Acute exercise tolerance among Veterans with Gulf War Illness

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Key terms and arguments

Post-exertion malaise (PEM): a short-term condition where symptoms are exacerbated 24-48 hours following physical or cognitive stress

- Similar but more rapid responses to physical stress (<1 hour) are not PEM

Adverse event (AE): undesirable or harmful outcome that occurs during or after an intervention but is not necessarily caused by it

- "Serious" (e.g., death from heart attack) or "non-serious" (e.g., fatigue)
  - Examples of non-serious AE's include PEM and other similar effects
  - National exercise testing and prescription guidelines provide strategies for minimizing serious AE's, but what about non-serious AE's?

Rationale: what do prior studies tell us about minimizing non-serious AE's when prescribing exercise?

- CMI's have an elevated risk for non-serious AE's following exercise:
  - ↑ severity of pain and fatigue symptoms
  - ↑ sensitivity to experimental pain
  - ↓ performance of cognitive tests

- Exercise challenge: physical stress→ provoke symptoms→ pathophysiology

- Informative for pathophysiology and risk awareness, but not always reflective of prescriptions used in exercise rehabilitation programs

- Lack of acute studies which compare risk of non-serious AE's across different exercise prescriptions makes guidance challenging

Specific aims and hypotheses

Aim(s): Examine dose-response relationship between exercise-intensity and:

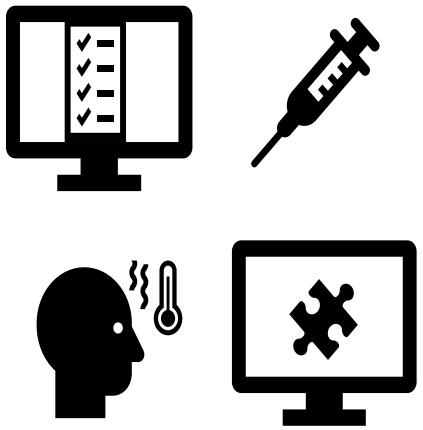
Psychometric outcomes: Symptoms, pain sensitivity, & cognitive performance (Aim 1)
Biological outcomes: Inflammatory cytokines (Aim 2)
Behavioral outcomes: Physical activity (Aim 3)

Central hypothesis: Relative to lower intensity exercise, higher intensity leads to larger:

↑ symptom severity (Aim 1a)
↑ sensitivity to experimental pain stimuli (Aim 1b)
↓ cognitive performance (Aim 1c)
↑ inflammatory cytokines (Aim 2)
↓ physical activity (Aim 3)

Randomized controlled crossover experiment

Pre-test outcomes



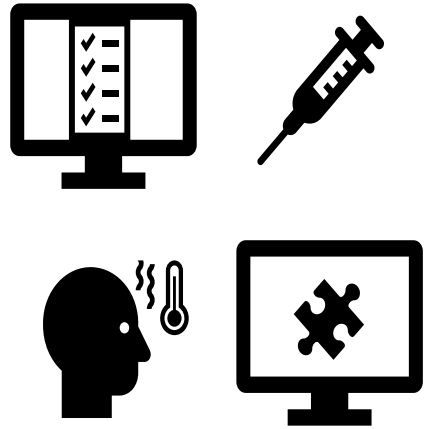
Vigorous intensity exercise (65% heart rate reserve)

Moderate intensity exercise (50% heart rate reserve)

Light intensity exercise (35% heart rate reserve)

Seated rest control condition

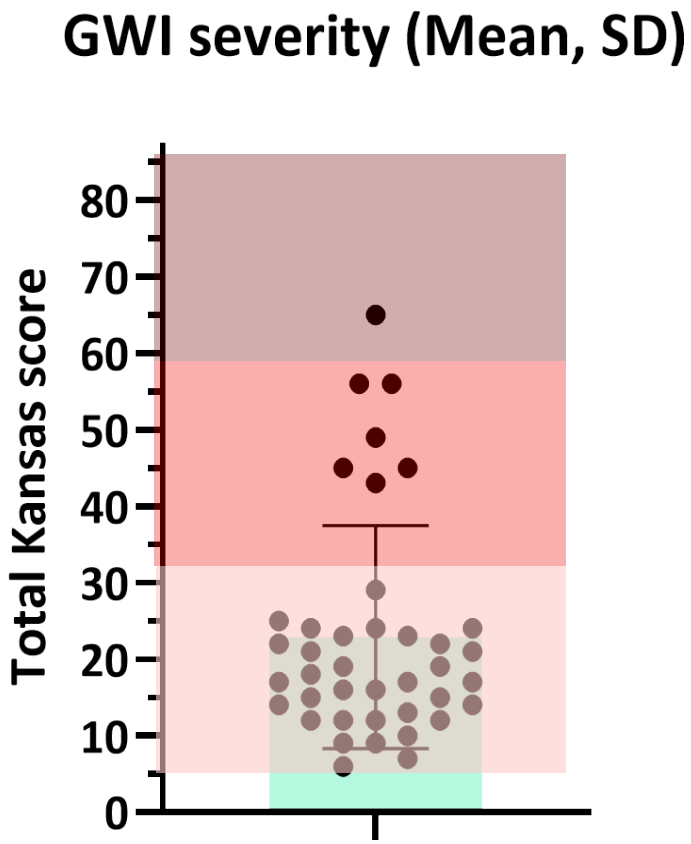
Post-test outcomes



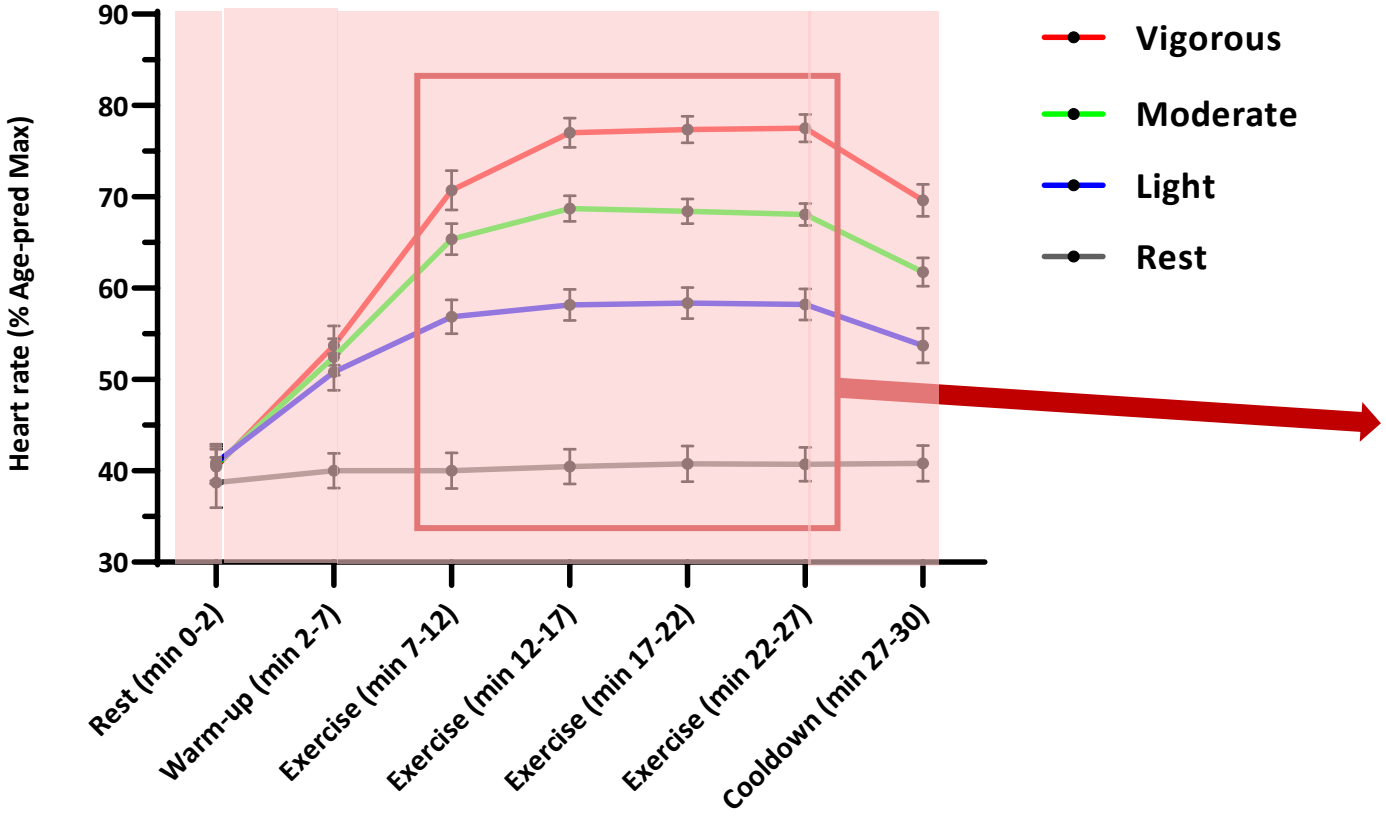
Results

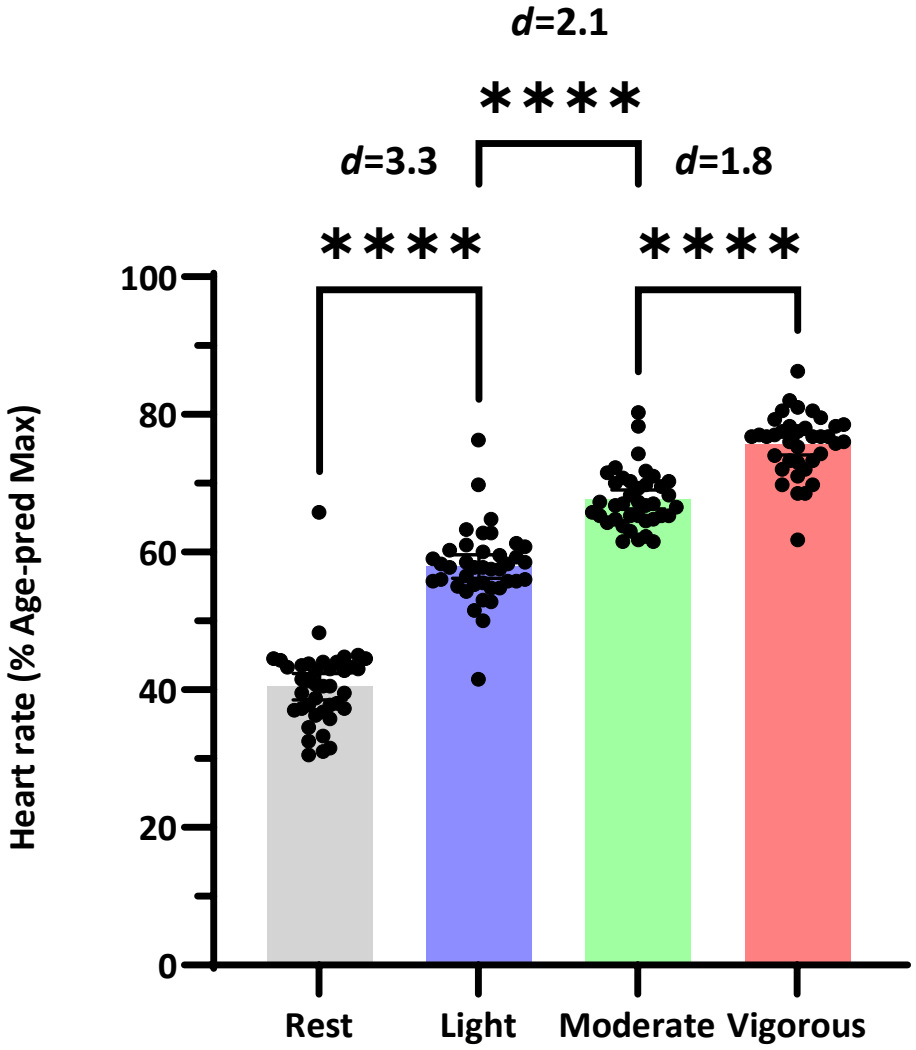
Characteristics of final sample (n=40)

Characteristics	Frequency
Male/Female	90/10
White/Black/Multiple Races	95/2.5/2.5
Kansas Fatigue	90%
Kansas Pain	87.5%
Kansas Neuro/Cognitive/Mood	100%
Kansas Gastrointestinal	42.5%
Kansas Respiratory	32.5%
Kansas Dermatological	22.5%



Success of exercise dosing





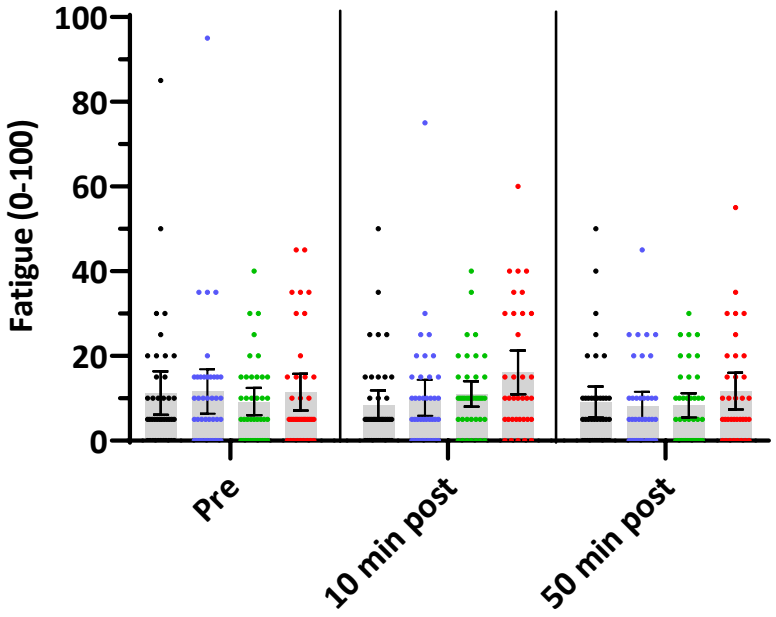
Note. Data represented as means (95% CI)

Note. Data averaged across 20-min exercise phase

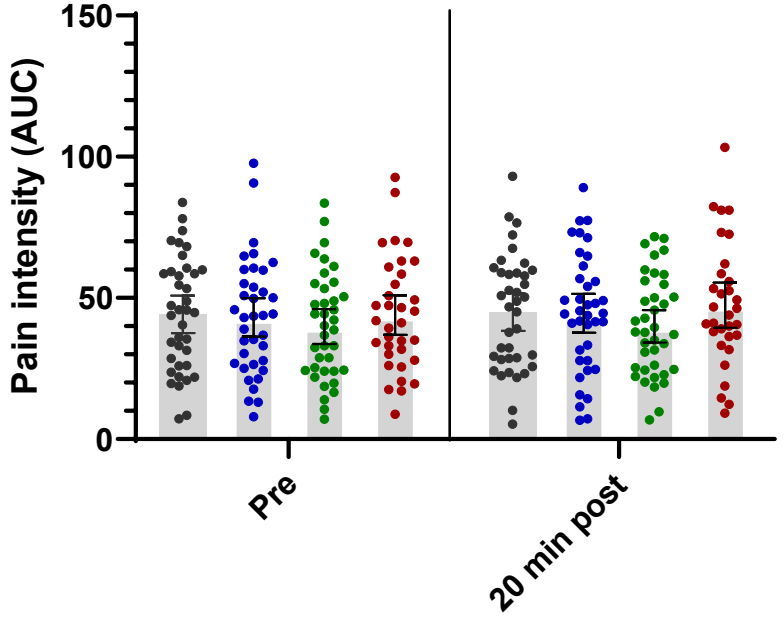
Primary results for Aims 1 & 3

Aim 1: Psychometric outcomes

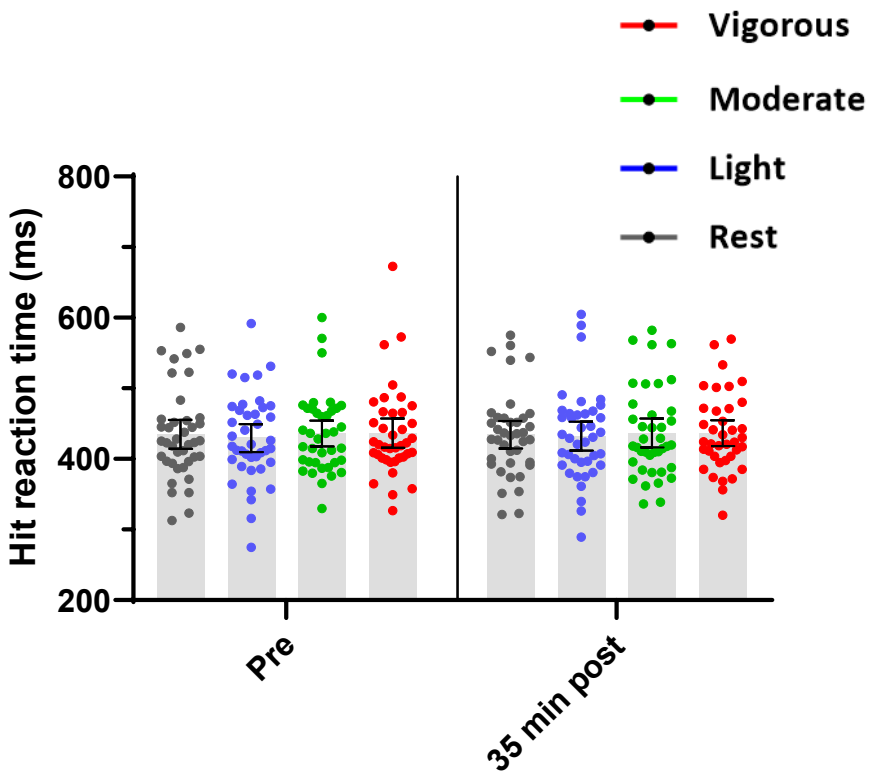
A. Fatigue symptoms



B. Pain sensitivity

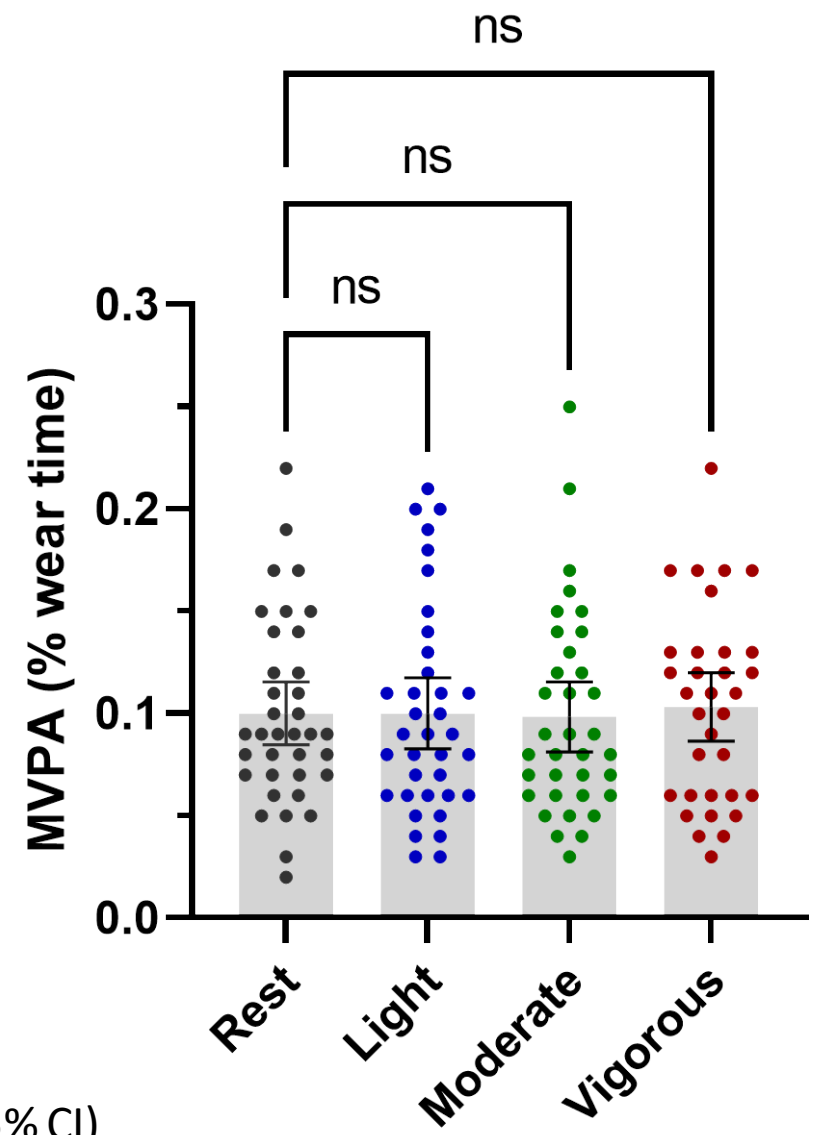


C. Cognitive performance



Note. Data represented as means (95% CI)

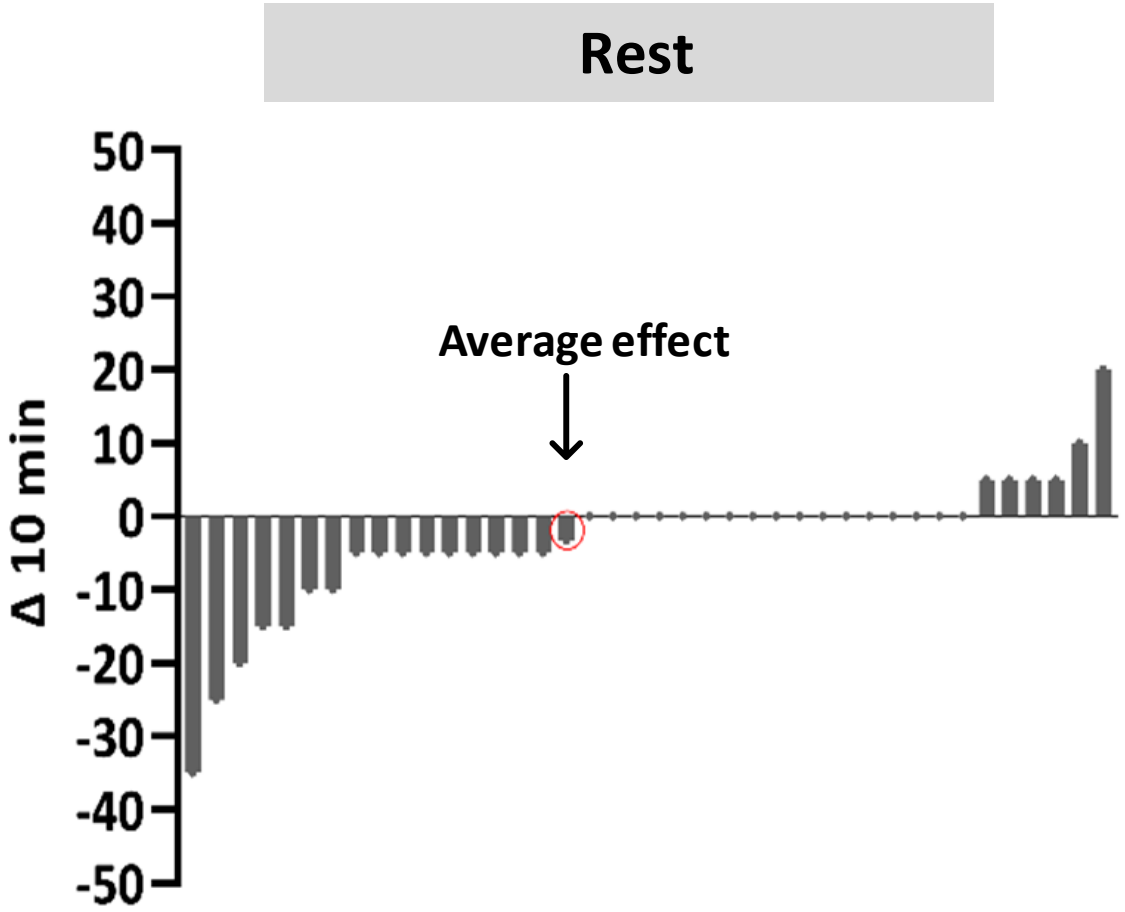
Aim 3: Moderate-to-vigorous physical activity

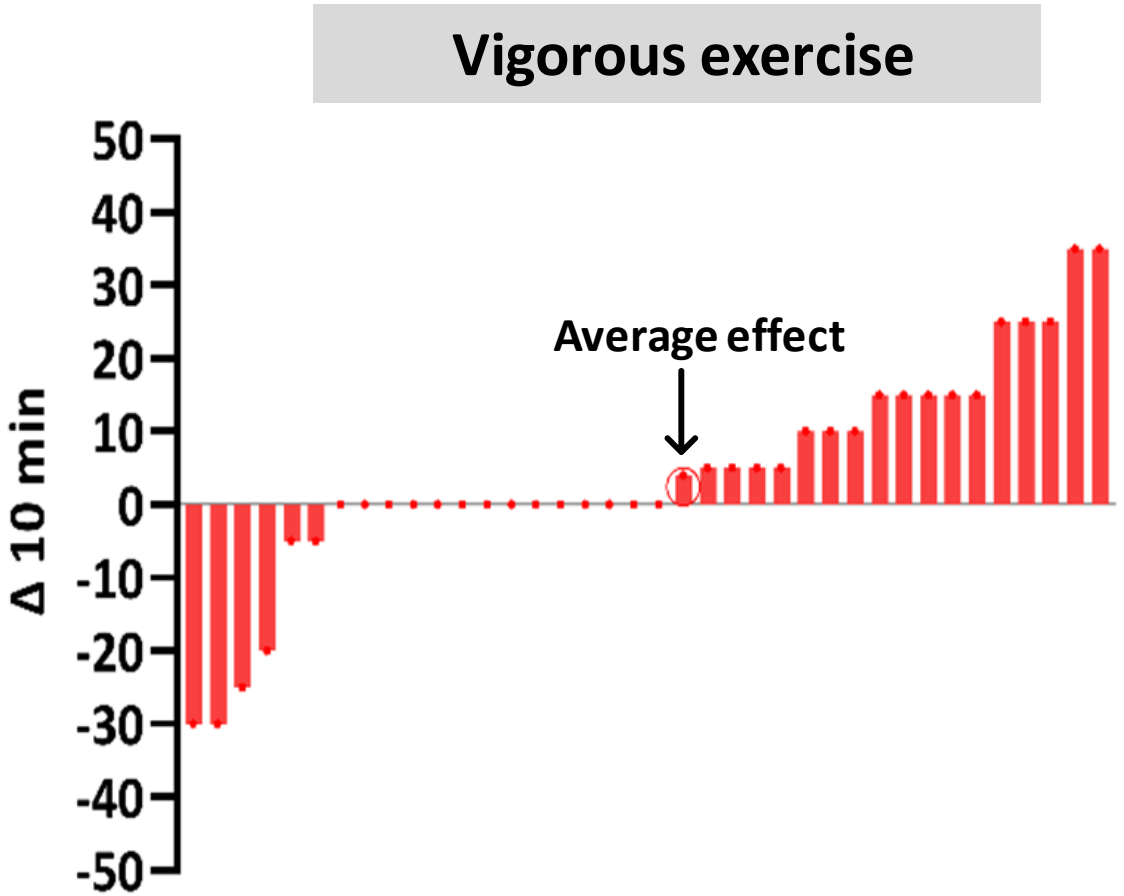


Note. Data represented as means (95% CI)

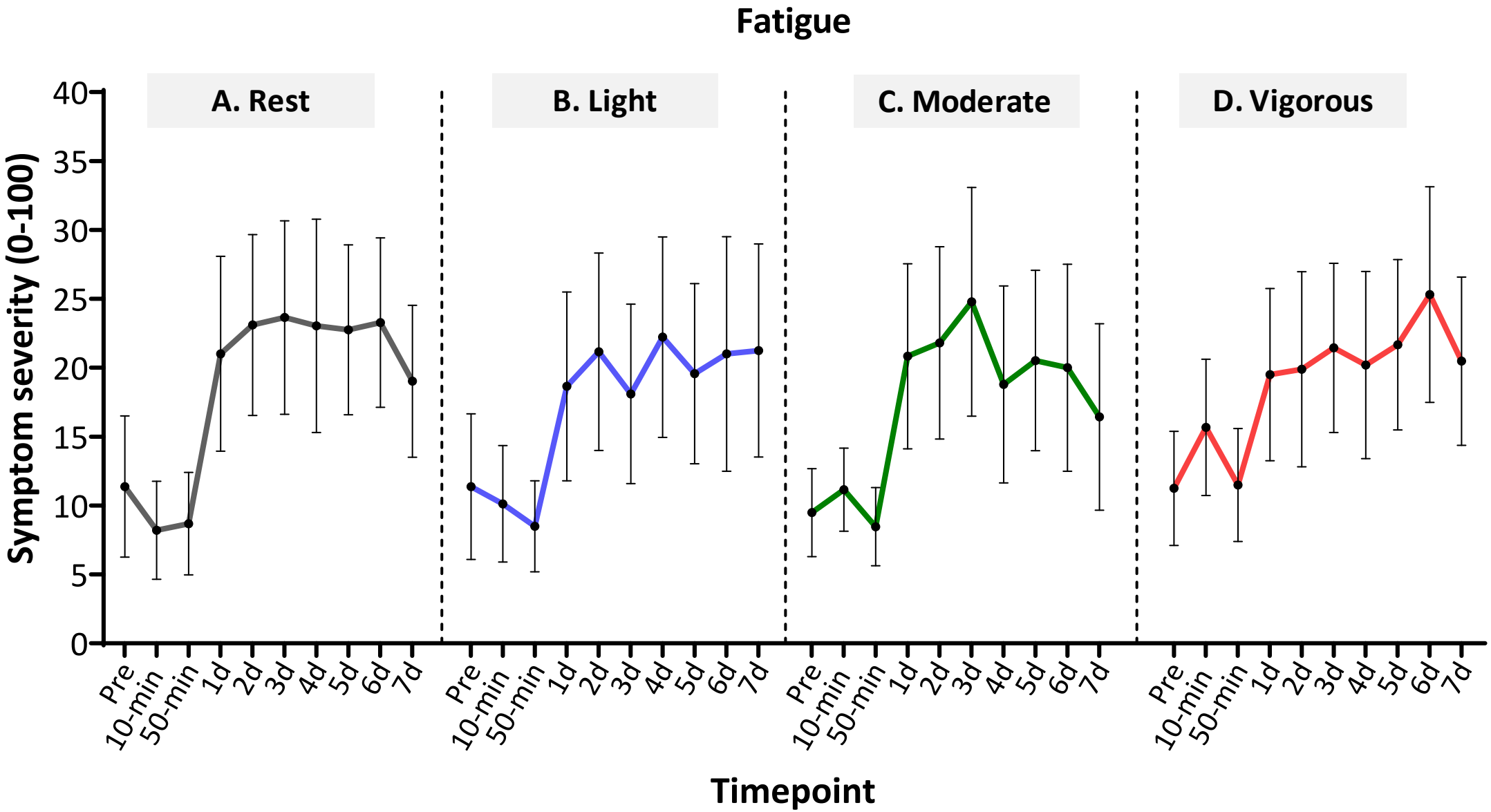
Exploratory results

Basing exercise prescriptions solely on group level analyses may have limited application for certain individuals





Fatigue symptoms were elevated in the natural setting



Discussion

Conclusions

***Scientific take home message*:** On average, aerobic exercise intensities ≤ 75% max HR did not lead to greater risk of non-serious AEs

***Clinical take home message*:** Regular moderate-to-vigorous physical activity (≤ 75% max HR) should be encouraged as part of the overall wellness plan for Veterans with GWI, especially those with milder symptom profiles.[1]

***Veteran take home message*:** Exercise is relatively safe and can improve your health and well-being. If you do experience pain and fatigue, exercising at lower intensities could reduce the risk of making your symptoms worse and can still provide some health benefits

[1] Exercise prescriptions should still take non-GWI related contraindications and risks into consideration

Limitations and future directions

Limitations

1. Unblinded study
2. Short-term effects
3. Generalizability

Future directions

1. Replication
2. Closer monitoring of non-serious adverse events
3. Risk stratification models

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