High Intensity Exercise Countermeasures Do Not Prevent Orthostatic Intolerance Following Prolonged Bed Rest

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Introduction

- Incidence of orthostatic intolerance during 80˚ head-up tilt increases with flight duration
  - ~20-25% Shuttle astronauts
  - >60% of Mir and ISS astronauts
- Post-flight orthostatic intolerance is a multi-factorial issue,
  - Contributing factors postulated to include reduced plasma volume, cardiac atrophy, altered baroreceptor function, impaired or attenuated vasoconstrictor responses, and decreased muscle tone.

Introduction

- Most previous bed rest studies have assessed effectiveness of a single countermeasure
  - Aerobic exercise
  - Resistive exercise
  - Orthostatic stress (LBNP, standing)
  - Fluid loading
- Few studies have examined an integrated countermeasures protocol, particularly one which is similar to that which might be used with current hardware on ISS

Introduction

- Countermeasure hardware on Mir and early ISS missions may have been inadequate to prevent significant cardiovascular deconditioning
- More advanced exercise capabilities (T2, ARED) allow for higher exercise intensities
- Could enhanced exercise capabilities be protective for ISS astronauts provide additional protection not previously achieved?

Objective

To determine whether an intense resistive and aerobic exercise countermeasure program designed to prevent cardiovascular and musculoskeletal deconditioning during 70 d of bed rest (BR), a space flight analog, would protect against post-BR orthostatic intolerance.

Methods

- 28 subjects randomly assigned to one of three groups:
  - Non-exercise controls (n=10 m, 1 f)
  - Exercise only plus placebo (n=9 m)
  - Exercise plus testosterone (n=8 m)
    - Exercise groups performed the same exercise countermeasures during BR
    - Testosterone vs. placebo administered in a placebo in a double-blinded fashion.

Pre-Bed Rest

- Control subjects did not perform any pre-bed rest exercise training but participated in the same pre-bed rest exercise testing
- Countermeasure subjects participated in pre-bed rest exercise training with a schedule similar to in-bed rest countermeasures
- No testosterone supplementation was administered before bed rest
- Intramuscular placebo or testosterone enanthate injections (100 mg/wk) were administered at the beginning of weeks 1, 2, 5, 6, 9, and 10 of bed rest

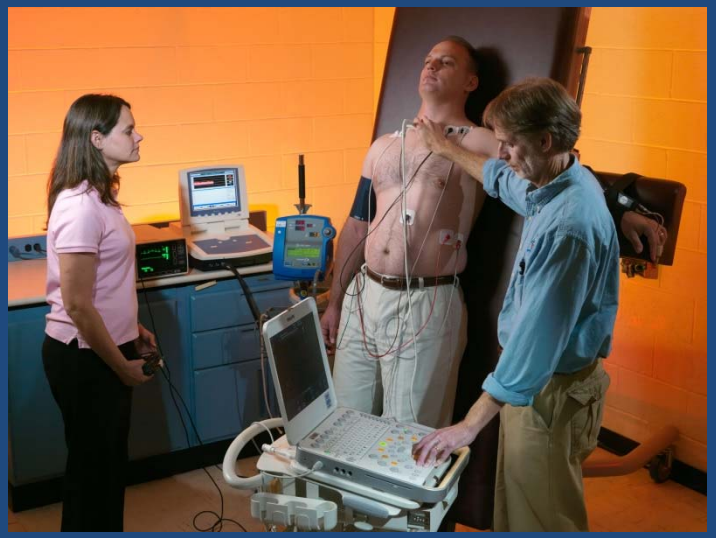
Methods

- Bed rest exercises were performed in the horizontal position
- Aerobic sessions used either the supine treadmill (sZLS) or supine cycle ergometer
  - Intervals 30 sec, 2 min and 4 min
  - Continuous at 75%
- Resistance sessions consisted of horizontal squat, leg press, leg curl, and heel raise

Integration of Aerobic and Resistance Training							
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Resistance	35 - 60 min		35 - 60 min		35 - 60 min		
Aerobic - Interval		32 min		15 min		35 min	
Aerobic - Continuous	30 min		30 min		30 min		

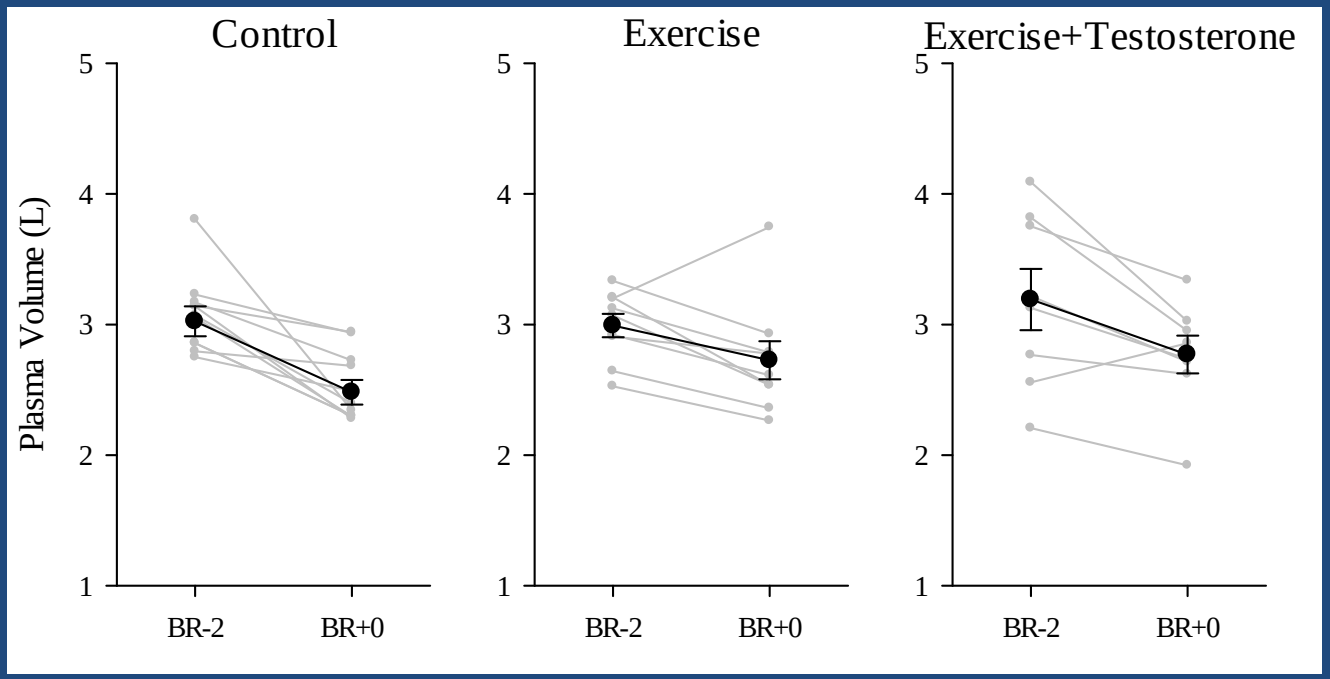
Methods

- Orthostatic intolerance
  - 15-min 80° head-up tilt
  - 2 d (BR-2) before start of and on the last day of BR (BR70).
- Plasma volume
  - Carbon monoxide rebreathing
  - BR-3 and before rising on the first recovery day (BR+0).

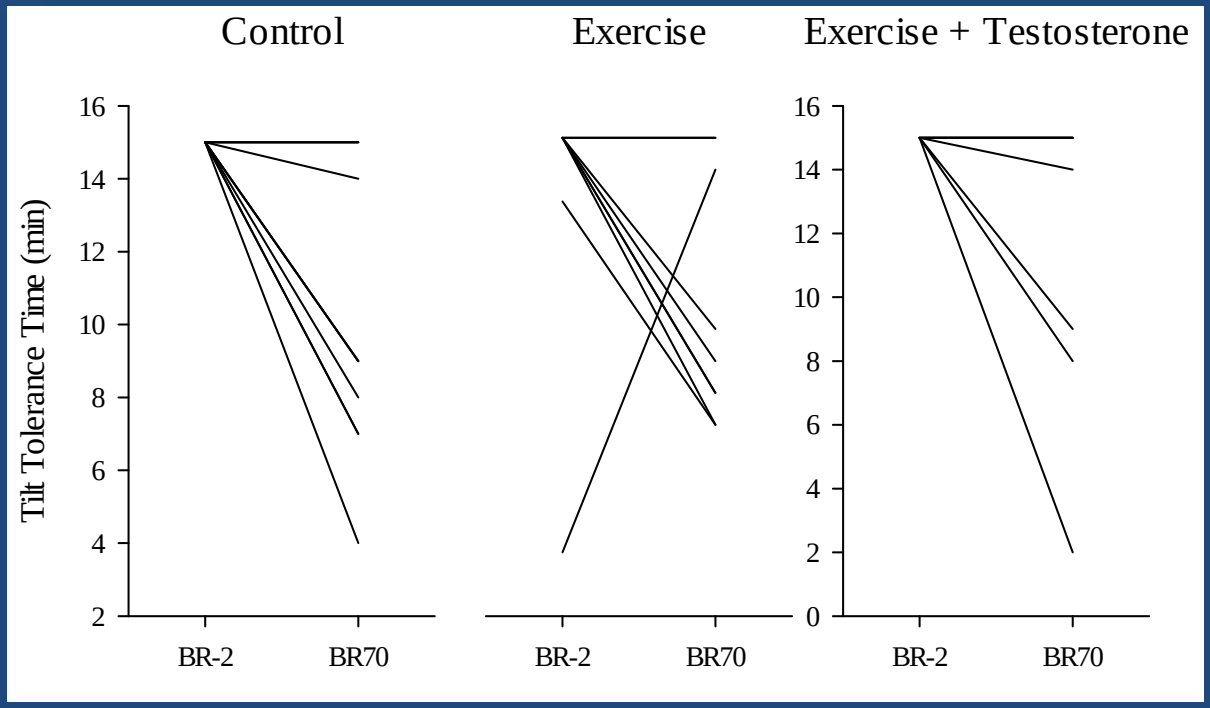


Results

- Plasma volume (absolute or relative to body mass index) decreased ($p<0.001$) from pre to post-BR, with no differences between groups.

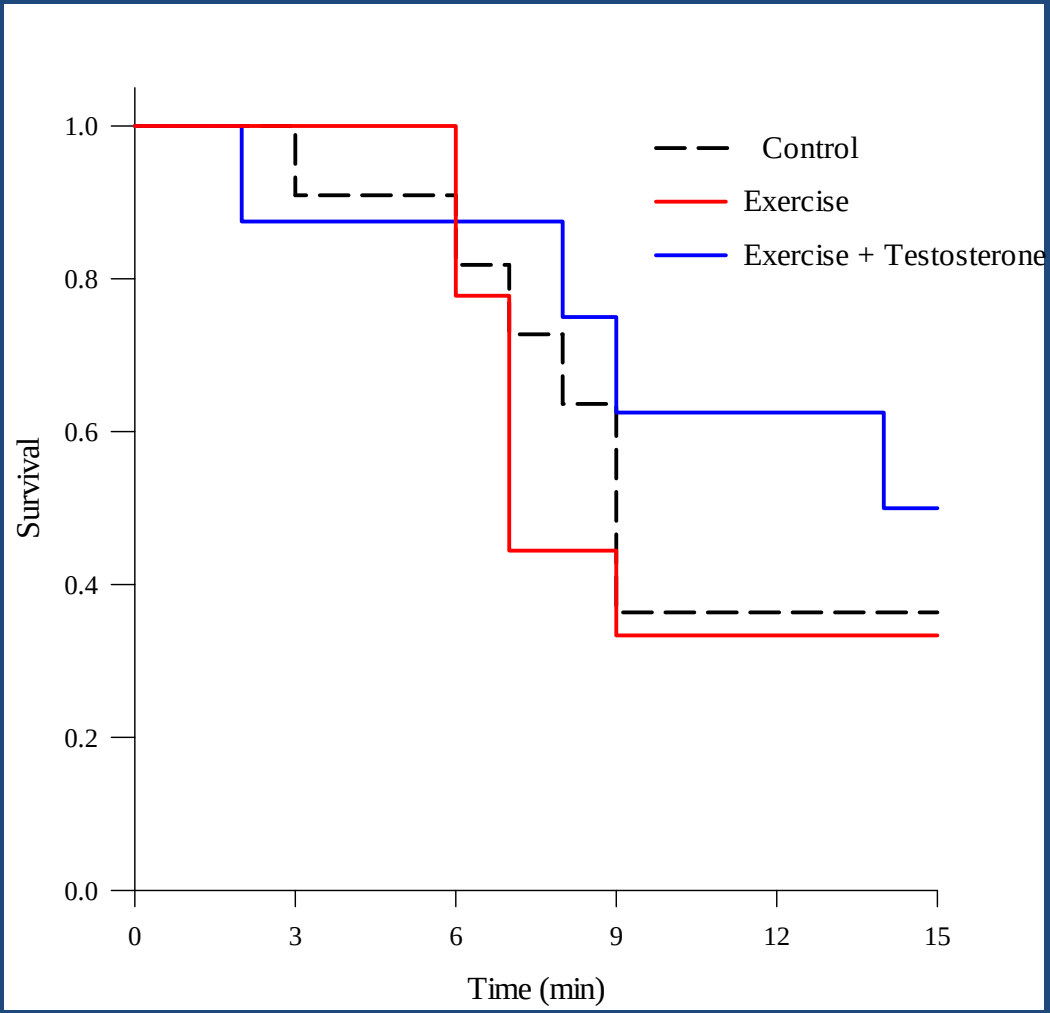


Results



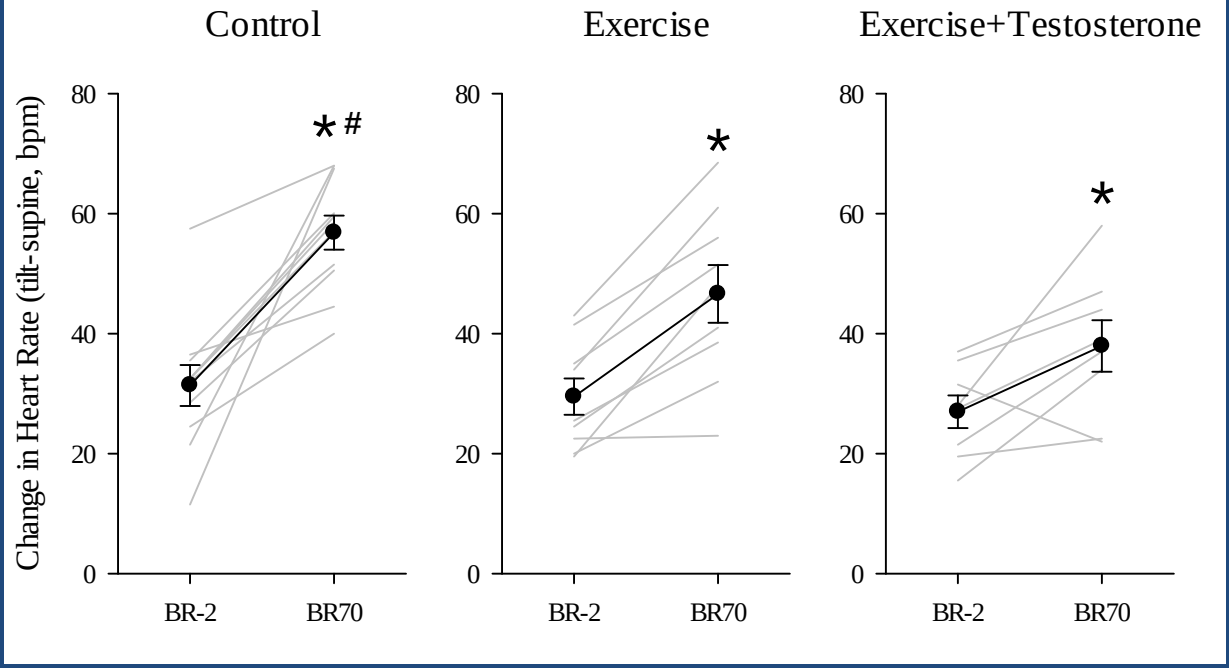
- BR-2: Only 2 presyncopal subjects during tilt (Exercise Only: 2 and 13 min)
- BR70: 7 of 11 (63%) Control, 6 of 9 (67%) Exercise Only, and 4 of 8 (50%) Exercise+Testosterone subjects became presyncopal

Results



No significant difference in survival time between groups on BR70 (p=0.55)

Results



- Change in heart rate from supine to standing was greater after bed rest in all three groups
- Heart rate response to tilt was larger in the Control group than in the Exercise+Testosterone group

Discussion

- Not without precedence that exercise alone did not protect against orthostatic intolerance
  - Schneider, 2002 (15-d BR): Exercise within LBNP
  - Shibata, 2010; Hastings, 2012 (18-d BR): cycle or rowing exercise
  - Greenleaf, 1989 (30-d BR): isokinetic resistive or supine cycle exercise
  - Belin de Chantemele, 2004 (90-d BR): Resistive exercise

Discussion

- Exercise plus orthostatic challenge or fluid loading attenuates or protects loss in tolerance
  - Watenpaugh, 1995 (5-d BR); Watenpaugh, 2007 (30-d BR); Guinet, 2009 (60-d BR): Exercise within LBNP with post-exercise LBNP challenge
  - Waters, 2005 (12-d BR): water and salt tablet fluid load
  - Shibata, 2010; Hastings, 2012 (18-d BR): Cycle or rowing exercise plus dextran to normalize filling pressures
  - Stenger, 2012 (21-d BR): Artificial gravity

Limitations

- Control group did not perform pre-BR exercise.
- PV not measured on day after tilt
- Exercise countermeasures (continuous aerobic and resistive) day before BR-2 tilt
- Exercise countermeasures not performed in the same schedule for all subjects relative to tilt test on BR70

Conclusions

- Performance of a vigorous exercise countermeasure protocol during BR, even with testosterone supplementation, does not protect against orthostatic intolerance or plasma volume loss.
- Preventing post-BR orthostatic intolerance may require additional countermeasures, such as orthostatic stress during BR or end-of-BR fluid infusion.

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