, and the researcher asked the subject how they were feeling on the thermal comfort scale. The water temperature was kept as close to 40° C

throughout the immersion. At the 12-minute mark, the subject stood up and got out of the hot tub.

Cold Water Immersion

After the completion of an exercise session consisting of a running TTF, a Wingate, and a leg press RTF the subject had a couple minutes to transition into suitable attire. Then the subject was instructed to submerge themselves into the cold tub to at least the waist level. Every 3 minutes, the water temperature was recorded, and ice could have been added to keep the water temperature as close to 12° C as possible. The researcher also asked the subject how they were feeling on the thermal comfort scale every 3 minutes. At the 12-minute mark, the subject stood up and got out of the cold tub.

Statistical analyses

All analyses were performed using SPSS Version 29.0 (IBM, Armonk, NY) and GraphPad Prism 9.0 (San Diego, CA). Measures of centrality and spread are presented as mean \pm standard deviation (SD). Paired samples t-tests were performed on the "pre" vs "post" recovery performance measures (TTF, power drop percentage, and RTF). One-way repeated measures ANOVAs were run on Δ each performance measure between test 1 and test 2 by treatment (CON, HWI, CWI). A chi-square test for independence was used to determine if the proportion of participants who

increased/maintained or decreased their combined exercise performances was associated with treatment (CON, HWI, CWI).

The probability of making a Type I error was set at $p \leq 0.05$ for all statistical analyses.

Results

12 subjects initially provided informed consent. One dropped out due to injury and two dropped out due to outside commitments. The physical and physiological attributes of the nine subjects who completed the entire intervention are presented in Table 1.

Table 1. Physical and physiological subject characteristics (mean \pm SD).

Age (years)	Height (cm)	Weight (kg)	Body fat percentage	VO ₂ max (mL/kg/min)	Leg press 1RM (lbs)
21.8 \pm 4.5	175.8 \pm 6	83.2 \pm 15.8	20.8 \pm 7.7	40.4 \pm 4.9	709 \pm 193

Time to Fatigue

Paired samples t-tests were run for all conditions between the pre- and post-recovery exercise bouts. For the control condition, the pre-recovery TTF mean (M=1576, SD=916) was 251 seconds longer than the post-recovery mean (M=1325, SD=776, $p=.0712$). For the HWI condition, the pre-recovery mean (M=1211, SD=513) was 58 seconds shorter than the post-recovery mean (M=1269, SD=532, $p=.5346$). For the CWI condition, the pre-recovery mean (M=1413, SD=624) was 166 seconds longer than the post-recovery mean (M=1247, SD=630, $p=.4392$). All mean

differences between pre- and post-recovery within the control, HWI, and CWI trials showed no statistical significance ($p>.05$). Though no statistical significance was found between pre- and post-recovery, a one-way repeated measures ANOVA was run to assess the effects of recovery modality between control, HWI, and CWI on TTF decrement. An insignificant recovery modality effect was found ($F(2, 8) = .6645, p=.7150$). The Δ in TTF (seconds) between exercise session and +24hr exercise session across recovery conditions is shown in Figure 2.

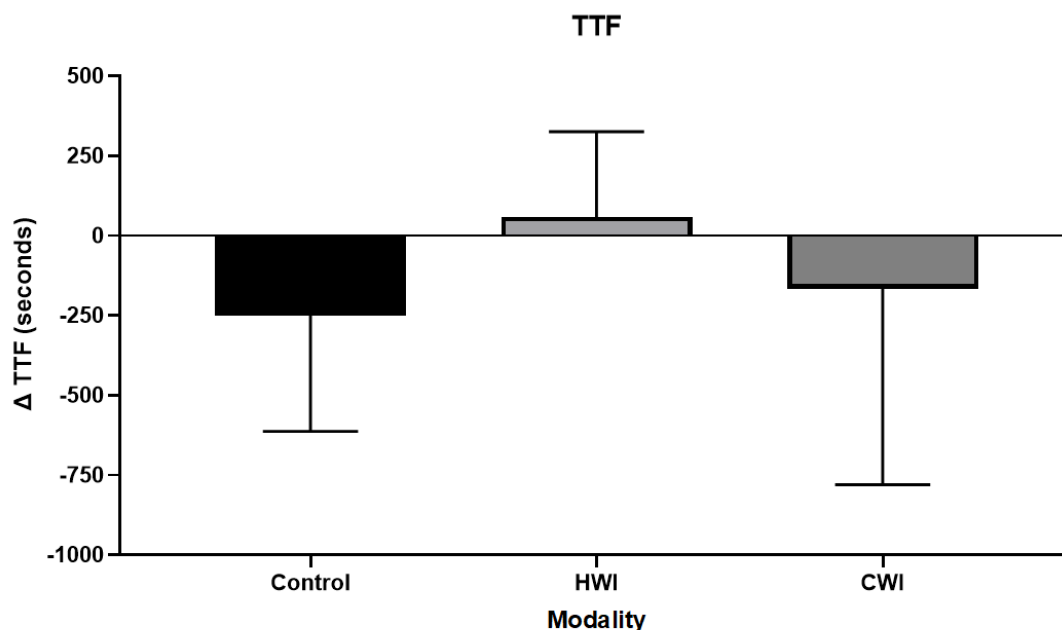


Figure 2. The Δ in TTF (seconds) between exercise session and +24hr exercise session across recovery conditions (Control vs. HWI vs. CWI).

Wingate Power Drop

Paired samples t-tests were run for all conditions between the pre- and post-recovery exercise bouts. For the control condition, the pre-recovery mean power drop ($M=60.50$, $SD=7.09$) was .7 percent less than the post-recovery mean ($M=61.20$, $SD=6.05$, $p=.6635$). For the HWI condition, the pre-recovery mean power drop ($M=61.42$, $SD=5.00$) was .91 percent greater than the post-recovery mean ($M=60.51$, $SD=4.45$, $p=.4395$). For the CWI condition, the pre-recovery mean power drop ($M=60.80$, $SD=3.93$) was .51 percent greater than the post-recovery mean ($M=60.29$, $SD=6.49$,

$p=.6911$). All mean differences for power drop percentage between pre- and post-recovery within the control, HWI, and CWI trials showed no statistical significance ($p>.05$). Following these paired samples t-tests, a one-way repeated measures ANOVA was run to examine the effects of recovery modality between control, HWI, and CWI on TTF decrement. An insignificant recovery modality effect was found ($F(2, 8) = .3954$, $p=.6164$). The Δ in Wingate Power Drop (%) between exercise session and +24hr exercise session across recovery conditions is shown in Figure 3.

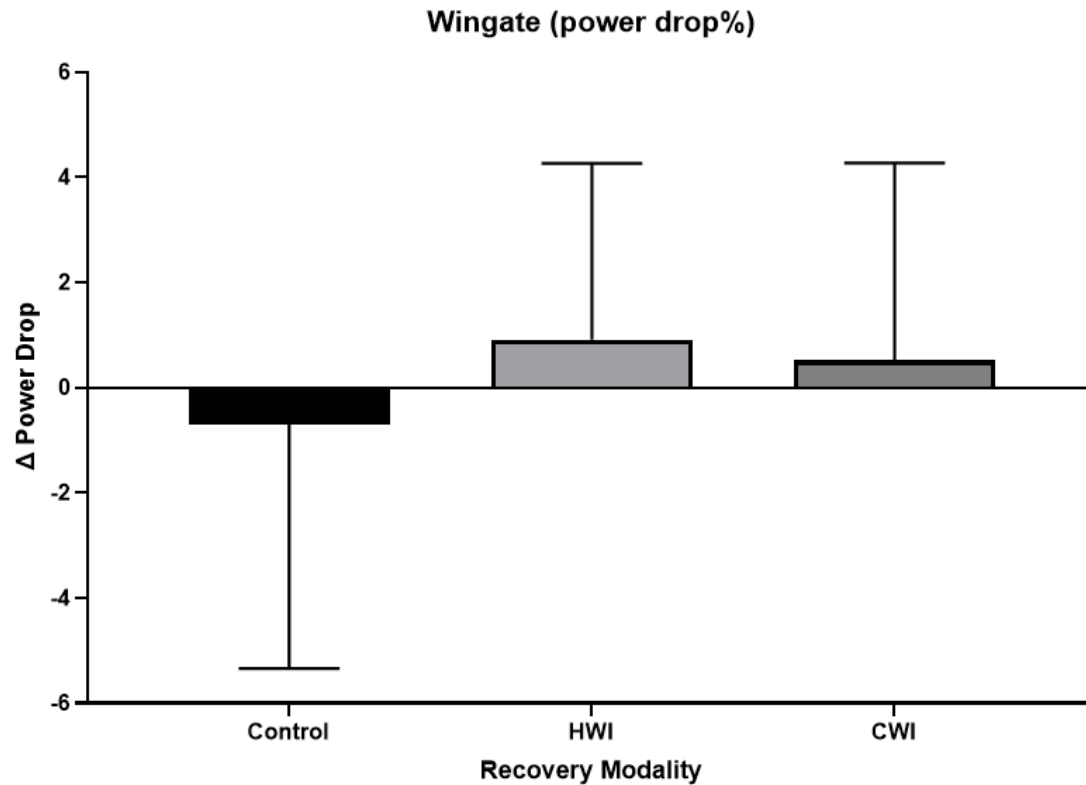


Figure 3. The Δ in Wingate Power Drop (%) between exercise session and +24hr exercise session across recovery conditions (Control vs. HWI vs. CWI).

Repetitions to Fatigue

Paired samples t-tests were run for all conditions between the pre- and post-recovery exercise bouts. For the control condition, the pre-recovery mean repetitions to fatigue (RTF) (M=15.6, SD=6.9) was 1.6 less than the post-recovery mean (M=17.2, SD=9.1, $p=.2598$). For the HWI condition, the pre-recovery mean RTF (M=17.7, SD=7.1) was 4.2 less than the post-recovery mean (M=21.9, SD=12.9, $p=.0730$). For the CWI condition, the pre-recovery mean RTF (M=18.8, SD=10.0) was 2.8 less than the post-

recovery mean (M=21.6, SD=10.1, $p=.0056$). The difference between pre- and post-recovery RTF was not statistically significant ($p>.05$) for the control or HWI trial but was statistically significant ($p\leq.05$) for the CWI trial. Following these paired samples t-tests, a one-way repeated measures ANOVA was run to gauge the effects of recovery modality between control, HWI, and CWI on RTF performance. The Δ in Repetitions to Fatigue on the leg press between exercise session and +24hr exercise session across recovery conditions is shown in Figure 4.

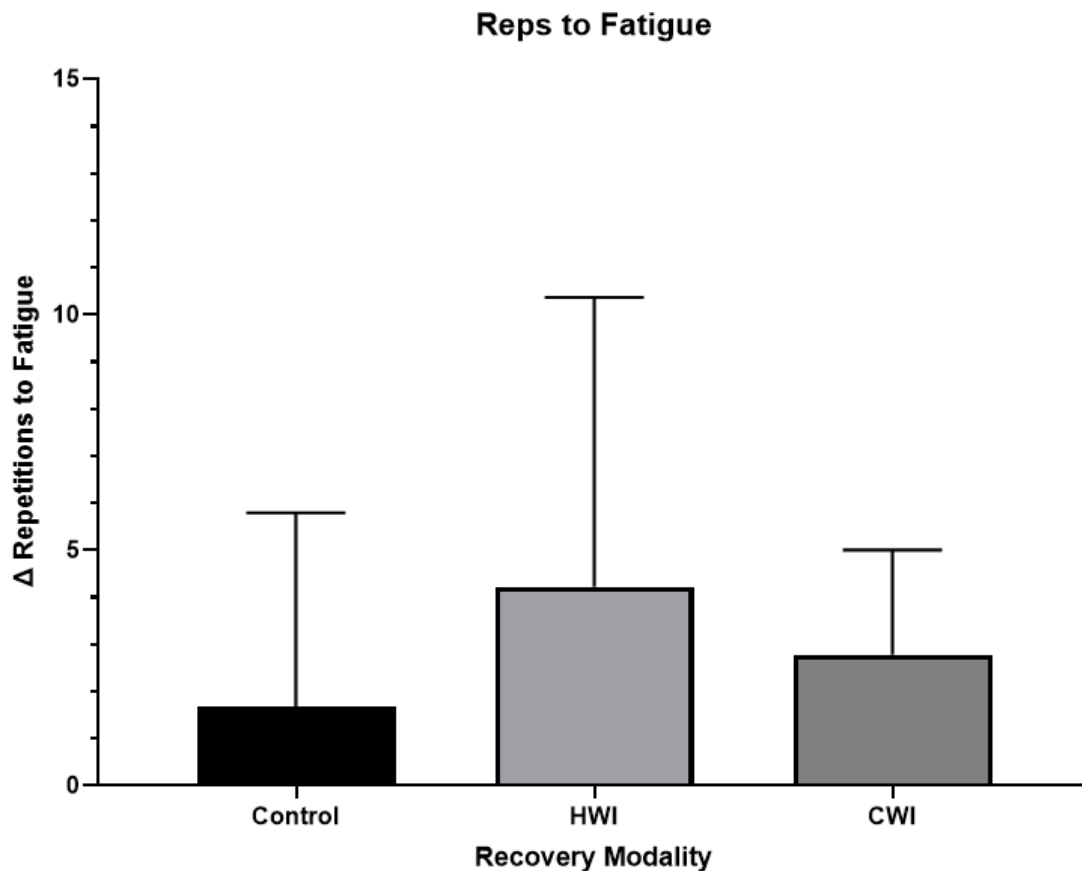


Figure 4. The Δ in Repetitions to Fatigue on the leg press between exercise session and +24hr exercise session across recovery conditions (Control vs. HWI vs. CWI).

Overall Individual Exercise Performance
A Chi-square test for independence indicated a significant association between recovery method (CON vs. HWI vs. CWI) and overall individual exercise performance, $\chi^2 (1, n = 81) = 7.264, p < .05, \phi = .299$. The proportion of individuals who exhibited a positive change in exercise performance following either HWI or CWI was significantly greater from the proportion of CON individuals ($p < 0.05$). Following

HWI and CWI recovery methods, there were 63.0% and 66.7%, respectively, of individuals that exhibited maintained or increased exercise performance. In comparison, in the CON recovery condition, there were 33.3% of individuals who exhibited maintained or increased exercise performance. The Phi coefficient value ($\phi = .299$) indicates a medium-to-large effect size. See Figure 5 below.

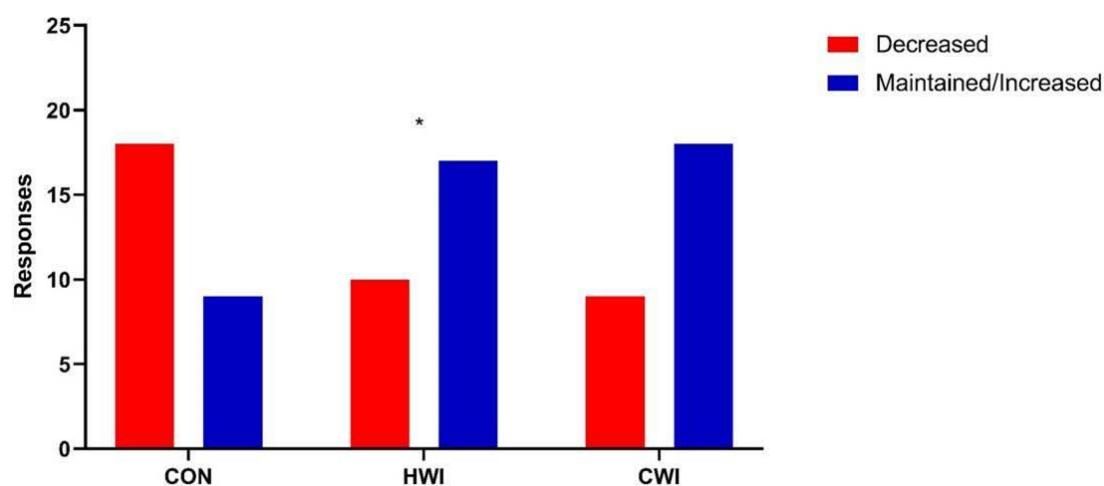


Figure 5. The proportion of individuals who exhibited a positive change in exercise performance following either HWI or CWI was significantly greater from the proportion of CON individuals ($p < 0.05$); * denotes $p < 0.05$.

Discussion

The main finding of this study was that there is a higher likelihood of maintained or improved overall lower body performance with either HWI or CWI post-exercise compared to control with a recovery period of about 24 hours. This preliminary finding is a step forward in furthering the research into how HWI and CWI can benefit recovery. Overall, recovery is becoming increasingly important to the performance of fitness enthusiasts and personal trainers alike in a bid to reduce fatigue and enhance performance. This study will provide those groups with important evidence for the use of various recovery methods as an effective training recovery strategy and help point to which may be most effective.

In contrast to our findings, where we found no significant differences in Wingate power drop index or leg press repetitions, Vaile and colleagues HWI group did observe better peak force compared to control 24 hours after the fatiguing exercise¹⁴. Some possible reasons for these differences could be due to the different exercise protocols utilized. We used a 3-exercise session that included a cardiorespiratory performance, anaerobic power, and strength-focused exercise bout, while Vaile and colleagues¹⁴ used a DOMS-inducing workout to simulate fatigue with a peak force and a peak power exercise at baseline and post-DOMS-inducing workout to measure change in performance. With regard to the similarities in HWI and CWI protocols,

overall dose is quite similar, Vaile and colleagues¹⁴ used 15° C and 38° C for 14 minutes each while we used 12° C and 40° C for 12 minutes each for CWI and HWI respectively.

Another study, this one by Pournot and colleagues¹¹, reported recovery benefits from CWI. The study involved 3 main exercises: knee extension maximal isometric voluntary contraction (MVC), countermovement jump (CMJ), and rowing. Primary outcome measures were MVC peak torque, CMJ height, and 30-second row mean power (P_{30s}). For the fatigue-inducing exercise, 2 segments of 10 minutes of work separated by a 10-minute rest was used. During each segment of work, subjects performed cycles of CMJ at a rate of 21 per 30 seconds for 30 seconds and rowing at roughly 80% of their maximal average power over 30 seconds. Each 30 period of exercise was separated by 30 seconds of rest. As for recovery, their control was sitting still in a chair for 15 minutes and CWI was a 15-minute immersion up to the iliac crest in 10° C water. It was reported that immediately after the fatiguing exercise, there were significant decreases in all performance measures, but 1 hour later, after the recovery, MVC and CMJ were insignificantly different than baseline for CWI, while P_{30s} for CWI and all performance measures for control were significantly lower than baseline. Additionally, 24 hours post-exercise, all

performance measures for the CWI group were insignificantly different from baseline, while the control group's MVC was still significantly less than baseline. Most of the power output-related measures from this study are approximately comparable to our Wingate test, which showed that CWI may have been better than control despite the absence of statistical significance. As Pournot and colleagues¹¹ had subjects perform multiple post-tests at various time points after the fatiguing exercise, the researchers may have obtained a fuller picture of the recovery process in action or ideal recovery modality to use for different recovery timeframes. Furthermore, having separate performance metric exercises to fatiguing exercises could explain some of the differences between studies as less additional fatigue is incurred compared to our study design where performance metric exercises are fatiguing and potentially causing a cascade of performance effects. In summary, Pournot et al.¹¹ found more conclusive evidence of CWI being beneficial to recovery than we did.

Finally, Jackman and colleagues¹⁶ investigated just HWI compared to control. Their study primarily focused on blood markers but also included data on MVIC. For their fatiguing exercise session, they had subjects perform 4 sets of 6 reps at their 6RM for each of

the following exercises: back squat, front squat, good mornings, and Bulgarian split squats. As for recovery, body position was standardized as $\sim 90^\circ$ hip angle, with legs outstretched and relaxed. The HWI group sat like this in a hot tub which was 40°C for 10 minutes, while the control group sat like this on a physiotherapy bed for 10 minutes. MVIC was measured 2 and 24 hours after the completion of exercise. It was found that there was no significant difference between the effects of control and HWI at either the two- or 24-hour post-exercise timepoints. These findings are similar to our results in which HWI recovery post-exercise failed to elicit a statistically significant effect on any one individual exercise performance. It is possible that with a larger sample size or pooled performance measures from multiple exercises a significant effect would be discovered.

Potential mechanistic reasons for the higher probability for improved or maintained performance with the use of HWI could be due to increased intramuscular temperature (IMT). Increased IMT has been shown to be a result of HWI¹⁶. Some researchers have suggested that increased IMT leads to improved blood flow in the affected tissues which allows harmful exercise byproducts to be flushed out of the muscle and nutrients to be delivered to help expedite the recovery process^{14,16-17}. The predominant thinking to CWI

being beneficial for recovery is that the measured reduction in IMT has a multitude of ergogenic effects on the muscle tissue¹⁸⁻¹⁹. These effects potentially include reduced creatine kinase activity, slowed metabolism, reduced capillary permeability, reduced blood flow, decreasing intracellular water content, and inhibited release of circulating hormones such as insulin-like growth factor-1, testosterone, and growth hormone¹⁹⁻²⁰. Both the reduced activity of creatine kinase and slowed metabolism could be reasons that indicate a lesser amount of muscle damage which leads to the maintenance/improvement of performance.

Our research is helpful in progressing knowledge of the effects of both HWI and CWI by providing another building block upon prior studies as a means to bolster protocols for future research. The main limitations of this study were the small sample size and the limited control we had on subject preparation and recovery outside of the laboratory. The small sample size may have resulted in low power and therefore an inability to detect potential true differences in the effect of CWI and HWI on recovery and recurrent exercise performances bouts. Whereas the limited control of subjects' active and busy lifestyles outside of the study could have led to inconsistent day-to-day performances through how well they were able to

sleep and eat prior to and between sessions. A strength of our study was the recreationally active cohort we investigated as their physical and physiological attributes are comparable to that of the average gym-goer. Additionally, the range of exercise performance bouts participants performed are comparable to usual domains (i.e., cardiorespiratory and muscular fitness) that fitness enthusiasts are likely to integrate into week-to-week training regimens.

Conclusion

There are three key 'take-home messages' based on findings from the present study:

1. There was a two-fold greater likelihood of maintained or improved exercise performance with either CWI or HWI post-exercise recovery strategies relative to control (i.e., a passive recovery).
2. Recovery is becoming increasingly important to the performance of fitness enthusiasts and athletes alike in a bid to reduce fatigue and enhance performance. This study provides ACE certified professionals with important evidence for the use of various recovery methods (CWI vs. HWI vs. passive recovery) as effective training recovery strategies and helps point to which is best.

3. Training recovery can be optimized by correctly managing the various components surrounding the exercise program. To accomplish this endeavor, ACE certified professionals can apply the F.I.T.T. paradigm to training recovery itself. The present study examined several of the F.I.T.T. parameters for training recovery:

- Type/Mode: CWI vs. HWI vs. Control (i.e., passive recovery) were studied. Both CWI and HWI were found to be safe and effective post-exercise recovery strategies.
- Intensity: Specific water temperatures for CWI (12° C) and HWI (40° C) that were safe and effective were identified.
- Time: Specific durations for CWI (12 minutes) and HWI (12 minutes) that were safe and effective were identified.

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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