Arterial Baroreflex Control of Arterial Blood Pressure: Dynamic Exercise

By

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1977 - Present
Neural mechanisms mediating the neural cardiovascular adjustments to exercise – Traditional Model (1980’s)

**Central command** is the primary feed-forward mechanism

**The exercise pressor reflex** is the primary feedback mechanism
Workload

Heart rate

Blood pressure

↑ Heart rate
↑ Blood pressure

Workload
Arterial Baroreflex

- At rest ABP and HR are inversely related.

However, during exercise as ABP increases the HR increases.

The question:
- Is the baroreflex switched off, Reset or just noise in the system?
Carotid sinus baroreceptor

Aortic baroreceptor

Arterial Pressure

NP

NS

Carotid-sinus nerve

Aortic nerve

Sympath. cardiac nerves

Sympath. vasoconstrictor nerves

Heart Rate

Exercise Pressor Reflex

Vasoconstriction

Vasodilation

Blood pressure

Heart Rate

Vasodilation
Importance of vasculature for arterial baroreflex control of blood pressure at rest and during exercise

\[ \Delta \text{HR or MAP} \]

\[ \text{MAP} = \text{HR} \times \text{SV} / \text{TVC} \]

Sympathetically-mediated Vasomotor Response

% contribution to CBR-MAP response

Ogoh et al., 2002, 2003
Collins et al., 2001

5 sec NP (40mmHg)
Central Command

CNS Baroreflex Neurons

Muscle Mechano-& Chemo-reflex

Sympathetic Nervous System

Rowell and O'Leary- JAP, 1990
Central Command

Arterial Baroreflex Resetting

Location of central command?

Medullary Cardiovascular Areas

Exercise Pressor Reflex

Exercise
Central Command and Baroreflex Resetting during Exercise

- 13 young healthy subjects
- Cycling at 20% VO$_{2\text{peak}}$ before and after systemic Norcuron (curare) used to effectively reduce strength by approximately 50%.
- Same work rate required greater motor unit recruitment in the weakened muscle and thus, greater central effort.
- Neck pressure - neck suction to model carotid baroreflex function curves


Gallagher KG et al., 2001
Knee Extension

Control extension vs Vibration

*p<0.05

Ogoh et al. J Physiol. 2002
Knee Flexion

- Control flexion
- Vibration

**Mean arterial pressure (mmHg)**
- Rest
- Flexion
- Vibration

**HR (bpm/min)**
- Rest
- Flexion
- Vibration

*p<0.05

Ogoh et al. J Physiol. 2002
Perceptual and metabolic responsivity to standard bicycle ergometry following various hypnotic suggestions.

Morgan WP, Raven PB, Drinkwater BL and Horvath SM.


Hypnotic manipulation of effort sense during dynamic exercise: cardiovascular responses and brain activation.

Williamson JW, McColl R, Mathews D, Mitchell JH, Raven PB and Morgan WP.

J Appl Physiol 2001 Apr;90(4):1392-9
Williamson et al. JAP, 2001
Uphill vs. Baseline

Downhill vs. Baseline

Williamson et al. JAP, 2001
Differences in Brain Activation Between Actual and Imagined Handgrip for Subjects With (A) and Without (B) Cardiovascular Responses

Williamson et al. JAP, 2002
Exercise Pressor Reflex and Baroreflex Resetting during Exercise

- 10 young healthy subjects

- Cycling at 20% VO\textsubscript{2peak} with and without medical anti-shock trousers applied to both lower extremities and inflated to 100 mmHg.

- MAS trousers used to enhance the stimulation of the exercise pressor reflex.

- Neck pressure- neck suction to model carotid baroreflex function curves

Gallagher KG et al., 2001
Experimental Set-up
Exercise Pressor Reflex and Baroreflex Resetting during Exercise

- 9 young healthy subjects
- Cycling at 30% VO$_{2\text{peak}}$ before and after lidocaine administered through the intervertebral space of the 2nd and 3rd lumbar vertebrae
- Epidural anaesthesia used to provide partial blockade of skeletal muscle afferents to reduce stimulation of the exercise pressor reflex.
- Neck pressure-neck suction to model carotid baroreflex function curves

Smith SA et al., 2003
<table>
<thead>
<tr>
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<th>Central Command</th>
<th>Exercise Pressor Reflex</th>
<th>Arterial Baro Reflex</th>
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<tbody>
<tr>
<td><strong>Voluntary Exercise</strong></td>
<td>+</td>
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<tr>
<td><strong>Electrically Induced Exercise</strong></td>
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<td><strong>Electrically Induced Exercise during Epidural Anesthesia</strong></td>
<td>0</td>
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Strange et al. JP 1993
Ogoh et al., JP (2007)
Ogoh et al., JP (2007)
Ogoh et al., JP (2007)
Exercise-induced hypertension (EIHt)

- EIHt carried 36% greater rate of CV events and mortality
- Independent risk factor for CV events and mortality

Exaggerated Blood Pressure Response to Exercise Is Associated With Augmented Rise of Angiotensin II During Exercise

Chi Young Shim, MD, Jong-Won Ha, MD, PhD, Sungha Park, MD, PhD, Eui-Young Choi, MD, Donghoon Choi, MD, PhD, Se-Joong Rim, MD, PhD, Namsik Chung, MD, PhD

Seoul, South Korea

Objectives
The aim of this study was to investigate the association between an exaggerated blood pressure (BP) response to exercise and augmented angiotensin (Ang) II rise during exercise.

Background
Although a central pressor effect of Ang II has been implicated in the pathogenesis of hypertension, the relationship between Ang II and exaggerated BP response to exercise is unclear.

Methods
Thirty-six subjects with an exaggerated BP response to exercise (18 men, age 50 ± 16 years, Group II) were compared with 36 age- and gender-matched control subjects (18 men, age 50 ± 16 years, Group I) with normal BP reactivity. The subjects who had resting BP =140/90 mm Hg or were treated with any antihypertensive drugs were excluded. The blood was sampled at rest and immediately after peak exercise for measurement of renin, Ang II, aldosterone, and catecholamine.
NP/NS over the past 25 years we have established that in humans activation

Exercise increases metabolic production of Free Radicals

Intensity related production of O$_2•^-$:

- Increases electron transport chain flux
- With increase tissue metabolism

Central sympathetic outflow is inhibited by central nitric oxide.

Mediator of the Intensity-dependent resetting of the carotid baroreflex?

Healthy

EIHt

Proposed schematic of the use of different lipid soluble pharmacological agents

Rationale

- Equivalent dosages (BP) - (Jankowski et al., 1995 & Chik et al., 2010)

- Similar reductions in circulating Ang II - (Hollenberg et al., 1981) & (Bussien et al., 1986)
Instrumentation and measurements

- ECG
- HR
- Finometer
- BP
- Measurement of Free Radicals: Electron paramagnetic resonance
- Blood Sampling - antecubital vein
- Muscle Sympathetic Nerve Activity (MSNA)
Measurement of MSNA
Measurement of MSNA during exercise EX150
Results – Hemodynamics (n=14)
Results – MSNA n=7
ABR stimulus-response function curves - Rest & E120 n=9
Conclusion of main results and discussion

- Peripheral superoxide concentrations were not significantly altered by ACEi
- Baseline MSNA and MAP were unchanged
- PER attenuated the increases in MSNA and MAP compared to PL and CAP during exercise.
- Resetting of OP and threshold pressures (THR) were attenuated with PER from baseline to EX120 compared to PL.
Arterial baroreceptor reflex pathway

(modified from Schreihofer, AM, core course lecture 2012).

- Slows (at rest)
- But during exercise Heart rate increases

NTS: nucleus tractus solitarius
NA: nucleus ambiguus
RVLM: rostral ventrolateral medulla
CVLM: caudal ventrolateral medulla

Why?
Superoxide-dependent electron spin resonance (ESR) spectroscopy - n=8