Tolerance to central hypovolemia: The influence of oscillations in arterial pressure and cerebral blood velocity

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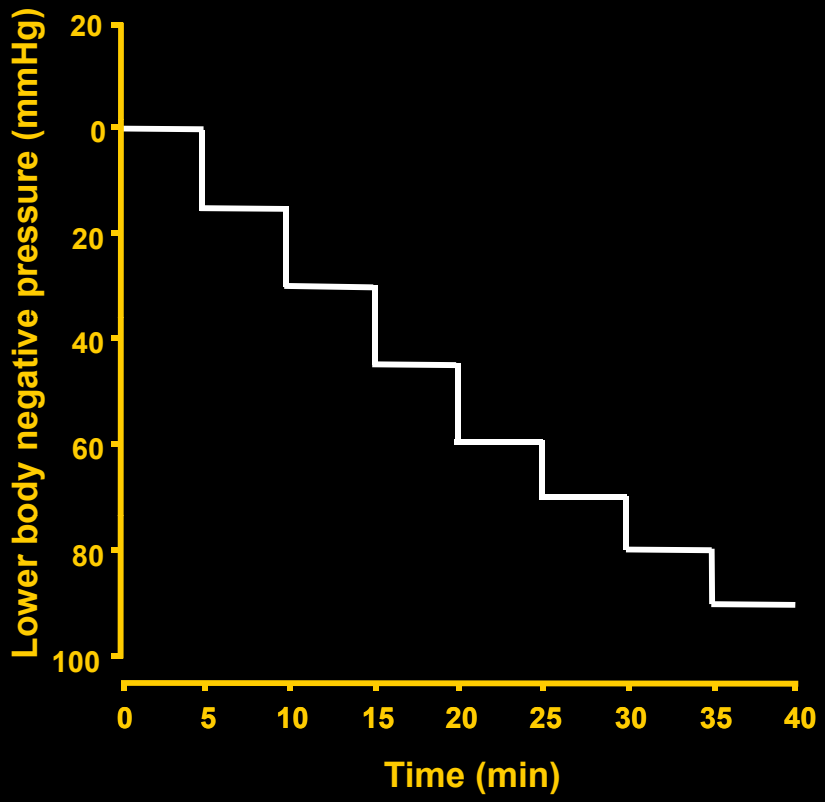
Tolerance to Hemorrhage

- Humans and animals with traumatic and/or hemorrhagic injuries – differential ability to survive
  (Shoemaker et al., Arch Surg 1973; Bishop et al., Crit Care Med 1993;Torres et al., Am J Physiol 2004; Klemcke et al., Shock 2008)
- Protective physiological mechanisms
  - Genetic and/or environmental
    - Reflex cardiovascular responses to maintain perfusion?
    - Tolerance to tissue ischemia?
- Can you predict a “survivor” prior to injury, or during the early phase of injury?
- Can a “non-survivor” be transformed into a “survivor”?

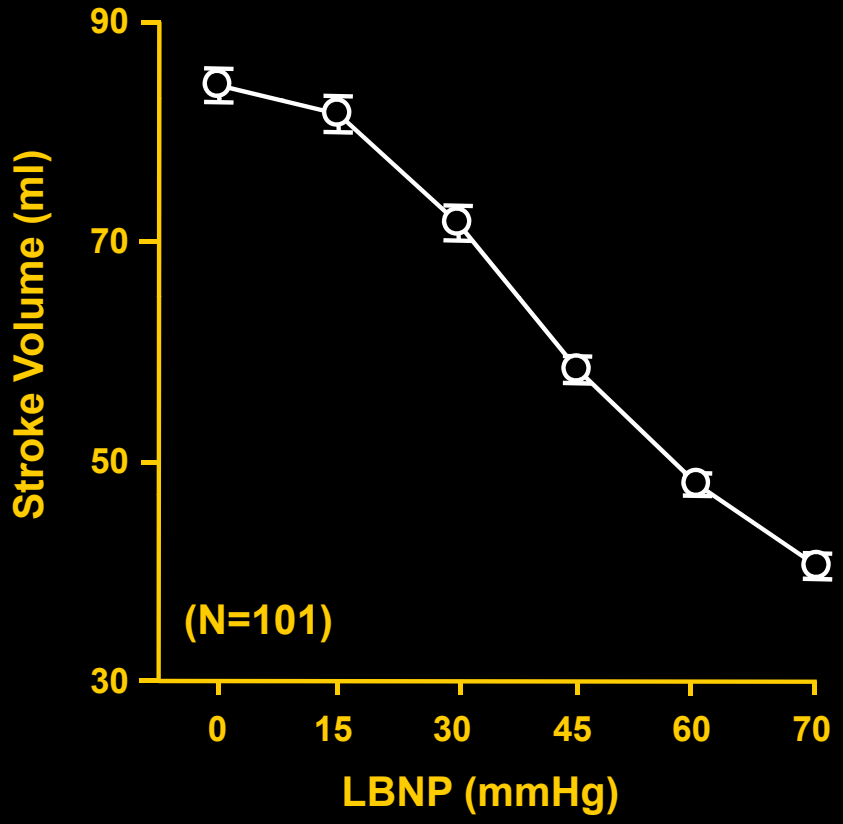
Model of Hemorrhage

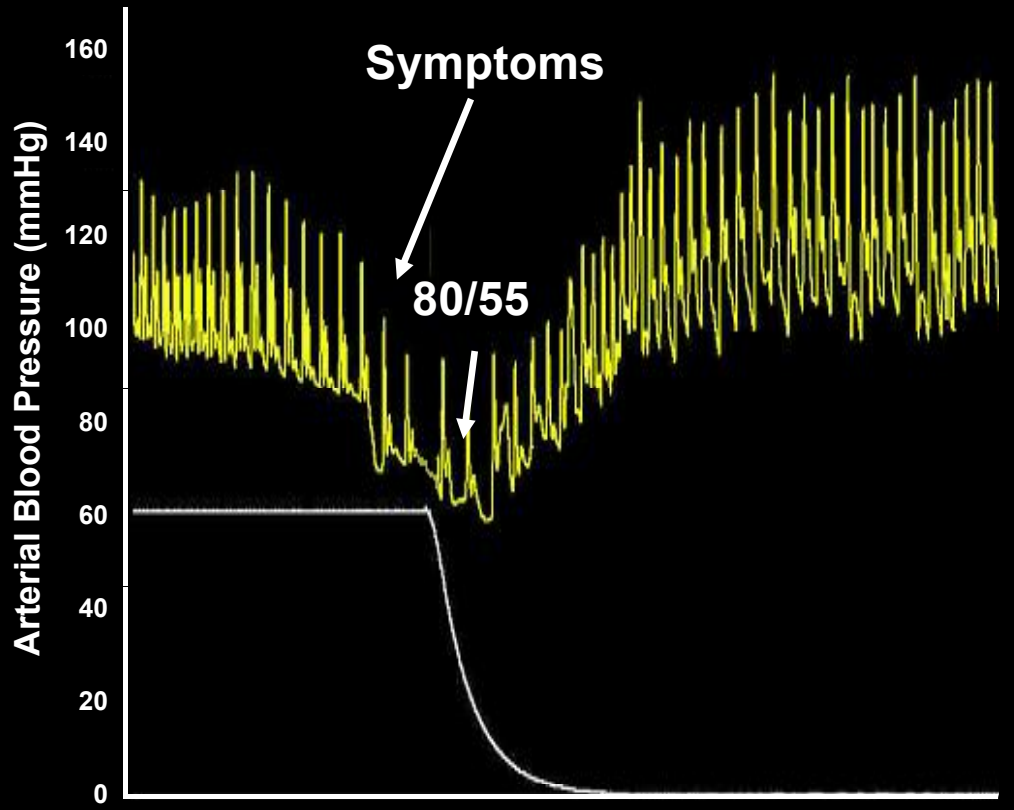
Lower Body Negative Pressure (LBNP)

Experimental Protocol



LBNP vs. Hemorrhage





Research Objectives

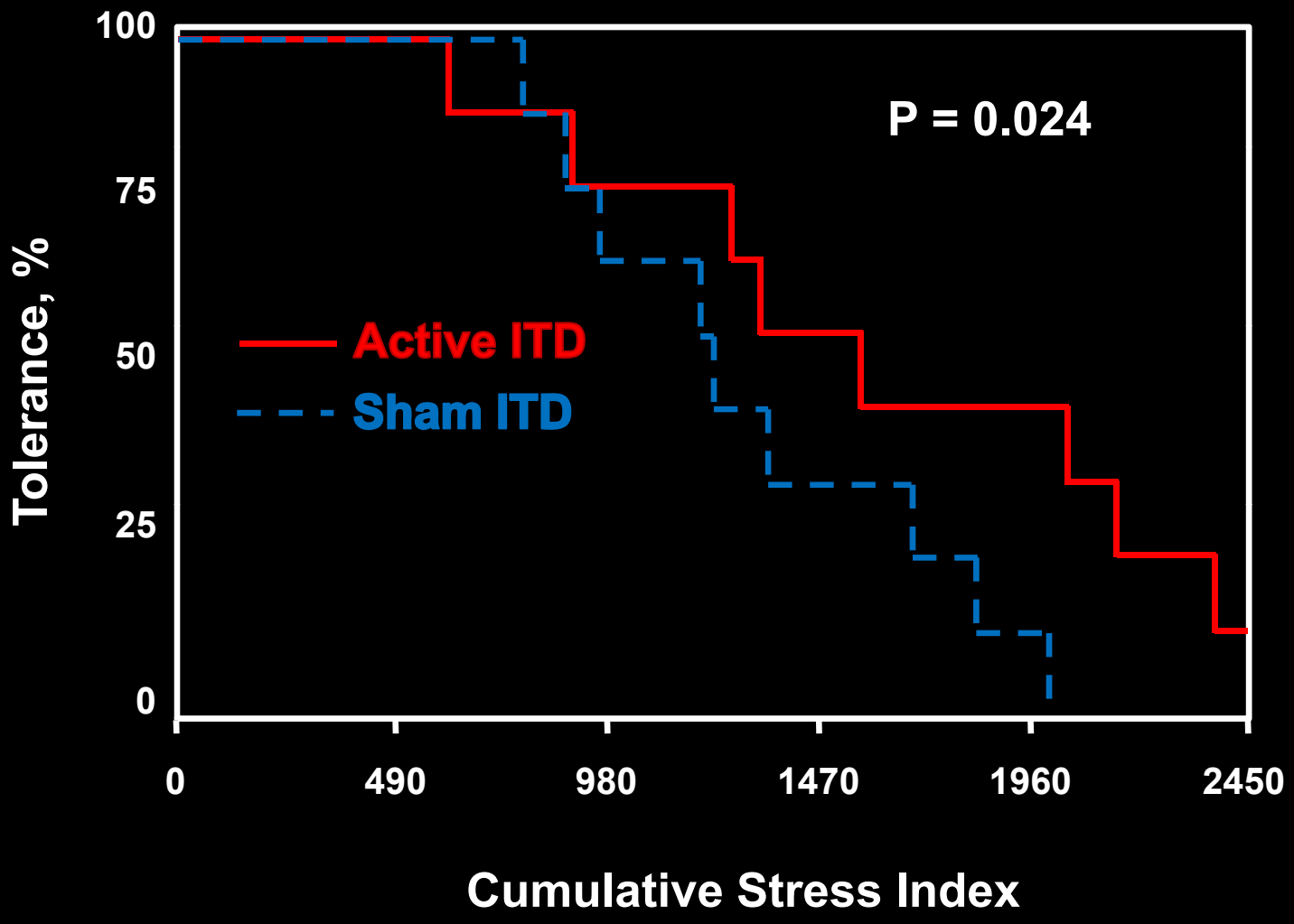
1. Identify *early* physiological markers of central hypovolemia (i.e., hemorrhage)
2. Determine the physiological *differences* between individuals with high and low tolerance to central hypovolemia
3. Investigate methods of *improving* tolerance to central hypovolemia

Inspiratory Resistance

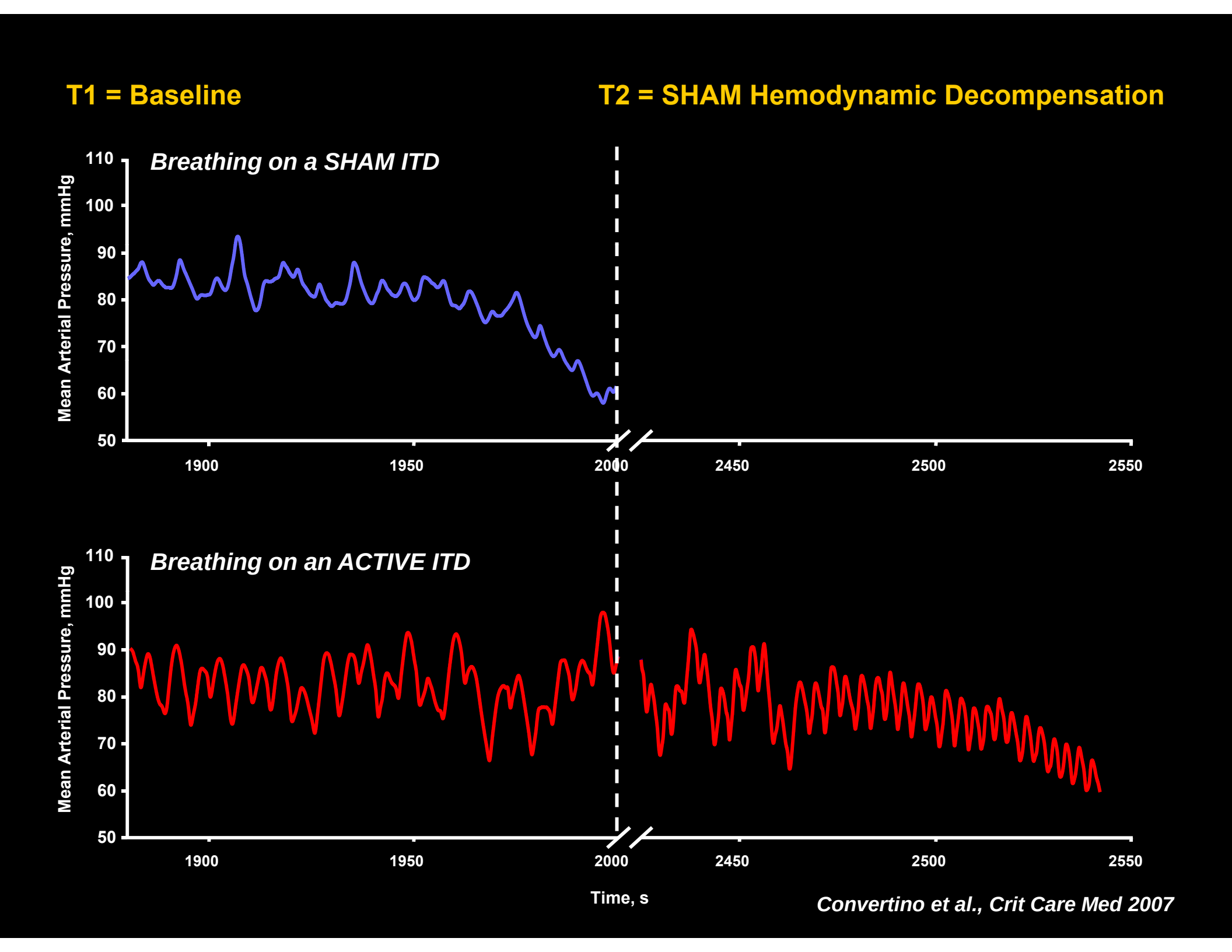
- ResQGARD™ Impedance Threshold Device *(Advanced Circulatory Systems Inc.)*
- Further reduces intrathoracic pressure during spontaneous inspiration *(Lurie et al. Crit Care Med 2004)*
- Increases venous return and ventricular preload
- Elevates cardiac output and arterial blood pressure *(Convertino et al. Crit Care Med 2004; Lurie et al. Crit Care Med 2004; Ryan et al., J Appl Physiol 2008)*

Inspiratory Resistance & Central Hypovolemia

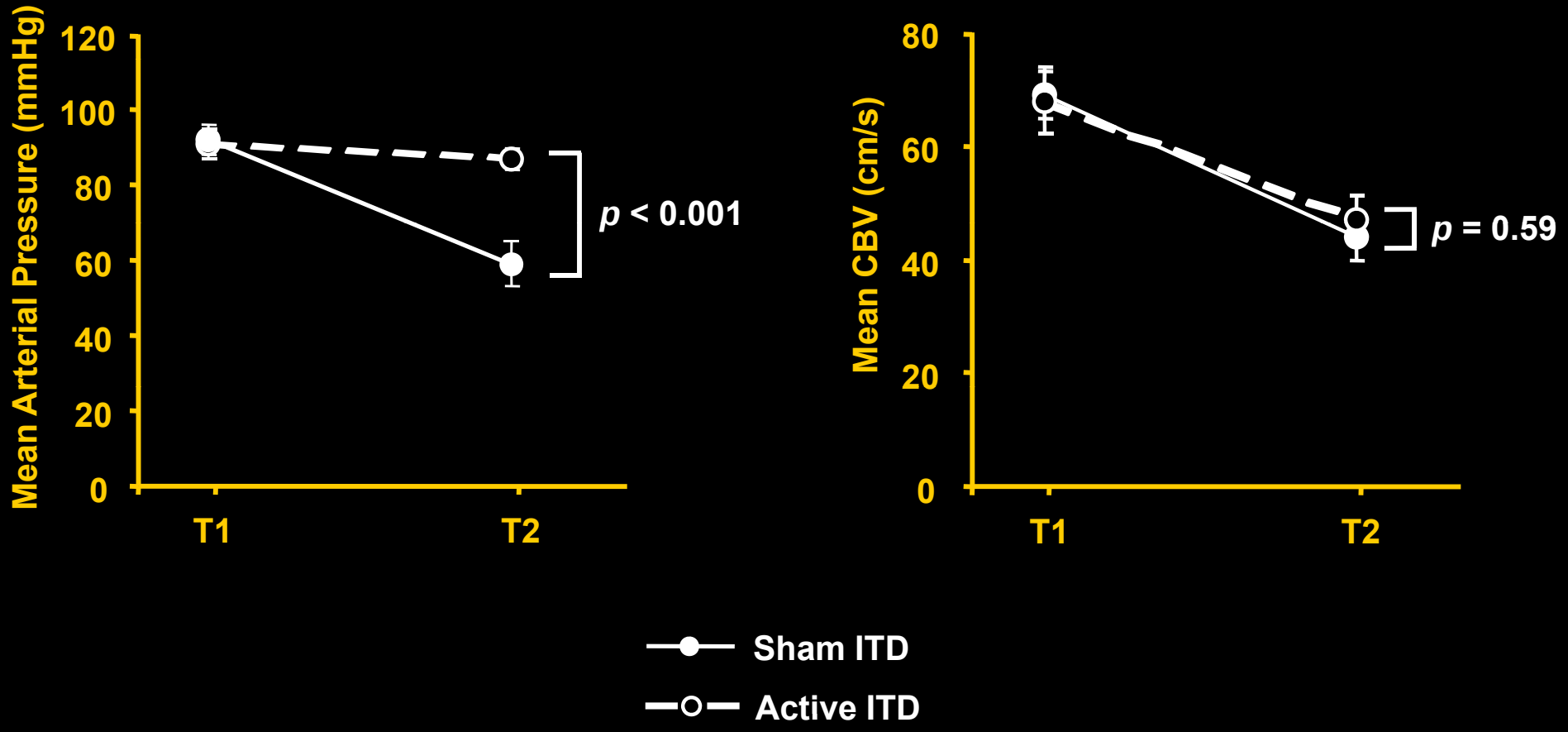
ITD breathing *increased* tolerance to central hypovolemia



Convertino et al., Crit Care Med 2007

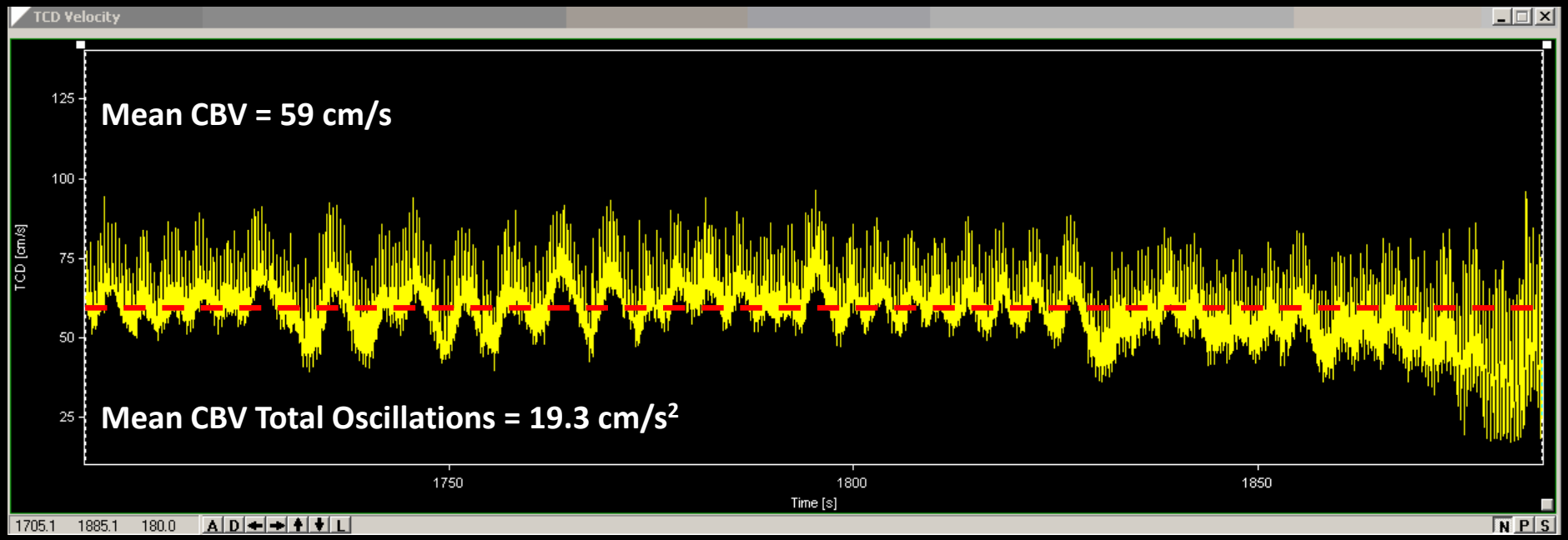

T1 = Baseline
T2 = SHAM Hemodynamic Decompensation
Breathing on a SHAM ITD
Breathing on an ACTIVE ITD
Mean Arterial Pressure, mmHg
110
100
90
80
70
60
50
1900
1950
2000
2450
2500
2550
Time, s
Convertino et al., Crit Care Med 2007

Protective Mechanism?

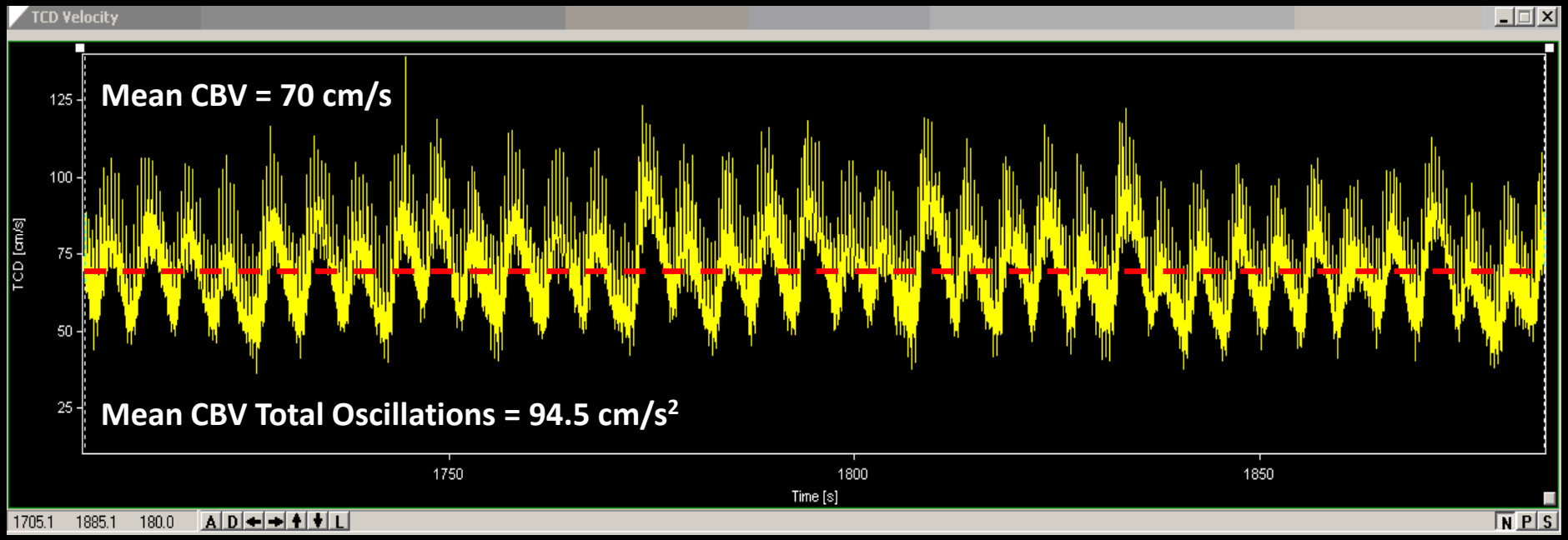


Rickards et al., Am J Physiol 2007

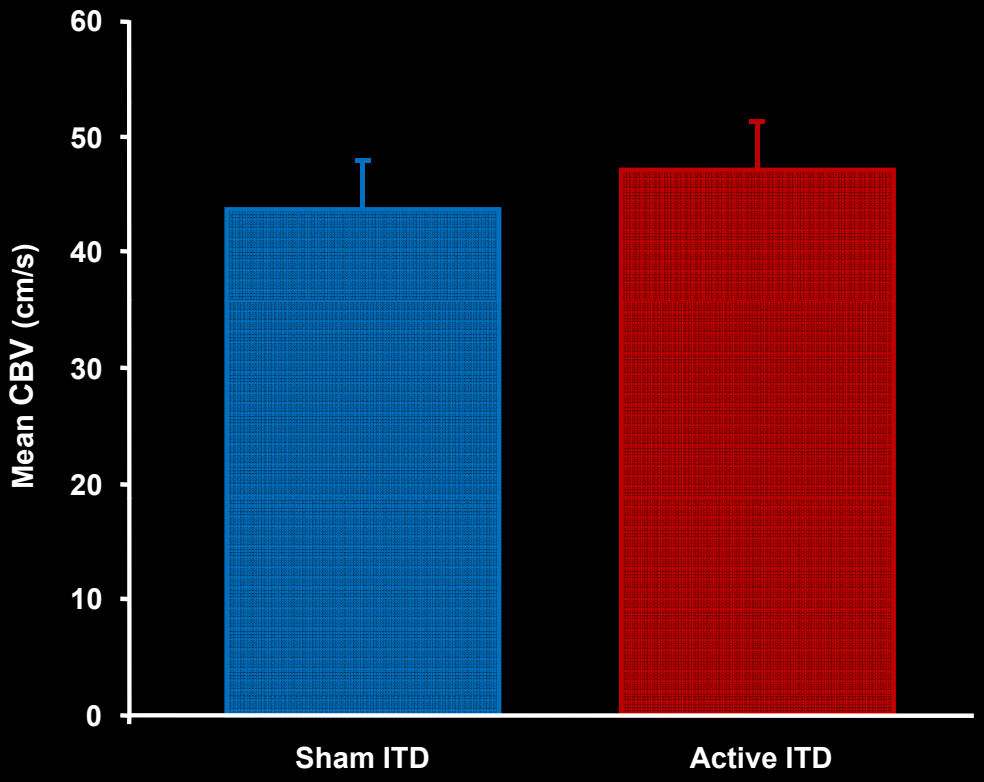
Sham ITD CBV (Presyncope – T2)

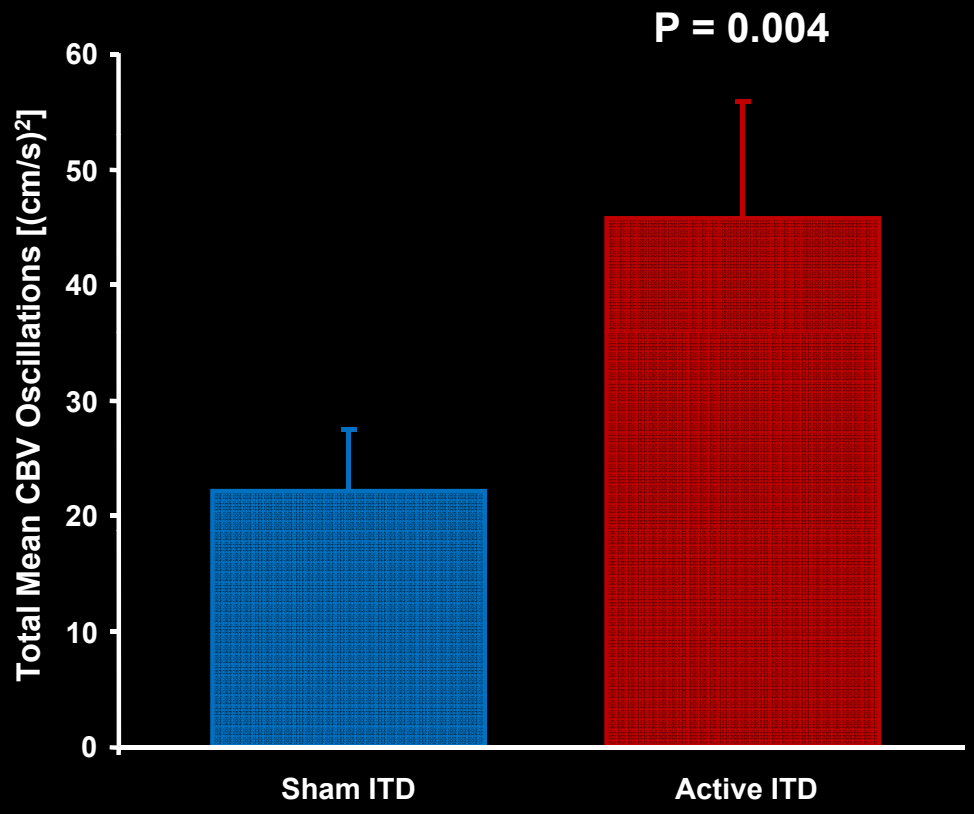


Active ITD CBV (Time of Sham Presyncope – T2)



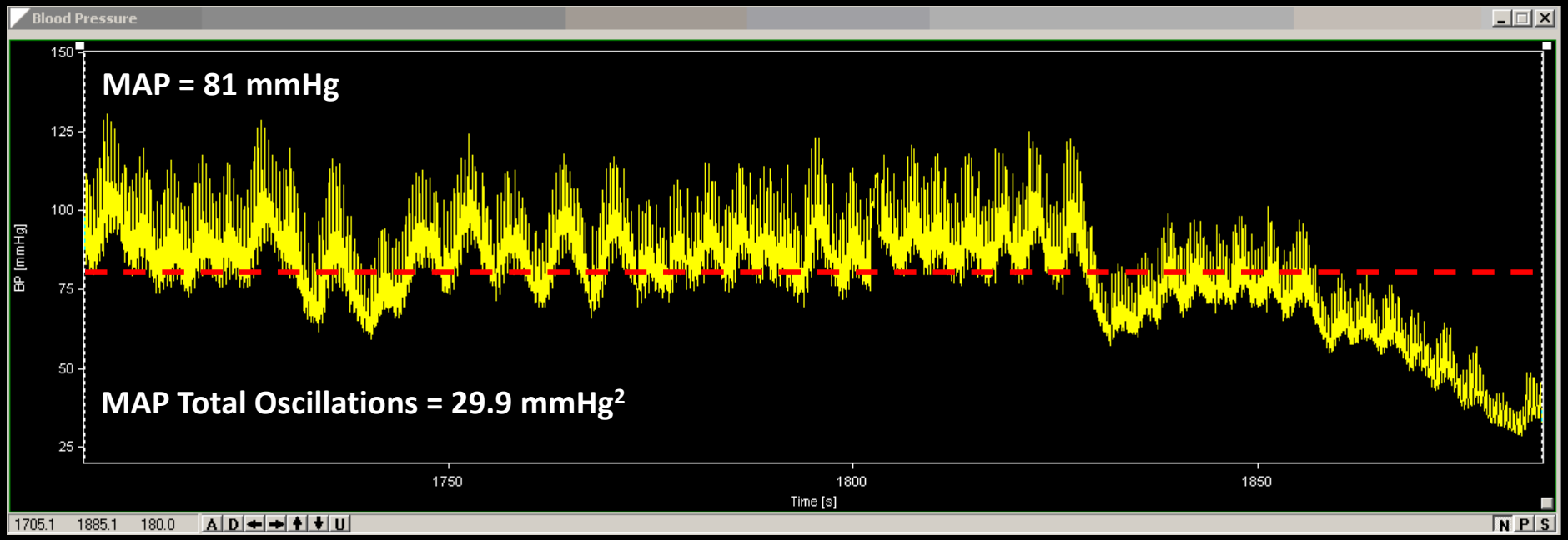
Oscillations - CBV



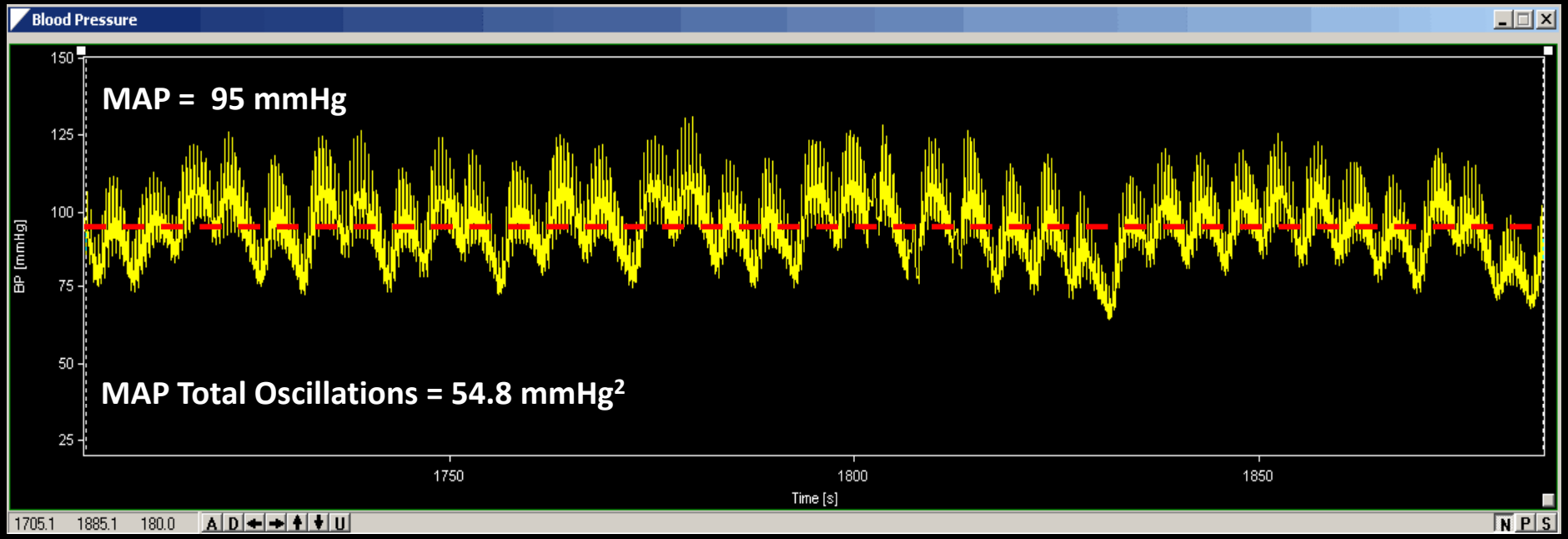


Rickards et al., Am J Physiol 2007

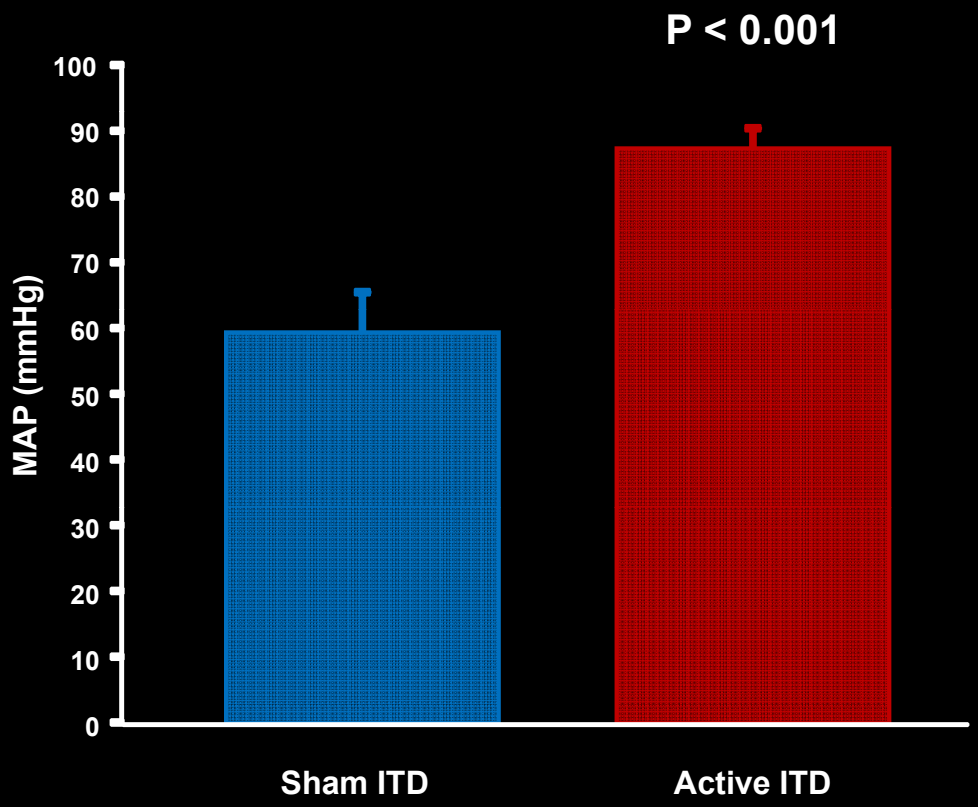
Sham ITD AP (Presyncope – T2)

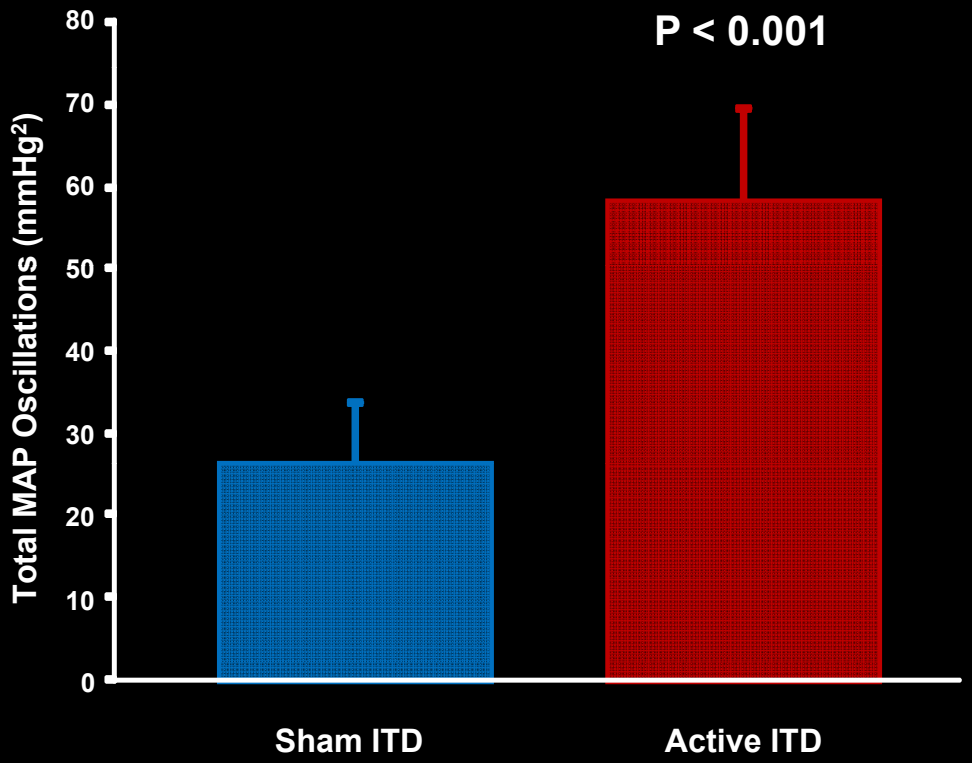


Active ITD AP (Time of Sham Presyncope – T2)



Oscillations – MAP



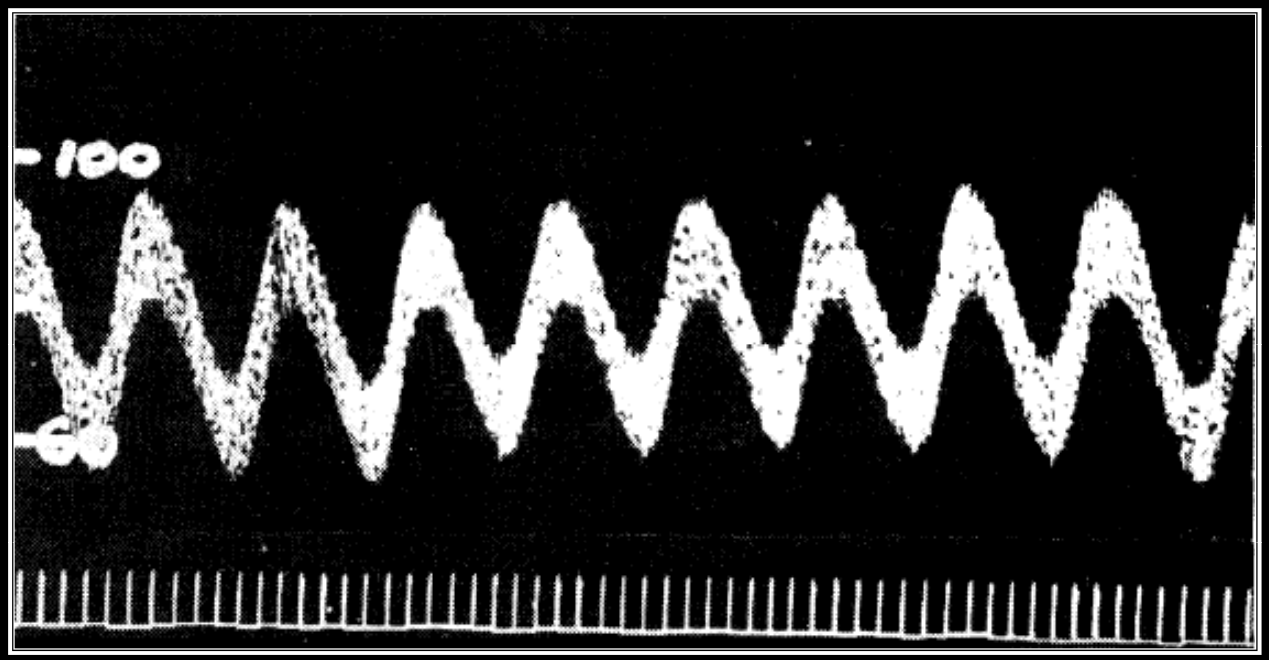


Rickards et al., Am J Physiol 2007

Summary

- Breathing with inspiratory resistance
  - *does not attenuate* the decrease in *mean* cerebral blood flow with reductions in central blood volume
  - *maintains* arterial blood pressure
  - *increases* oscillations in cerebral blood velocity and blood pressure
  - *delays* the onset of cardiovascular collapse and the reporting of presyncopal symptoms
  - *prolongs* tolerance to the reduction in central blood volume
- *Oscillations* in cerebral blood velocity and arterial blood pressure appear to be *protective*

Oscillations with Hemorrhage



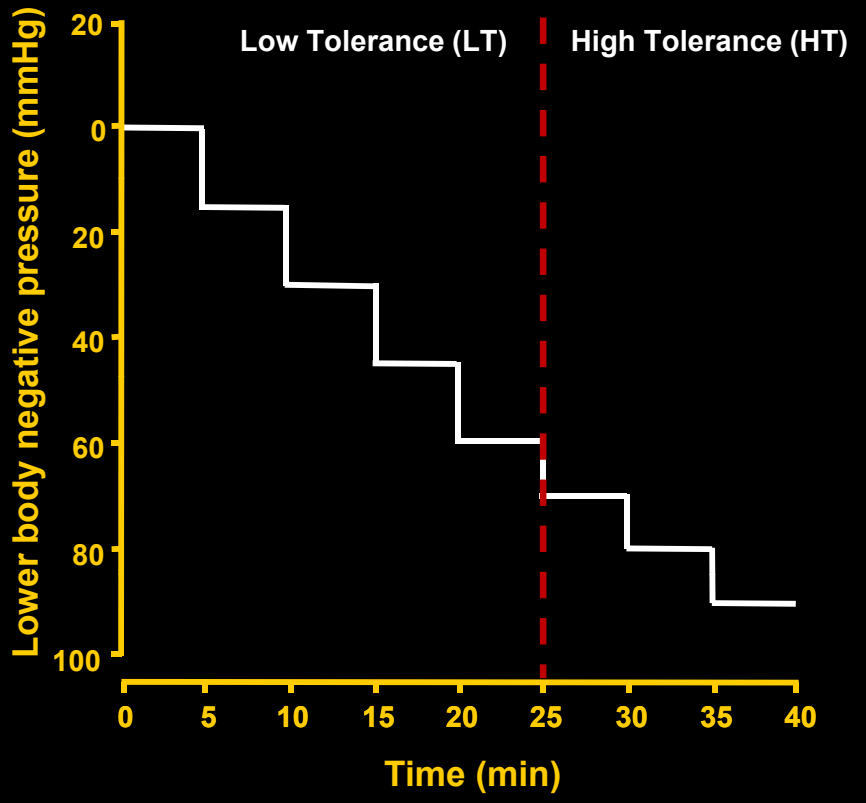
Arterial blood pressure oscillations 1-hour following 25% hemorrhage in a dog

Guyton & Harris. Am J Physiol, 1951

Hypothesis

As induced oscillations in CBV and ABP are associated with an increase tolerance to central hypovolemia, subjects with high tolerance (HT) will display higher endogenous oscillations than subjects with low tolerance (LT)

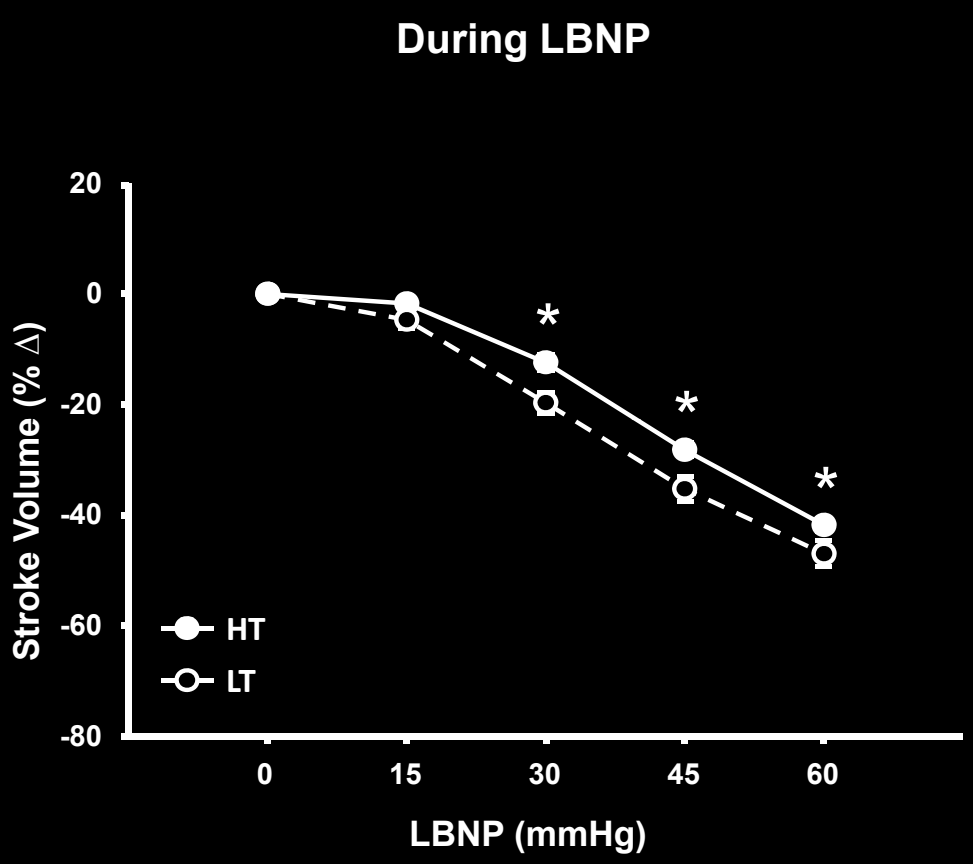
Tolerance to Central Hypovolemia

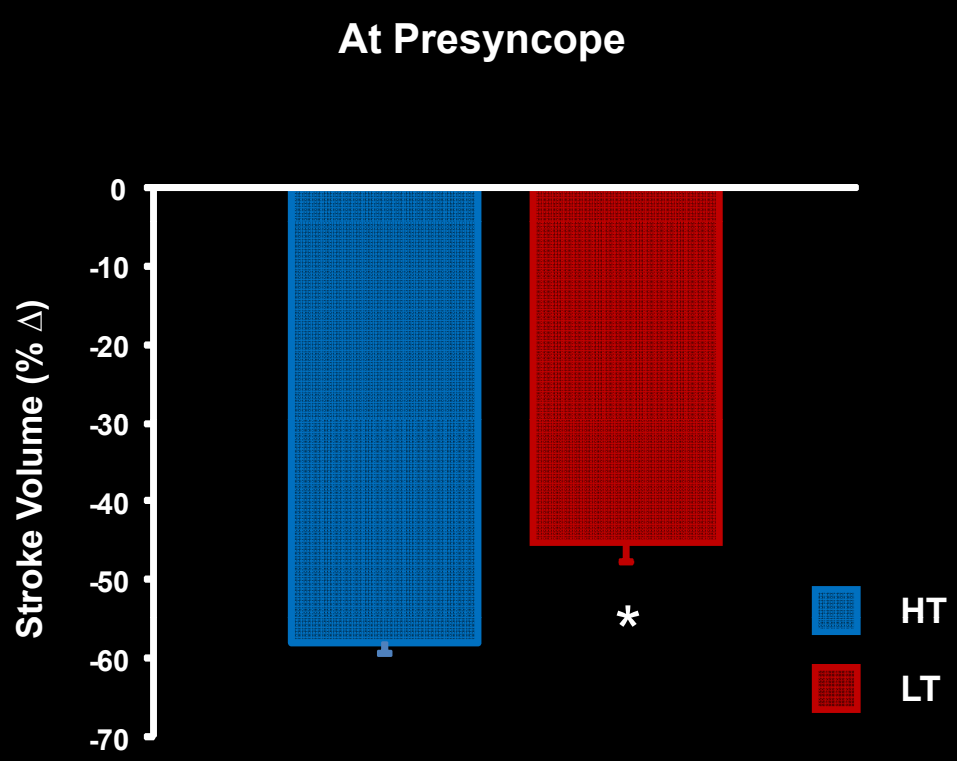


Subject Demographics

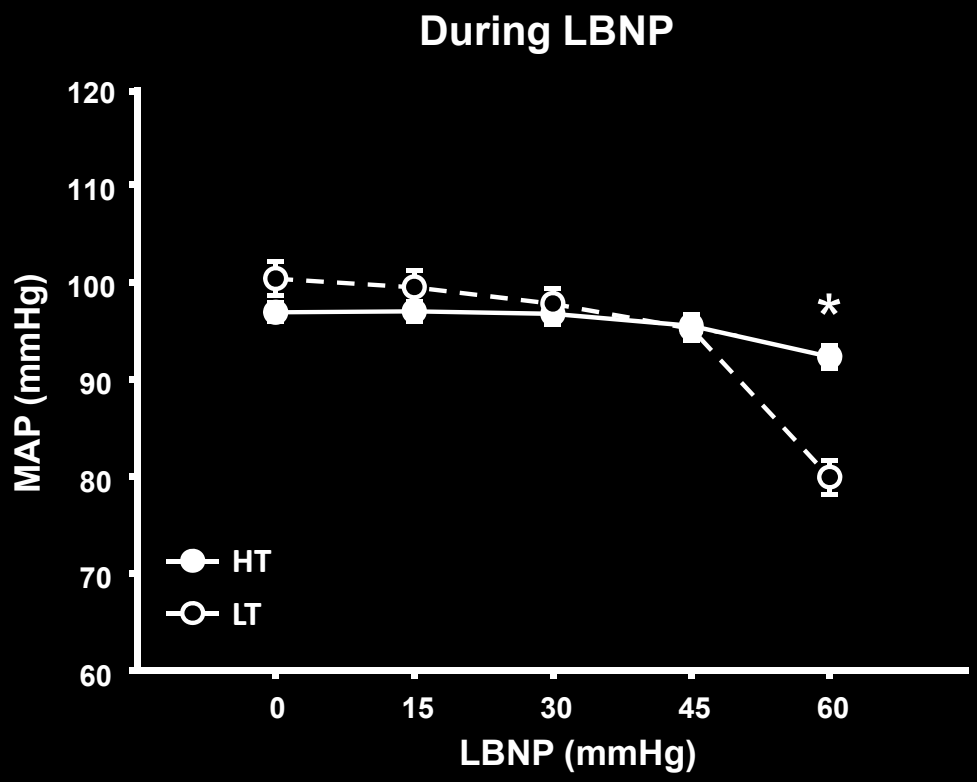
	High Tolerant (HT)	Low Tolerant (LT)	P-Value
N	76 (71%)	31 (29%)	-
LBNP Tolerance Time (sec)	1893 ± 31	1333 ± 21	-
Sex	29F (38%) 47M (62%)	16F (52%) 15M (48%)	0.29
Age (yrs)	29 ± 1	28 ± 1	0.57
Height (cm)	174 ± 1	172 ± 2	0.42
Weight (kg)	76 ± 2	78 ± 4	0.69

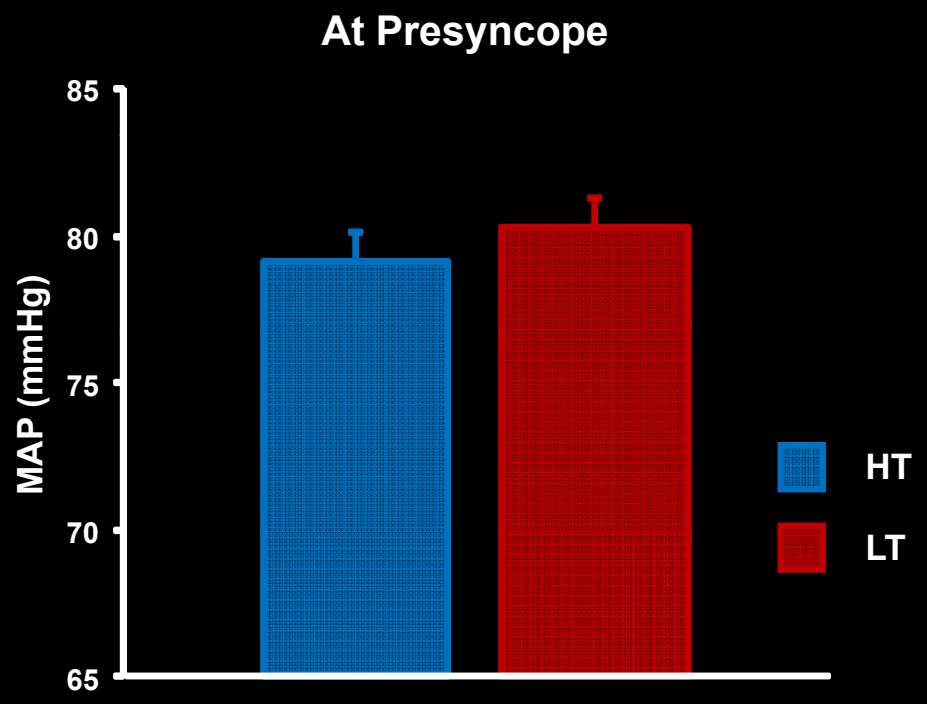
Tolerance to Central Hypovolemia





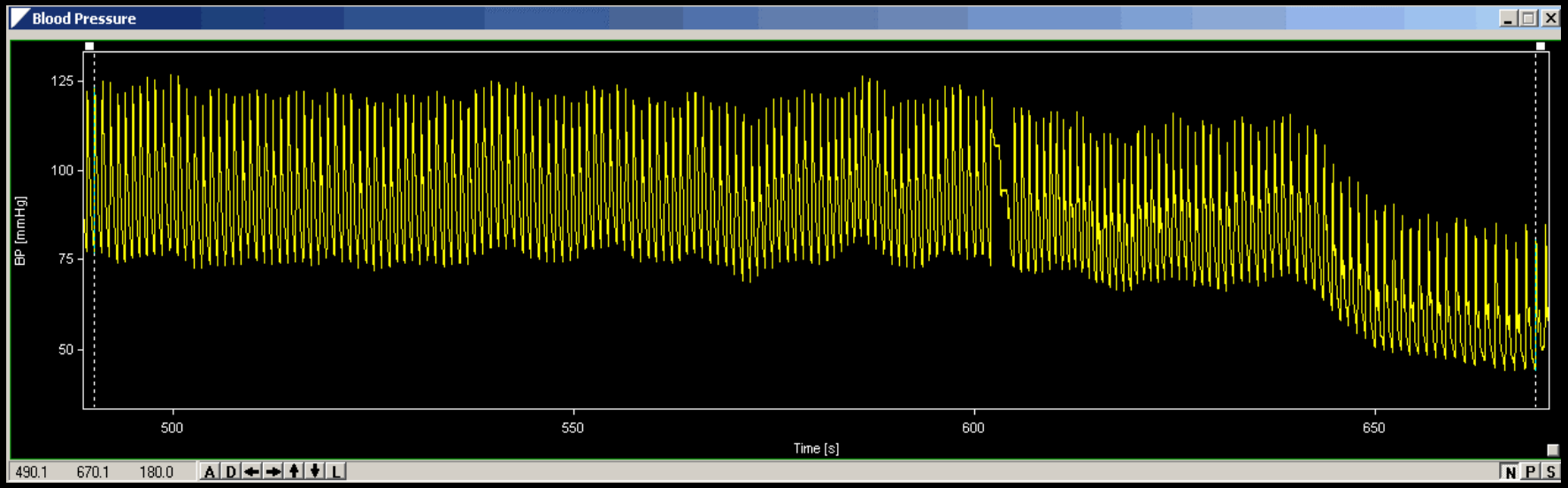
* denotes P ≤ 0.032 between HT and LT





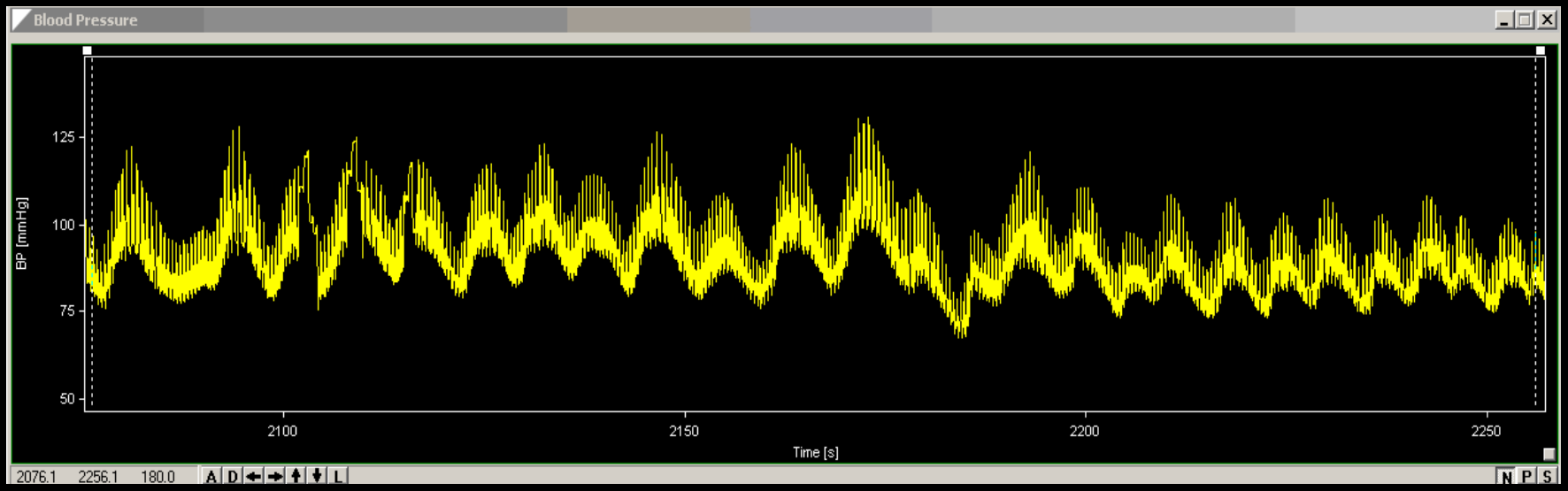
* denotes P ≤ 0.001 between HT and LT

Low Tolerant (max LBNP = -30 mmHg)

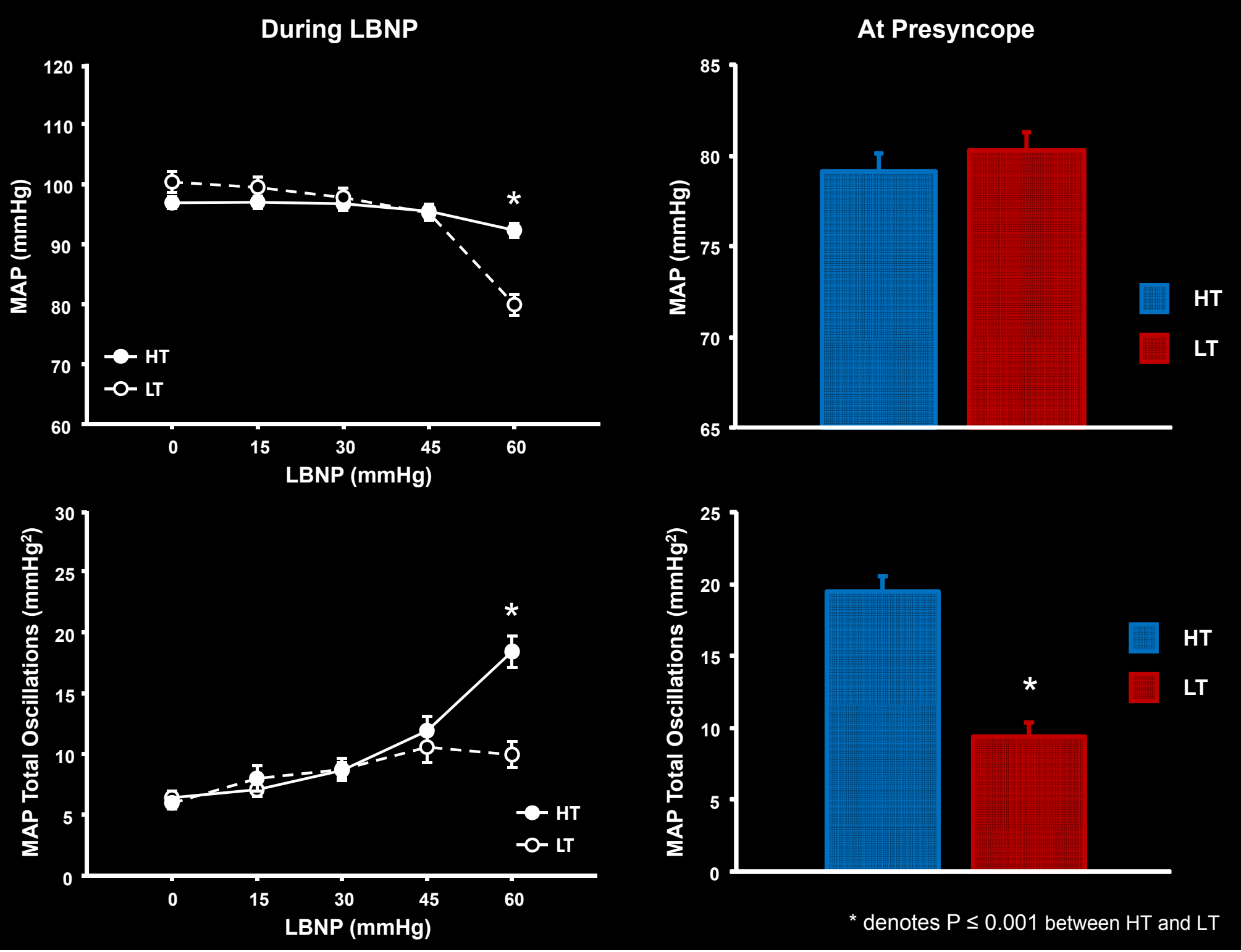


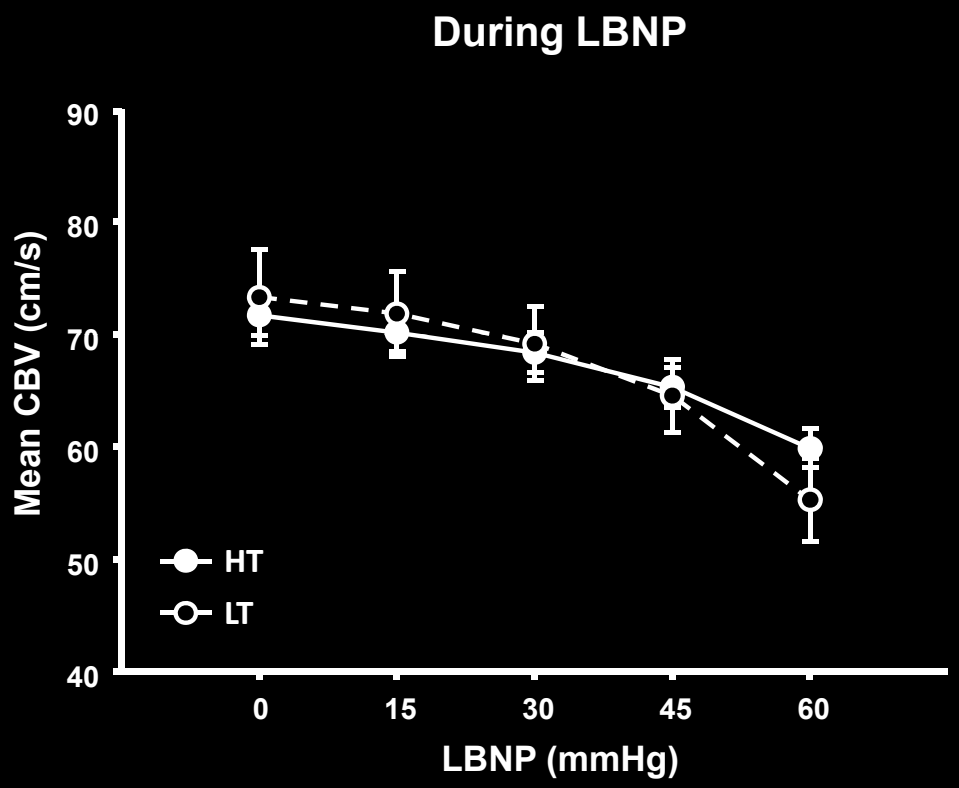
SBP = 116 mmHg, DBP = 70 mmHg, MAP = 87 mmHg

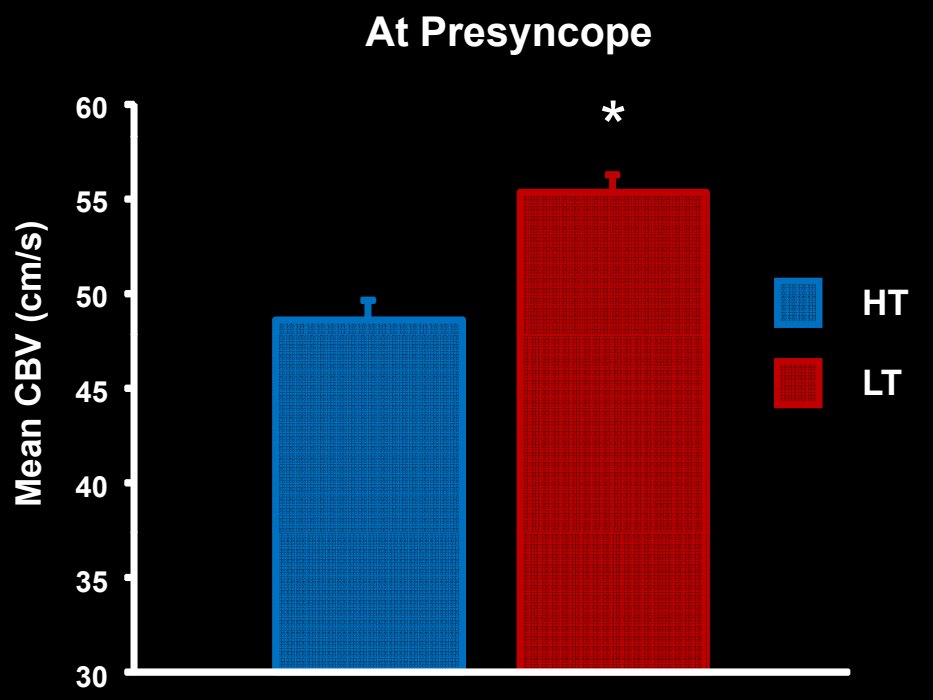
High Tolerant (max LBNP = -80 mmHg)



SBP = 104 mmHg, DBP = 83 mmHg, MAP = 91 mmHg

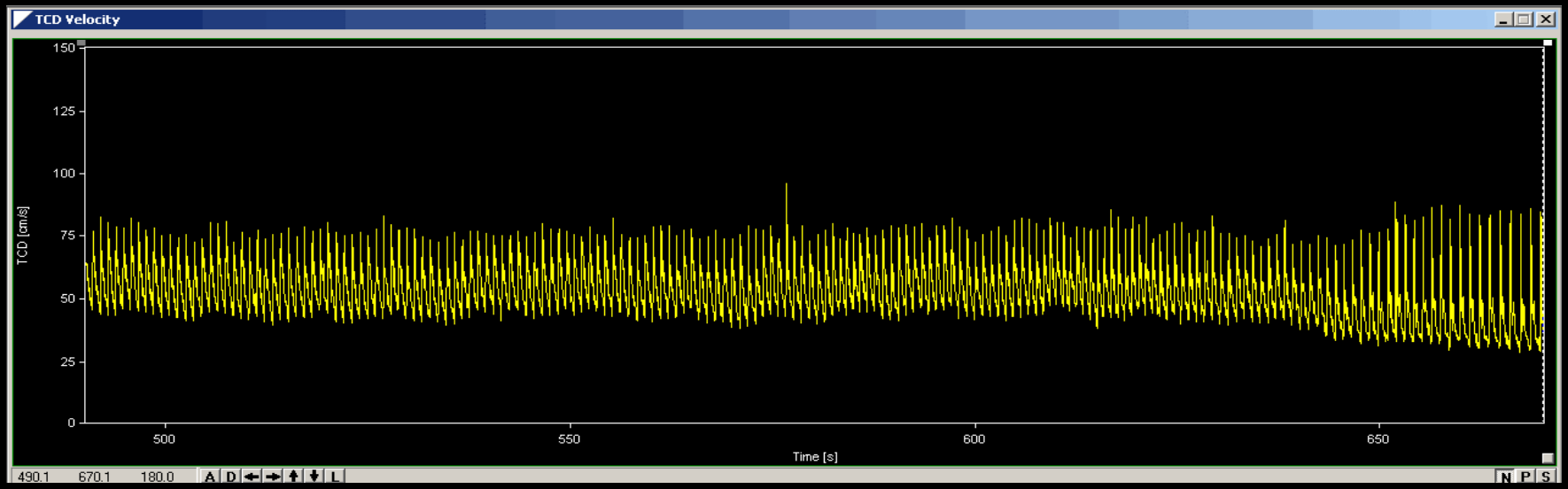

During LBNP
MAP (mmHg)
120
110
100
90
80
70
60
0
15
30
45
60
LBNP (mmHg)
HT
LT
*
At Presyncope
MAP (mmHg)
85
80
75
70
65
HT
LT
MAP Total Oscillations (mmHg²)
30
25
20
15
10
5
0
0
15
30
45
60
LBNP (mmHg)
HT
LT
*
MAP Total Oscillations (mmHg²)
25
20
15
10
5
0
HT
LT
*
* denotes P ≤ 0.001 between HT and LT





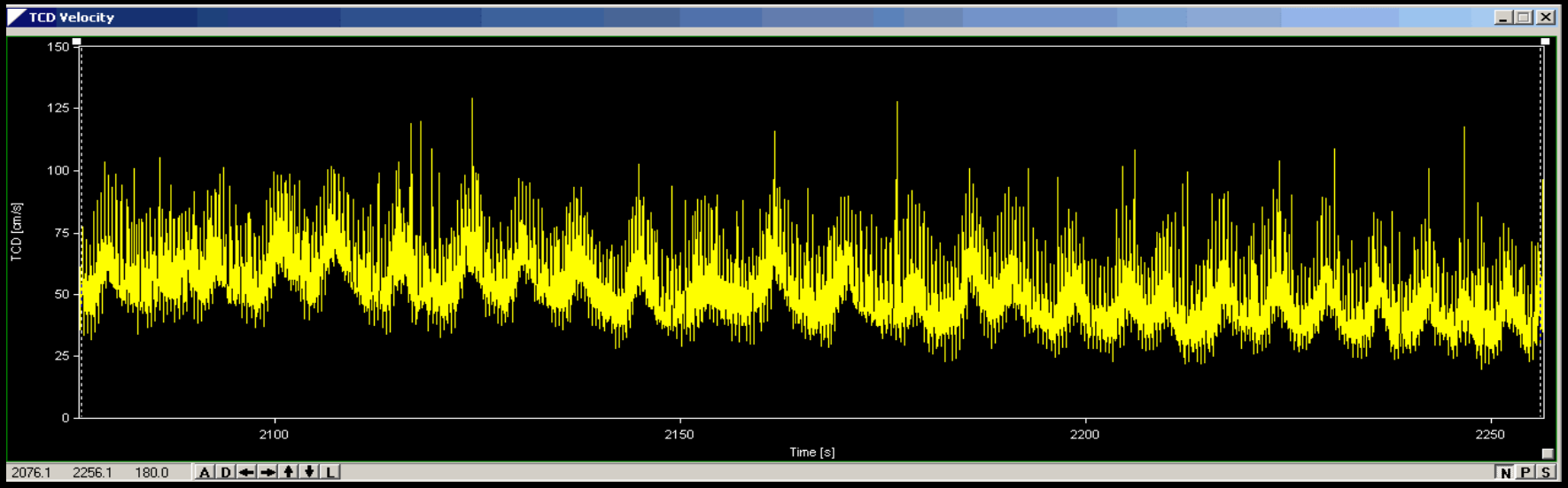
* denotes P ≤ 0.052 between HT and LT

Low Tolerant (max LBNP = -30 mmHg)

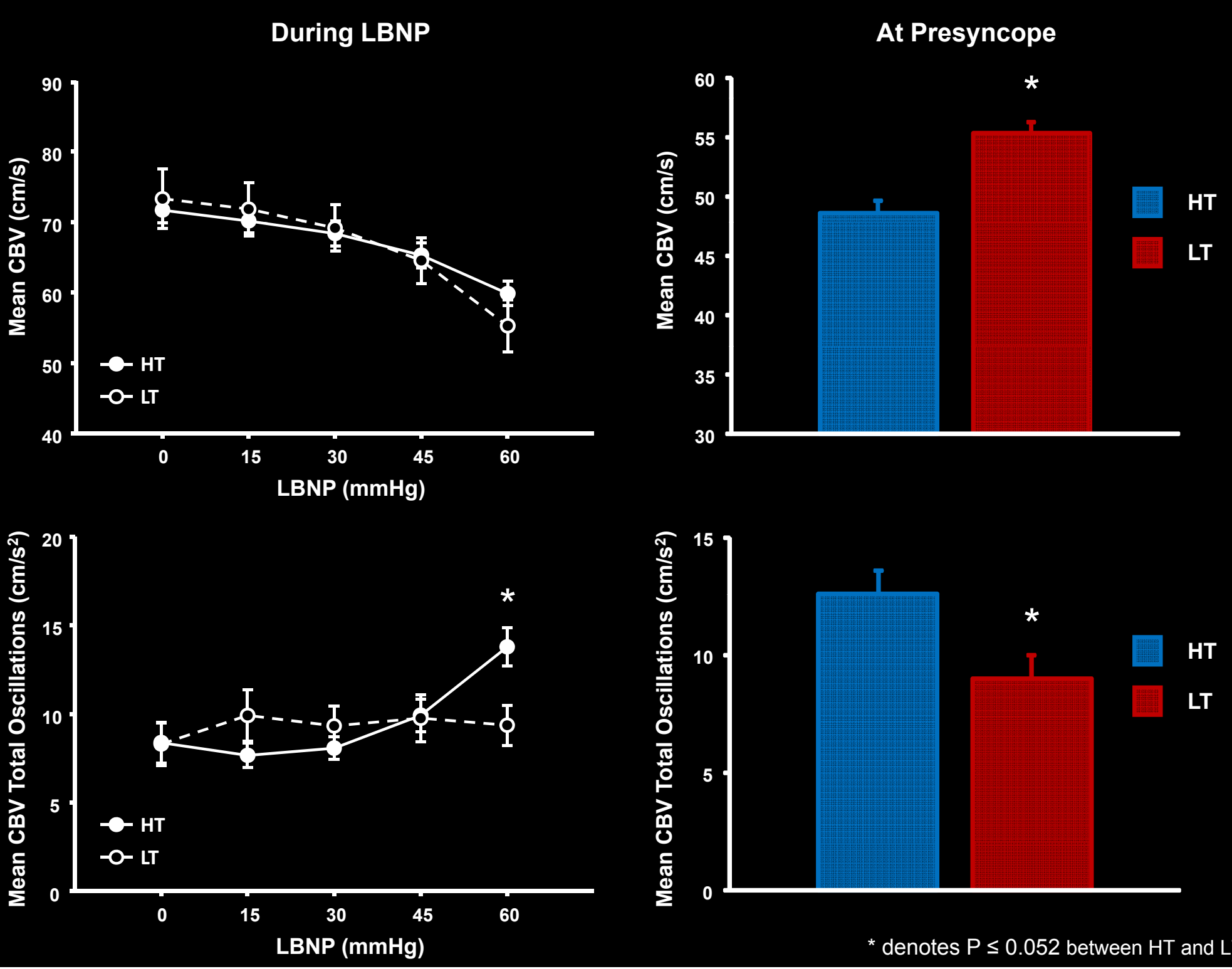


Systolic CBV = 79 cm/s; Diastolic CBV = 40 cm/s; Mean CBFV = 53 cm/s

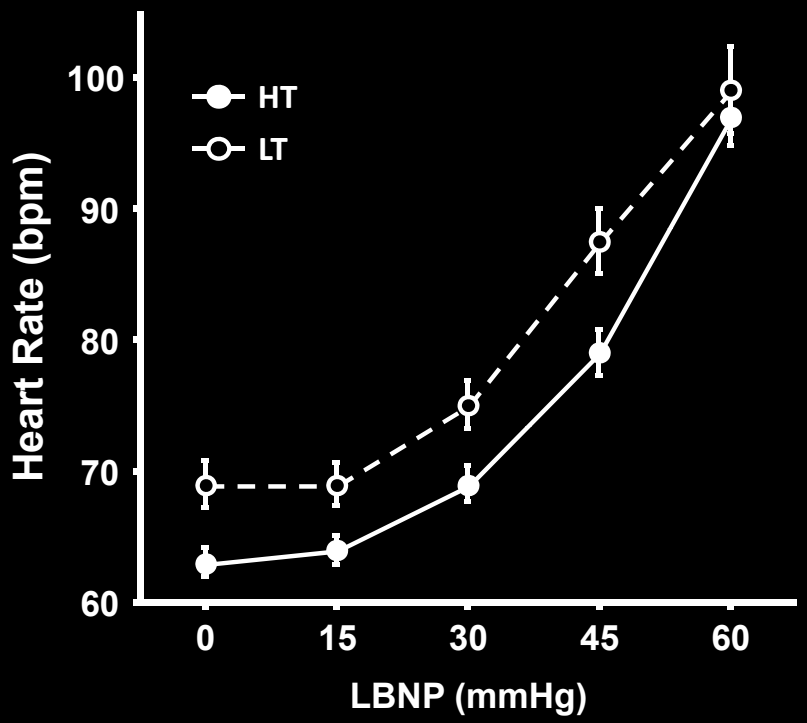
High Tolerant (max LBNP = -80 mmHg)

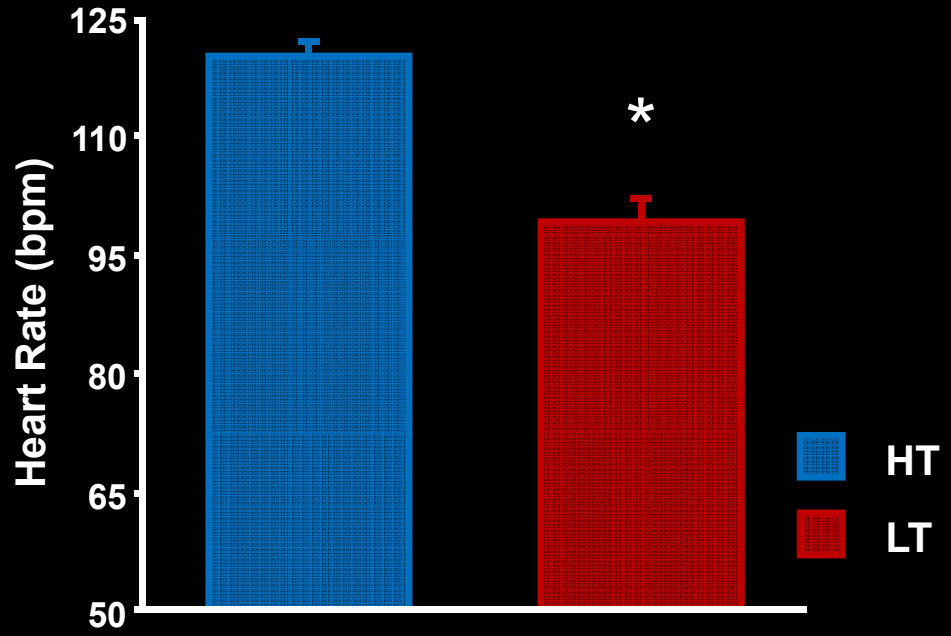


Systolic CBV = 80 cm/s; Diastolic CBV = 41 cm/s; Mean CBV = 54 cm/s


During LBNP
At Presyncope
Mean CBV (cm/s)
90
80
70
60
50
40
HT
LT
0
15
30
45
60
LBNP (mmHg)
60
55
50
45
40
35
30
*
HT
LT
Mean CBV Total Oscillations (cm/s²)
20
15
10
5
0
*
HT
LT
0
15
30
45
60
LBNP (mmHg)
15
10
5
0
*
HT
LT
* denotes P ≤ 0.052 between HT and LT

Heart Rate Response





* denotes P ≤ 0.001 between HT and LT

Summary

- HT subjects able to tolerate greater reductions in central blood volume (i.e., SV) and cerebral blood flow (i.e., mean CBV)
- Spontaneous oscillations in CBV and MAP associated with higher tolerance to central hypovolemia, consistent with previous findings using inspiratory resistance
- Hemodynamic oscillations associated with protection against the development of presyncopal symptoms
- Possible mechanisms for this protective effect include:
  - Higher peak CBV transiently increases flow and oxygen delivery to cerebral tissue
  - Increased shear stress on cerebral vessel walls elicits release of vasodilators, reducing vascular resistance on cerebral vessels, increasing flow, and subsequently enhancing oxygen delivery to cerebral tissue

Implications

- Assessing *mean* responses alone may not provide a complete clinical picture
  - Continuous monitoring necessary
- Oscillations (e.g., in BP, CBV) could be integrated into algorithms for monitoring hemorrhaging patients
- A patient with “low tolerance” to hemorrhage could be transformed into “high tolerant” by eliciting oscillations with therapeutics (e.g., via inspiratory resistance)

Acknowledgements

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  Caroline Rickards
- ***US Army Institute of Surgical Research***
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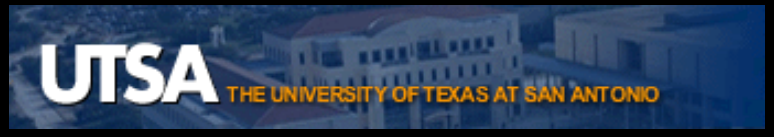
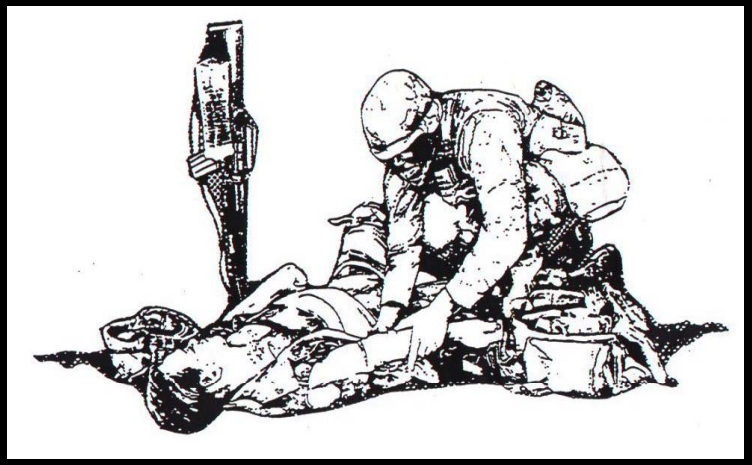
  Kathy Ryan
  Gary Muniz
- ***The University of Texas at San Antonio***
  William Cooke
- ***Advanced Circulatory Systems, Inc.***
  Keith Lurie
- ***Medical Research and Materiel Command, US Army***



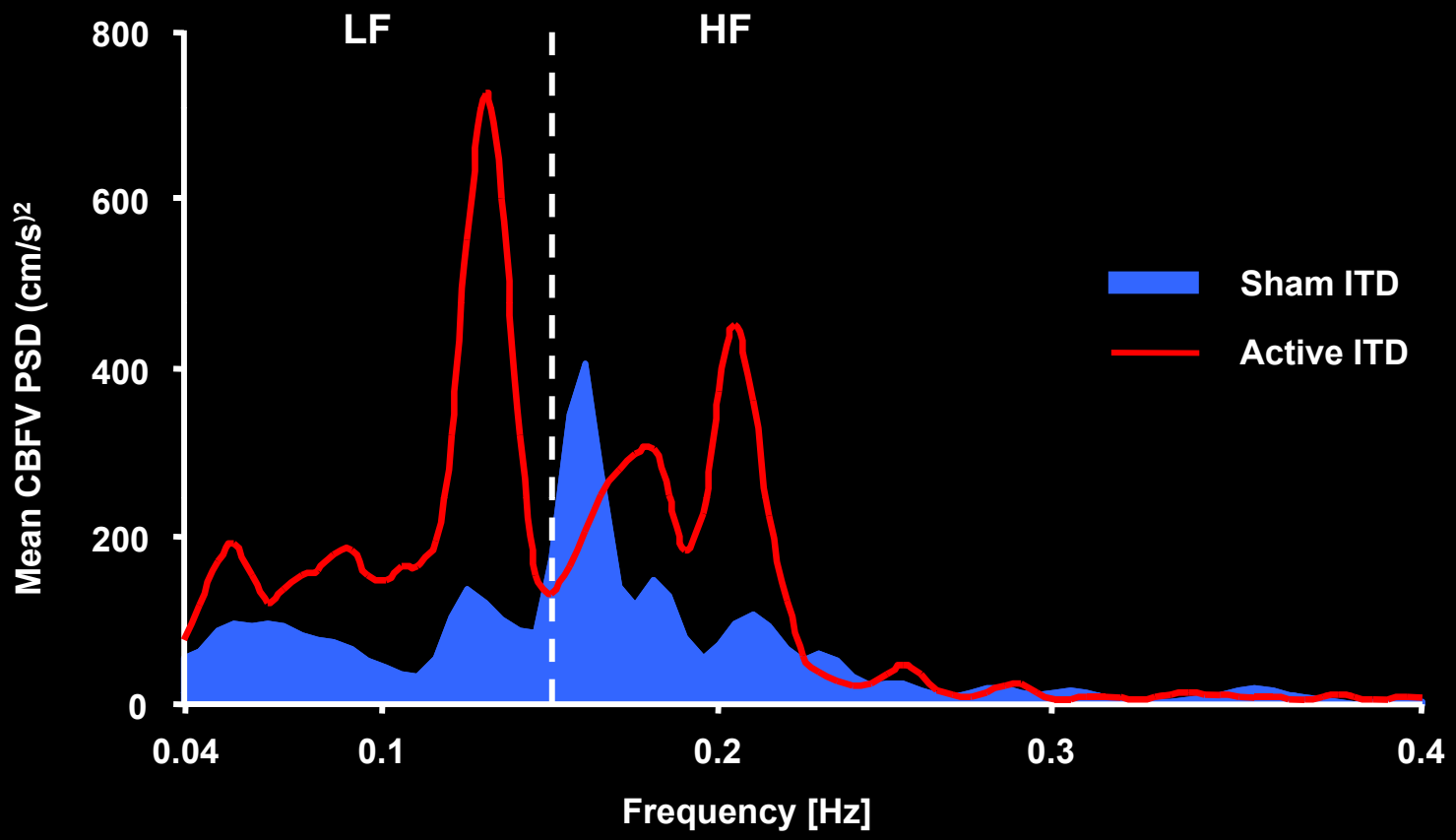
Questions

Combat Casualty Care



Research for the Soldier

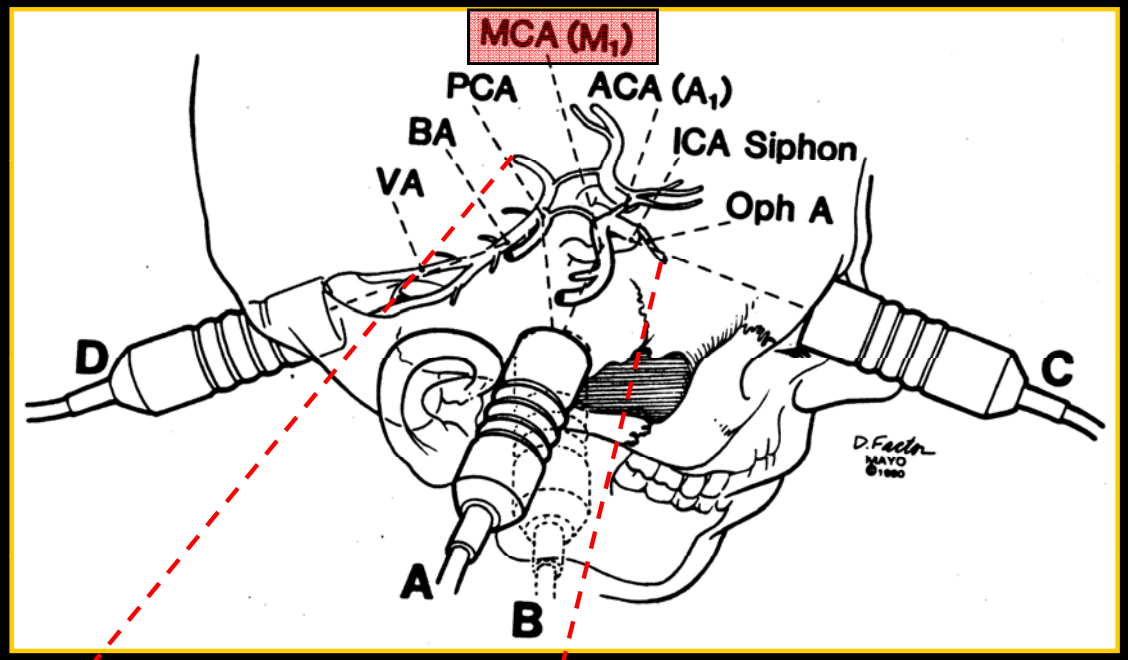
CBFV Oscillations

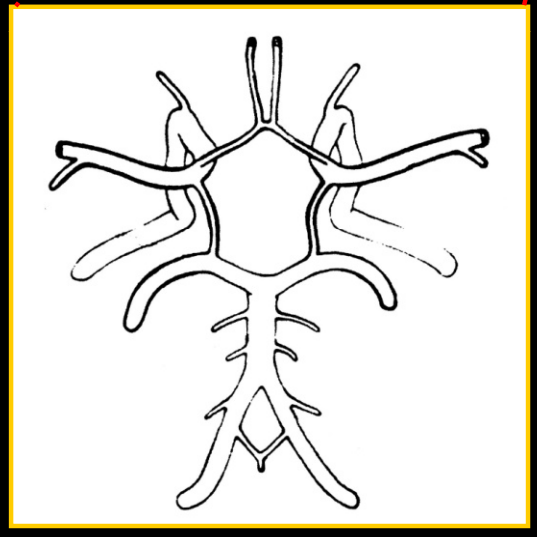


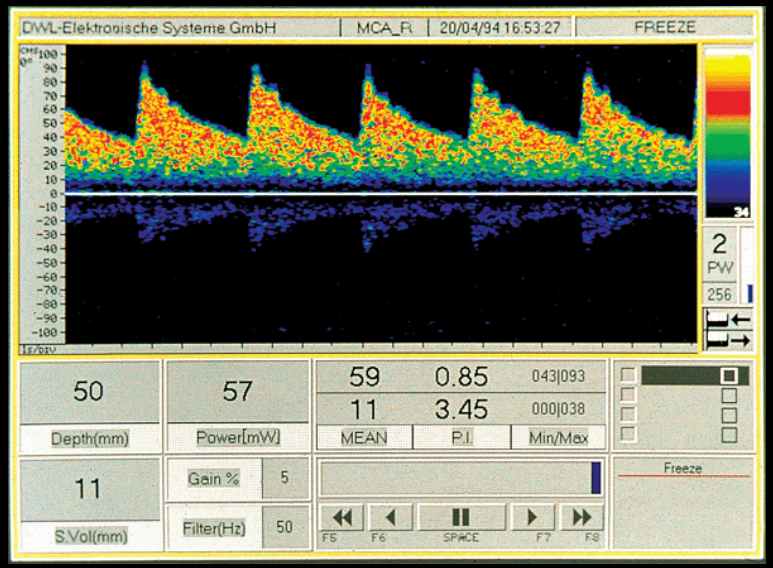
	Sham ITD	Active ITD	P-Value
LF, cm/s²	9.0 ± 2.4	24.7 ± 7.2	0.007
HF, cm/s²	13.1 ± 3.8	20.9 ± 8.3	0.234
TOTAL, cm/s²	22.1 ± 5.4	45.6 ± 10.2	0.004

Rickards et al., Am J Physiol 2007

Transcranial Doppler (TCD)







MCA Velocity waveform via Spectral Analysis

Continuous Non-invasive Blood Pressure