Neural Regulation of the Heart

Jean Hardwick
Ithaca College
NEUROSCIENCE, Fourth Edition, Figure 21.1
Autonomic Nervous System

Parasympathetic:
- Cranial Sacral
- Pre
- Ach
- Ganglion
- Pst

Sympathetic:
- Thoracic Lumbar
- Pre
- Ach
- Ganglion
- Pst
- NE
Sensory innervation

Sensory Inputs
- BP
- pH
- pO₂

Nodose Ganglia
Vagus Nerve
Dorsal Root Ganglia
Autonomic Innervation of the Heart

Parasympathetic

ACh
↓ Heart Rate
↓ Contractility
↓ Cardiac Output

Sympathetic

NE
↑ Heart Rate
↑ Contractility
↑ Cardiac Output
Cardiac Ganglion

Parasympathetic:
- Cranial Sacral

Sympathetic:
- Thoracic Lumbar

Ganglion

Pre

ACH

Pst

NE
CNS Preganglionic Neurons

Parasympathetic Postganglionic Neurons

Cardiac Sensory Neurons

Cardiac Target Cells

Sympathetic Postganglionic Fibers
Parasympathetic Cardiac Ganglion

- Fast synaptic transmission (excitatory)
  - ACh (nicotinic receptors)

- Other signals
  - ACh (muscarinic receptors)
  - NE
  - Neuropeptides
  - Locally-generated signals
Guinea pig cardiac ganglion

Neurotransmitters

- Neuropeptides
  - Sensory peptides
    - Substance P, CGRP
  - PACAP
    - PACAP38, PACAP27
Physiology

“puffer” containing test substance
Stimulation of fiber inputs

A
Control

B
0 Ca++

C
Wash

fts

7.5 mV

15 sec
Substance P
Substance P

Control

SP

Wash
PACAP

A1 PACAP27

A2 PACAP27

B1 CONTROL

B2 PACAP27

B3 VIP

C1 CONTROL

C2 PACAP38

C3 PACAP27
Non-traditional Neuromodulators

- Immune mediators
  - Mast cell activation
    - Histamine
    - Prostaglandins

- Nitric Oxide
Cardiac Mast Cells

- Found in high density in mammalian heart
- Stimulated by:
  - Antigen exposure
  - Sensory neuropeptides
  - Chemoreceptors
    - pH changes, low oxygen
- Upon stimulation, release
  - Histamine
  - Prostaglandins (synthesized from phospholipids)
Parasympathetic Cardiac Ganglion

Preganglionic Fibers

Sympathetic Postganglionic Fibers

Sensory Afferents

Mast cells

Postganglionic Fibers
Sensitization

Inject with OVA every other day (3 injections total)

Wait 3 weeks

Collect Tissue

Apply OVA to tissue to induce mast cell degranulation
Response to Mast Cell Degranulation

1. OVALBUMIN

2. OVALBUMIN

3. HISTAMINE

10 mV 10 sec
Excitability

- **Excitability**
- **Stimulus (nA)** vs **AP Frequency (Hz)**
  - **Control, All cells** vs **Histamine, All cells**
  - **Phasic Control** vs **Phasic Histamine**
  - **Tonic Control** vs **Tonic Histamine**
Nitric Oxide in the Heart
Nitric Oxide

NOS

Ca++

NO

Guanylate Cyclase

cGMP
Physiological Actions of NO

- Electrophysiological recordings from the cardiac plexus

Preganglionic fiber  ACh  SNP  Intracardiac neuron
Nitric Oxide

SNP

Control

20 mV

50 msec
Regulation of neuronal firing

- Preganglionic fibers
  - ACh - fast depolarization, AP generation
  - PACAP – slow, long lasting depolarization, increase in excitability

- Sensory afferent fibers
  - SP – slow depolarization, increase in excitability

- Mast cells
  - Histamine – depolarization, increase in excitability

- Intracardiac neurons
  - NO – presynaptic increase in EPSP amplitude
Chronic Heart Disease and Neuronal Regulation

Am J Physiol Heart Circ Physiol 287: H1599-H1608
Models of Heart Disease

- **Myocardial infarction**
  - Ligate left ventricular coronary artery
  - 6-9 weeks recovery

- **Pressure Overload**
  - Band descending dorsal aorta
  - Produces left ventricular hypertrophy
  - 8-10 weeks recovery

- **Sham surgery**
Regulation of NOS levels

Control

Chronic MI

nNOS and MAP2
Regulation of NOS levels

![Bar graph showing the regulation of NOS levels with different control groups: Control, CMI, Sham surgery, and CPO. The graph indicates that CMI has a significantly higher %nNOS cells compared to other groups.](image-url)
Mast Cell Density

Control

CMI
Mast Cells

![Graph showing mast cell density in control, MI, and PO groups.](image)
Physiological Changes with Chronic MI

A
UNTREATED

B
CHRONIC MI

Control

Histamine

20 mV
100 msec
Physiological Changes with Disease

![Graph showing physiological changes with disease](image-url)

- Control
- Control with Histamine
- PO with Histamine
- MI with Histamine

**Axes:**
- Y-axis: AP Frequency (Hz)
- X-axis: Stimulus Intensity (nA)
Physiological Changes with Disease

![Graph showing AP Frequency (Hz) against Stimulus Intensity (nA)]

- **Control**
- **Control with PACAP**
- **PO with PACAP**
- **MI with PACAP**
Preganglionic Inputs

Sensory Inputs

ACh

PACAP

NO

SP

CGRP

Histamine

Mast Cells

Target Cells
Acknowledgements

- National Institutes of Health
  - Heart Lung and Blood Institute
- Jeffrey Ardell – ETSU
- Marie Southerland, DVM – ETSU
- Rodney Parsons – UVM
<table>
<thead>
<tr>
<th>Student Collaborators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seth DePuy ('99)</td>
</tr>
<tr>
<td>Beth Peterson ('01)</td>
</tr>
<tr>
<td>Kristen Sager ('02)</td>
</tr>
<tr>
<td>Greg Jelson ('02)</td>
</tr>
<tr>
<td>Bekke Mapes ('03)</td>
</tr>
<tr>
<td>Amy Kotarski ('05)</td>
</tr>
<tr>
<td>Danielle Federico ('05)</td>
</tr>
<tr>
<td>Andrew Kelley ('05)</td>
</tr>
<tr>
<td>Robert Janelli ('07)</td>
</tr>
<tr>
<td>Ryan Bochacki ('07)</td>
</tr>
<tr>
<td>Caitlin Baran ('09)</td>
</tr>
<tr>
<td>Noah Mishkin ('11)</td>
</tr>
<tr>
<td>Melanie Powers ('01)</td>
</tr>
<tr>
<td>Gina DiMasi ('02)</td>
</tr>
<tr>
<td>Zach Goldsmith ('02)</td>
</tr>
<tr>
<td>Martha Morin ('03)</td>
</tr>
<tr>
<td>Brenna Corbett ('03)</td>
</tr>
<tr>
<td>Jay Sellers ('05)</td>
</tr>
<tr>
<td>Abby Wilkes ('06)</td>
</tr>
<tr>
<td>Megan McManus ('06)</td>
</tr>
<tr>
<td>Nancy Andersen ('07)</td>
</tr>
<tr>
<td>Amber Contrastan ('09)</td>
</tr>
<tr>
<td>Lauren Houdek ('10)</td>
</tr>
<tr>
<td>Alison Girasole ('11)</td>
</tr>
</tbody>
</table>