Hypovolemia-induced Orthostatic Hypotension Relates To Hypo-sympathetic Responsiveness

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- All astronauts experience a reduction in plasma volume during flight.
  - This is an underlying cause of orthostatic hypotension.

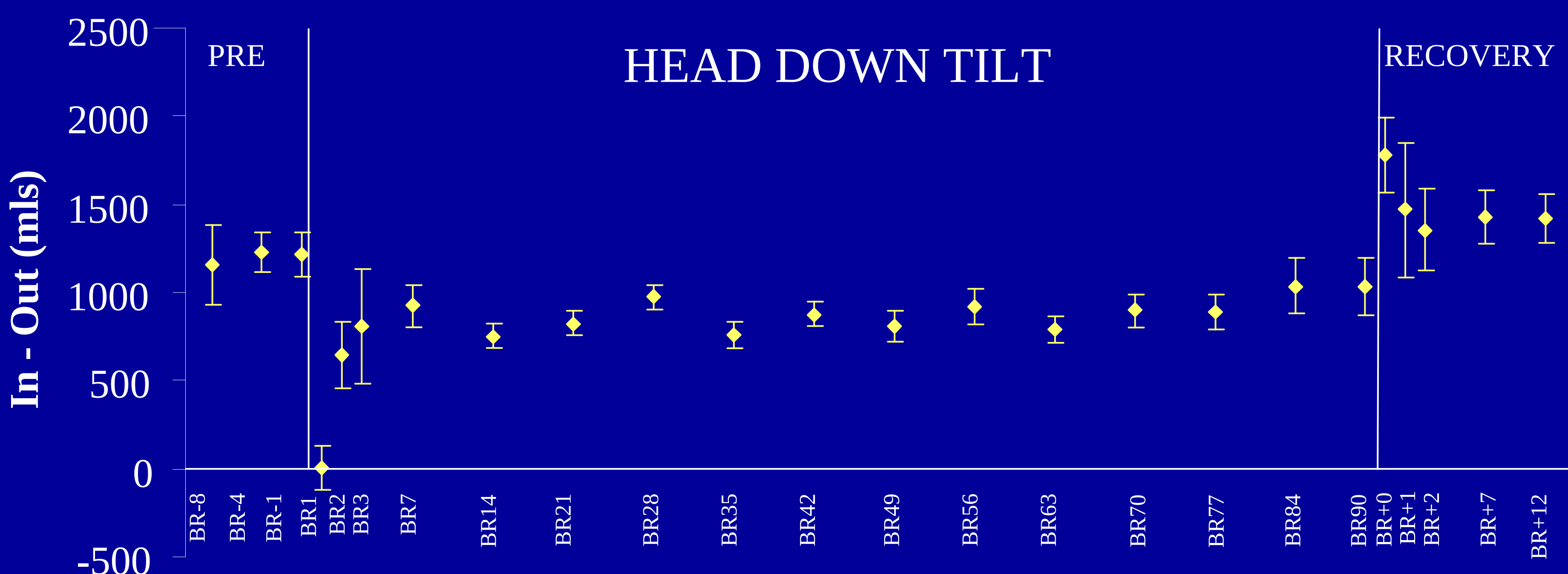
- Those who can mount a supra-sympathetic response can maintain blood pressures during tilt tests on landing day.
  - those who cannot, experience orthostatic hypotension and presyncope.

- Preflight identification of susceptible crew members is difficult
  - prior to flight, large sympathetic responses are not needed
  - incidents of presyncope are rare.

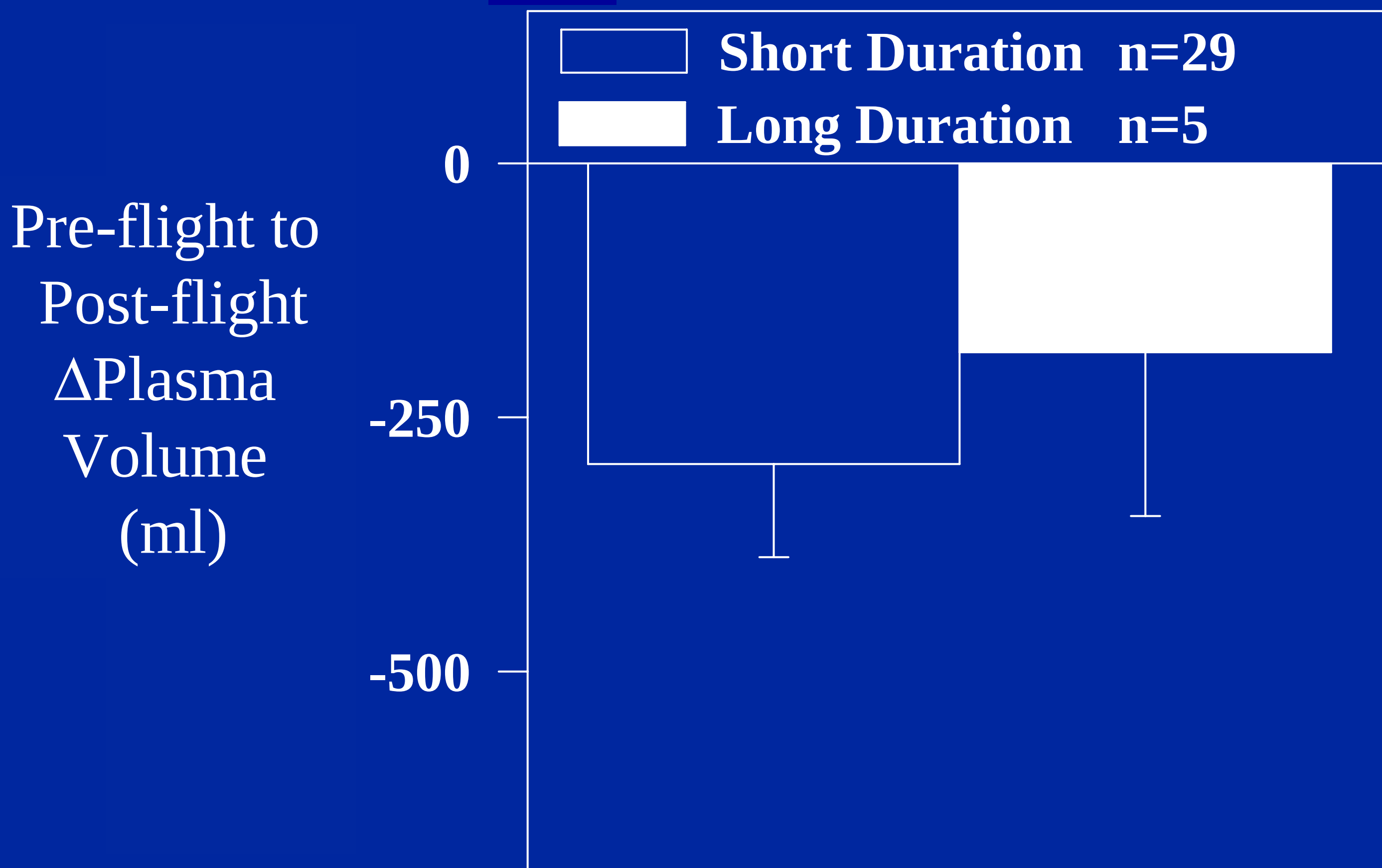
- We tested the hypotheses that experimentally-induced hypovolemia:
  - would reproduce the incidence of presyncope during upright tilt on landing day.
  - the underlying cause would be inadequate compensatory sympathetic responses.

- If true, we would be able to:
  - predict before flight individual susceptibility
  - prospectively prescribe countermeasures for them.

Fluid Intake Minus Urine Output



Plasma volume losses are similar after short and long-duration spaceflight



Meck JV, et al. Marked Exacerbation of Orthostatic Intolerance after Long- vs. Short-Duration Spaceflight in Veteran Astronauts. Psychosomatic Medicine 63:865-873, 2001.

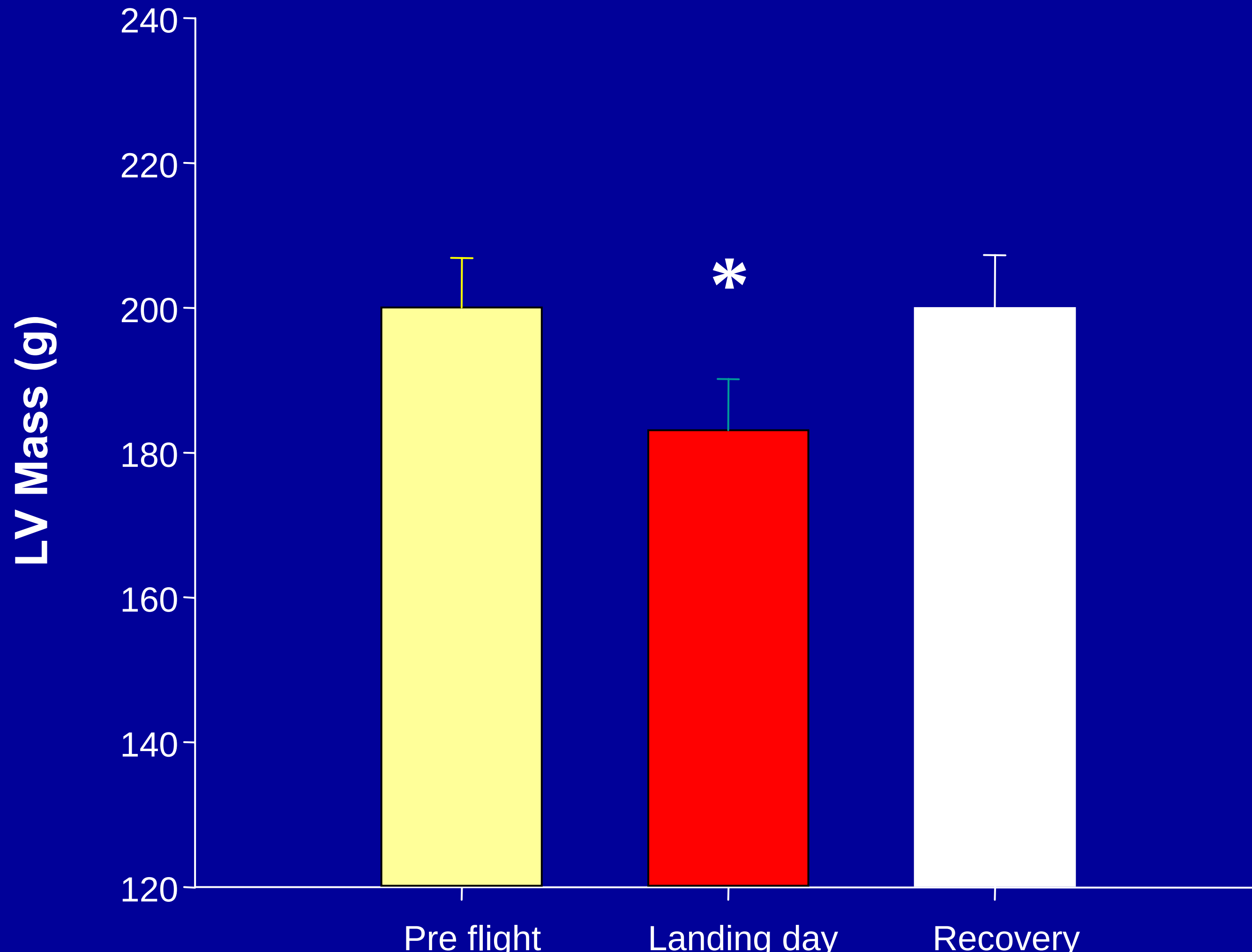
Reduced Plasma Volume affects:

- Orthostatic Tolerance
- Cardiac Function
- Renal Function (i.e. kidney stones)
- Aerobic Capacity
- Vascular Function

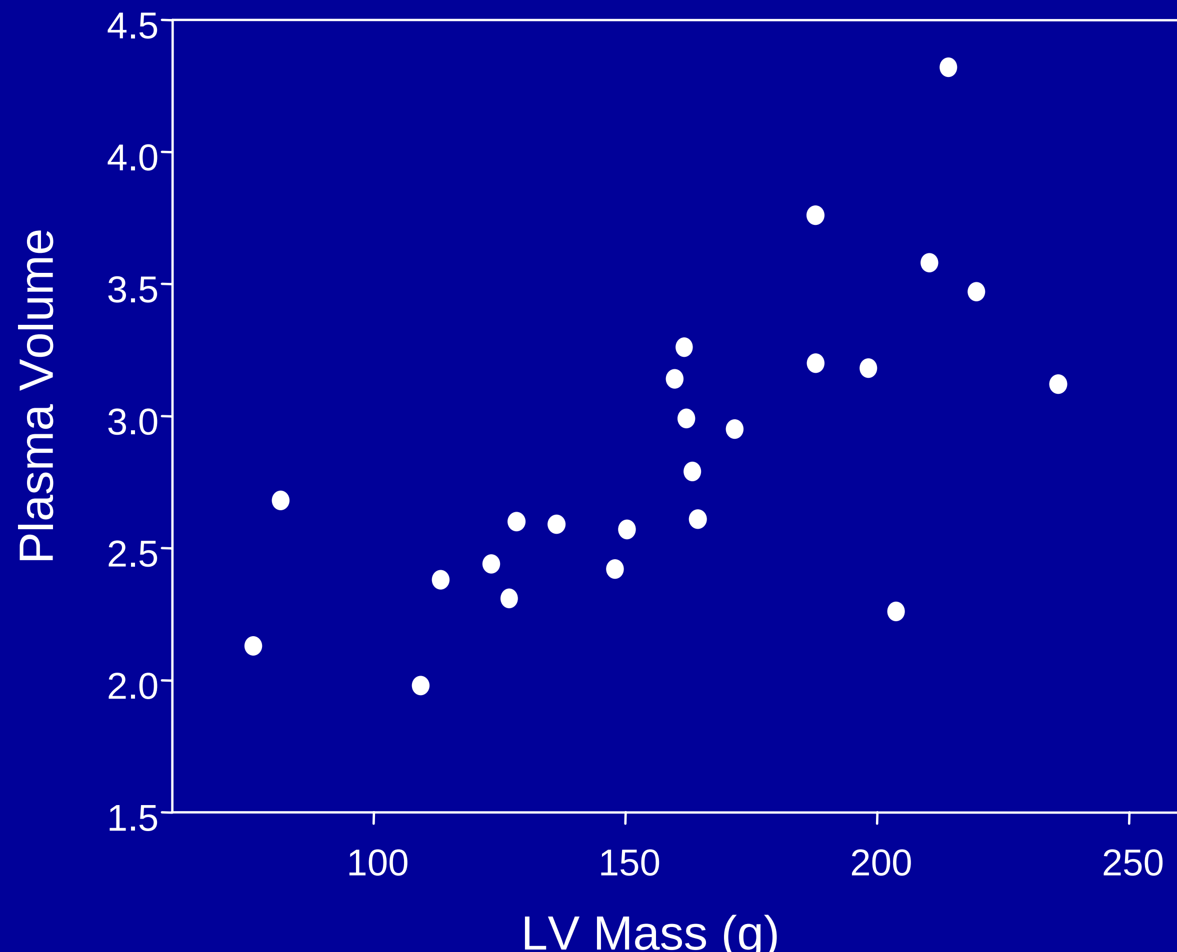
Effects of plasma volume losses on left ventricular mass

After Short-Duration Flight, LVM is Recovered at R+3 as Measured by Ultrasound

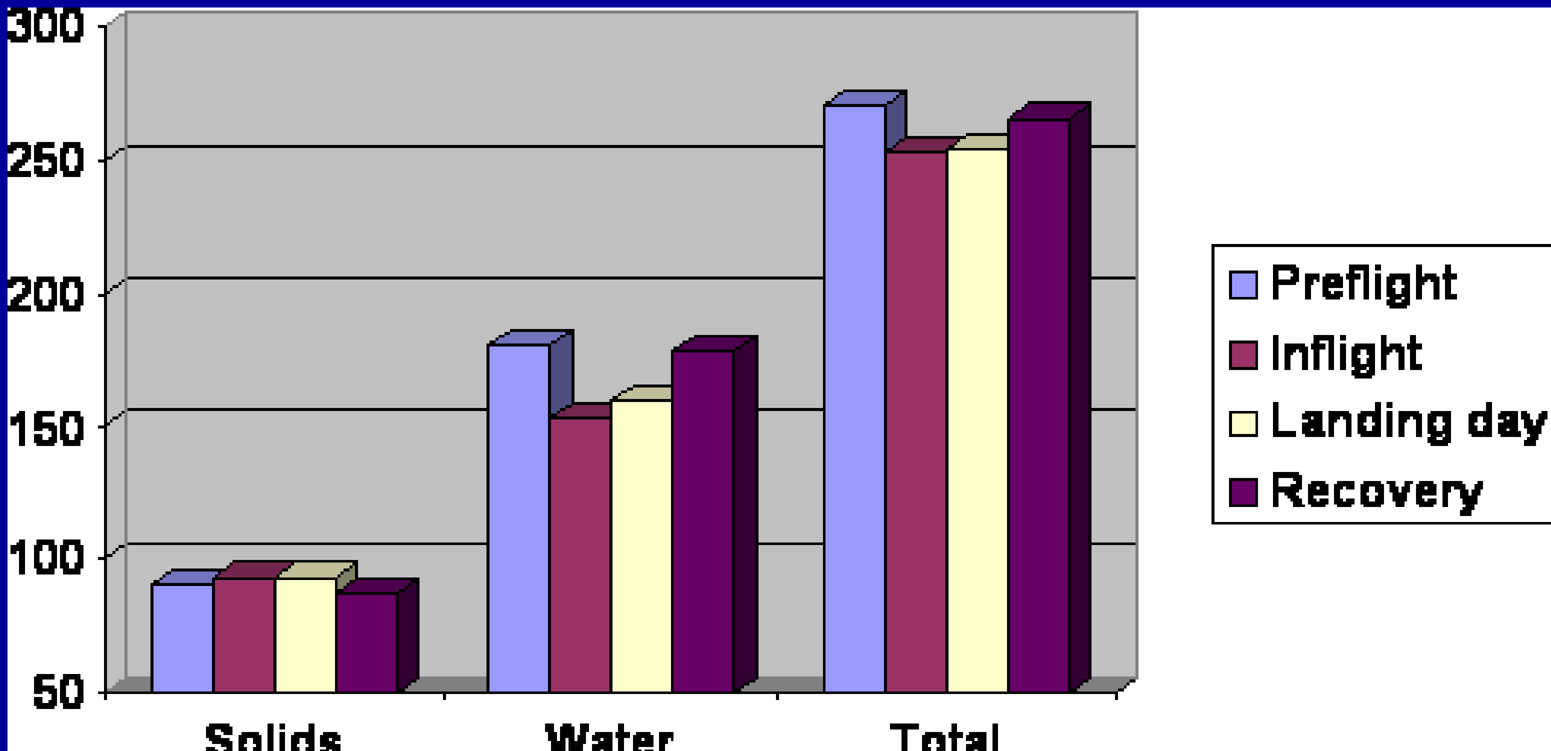
(loss of approximately 8%; n= 13)



LVM vs. Plasma Volume

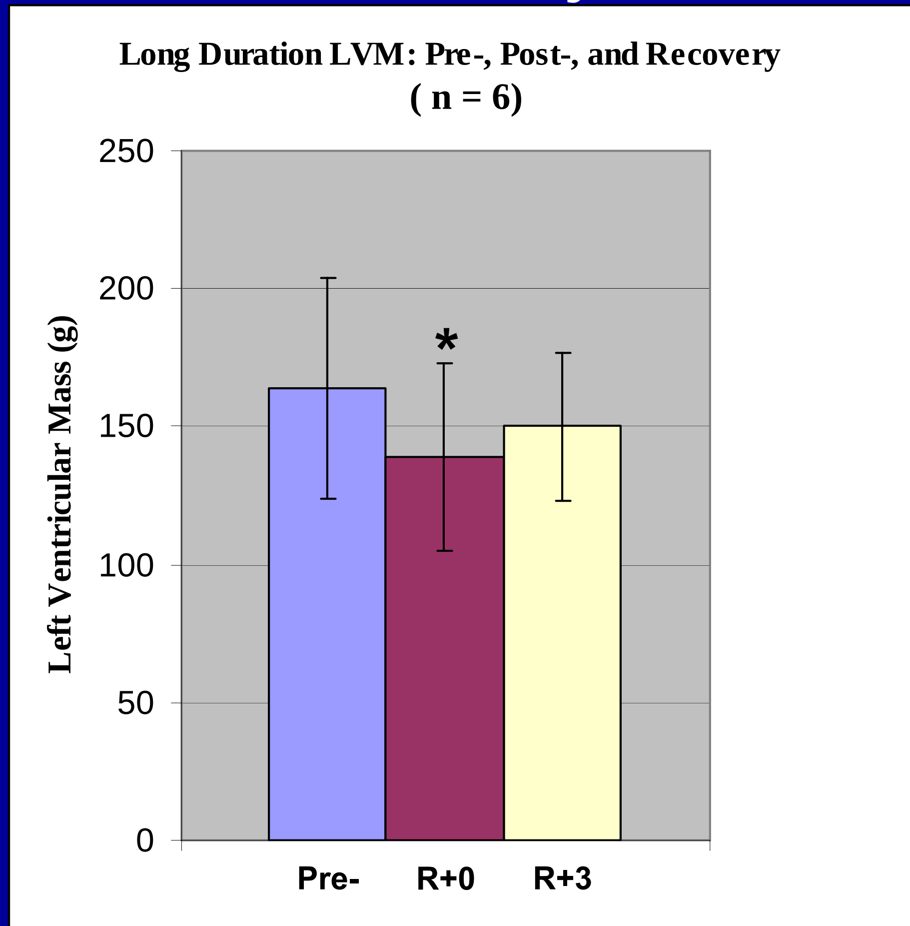


Mathematical Model Predicted Tissue Dehydration Effect



Computer model showing that changes in left ventricular mass during spaceflight are due to loss of water rather than solids.
These data reproduce our published R+0 findings

After Long-Duration Flight LVM is NOT Recovered by R+3



(Decrease of 15%)

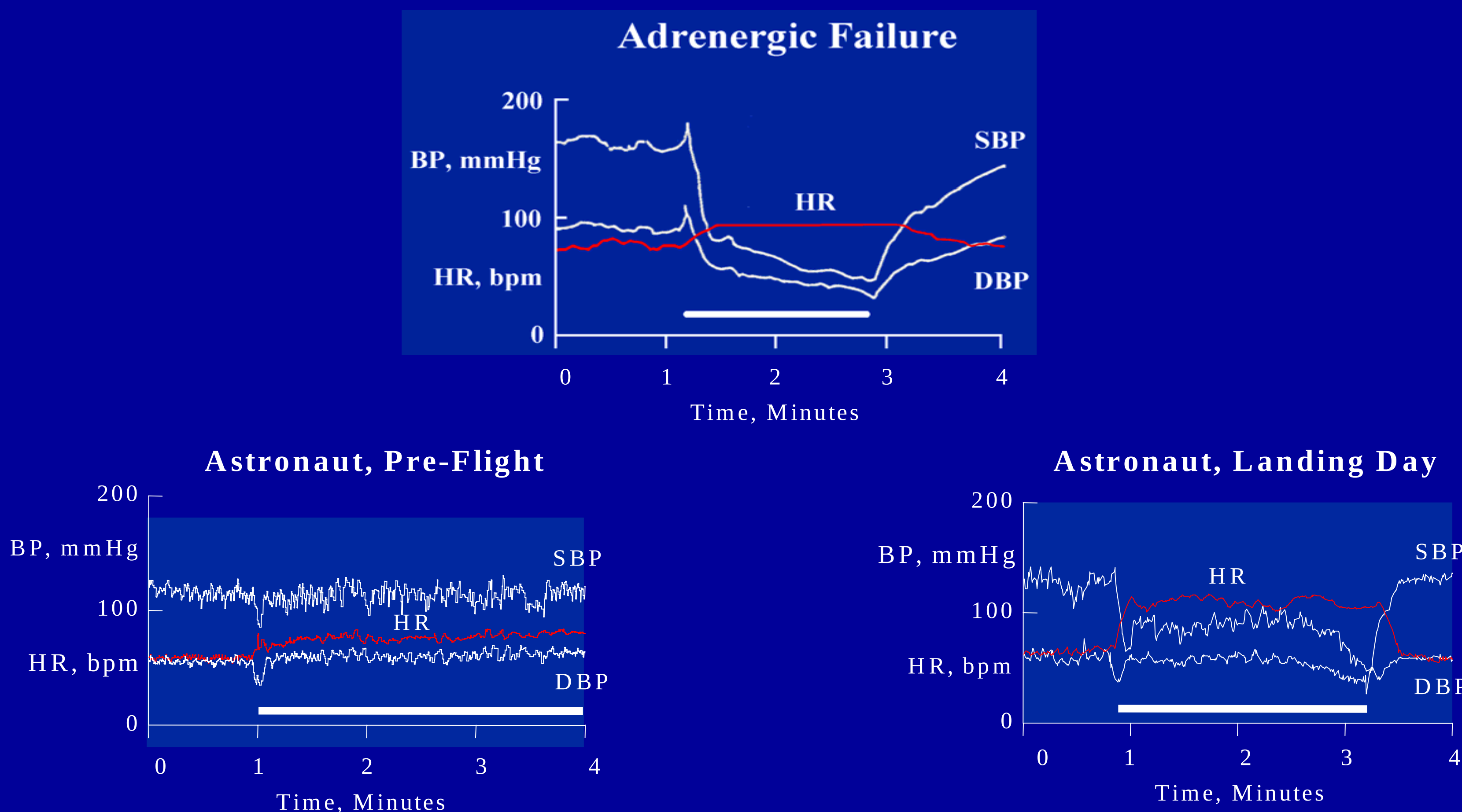
Effects of plasma volume losses on orthostatic tolerance

Loss of plasma volume is not different between astronauts who DO and astronauts who DO NOT suffer from postflight orthostatic hypotension.

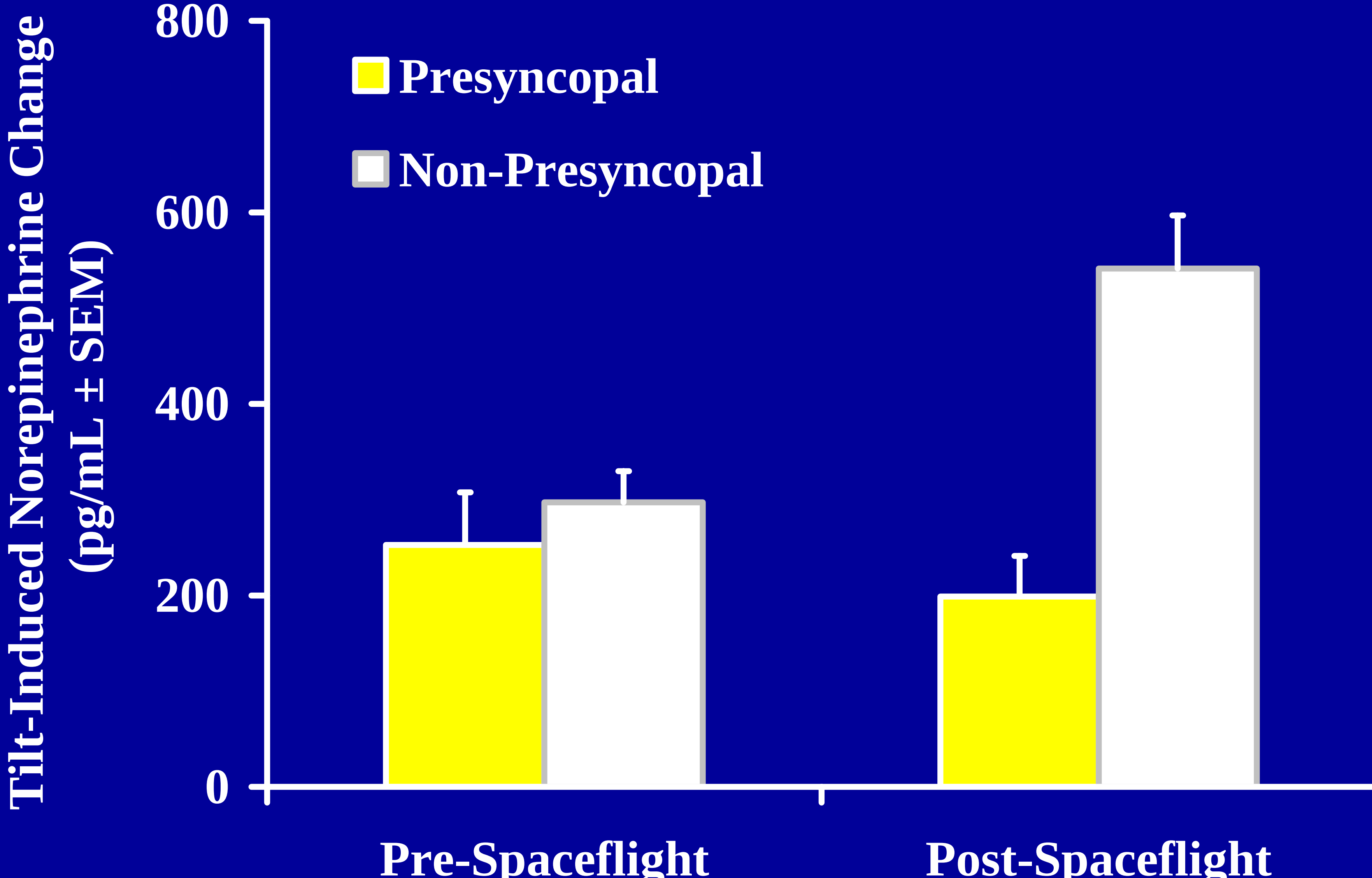
	Preflight Plasma Vol, l/m^2	Landing day PlasmaVol, l/m2	% Spaceflight-Induced Loss
Presyncopal Men (*n*=6)	1.67 ± 0.1	1.55 ± 0.12*	7.1 ± 0.03
Non-Presyncopal (*n*=24) Men	1.73 ± 0.0	1.60 ± 0.05 **	7.1 ± 0.03

Values are means ± SE; $*p \le 0.05$, $**p \le 0.01$, vs. preflight

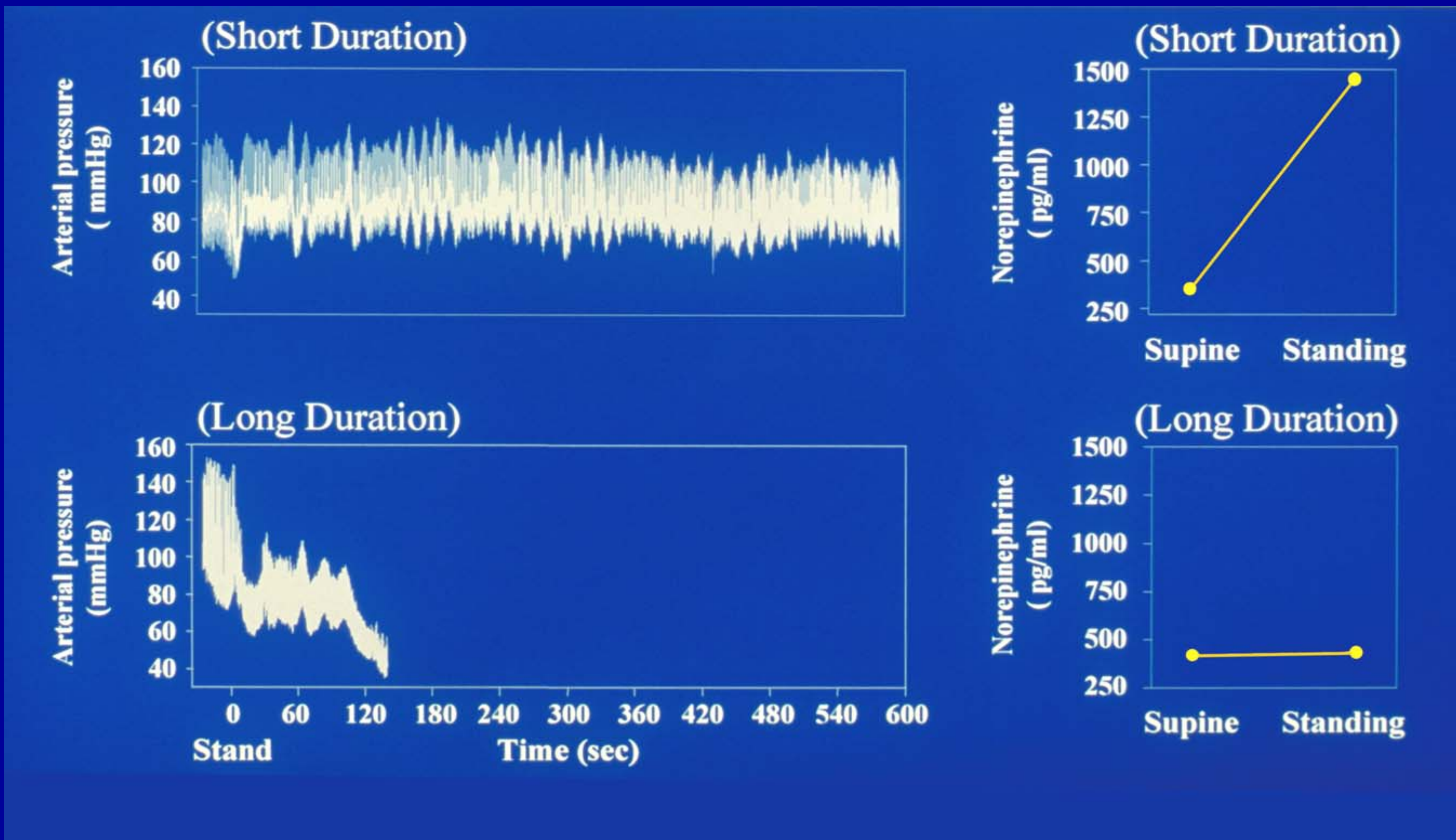
Cardiovascular responses to upright posture in a patient and an astronaut

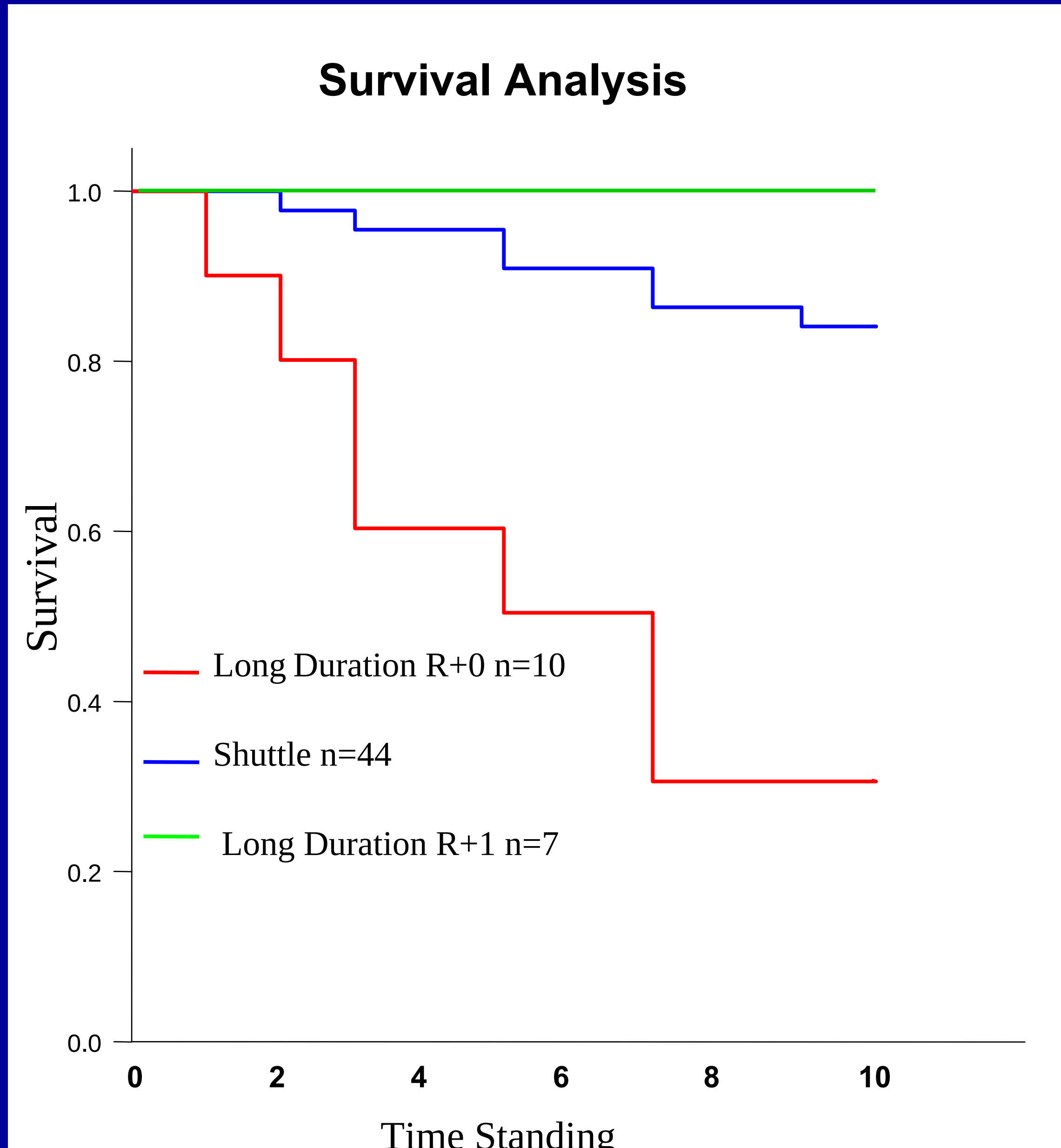


Norepinephrine Response to Tilt before and after Spaceflight



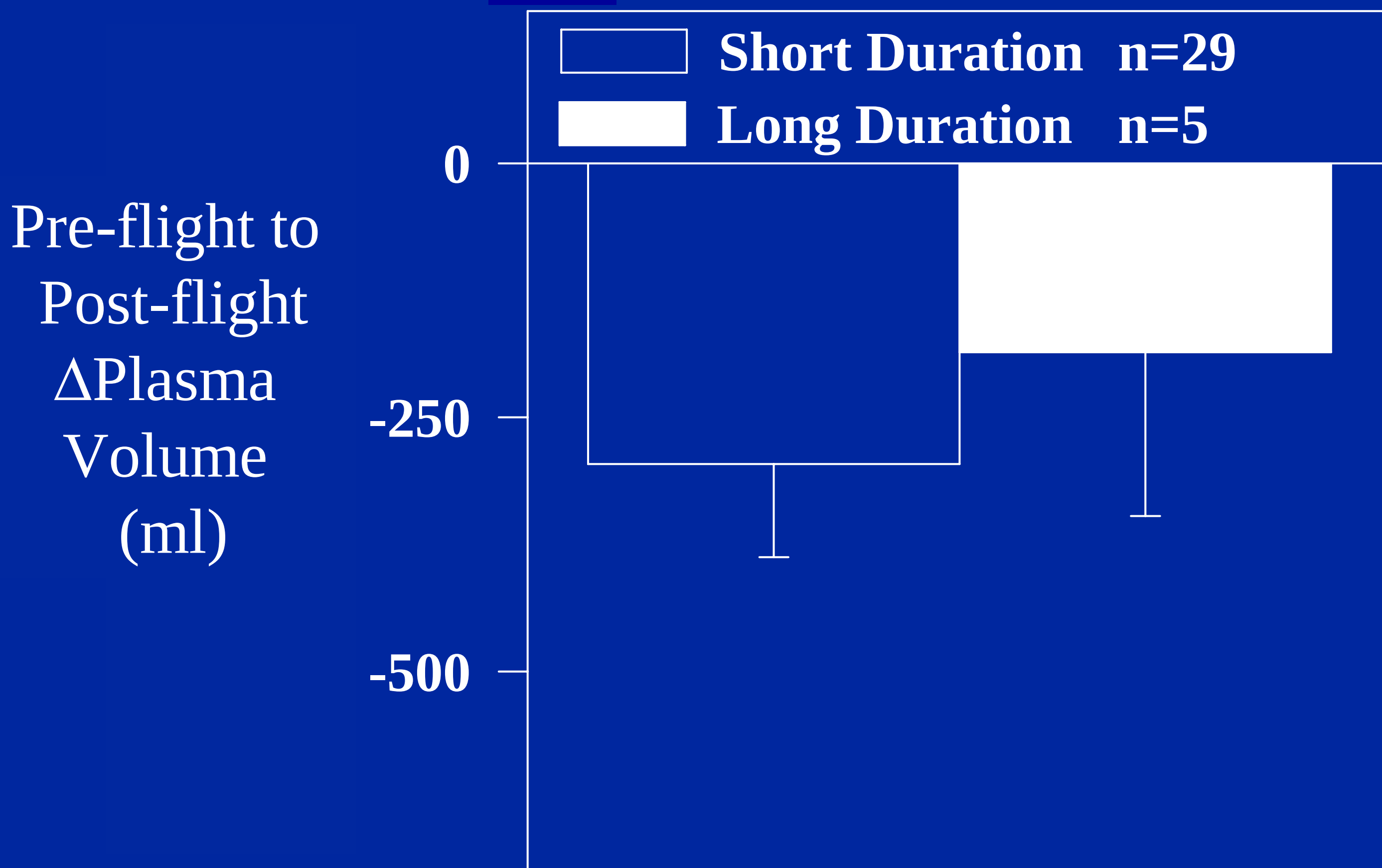
Responses to standing after a short (top) and a long (bottom) flight in the same astronaut





Shuttle vs. Long Duration R+0 = $p<0.02$
Long Duration R+0 vs. Long Duration R+1 = $p<0.03$

Plasma volume losses are similar after short and long-duration spaceflight



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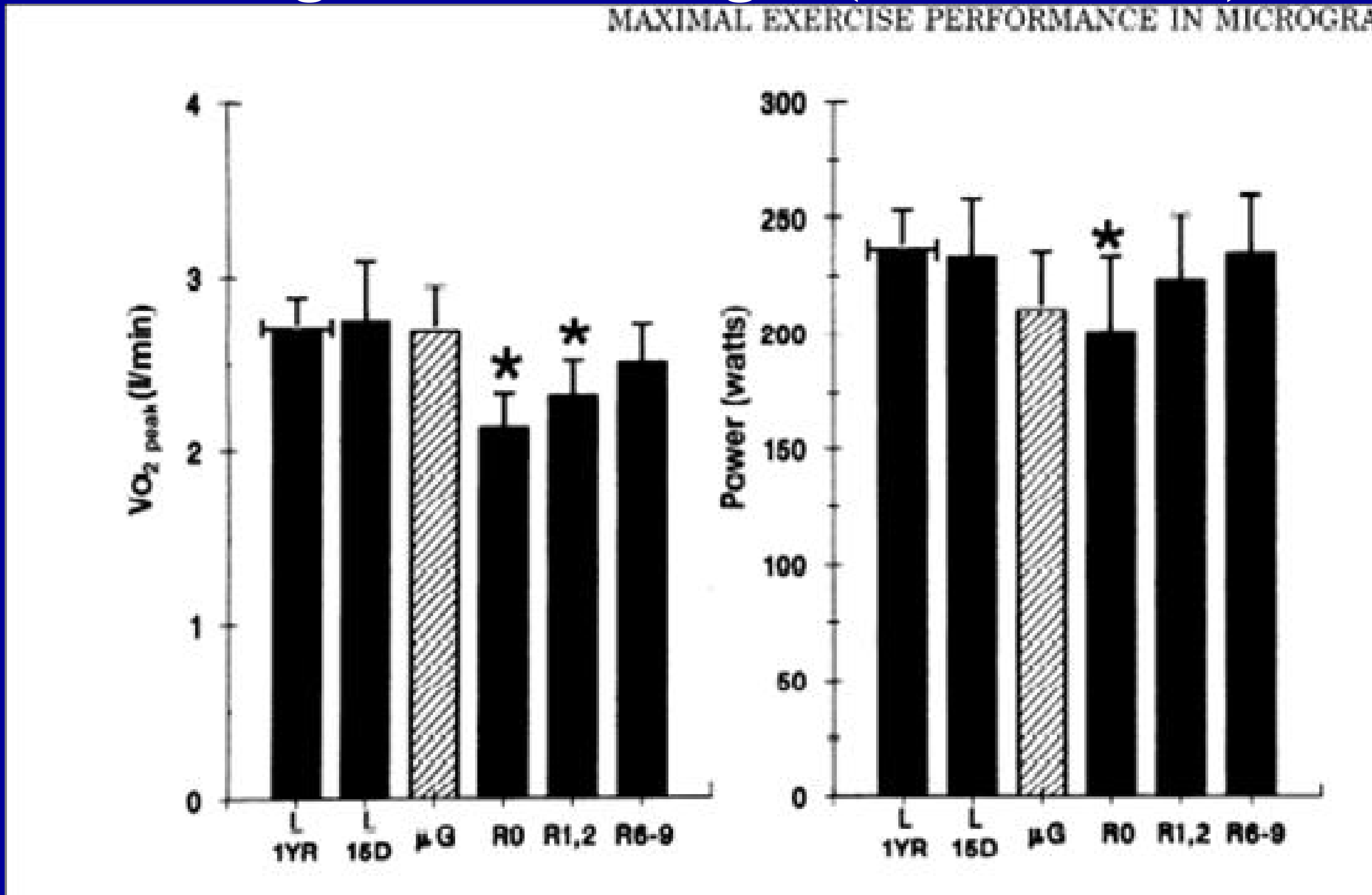
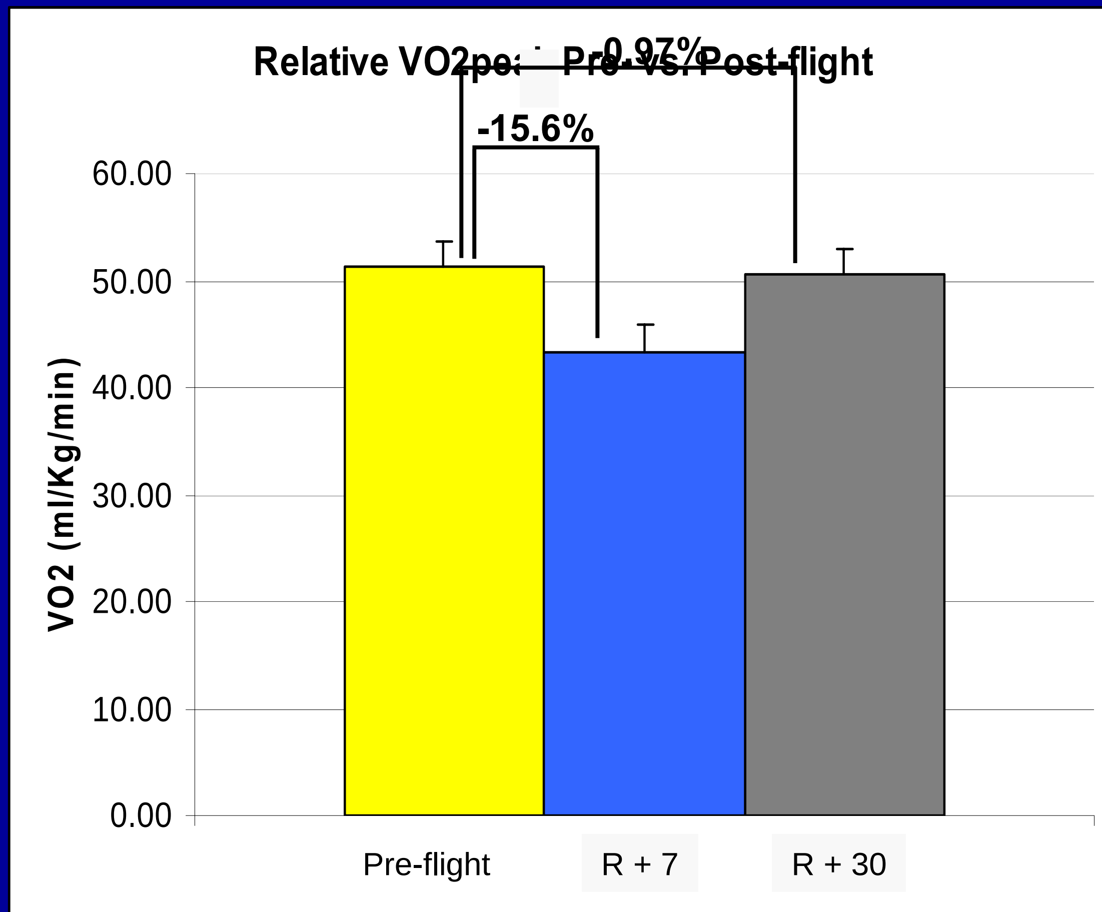
Effects of plasma volume losses on aerobic capacity

Maximum Oxygen Uptake Preflight, In-flight and Postflight (all max tests)



Levine et al., Maximal exercise performance after adaptation to microgravity. JAP 81(2): 686-694, 1996.

ISS Relative Oxygen Consumption
Pre- vs. Post-flight (max pre, sub-max post)



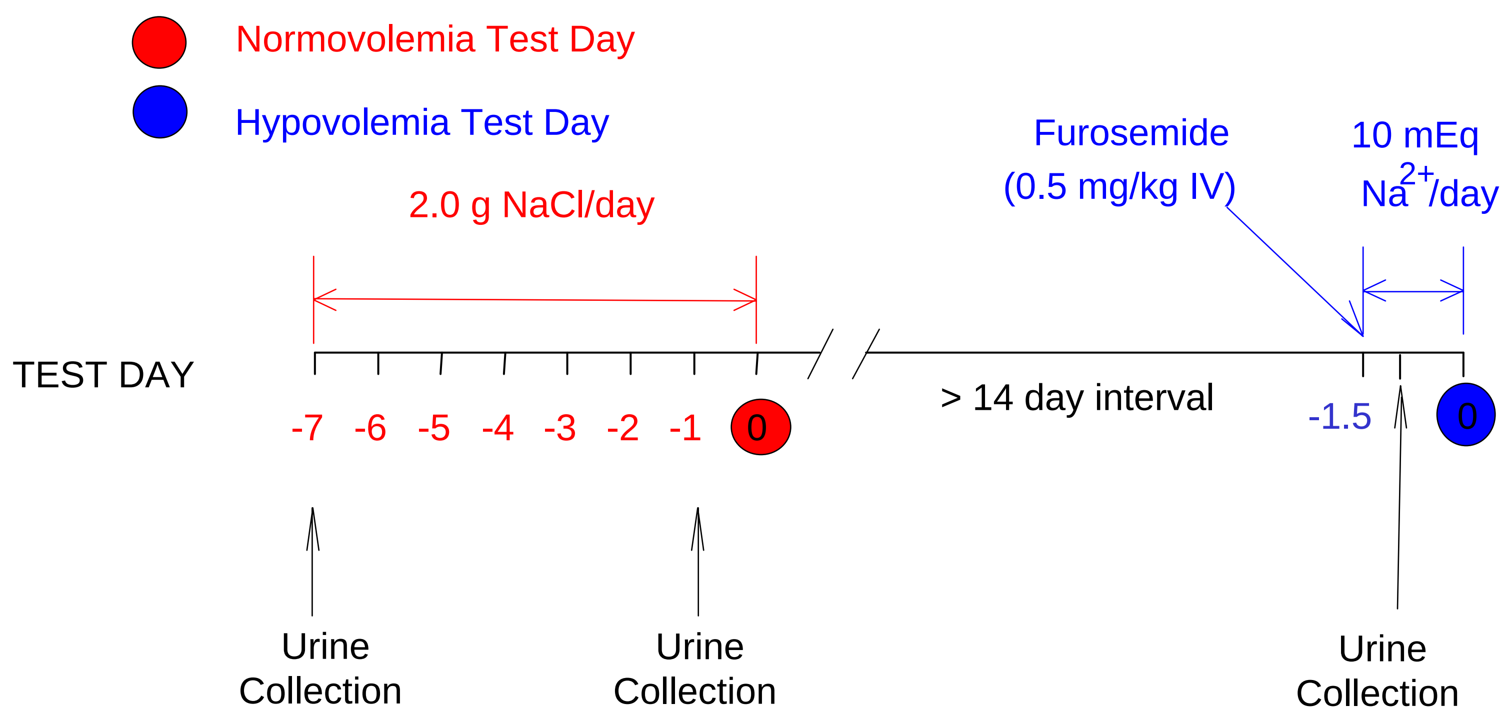
Hypovolemia Model

METHODS

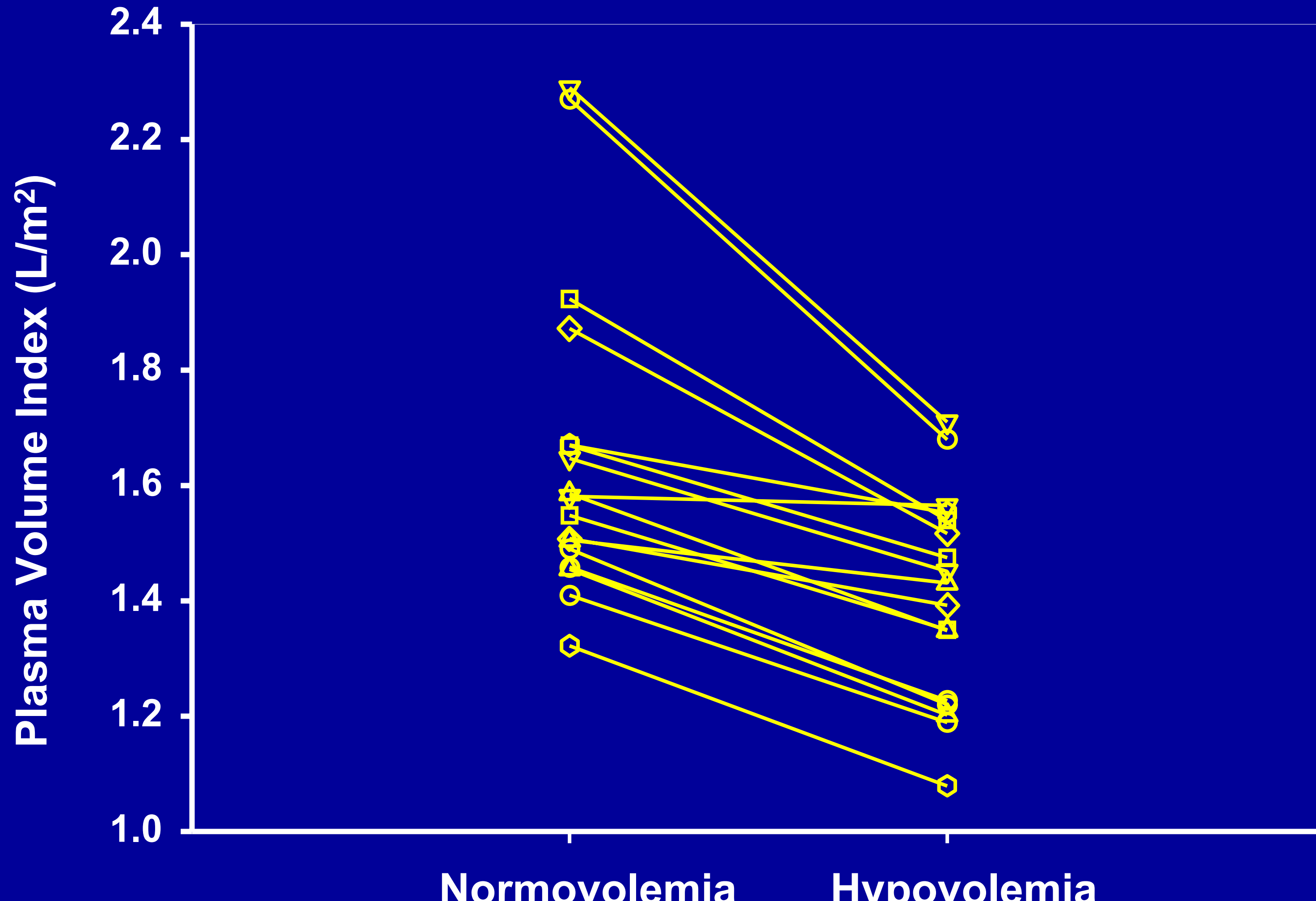
12 Men (40.1 ± 1.4 yrs; 182.5 ± 1.3 cm; 86.2 ± 2.4 kg)

5 Women (39.0 ± 3.6 yrs; 161.8 ± 2.7 cm; 56.6 ± 3.9 kg)

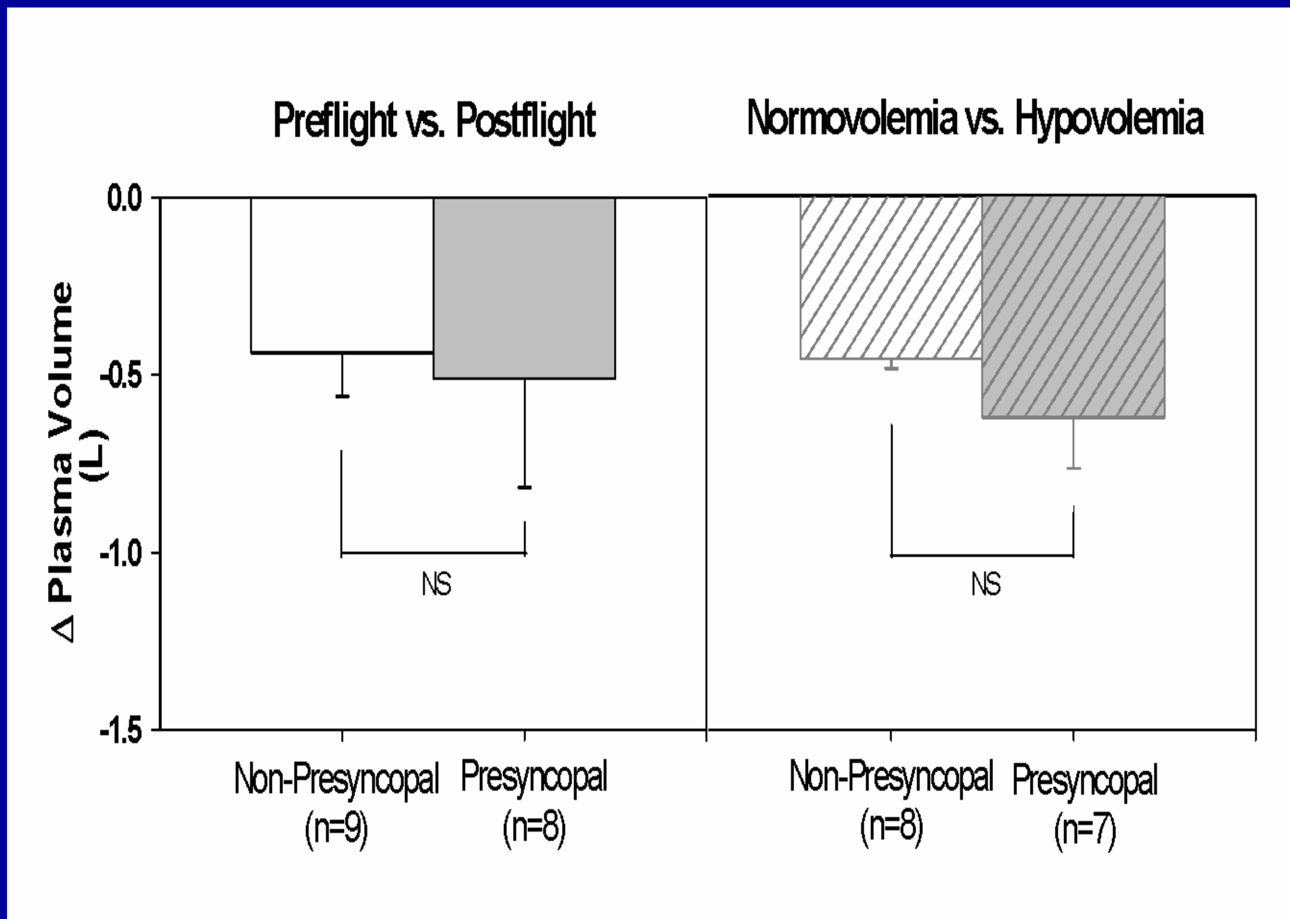
17 Total Subjects – 11 normal, 6 astronauts (5 male, 1 female)



Plasma Volume Change During Hypovolemia

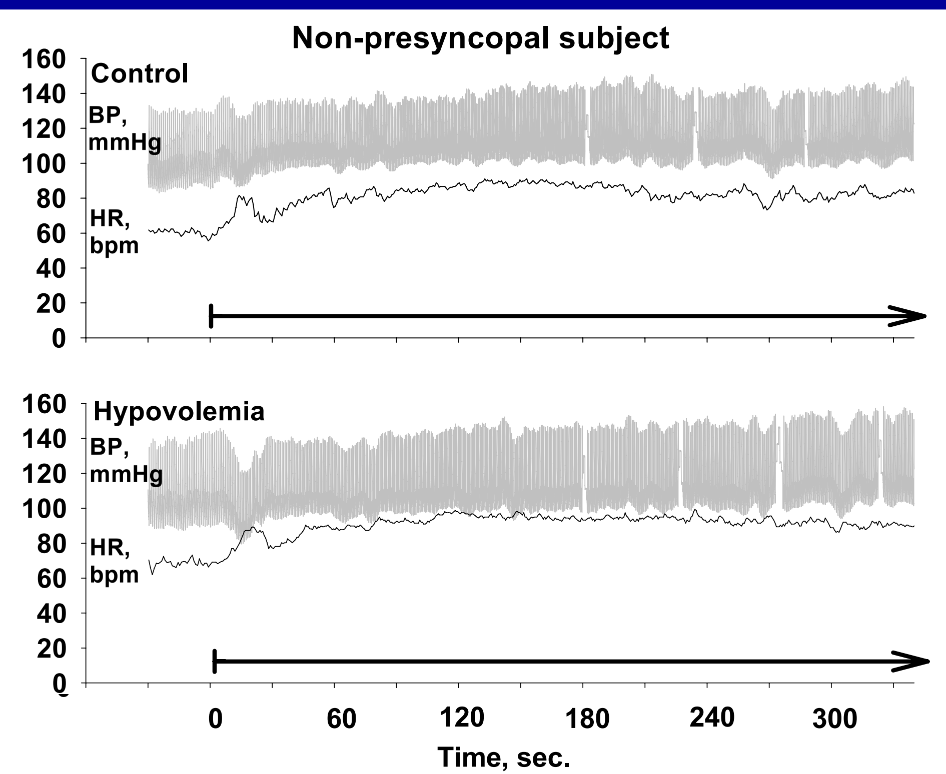


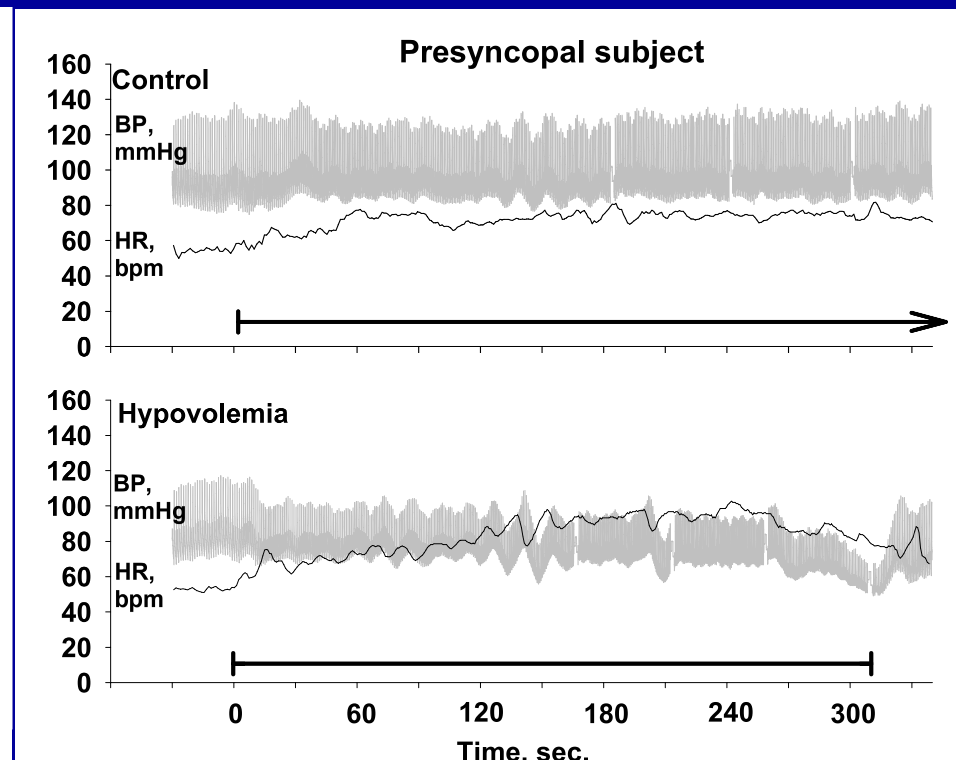
Plasma Volume Changes During Hypovolemia and After Spaceflight



Presyncopal?

	R+0 (Landing Day)	Hypovolemia
Astronaut 1	YES	YES
Astronaut 2	YES	YES
Astronaut 3	YES	YES
Astronaut 4	YES	YES
Astronaut 5	NO	NO
Astronaut 6	NO	NO


Non-presyncopal subject
Control
BP,
mmHg
HR,
bpm
Hypovolemia
BP,
mmHg
HR,
bpm
160
140
120
100
80
60
40
20
0
0
60
120
180
240
300
Time, sec.


Presyncopal subject
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BP,
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Hypovolemia
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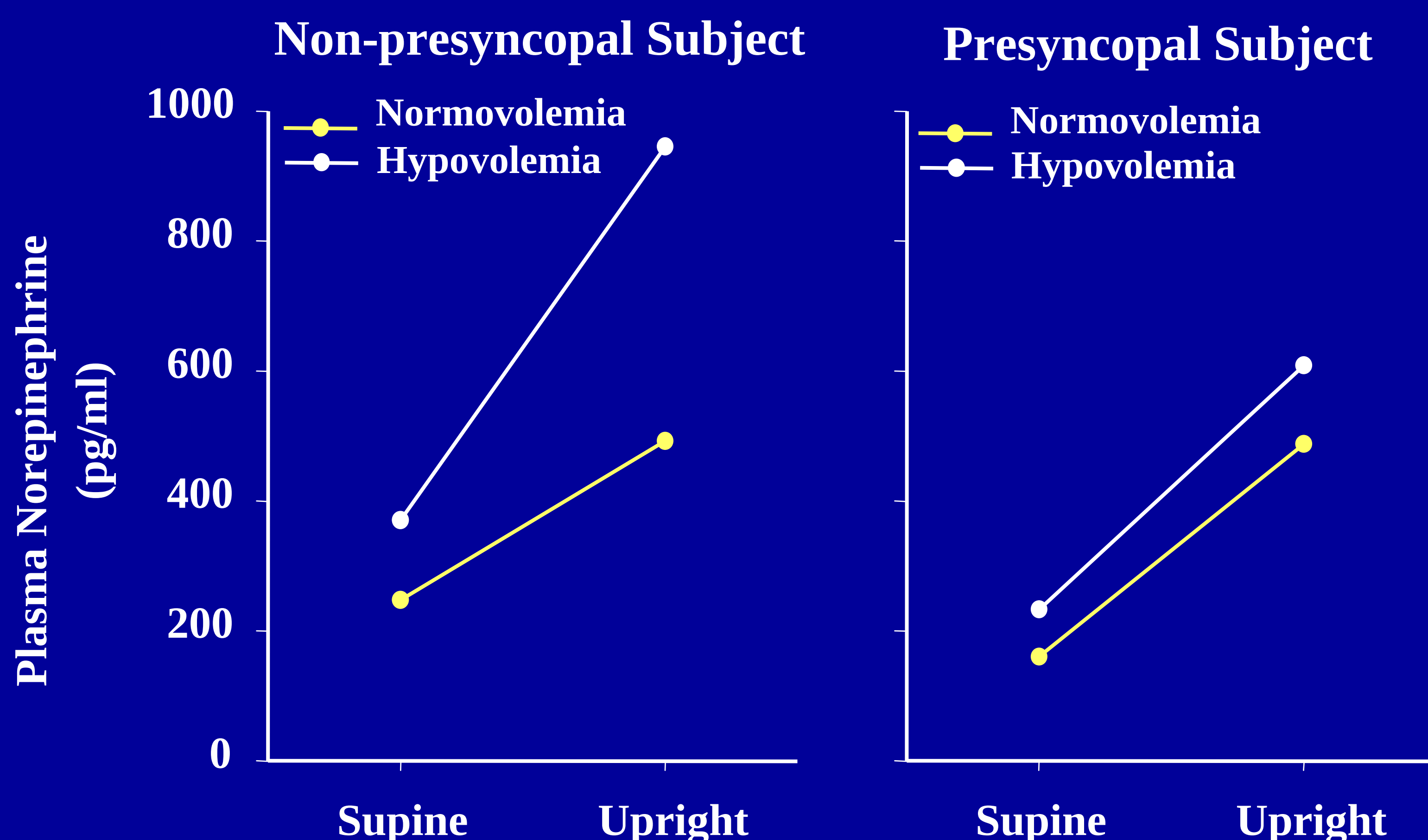
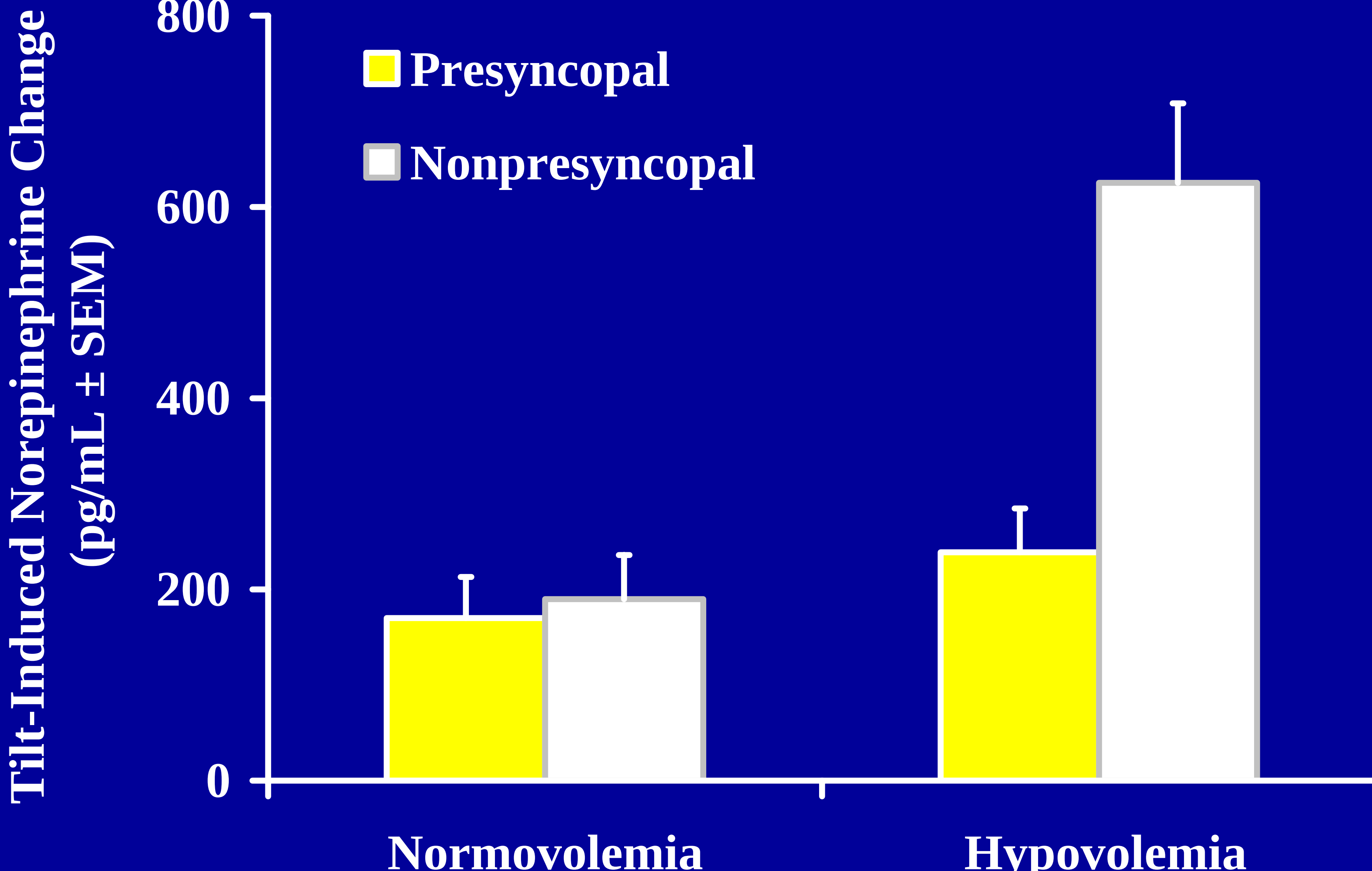
240
300
Time, sec.

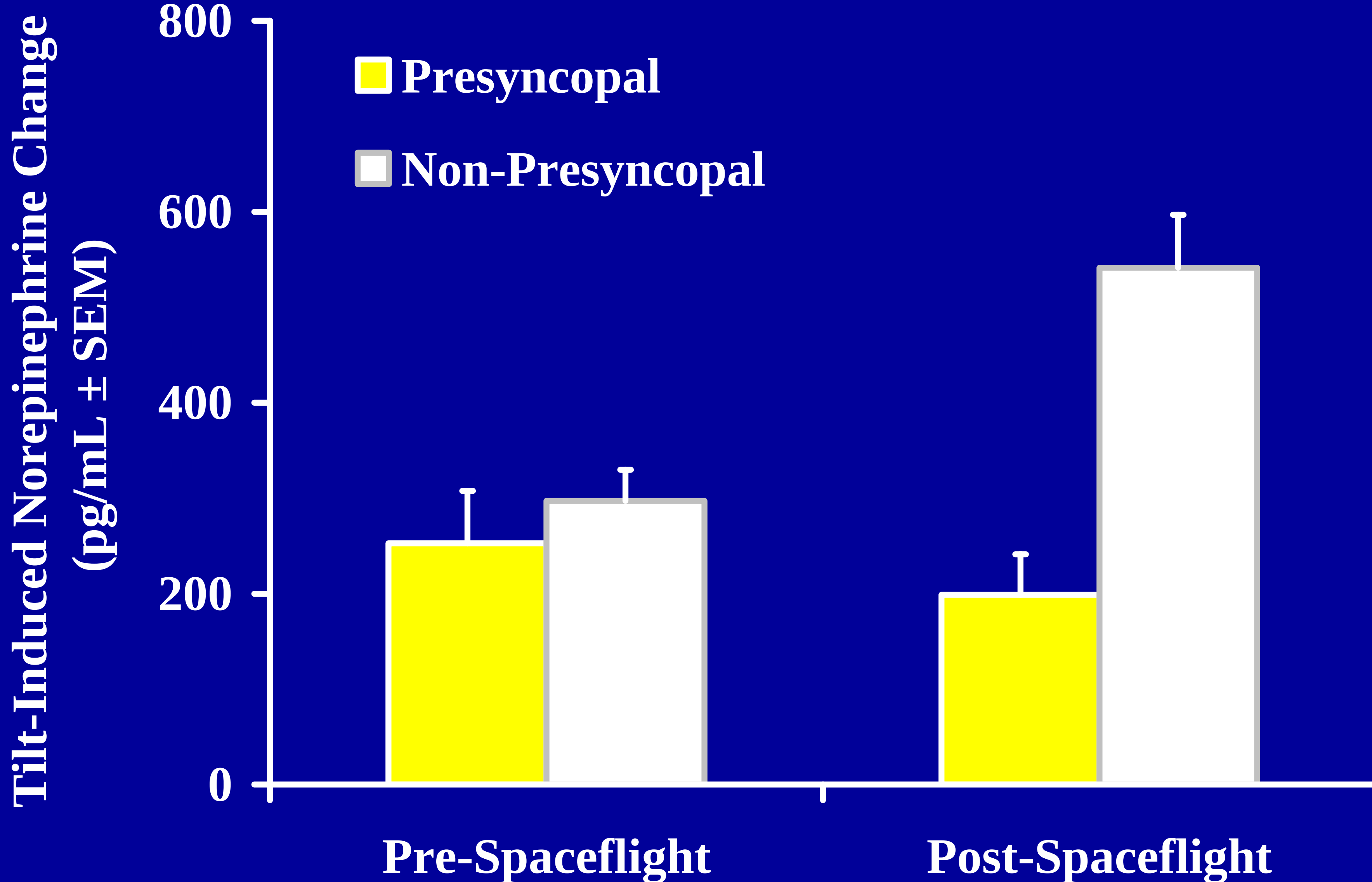
Norepinephrine Response to Tilt during Normovolemia and Hypovolemia



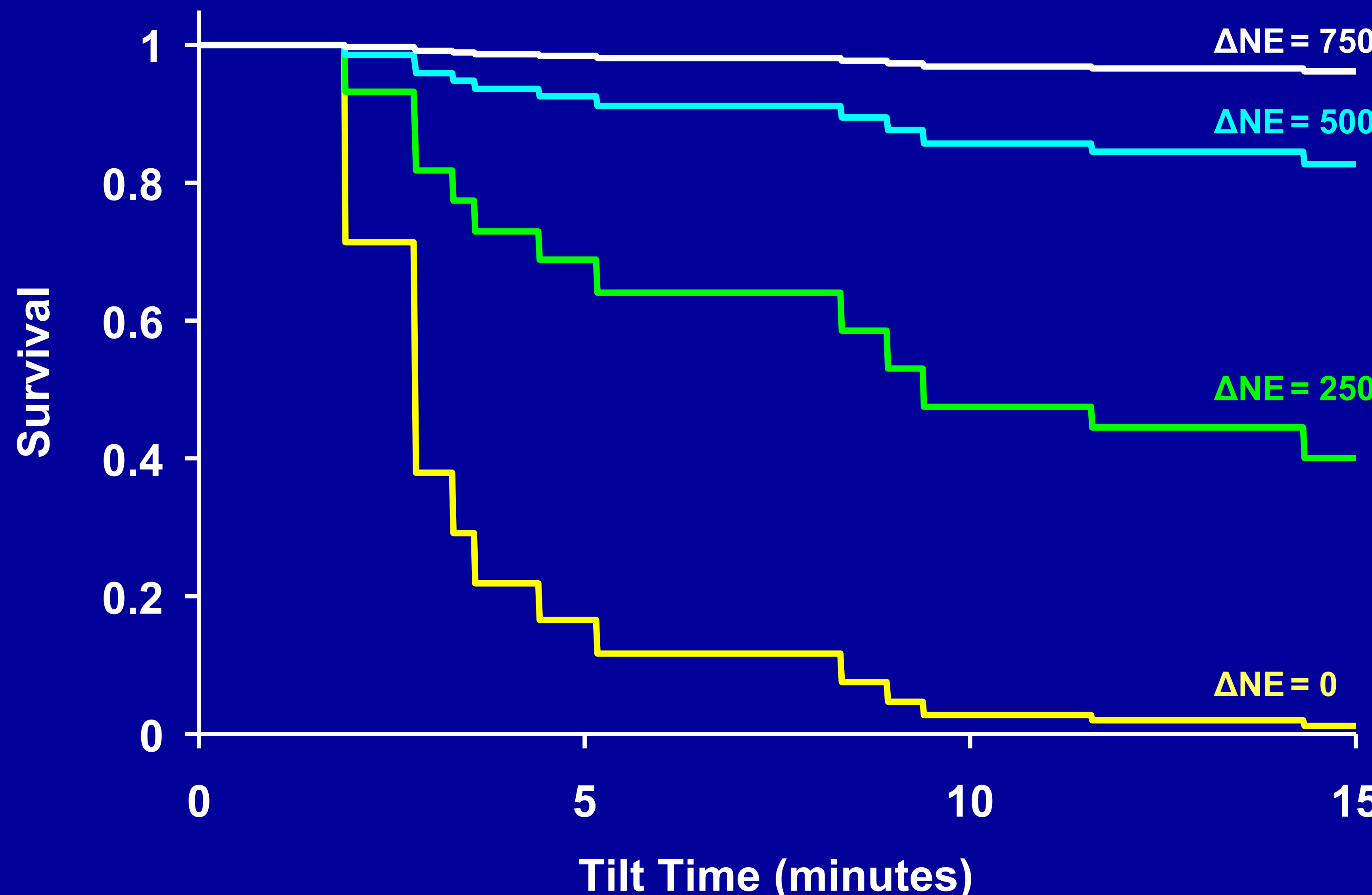
Norepinephrine Response to Tilt during Normovolemia and Hypovolemia



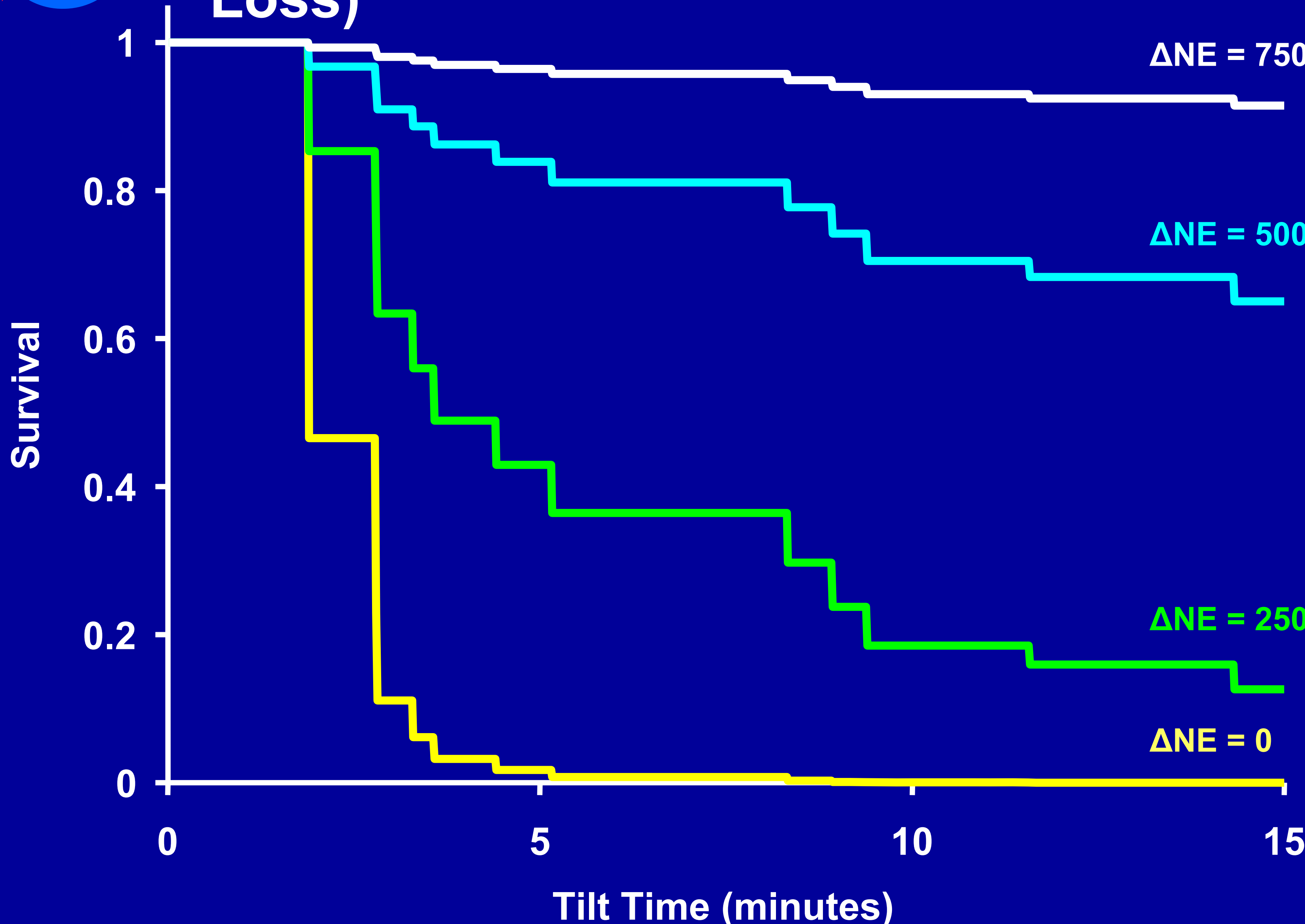
Norepinephrine Response to Tilt before and after Spaceflight



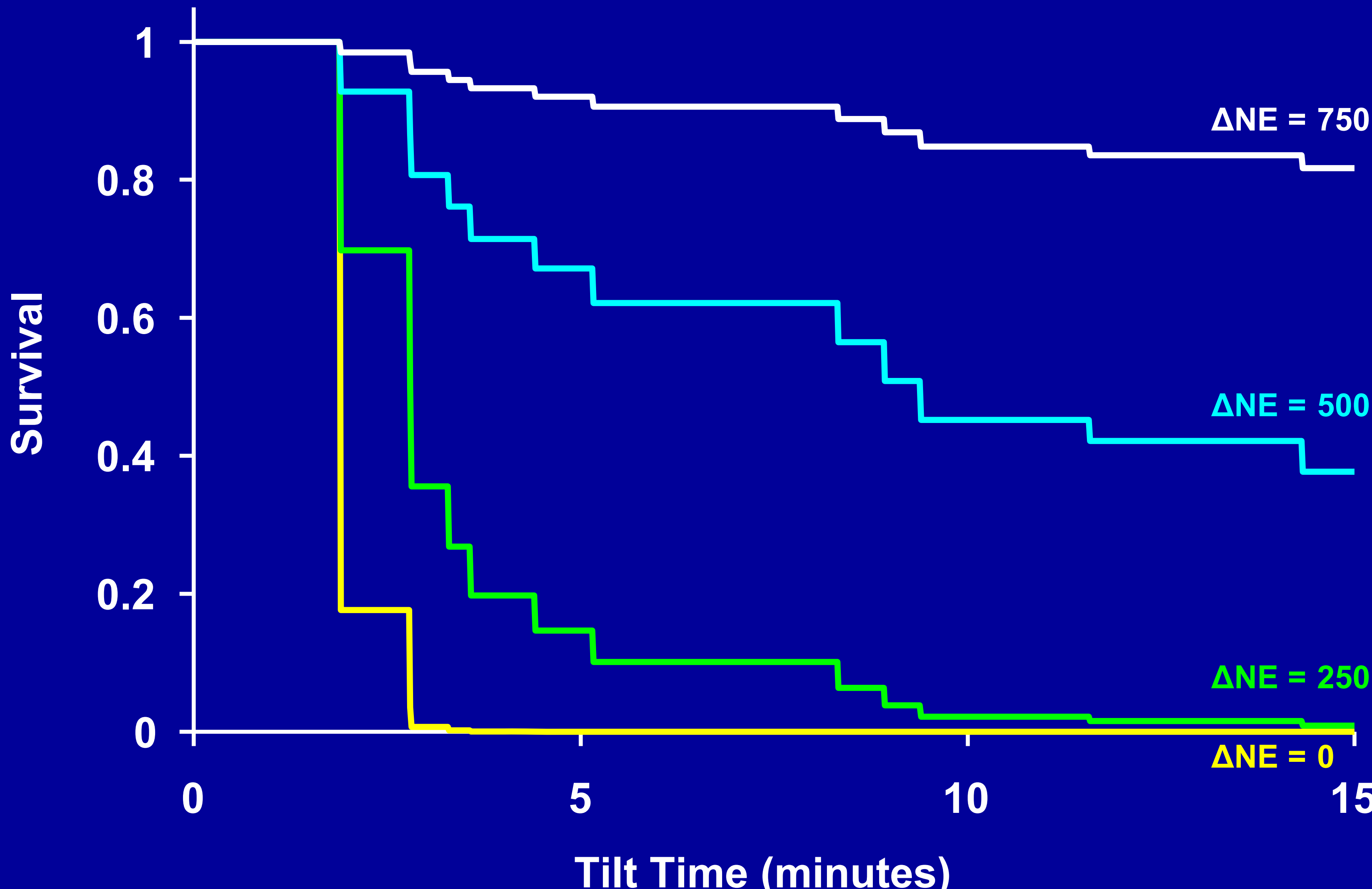
0.2 L/m² PVI Loss (13% Plasma Volume Loss)



0.4 L/m² PVI Loss (22% Plasma Volume Loss)



0.6 L/m^2 PVI Loss (30% Plasma Volume Loss)



Summary

- We report a new model which uses hypovolemia to force humans into a hemodynamic state that is similar to that after spaceflight.
- This model can be used to test candidate countermeasures for postflight orthostatic hypotension and to identify crewmembers who will be most susceptible to that symptom on landing day.