HUMAN CARDIOVASCULAR ADAPTATION TO WEIGHTLESSNESS

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Entering weightlessness (0 G) induces immediately a shift of blood and fluid from the lower to the upper parts of the body inducing expansion of the cardiac chambers (Bungo et al. 1986; Charles & Lathers 1991; Videbaek & Norsk 1997). For many years the effects of sudden 0 G on central venous pressure (CVP) was discussed, and it puzzled researchers that CVP compared to the 1-G supine position decreased during the initial hours of spaceflight, when at the same time left atrial diameter increased (Buckey et al. 1996). By measuring esophageal pressure as an estimate of inter-pleural pressure, it was later shown that this pressure decreases more than CVP does during 0 G induced by parabolic flights (Videbaek & Norsk 1997). Thus, transmural CVP is increased, which distends the cardiac chambers. This unique lung-heart interaction whereby 1) inter-pleural pressure decreases and 2) central blood volume is expanded is unique for 0 G. Because transmural CVP is increased, stroke volume increases according to the law of Frank-Starling leading to an increase in cardiac output, which is maintained increased during months of 0 G in space to levels of some 25 % above that of the 1-G seated position (Norsk unpublished). Simultaneously, sympathetic nervous activity is at the level of the upright 1-G posture, which is difficult to explain based on the high stroke volume and decreased blood pressure and systemic vascular resistance. This paradox should be explored and the mechanisms revealed, because it might have implications for estimating the cardiovascular risk of travelling in space.

Buckey, J. C. et al. Central venous pressure in space. J. Appl. Physiol. 81:19-25 (1996).

Bungo, M. W., et al. Echocardiographic investigation of the hemodynamics of weightlessness. J. Amer. Coll. Cardiol. 7(2): 192A (1986).

Charles, J. B. & Lathers C. M. Cardiovascular adaptation to spaceflight. J. Clin. Pharmacol. 31:1010-1023 (1991).

Videbaek, R. & Norsk, P. Atrial distension in humans during microgravity induced by parabolic flights. J. Appl. Physiol. 83:1862-66 (1997).

Norsk, P. & Christensen N. J. The paradox of systemic vasodilatation and sympathetic nervous stimulation in space. Resp. Physiol. Neurobiol. 169S: S26-S29 (2009).

Human Cardiovascular Adaptation to Weightlessness

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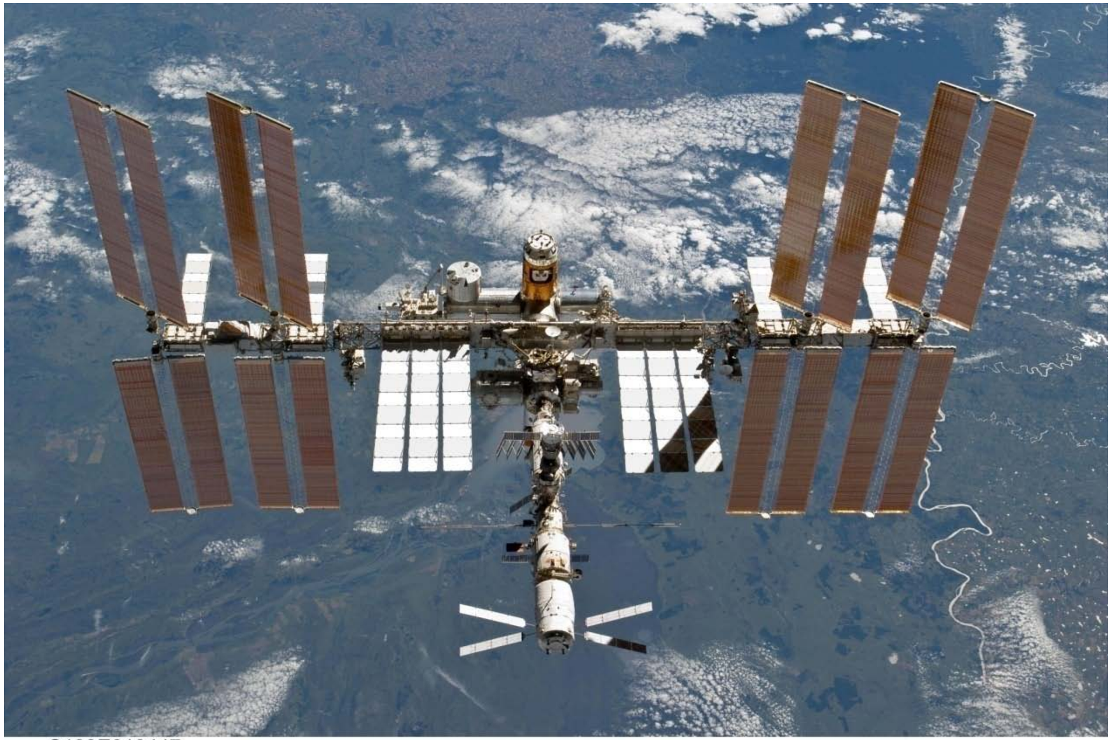


S133E010447

Background

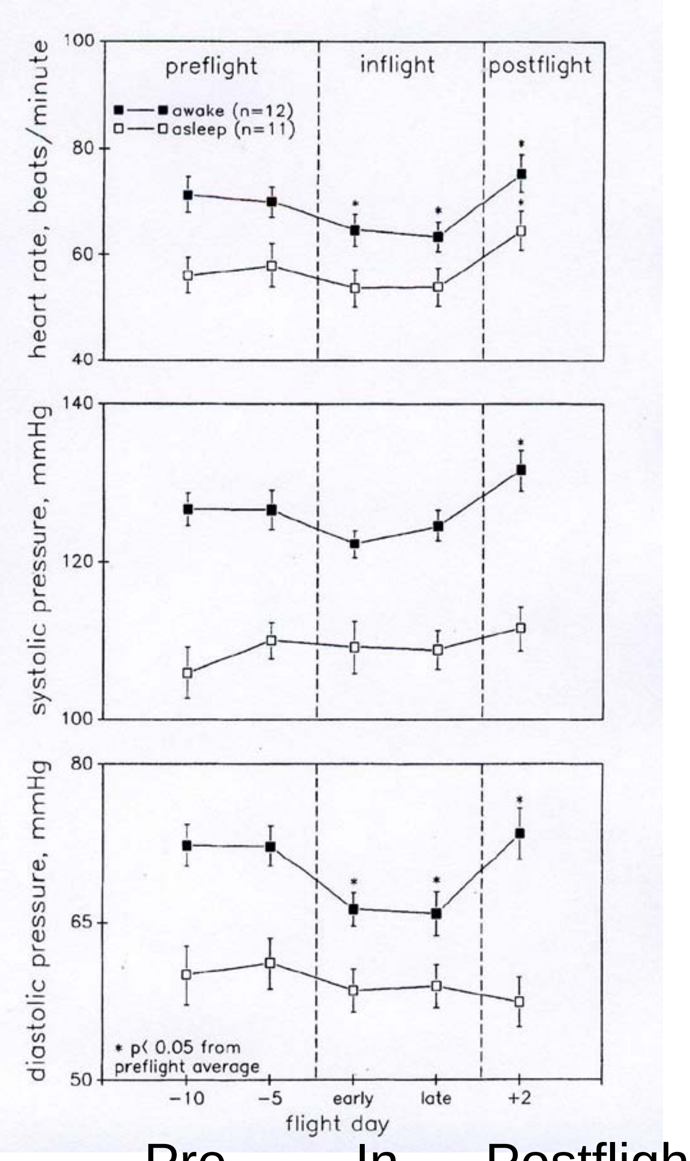
Short-term spaceflight (< 2 weeks):

Variable	Method	Effect (0 G/upright)	References
Blood pressure (BP)	24-h Brachial (Oscillometry)	$\downarrow$ (Only DAP)	Meck et al. (J. Appl. Physiol. 1996)
	Brachial (Auscultatory/ oscillometry)	$\downarrow$	Shykoff et al. (J. Appl. Physiol. 1996)
	Finger (infrared photoplethysmography)	$\rightarrow$	Norsk et al. (Hypertension 2006)
Cardiac output (CO)	Rebreathing (Acetylene)	$\uparrow\rightarrow$	Prisk et al. (J. Appl. Physiol. 1993)
	Rebreathing (N_2O)	$\uparrow$	Norsk et al. (Hypertension 2006)
	Rebreathing (CO_2)	$\uparrow$	Shykoff et al. (J. Appl. Physiol. 1996)
Systemic vascular resistance	MAP/CO	$\downarrow$	Shykoff et al. (J. Appl. Physiol. 1996)
	MAP/CO	$\downarrow$	Norsk et al. (Hypertension 2006)

Heart rate

Systolic

Diastolic



Pre- In- Postflight

Fritsch-Yelle et al.
J. Appl. Physiol.
80:919-914, 1996.

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Short-term spaceflight (< 2 weeks):

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Blood pressure (BP)	24-h Brachial (Oscillometry)	$\downarrow$ (Only DAP)	Meck et al. (J. Appl. Physiol. 1996)
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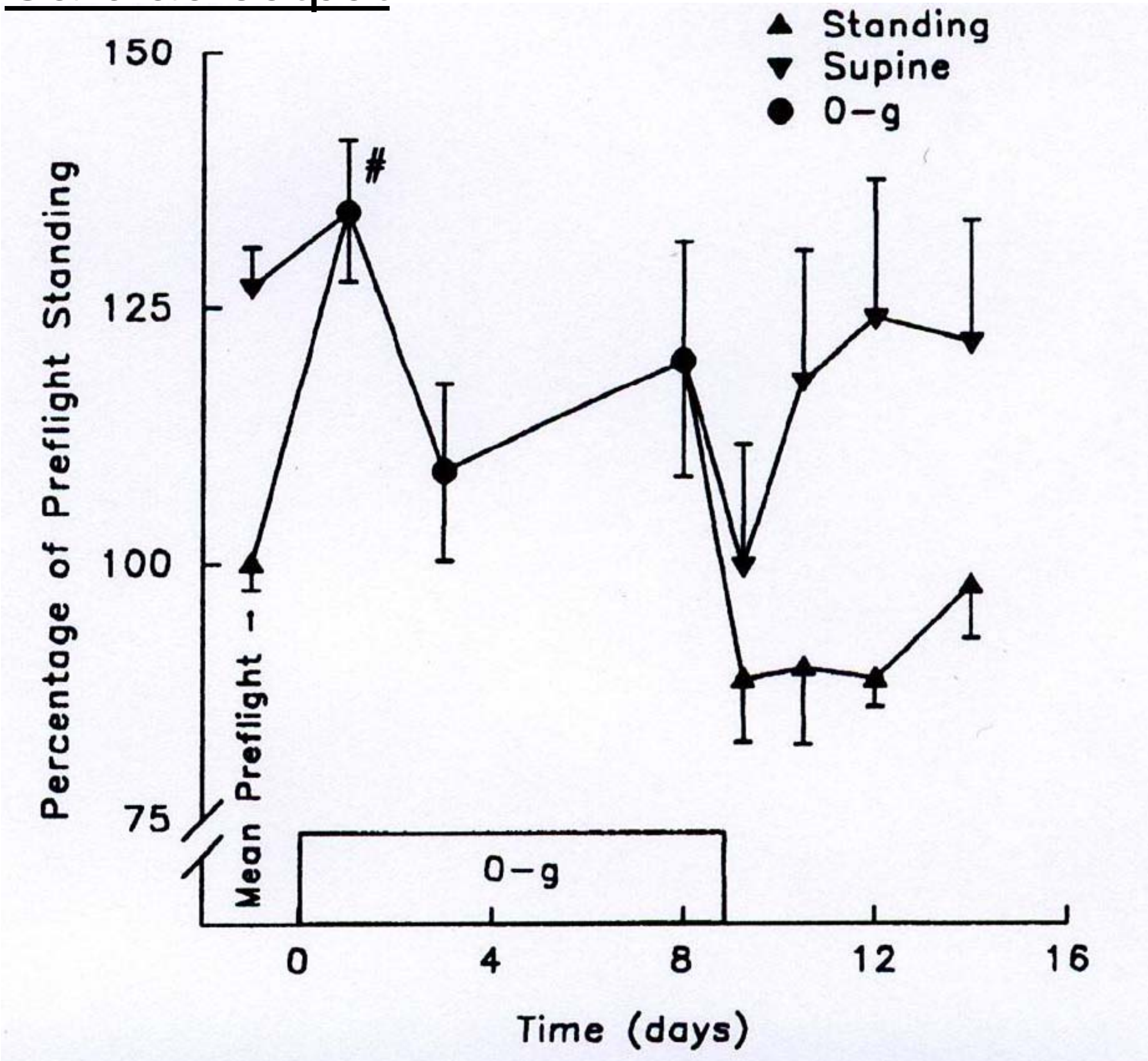
	MAP/CO	$\downarrow$	Norsk et al. (Hypertension 2006)

Cardiac output



Prisk et al.
J. Appl. Physiol.
75:15-26,1993.

Background

Short-term spaceflight (< 2 weeks):

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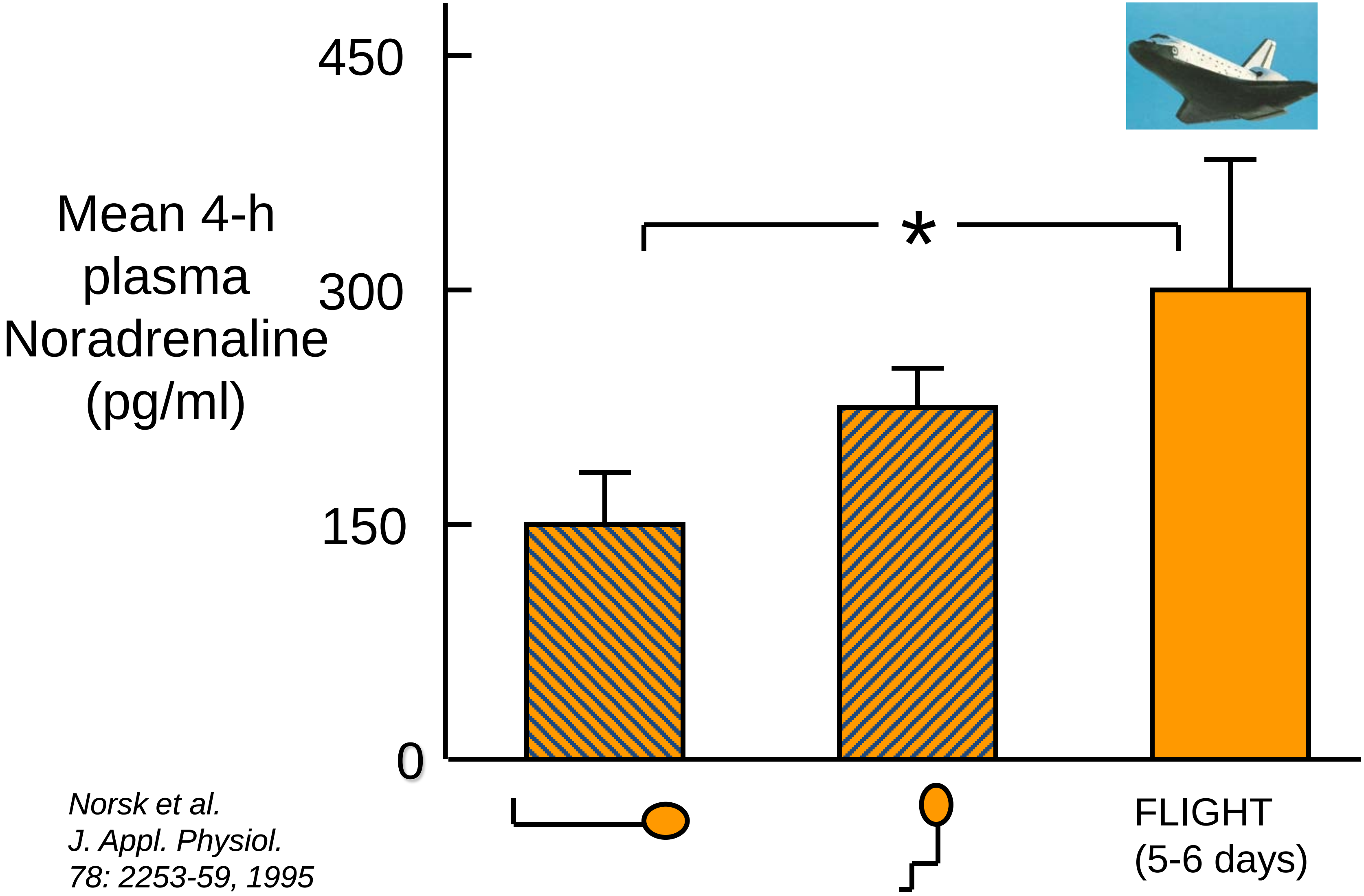
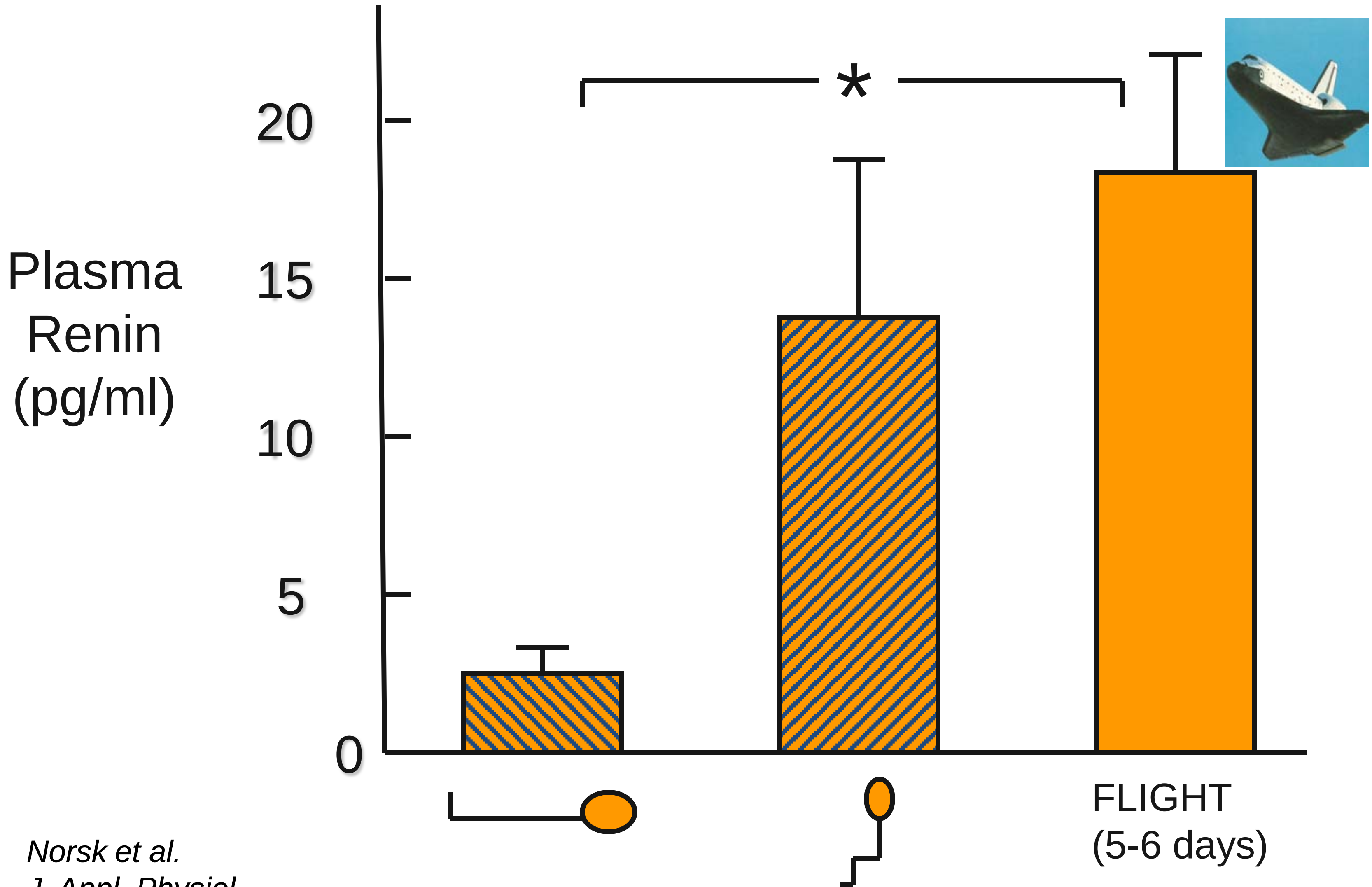
	Brachial (Auscultatory/ oscillometry)	↓	Shykoff et al. (J. Appl. Physiol. 1996)
	Finger (infrared photoplethysmography)	→	Norsk et al. (Hypertension 2006)
Cardiac output (CO)	Rebreathing (Acetylene)	↑ →	Prisk et al. (J. Appl. Physiol. 1993)
	Rebreathing (N_2O)	↑	Norsk et al. (Hypertension 2006)
	Rebreathing (CO_2)	↑	Shykoff et al. (J. Appl. Physiol. 1996)
Systemic vascular resistance	MAP/CO	↓	Shykoff et al. (J. Appl. Physiol. 1996)
	MAP/CO	↓	Norsk et al. (Hypertension 2006)



Norsk et al.
J. Appl. Physiol.
78: 2253-59, 1995



Norsk et al.
J. Appl. Physiol.
78: 2253-59, 1995

Background (2):

Long-term spaceflight (> 3 months):

Variable	Method	Effect (0 G/upright)	References
Blood pressure (BP)	Brachial or finger ? (Oscillometry/ photoplethysmography?)	↓ (Only DAP)	Baevsky et al. (J. Appl. Physiol. 2007)

Background (2):

Long-term spaceflight (> 3 months):

Variable	Method	Effect (0 G/semi-upright)	References
Blood pressure (BP)	Brachial or finger ? (Oscillometry/ photoplethysmography?)	↓ (Only DAP)	Baevsky et al. (J. Appl. Physiol. 2007)

Purpose

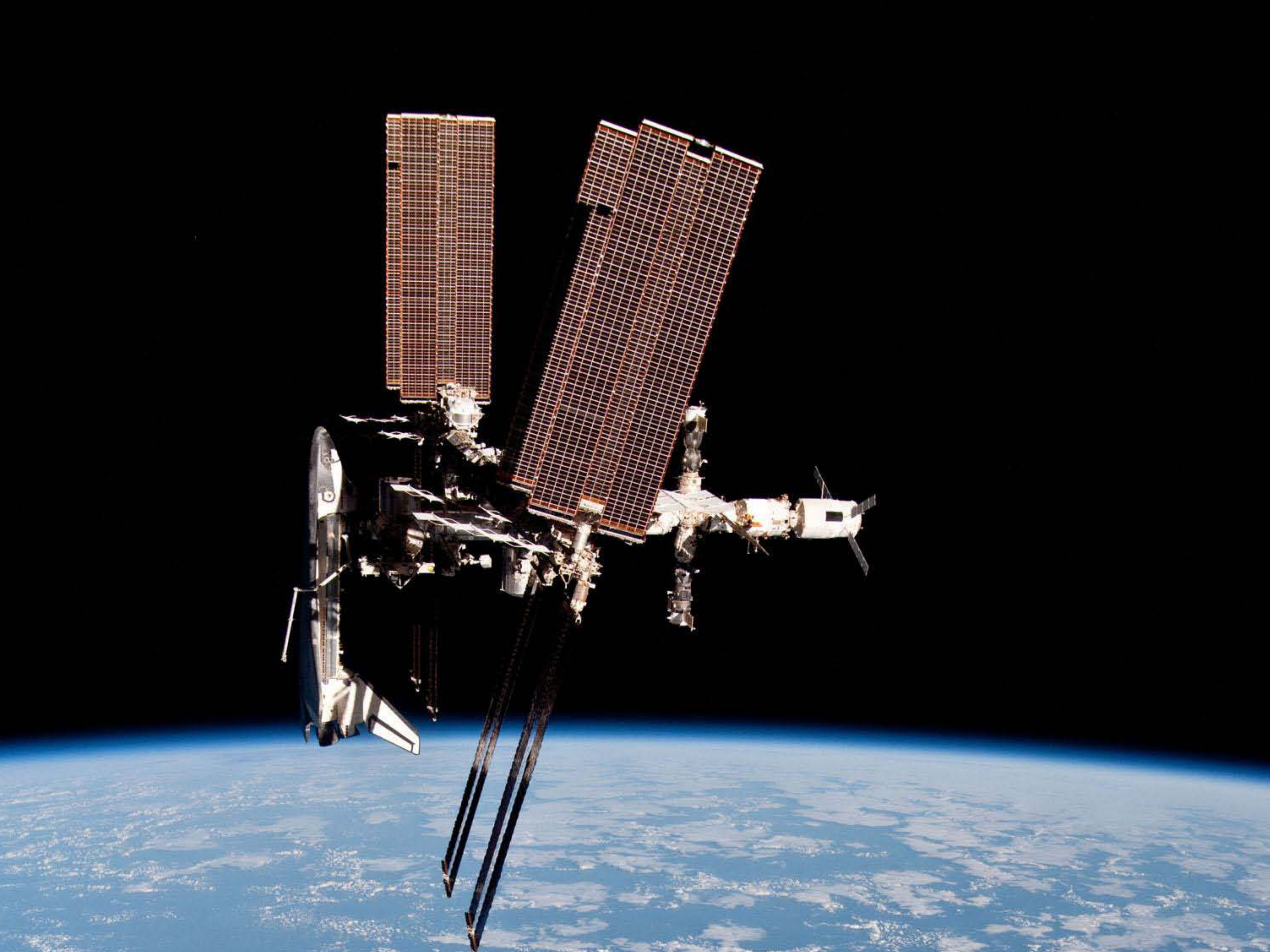
To investigate how 24-h ambulatory blood pressure and the cardiovascular system adapt to long-term (3-6 months) space flight and thus, how the daily load of gravity here on Earth affects our ambulatory blood pressure.

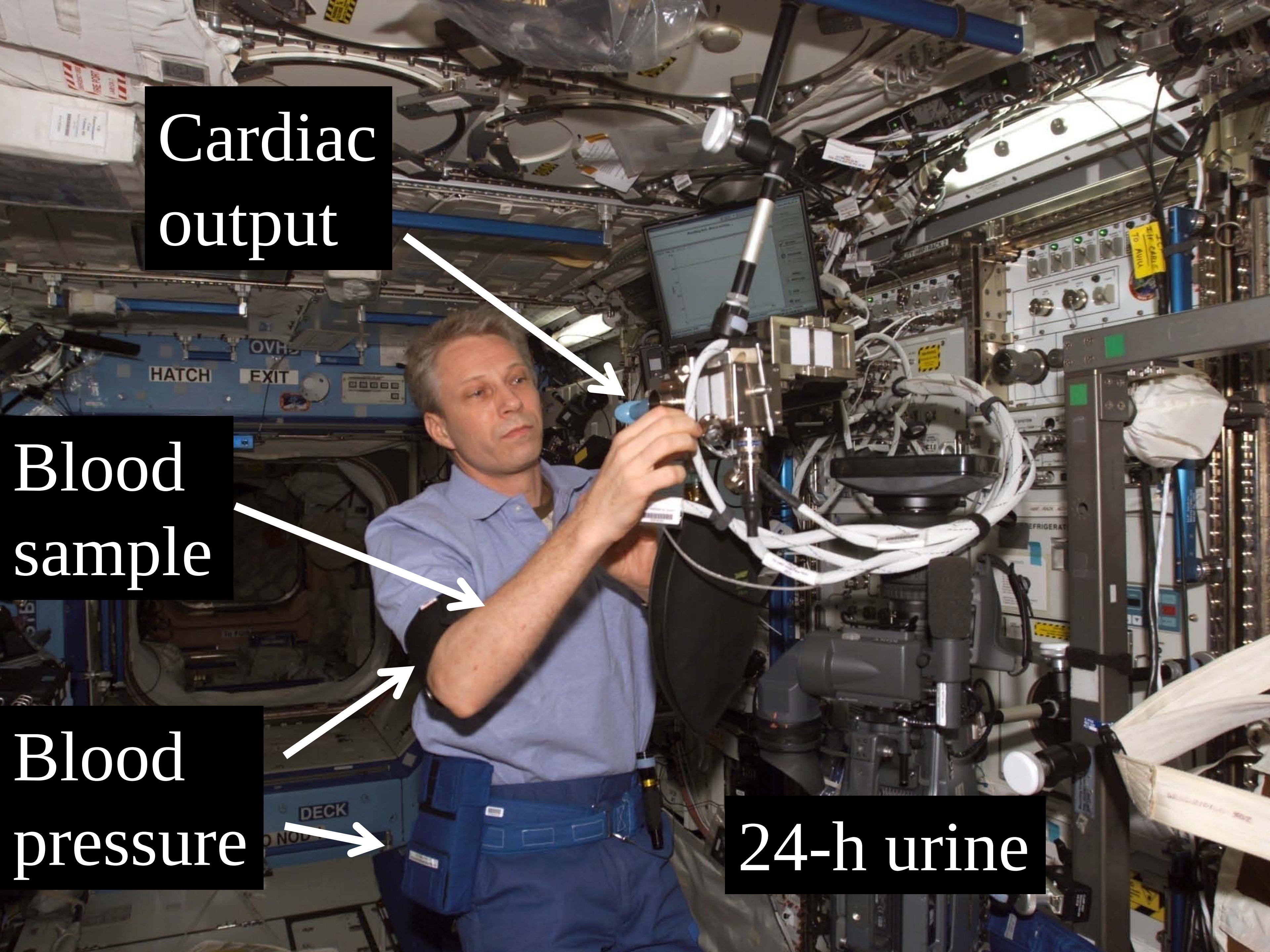
Hypothesis

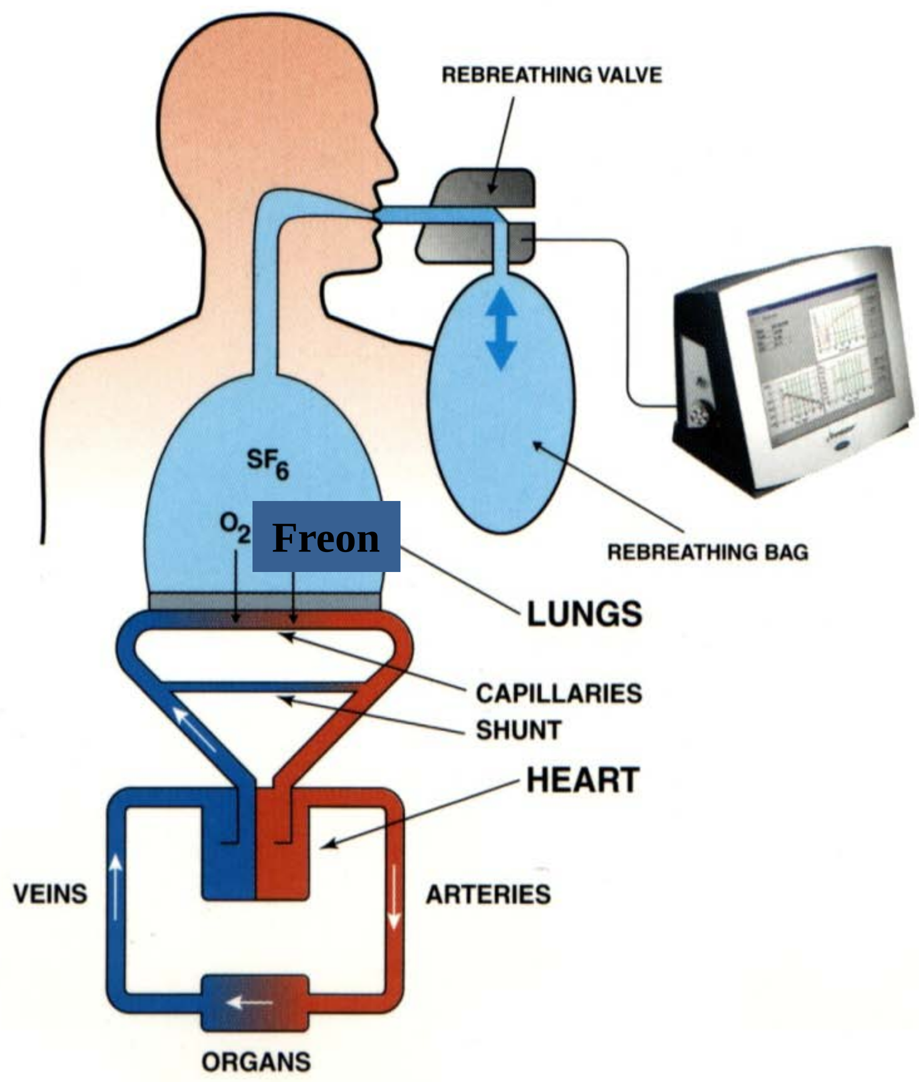
Despite an increase in cardiac output (CO), 24-h ambulatory brachial blood pressure (BP) is unchanged or decreased by chronic systemic arterial vasodilatation during long-term (months) space flight.

ISS026E012919

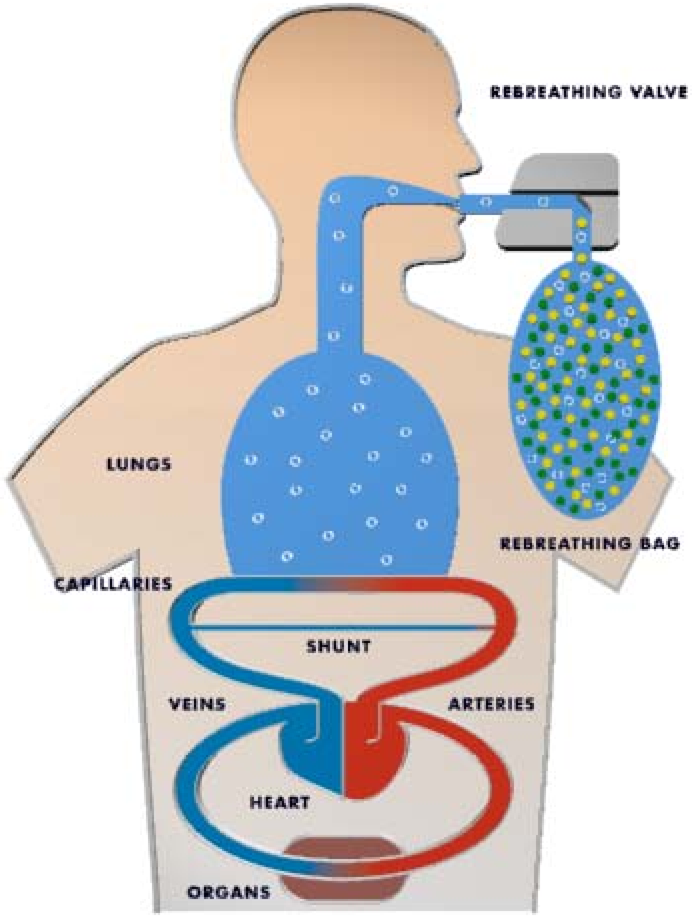
Paoli Nespoli
European Space Agency astronaut

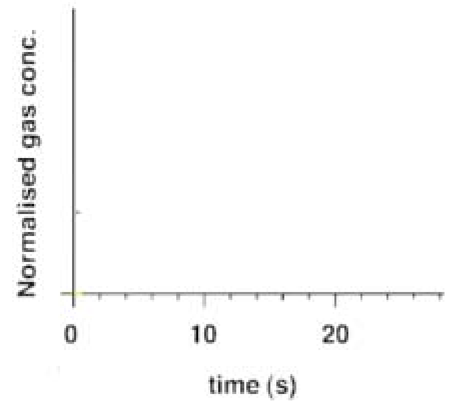



Cardiac output
Blood sample
Blood pressure
24-h urine



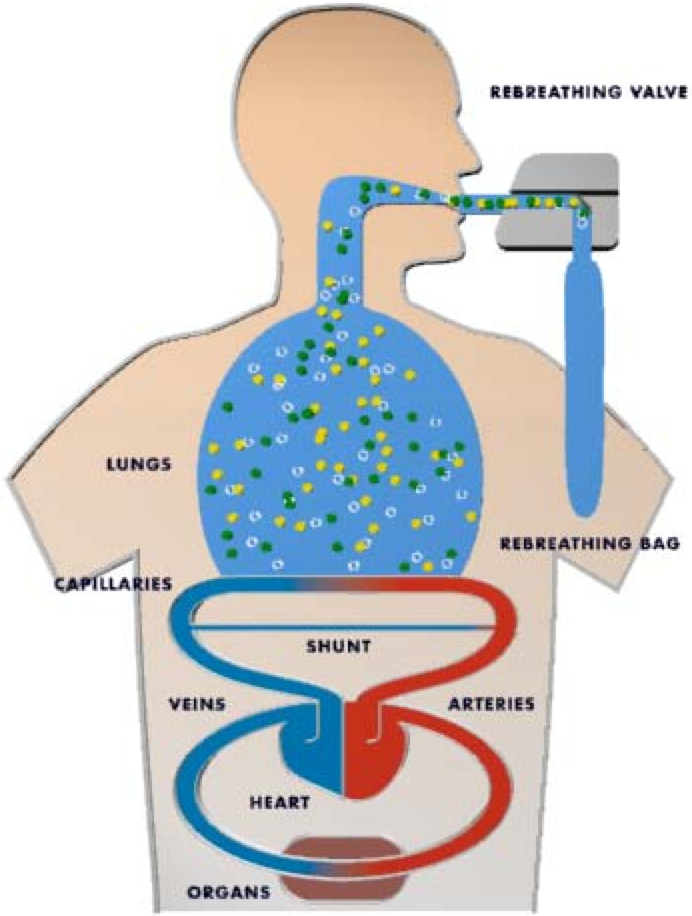
Cardiac output
by
rebreathing

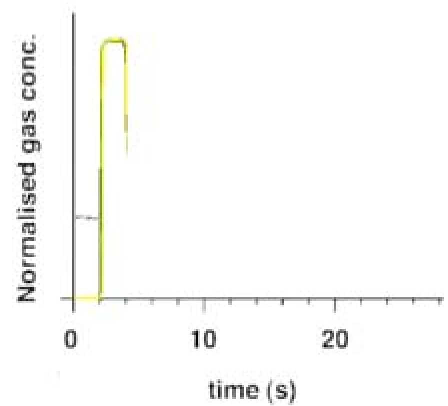




- Blood soluble gas
- Blood insoluble gas
- Oxygen

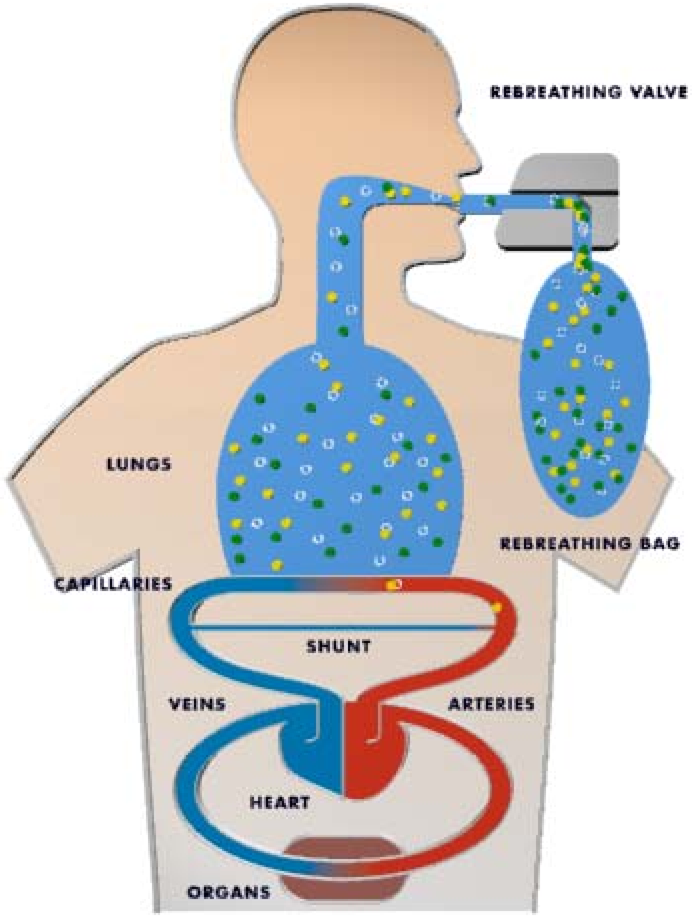
innocor™

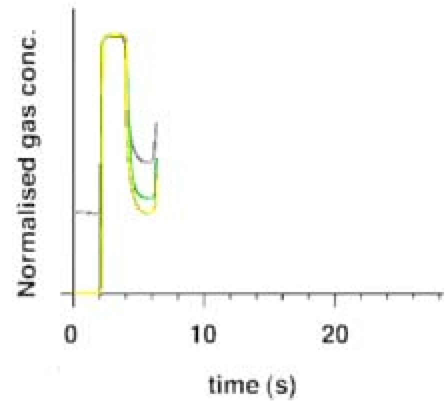




- Blood soluble gas
- Blood insoluble gas
- Oxygen

innocor™



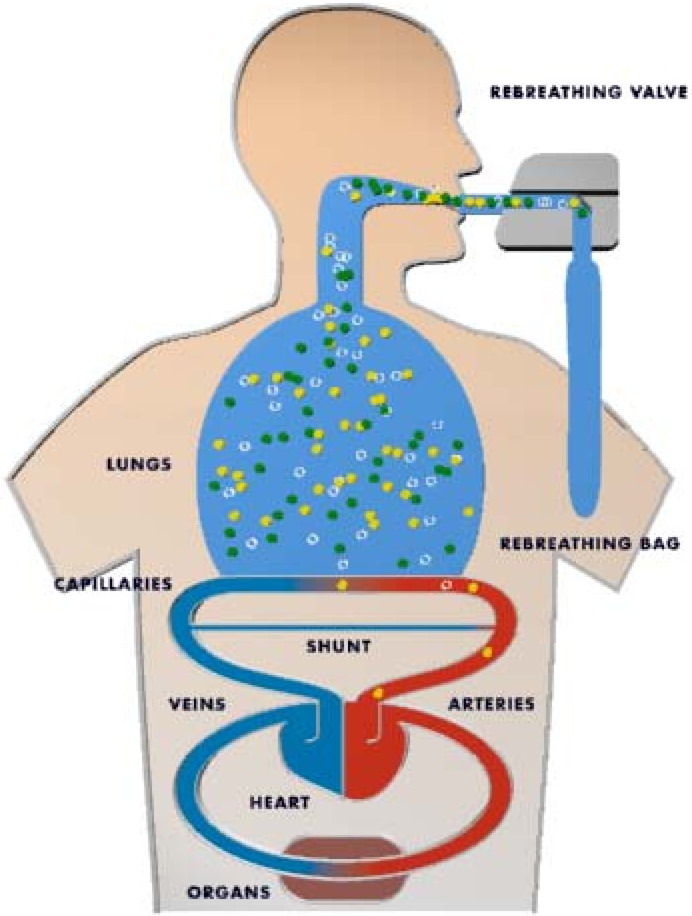


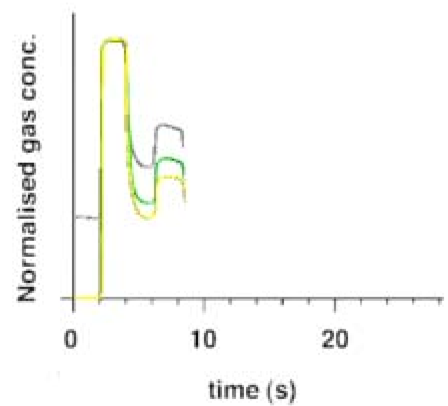
Blood soluble gas

Blood insoluble gas

Oxygen

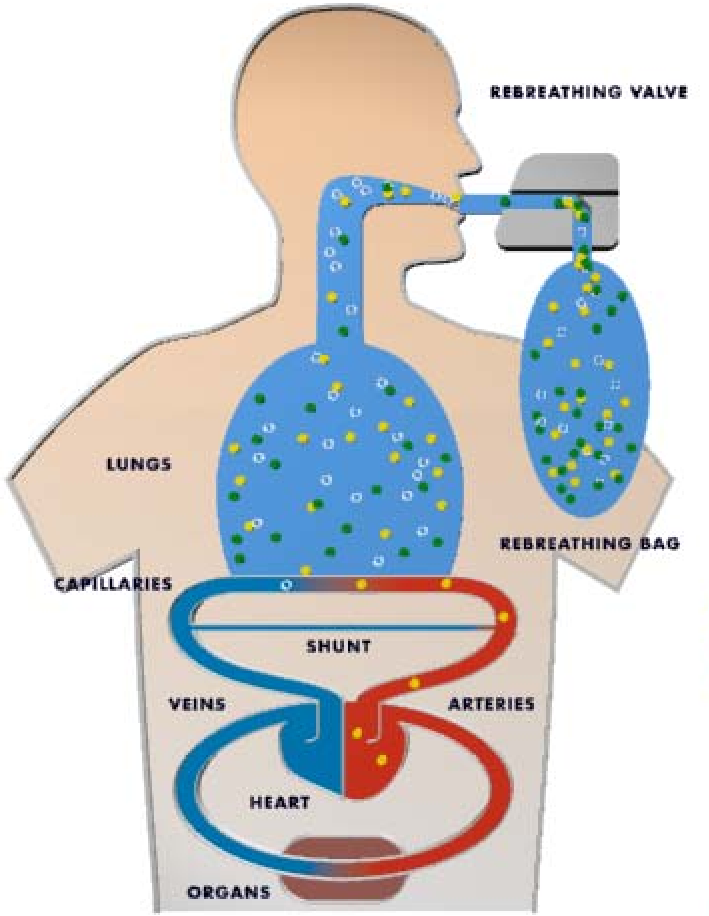
innocor™

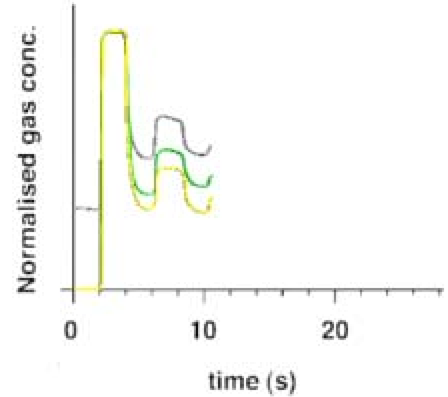




● Blood soluble gas
● Blood insoluble gas
○ Oxygen

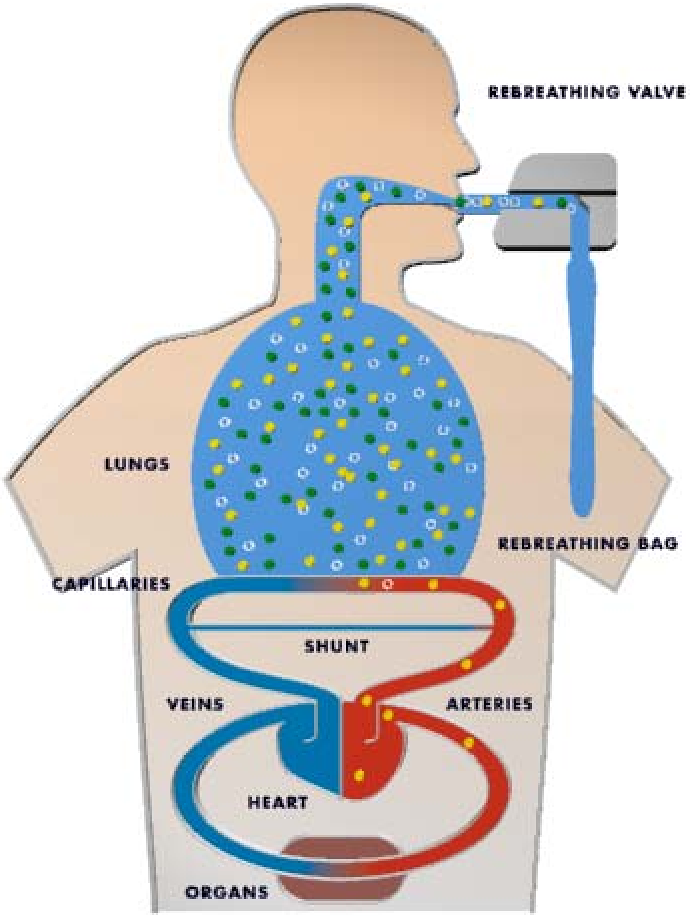
innocor™

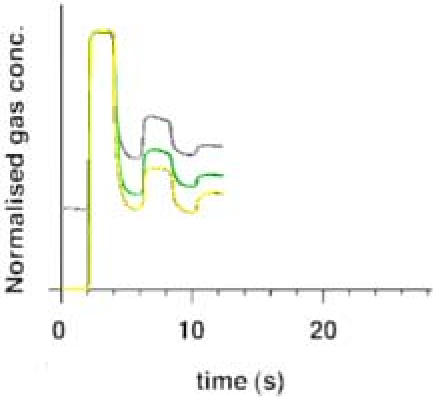




- Blood soluble gas
- Blood insoluble gas
- Oxygen

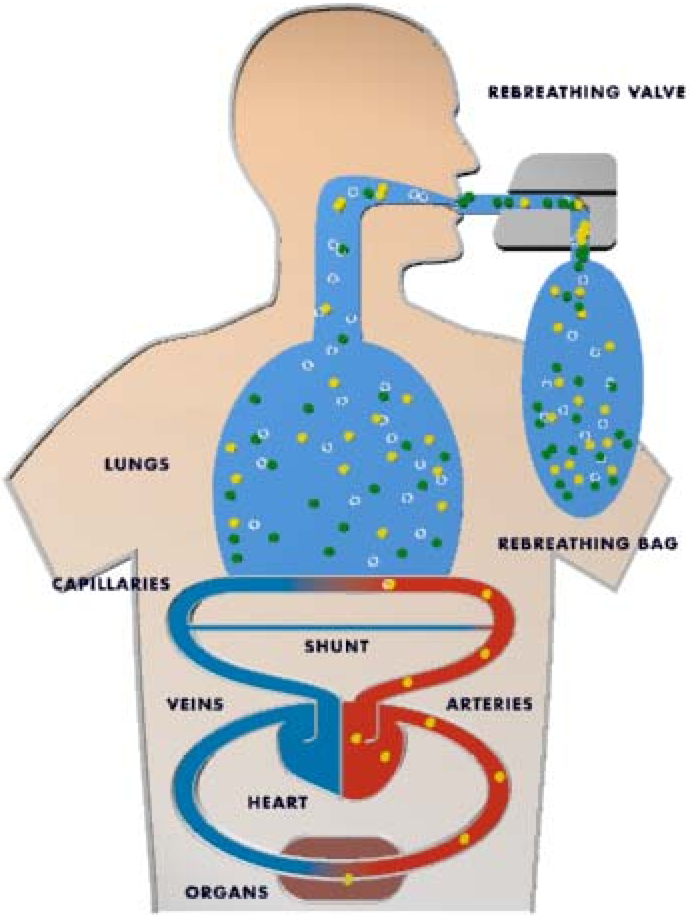
innocor™

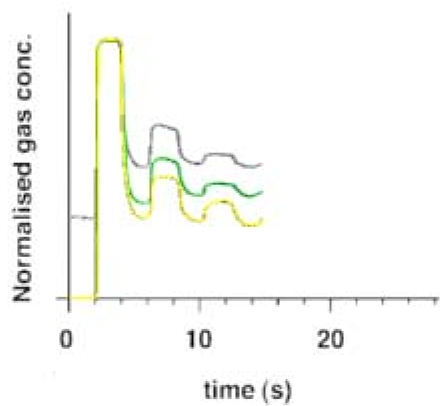




- Blood soluble gas
- Blood insoluble gas
- Oxygen

innocor™



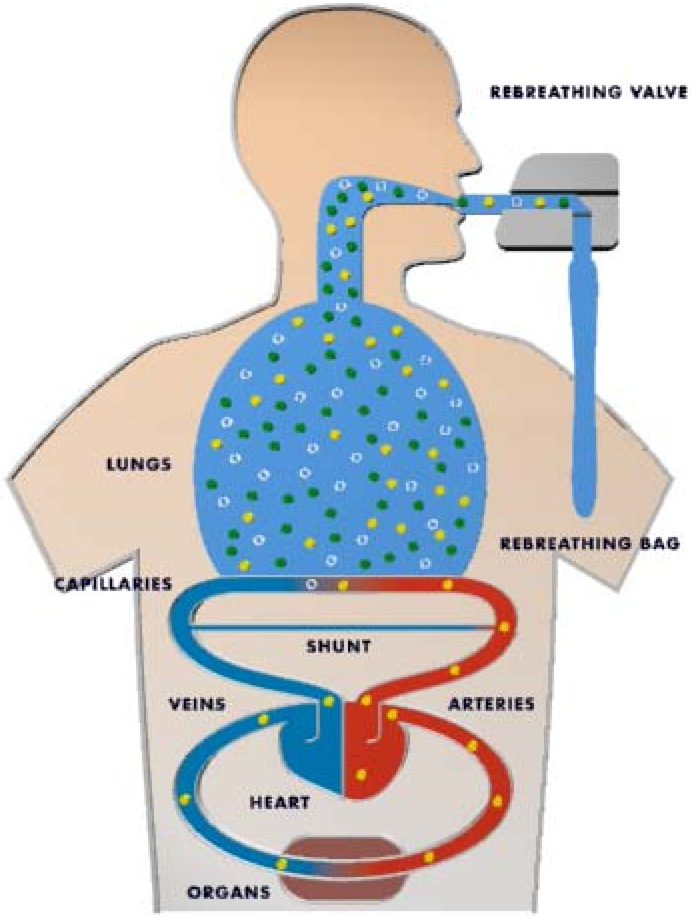


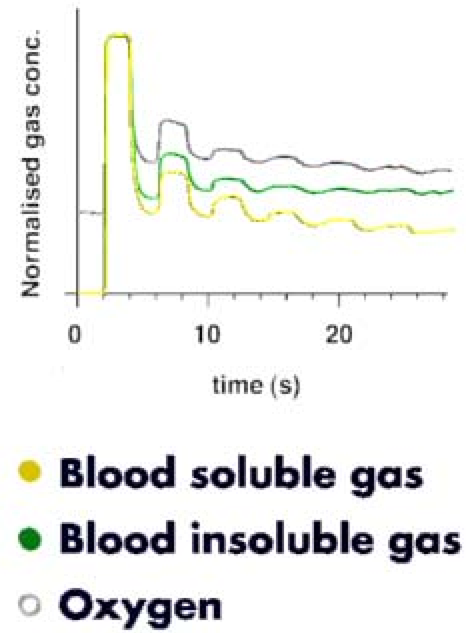
Blood soluble gas

Blood insoluble gas

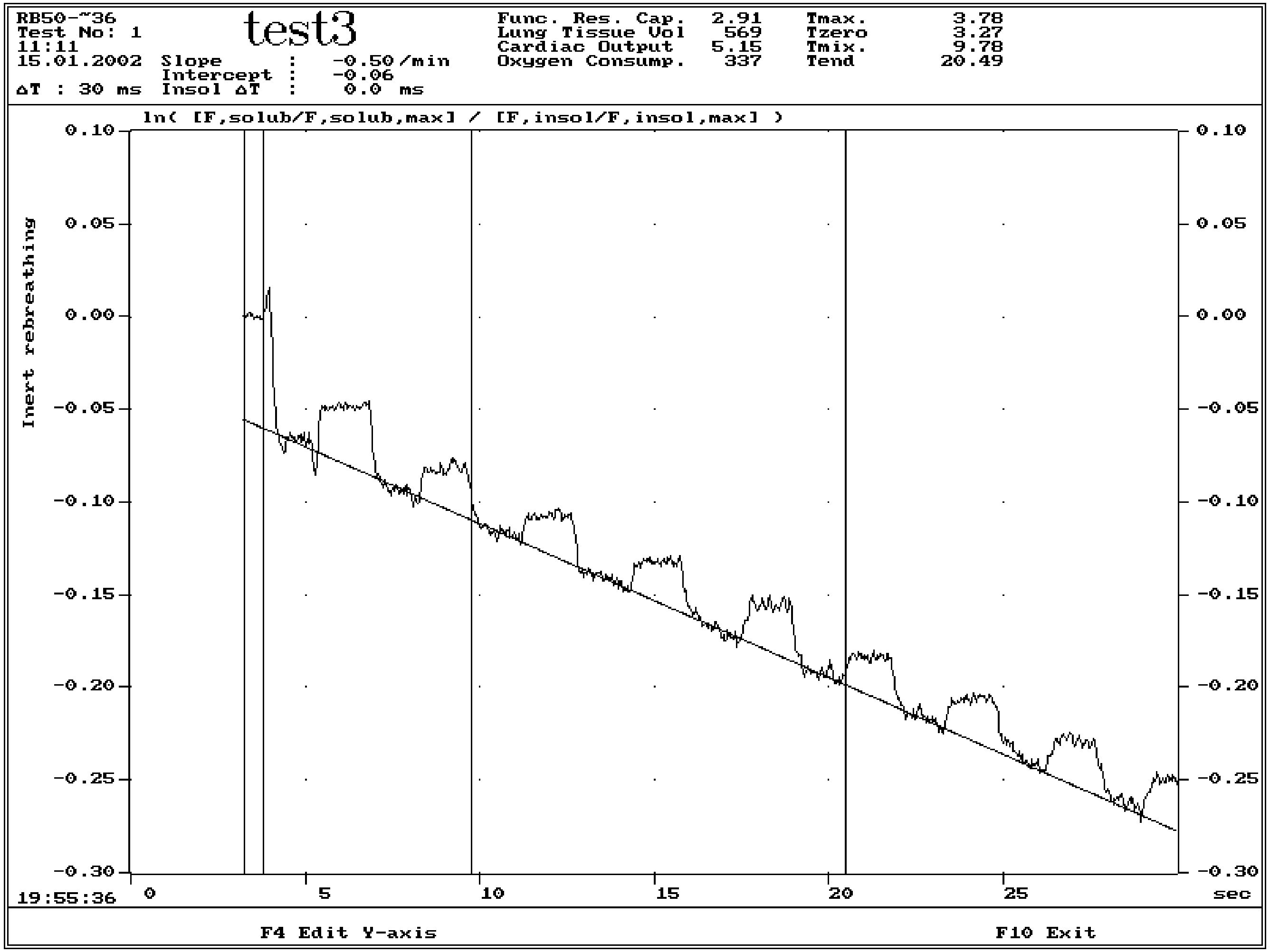
Oxygen

innocor™


REBREATHING VALVE
LUNGS
REBREATHING BAG
CAPILLARIES
SHUNT
VEINS
ARTERIES
HEART
ORGANS


Normalised gas conc.
0
10
20
time (s)
Blood soluble gas
Blood insoluble gas
Oxygen

innocor™


RB50-~36
Test No: 1
11:11
15.01.2002
ΔT : 30 ms
test3
Slope : -0.50 /min
Intercept : -0.06
Insol ΔT : 0.0 ms
Func. Res. Cap. 2.91
Lung Tissue Vol 569
Cardiac Output 5.15
Oxygen Consump. 337
Tmax. 3.78
Tzero 3.27
Tmix. 9.78
Tend 20.49
ln([F,solub/F,solub,max] / [F,insol/F,insol,max])
Inert rebreathing
0.10
0.05
0.00
-0.05
-0.10
-0.15
-0.20
-0.25
-0.30
0
5
10
15
20
25
sec
19:55:36
F4 Edit Y-axis
F10 Exit

Experimental protocol

Pre-flight: Launch minus 2 months or more
In-flight: Launch + 3 to 6 months
Post-flight: Landing + 2 months or more.

Time:	**12:00 14:00 16:00 18:00 20:00 22:00 24:00 02:00 04:00 06:00 08:00 10:00 12:00**
Blood pressure: (Ambulatory)	X X X X X X X X X X X X X X X X X X X X
Cardiac output: (Seated)	X X X X X
Blood sampling: (Seated)	X
Urine collection: (ambulatory)	**>--<**

X: Execution.

Experimental protocol

Pre-flight: Launch minus 2 months or more
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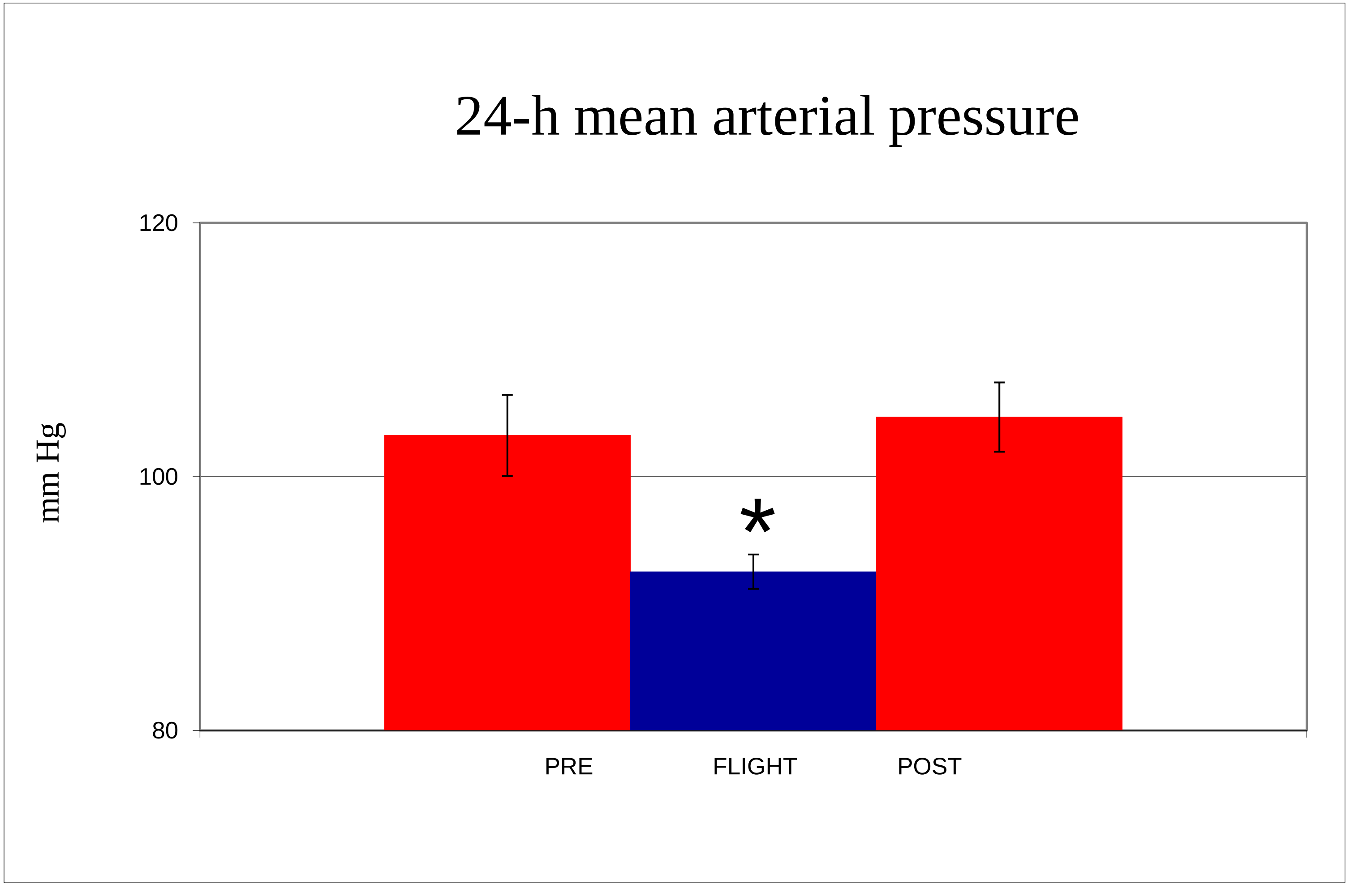
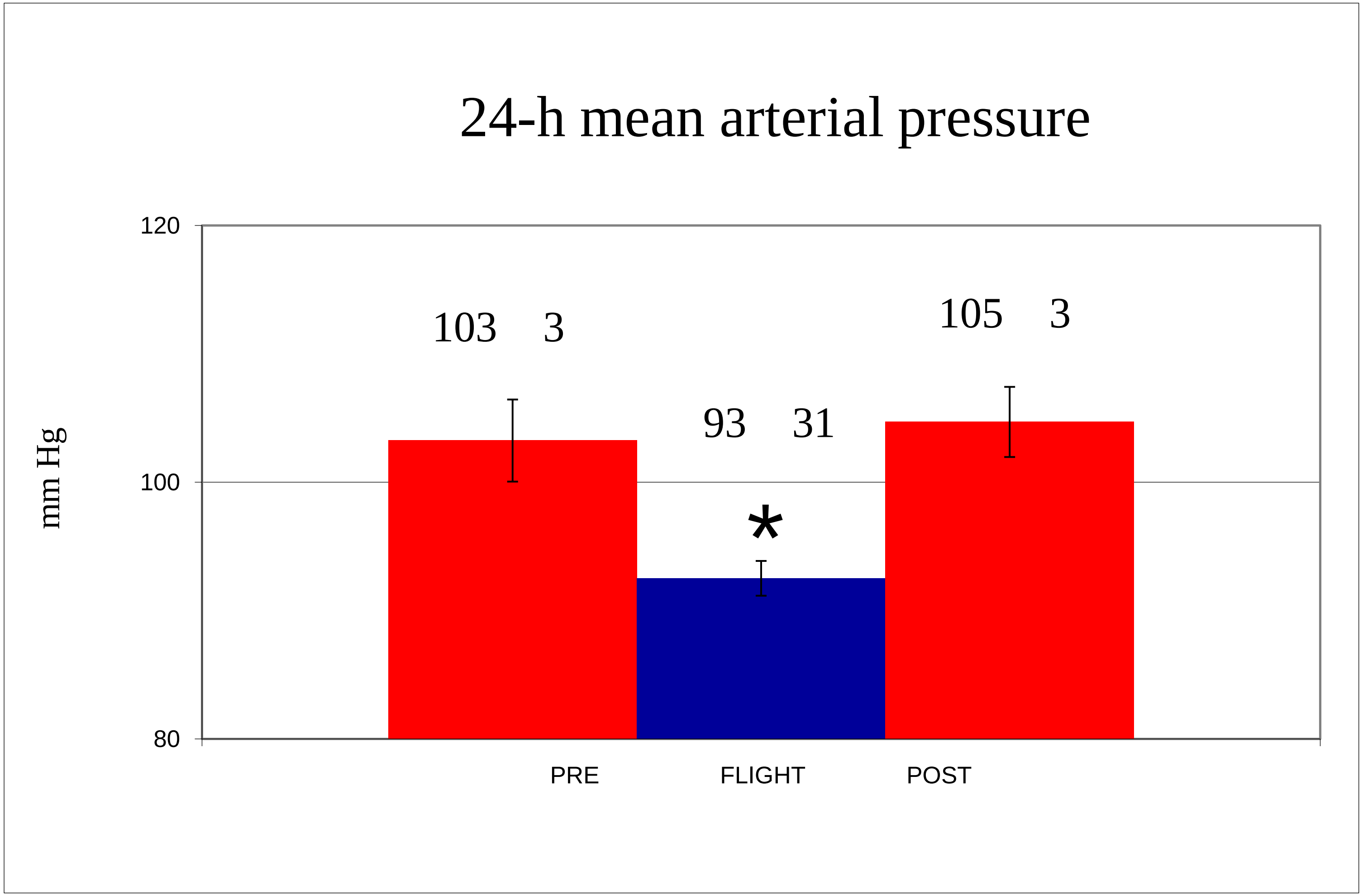
Time:	**12:00 14:00 16:00 18:00 20:00 22:00 24:00 02:00 04:00 06:00 08:00 10:00 12:00**
Blood pressure: (Ambulatory)	X X X X X X X X X X X X X X X X X X X X
Cardiac output: (Seated)	X X X X X
Blood sampling: (Seated)	X
Urine collection: (ambulatory)	>---<

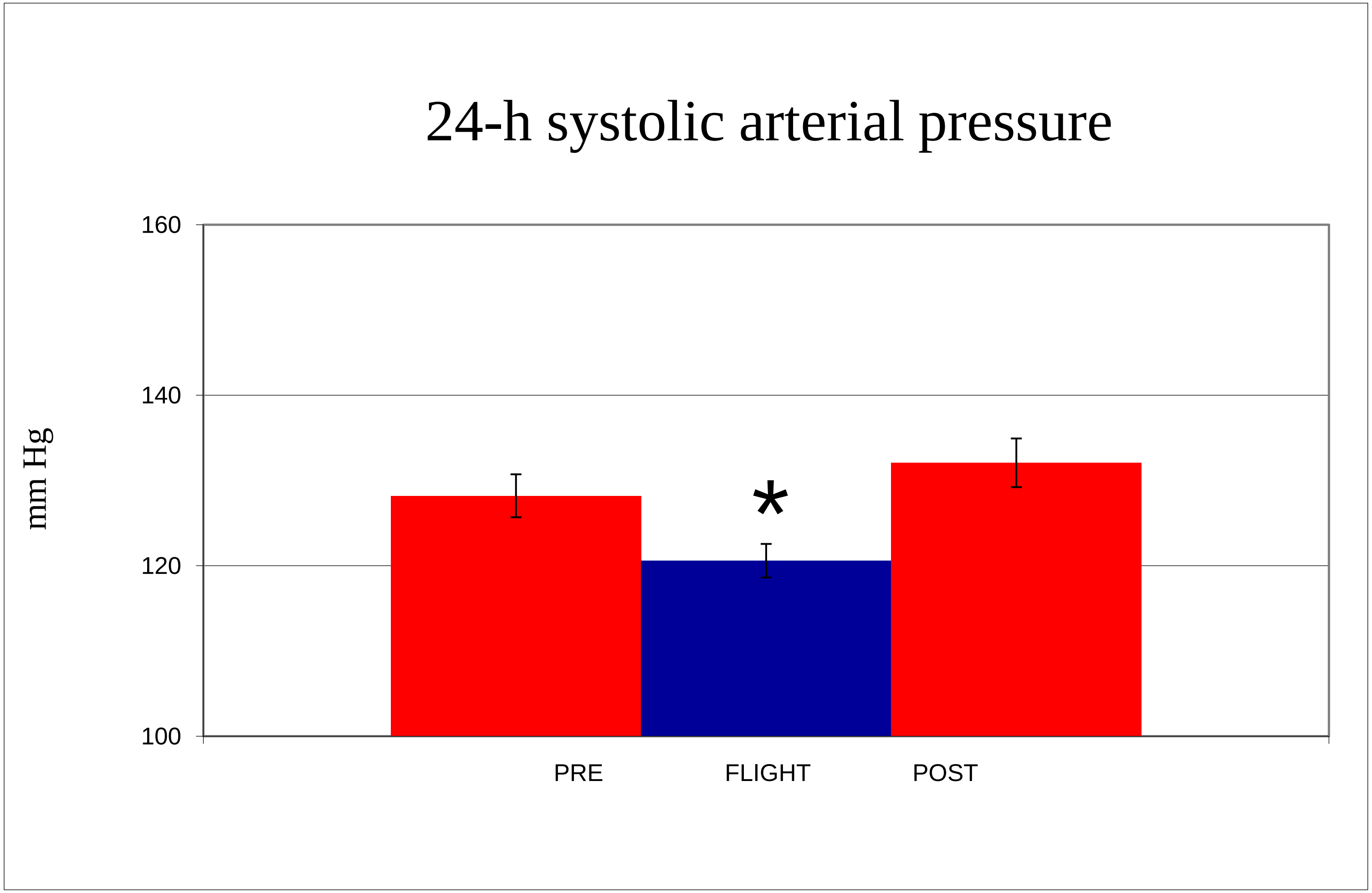
X: Execution

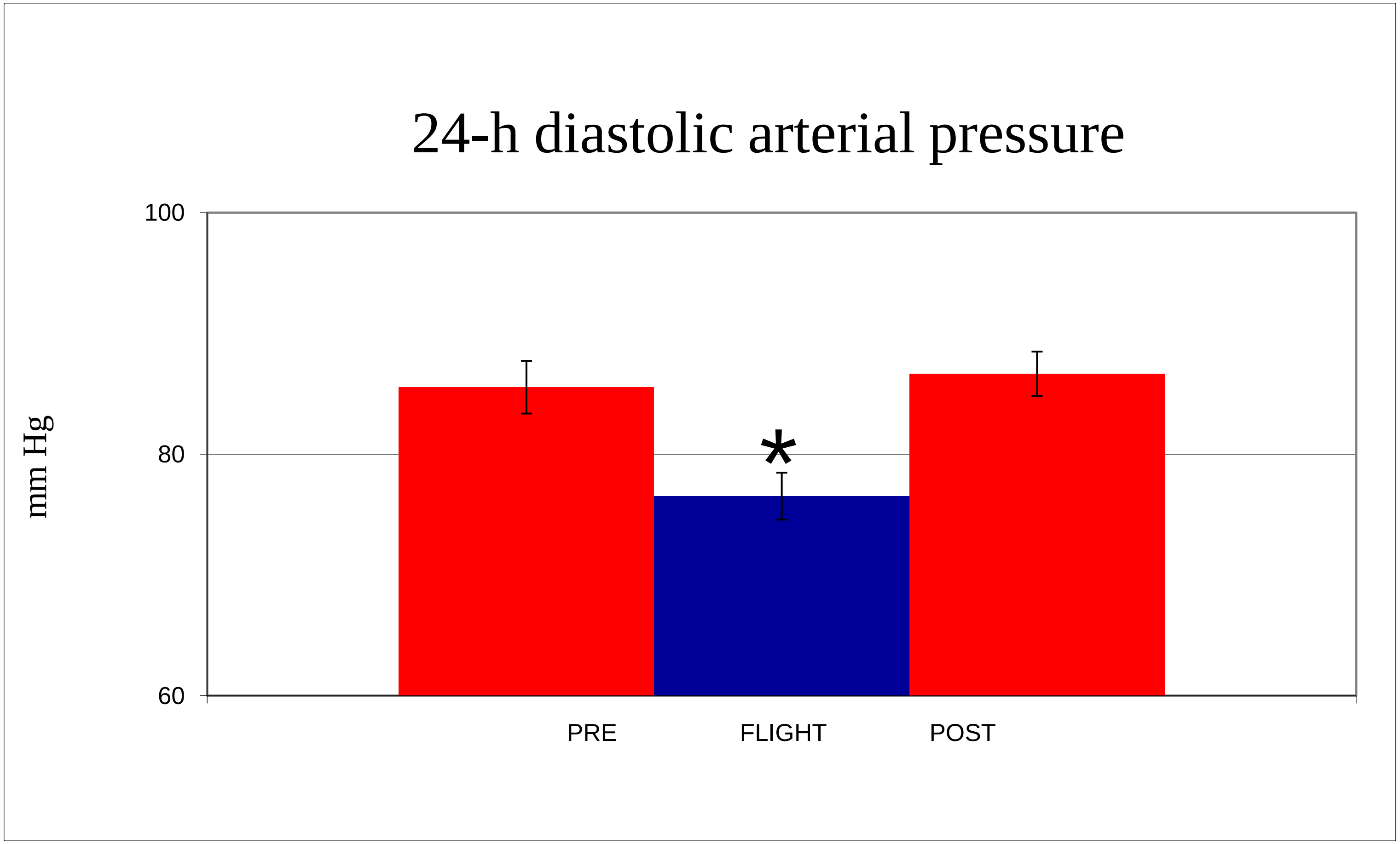
Results

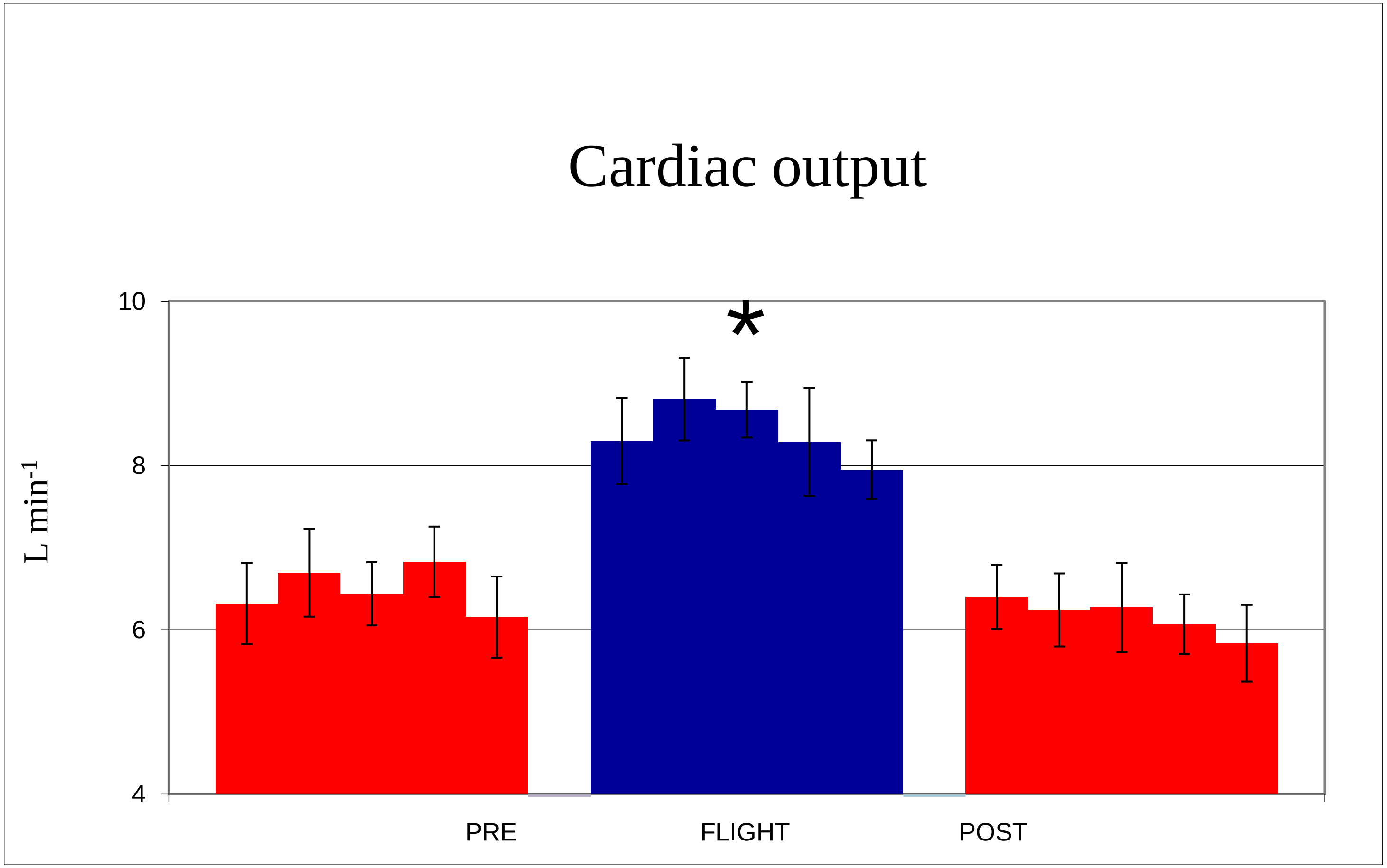
(N = 6 males)


24-h mean arterial pressure
mm Hg
120
100
80
*
PRE
FLIGHT
POST

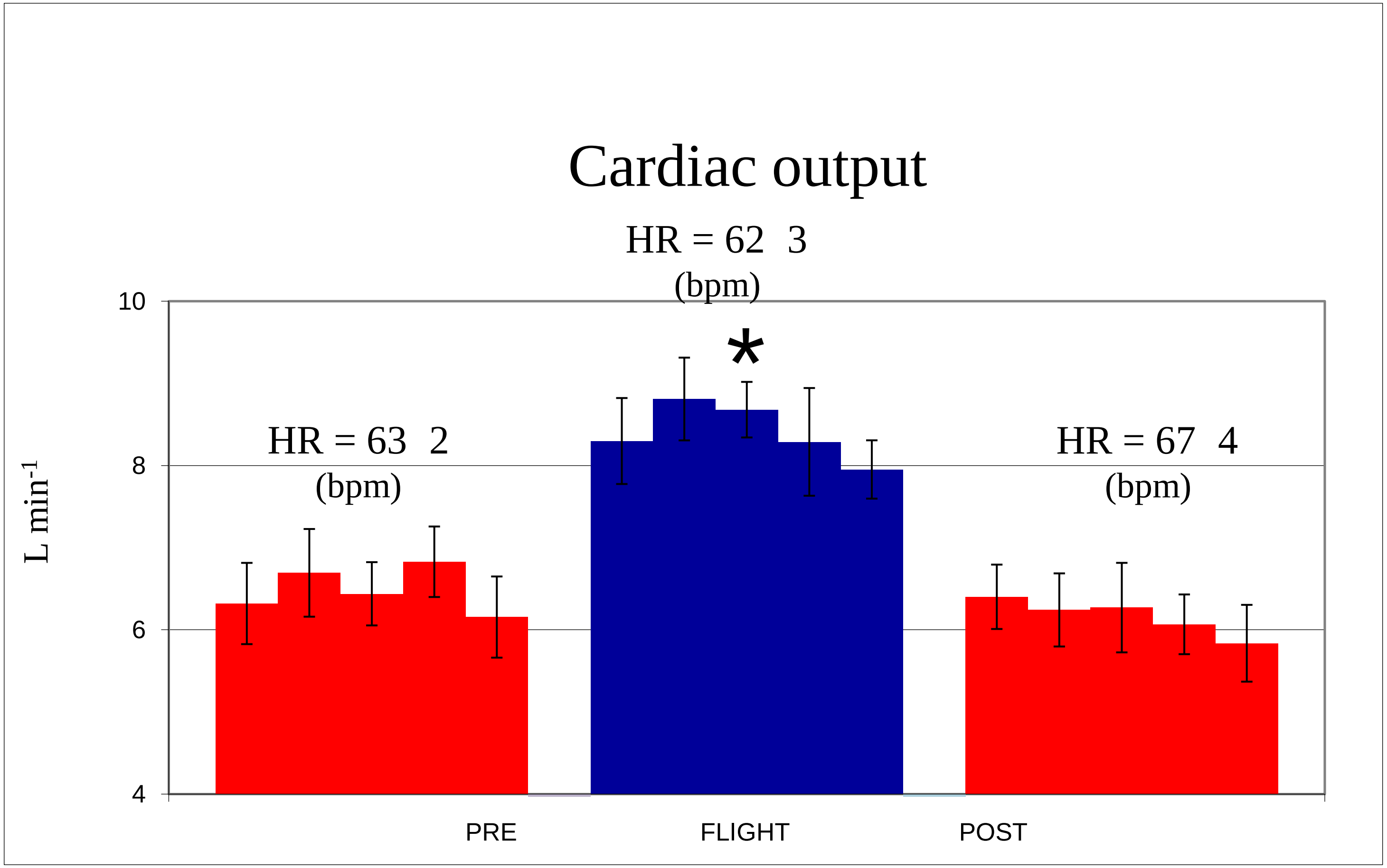

24-h mean arterial pressure
120
100
80
mm Hg
103 3
93 31
*
105 3
PRE
FLIGHT
POST


24-h systolic arterial pressure
mm Hg
160
140
120
100
*
PRE
FLIGHT
POST

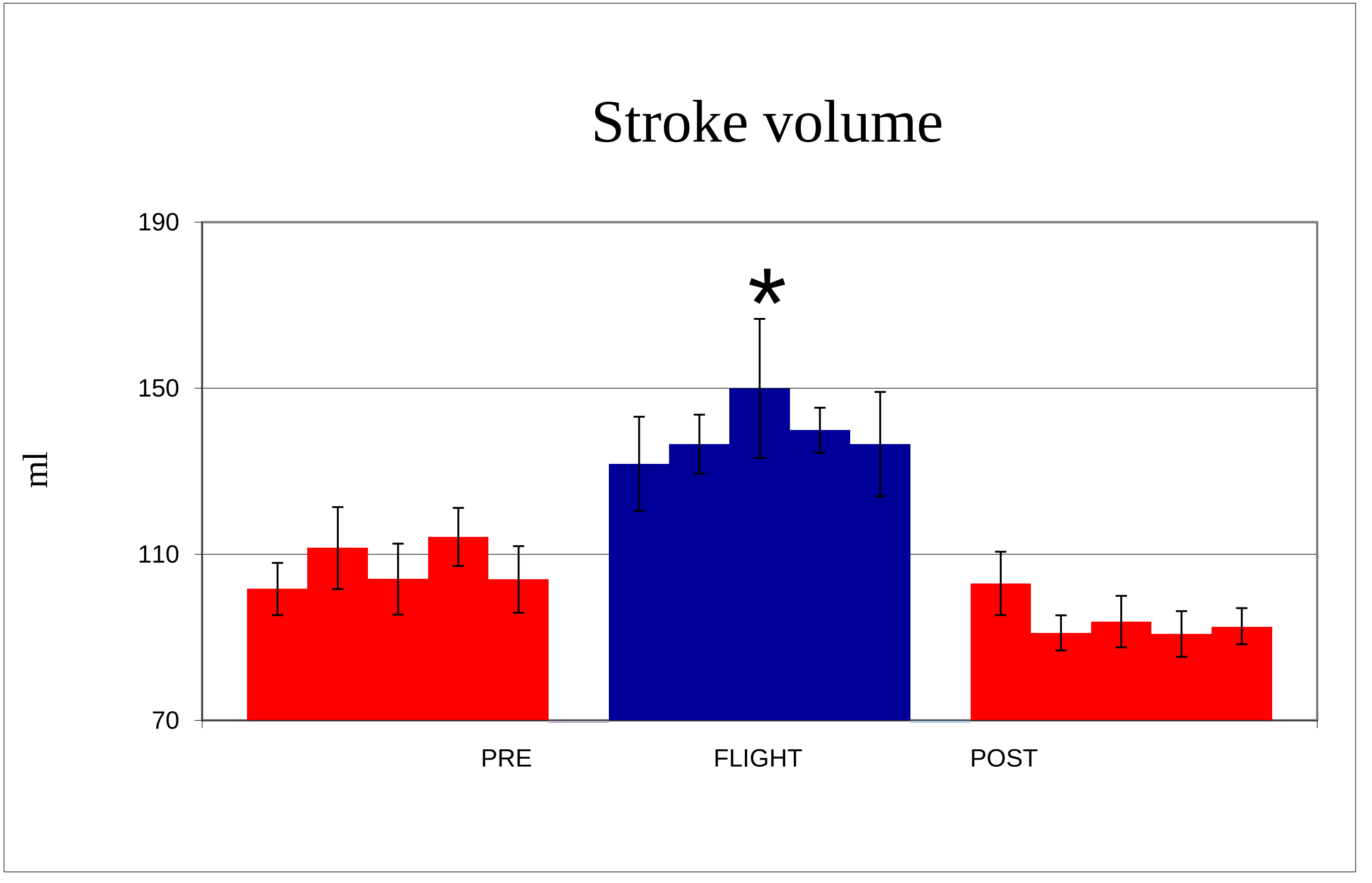

24-h diastolic arterial pressure
mm Hg
100
80
60
*
PRE
FLIGHT
POST



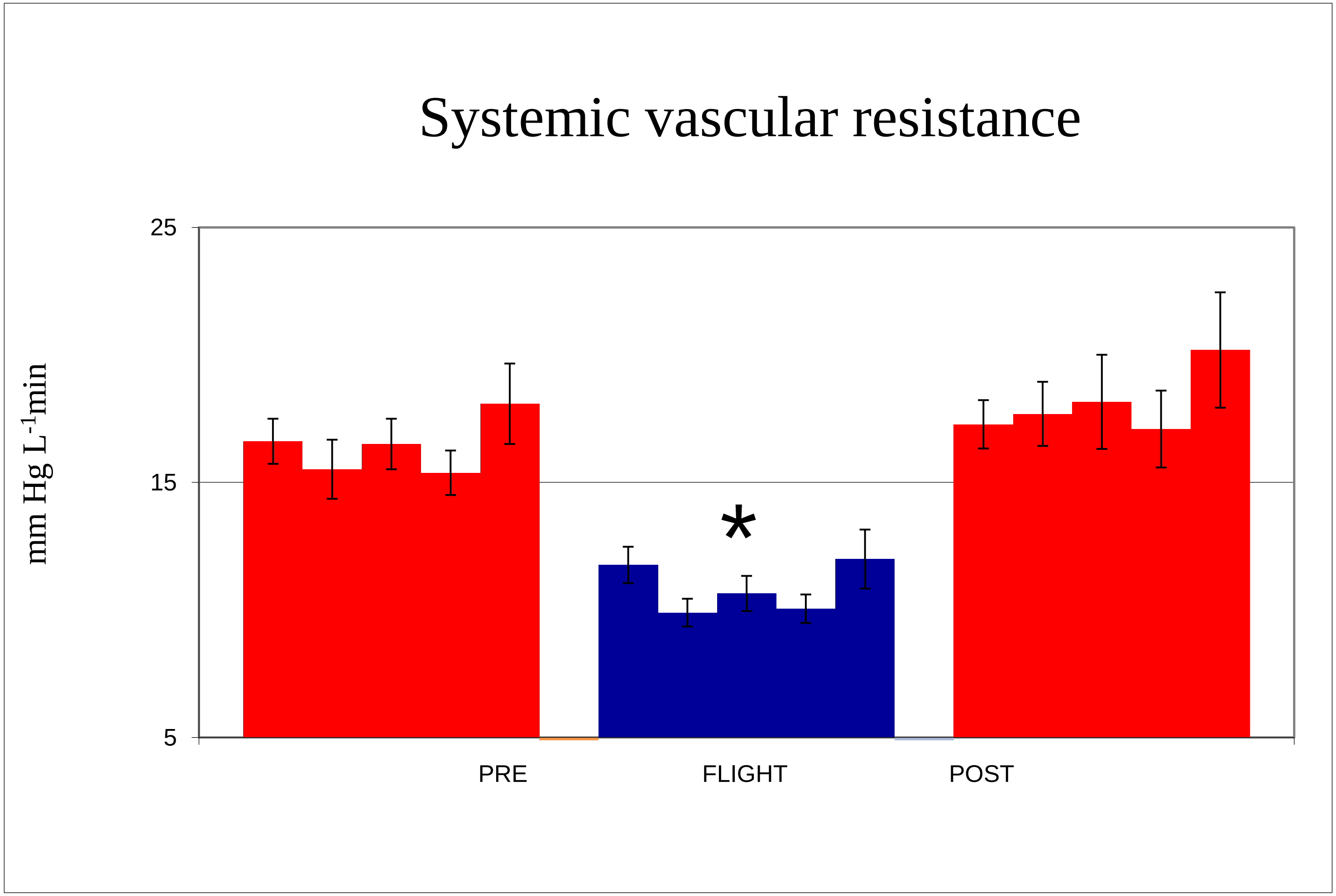
Cardiac output
L min-1
10
8
6
4
*
PRE
FLIGHT
POST

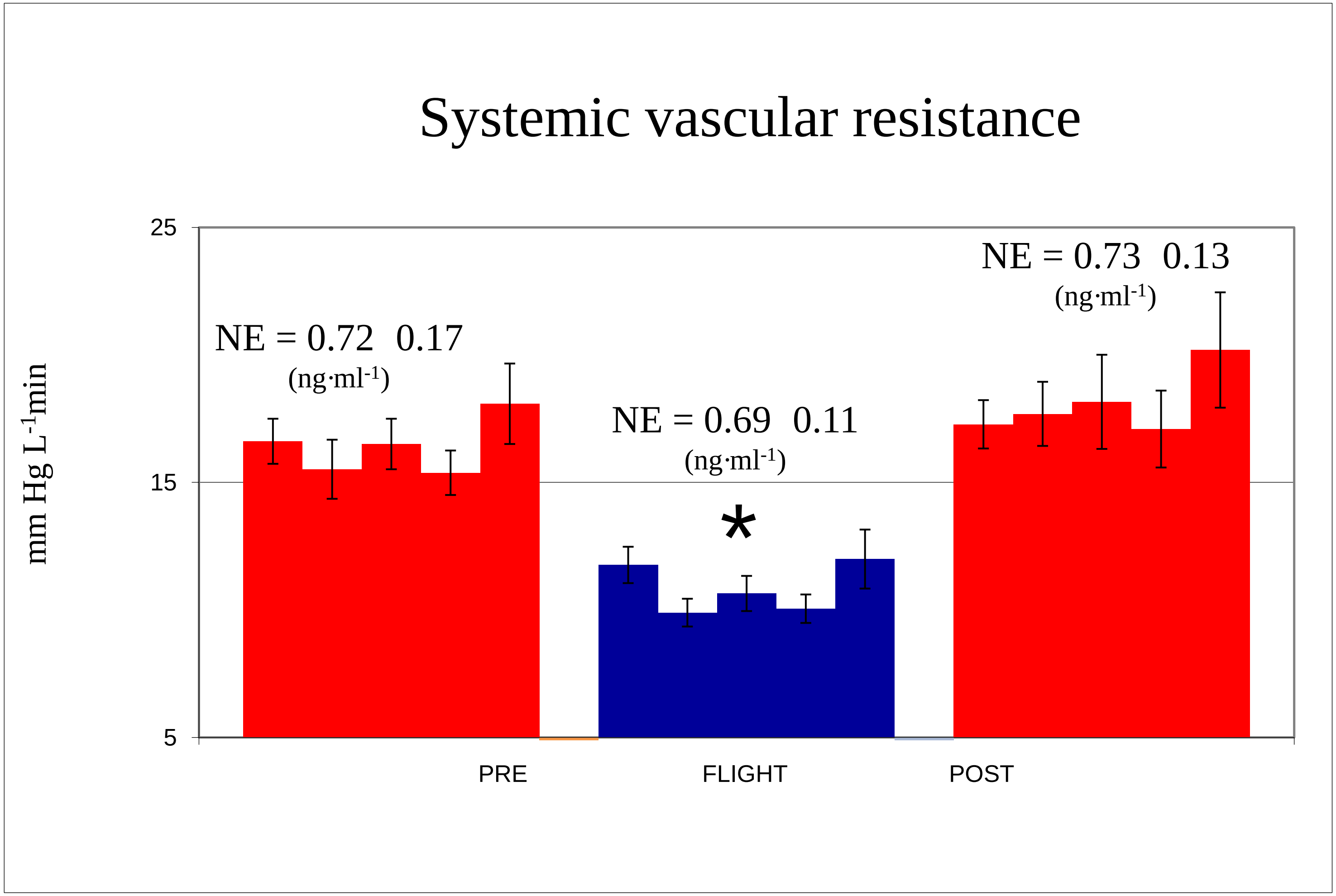


Cardiac output
HR = 62 3
(bpm)
*
HR = 63 2
(bpm)
HR = 67 4
(bpm)
L min-1
10
8
6
4
PRE
FLIGHT
POST

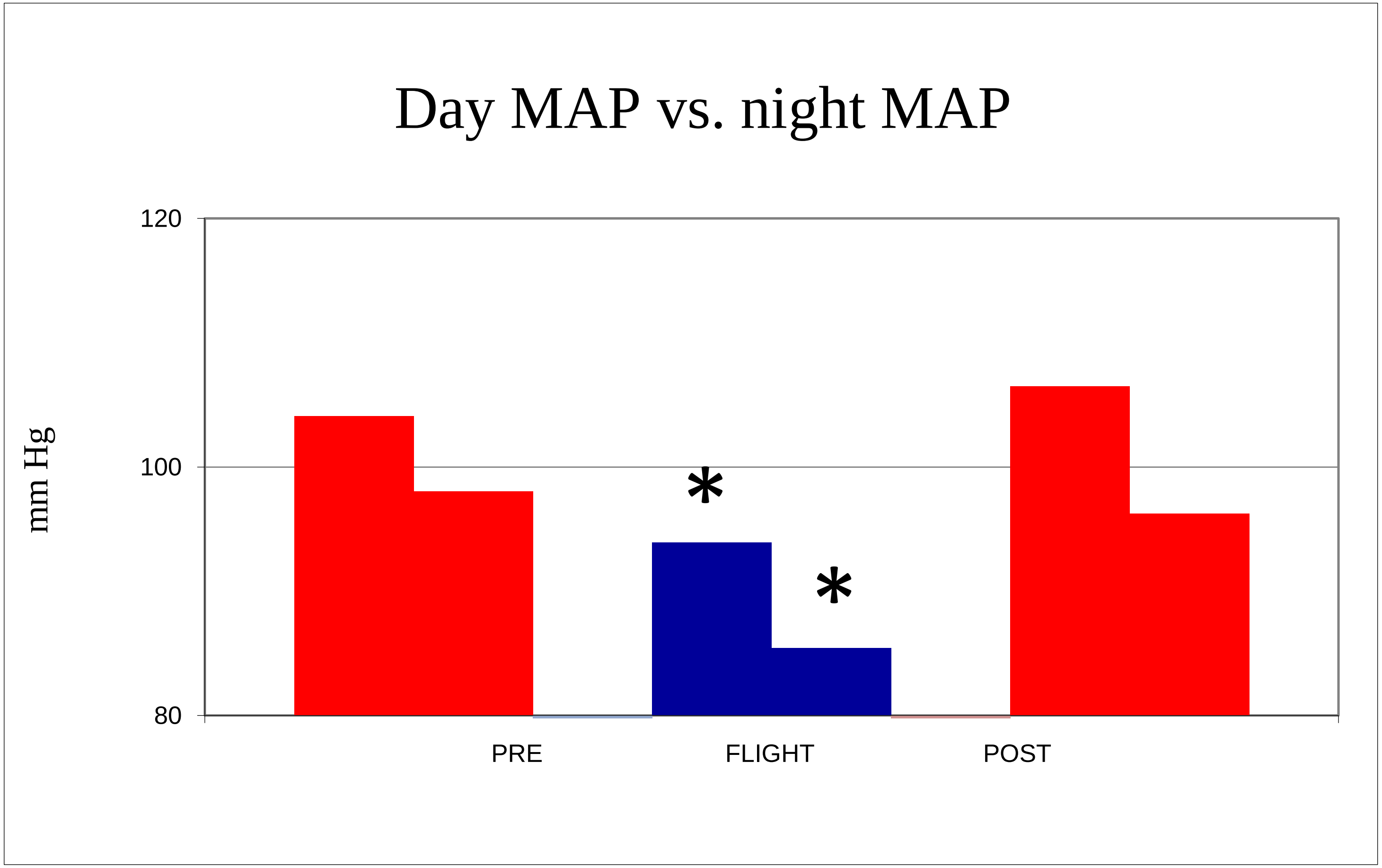


Stroke volume
ml
190
150
110
70
*
PRE
FLIGHT
POST


Systemic vascular resistance
mm Hg L^{-1}min
25
15
5
*
PRE
FLIGHT
POST



Systemic vascular resistance
mm Hg L-1min
25
15
5
NE = 0.72 0.17
(ng·ml-1)
NE = 0.69 0.11
(ng·ml-1)
*
NE = 0.73 0.13
(ng·ml-1)
PRE
FLIGHT
POST



Day MAP vs. night MAP
mm Hg
120
100
80
*
*
PRE
FLIGHT
POST

Conclusions:

Months of space flight on the ISS:

- 24-h ambulatory BP ↓
- SV and thus CO ↑
- Systemic vascular resistance ↓
- SNA →
- Night dip of BP →

Mechanisms:

Weightlesness?

Chronic pulsatile baroreceptor stimulation by increased central blood volume (increased SV and thus CO).

<u>But</u> what about the high SNA?

Exercise training effect?

<u>But</u> HR and plasma NE unchanged!

High salt intake?

<u>But</u> 24-h renal Na^+ excretion unchanged!

Other factors (radiation, oxidative stress etc.)?

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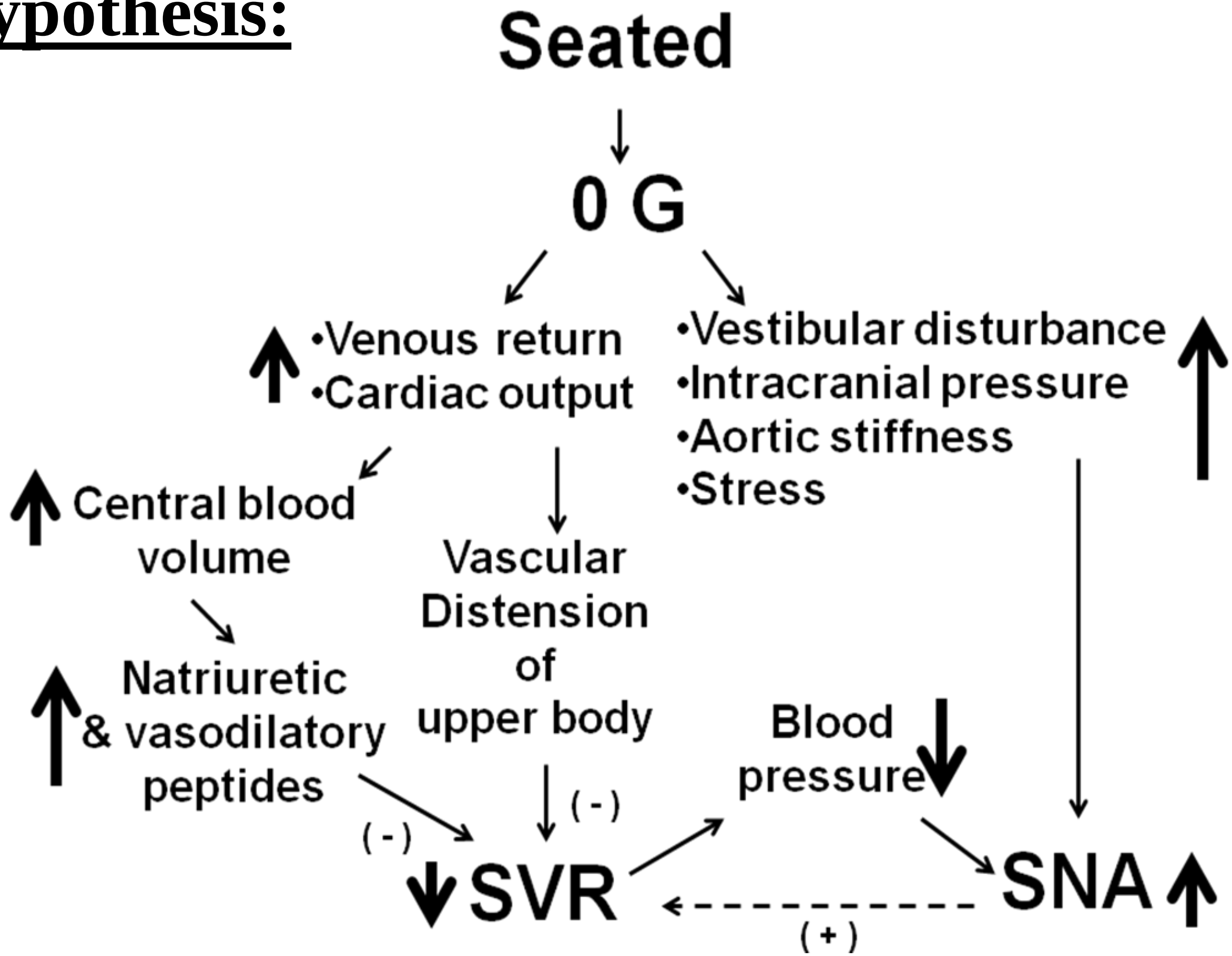
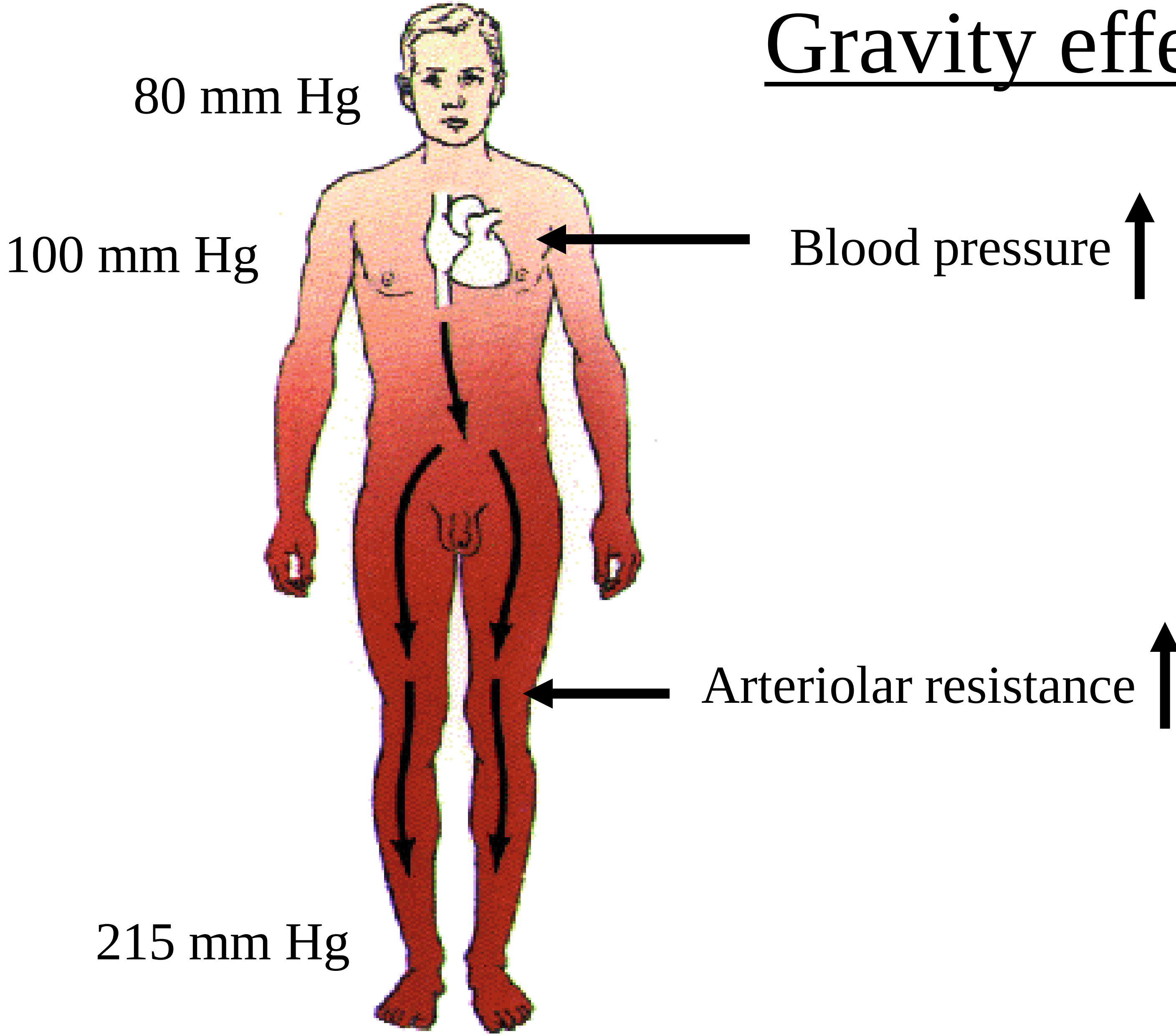
Other factors (radiation, oxidative stress etc.)?

Hypothesis:

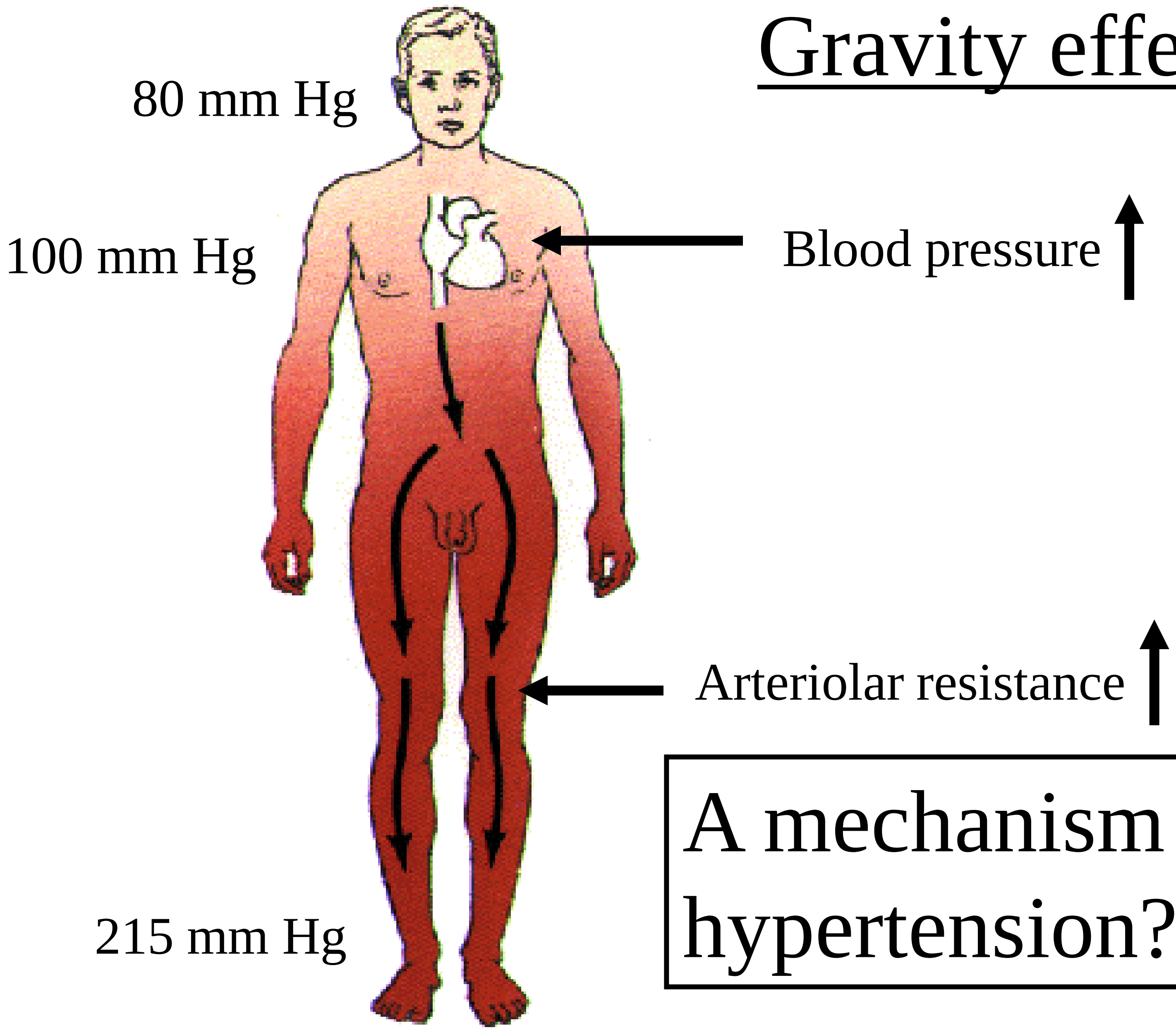


Norsk & Christensen
Respir .Physiol. Neurobiol.
169 (Suppl. 1):S26-9, 2009.

Gravity effects:



Gravity effects:



A mechanism for hypertension???

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<u>Co-authors</u>

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Simone Thomas (ESA)
Astronauts (ESA)

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Clinic at NASA-Johnson Space Center
Astronauts

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