“Chronic Sympathetic Nerve Recordings Using Telemetry”

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Rodent Instrumentation Symposium
Experimental Biology 2011, Washington, D.C.
Methods to Assess Sympathetic Function

- Plasma or urinary catecholamines
- Tissue catecholamine content
- Blockade of ganglionic transmission or peripheral adrenergic receptors
- Acute sympathetic nerve recordings (anesthetized preparations)
- Nerve transection/organ denervation
- Tissue or regional norepinephrine spillover
- Analysis of low versus high frequency spectrum (spectral analysis)

Each of these approaches is limited by a temporal resolution and lack of organ specific changes in sympathetic nerve activity.
Chronic Recording of Sympathetic Nerve Activity
Via Tethers and Hard-Wire System

Yoshimoto et al. Hypertension 2010
Telemetry for Chronic Sympathetic Nerve Recordings

- Telemetry – a wireless solution to chronically monitor various physiological variables

- Basic Components

  - Transmitter
  - Data Acquisition System
  - Receiver
  - End Product

*Data generated using DSI Telemetry System*
The “Materials”

List of equipment, suppliers, catalog numbers is provided at the end.
The “Materials” – Part II
The “Methods” – Lumbar SNA

Need to use aseptic technique – pictures are for demonstration purposes!
The “Methods” – Renal SNA

Need to use aseptic technique – pictures are for demonstration purposes!

1. [Diagram of renal anatomy]


2. Bruce Van Vliet & Telemetry Research
   (suture leads into muscle)
How do we assess the quality of the nerve signal?

- **Species differences** – basal level of sympathetic tone
- **Nerve differences** – renal versus lumbar versus splanchnic versus other
- **Cardiac-related bursts**

*Data generated using DSI Telemetry System*
How do we assess the quality of the nerve signal?

- **Species differences** – basal level of sympathetic tone
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- **Cardiac-related bursts** – rodents should exhibit obvious cardiac-related bursts
- **Change in voltage in response to phenylephrine (baroreflex) or ganglionic blockade**

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- **Change in voltage in response to phenylephrine (baroreflex) or ganglionic blockade**
- **Change in voltage in response to sodium nitroprusside?**

Sodium nitroprusside (4 ug/kg, iv)

![Graphs showing arterial blood pressure, rectified & integrated lumbar SNA, and raw lumbar SNA with TC: 10 ms and 5 s time marks.](data:image/png;base64,iVBORw0KGgoAAAANSUhEUgAAA...)

*Data generated using DSI Telemetry System*
Things to worry about?

- **EMG Artifacts** – not related to cardiac cycle and more prolonged

*Data generated using DSI Telemetry System*
Things to worry about – Part II

- **Noise** – different forms and different kinds

<table>
<thead>
<tr>
<th>Arterial Blood Pressure</th>
<th>Rectified &amp; Integrated Lumbar SNA</th>
<th>Raw Lumbar SNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>TC: 10 ms</td>
<td>0.5 s</td>
</tr>
<tr>
<td>Noise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium Noise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small Noise</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data generated using DSI Telemetry System*
Reasonable Expectations

- Success rate (viable nerve at Day 5 post-implant): ~70%
- Average duration of stable (post Day 5) sympathetic nerve recording: 14.1±1.2 days
- Time-related decline in sympathetic nerve activity

<table>
<thead>
<tr>
<th>Heart Rate</th>
<th>Day 2</th>
<th>Day 6</th>
<th>Day 15</th>
<th>Day 25</th>
<th>Day 33</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial Blood Pressure</td>
<td>431</td>
<td>381</td>
<td>331</td>
<td>341</td>
<td>338</td>
</tr>
<tr>
<td>Rectified &amp; Integrated Lumbar SNA</td>
<td>TC: 10 ms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw Lumbar SNA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data generated using DSI Telemetry System*
Reasonable Expectations

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- Thoughts related to **experimental design**: “Off-On-Off”
Reasonable Expectations

- Success rate (viable nerve at Day 5 post-implant): 70%
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- Time-related decline in sympathetic nerve activity
- Thoughts related to experimental design: “Off-On-Off”

![Graph showing sympathetic nerve activity over time with Nerve Viability? highlighted.](image)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Experimental Manipulation</th>
<th>Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>Nerve Activity</td>
<td>Baseline</td>
</tr>
</tbody>
</table>

Sympathetic Nerve Activity

Time
Sympathetic Nerve Activity Analysis

- Raw Signal – Spike or Action Potential Frequency (less common)
- Rectify & Integrate (subtract noise) – Normalize to baseline (100%) & report voltage
- Burst Frequency & Amplitude

Caution – may be difficult in rodents when an increase in SNA is expected

Phenylephrine (4 ug/kg, iv)

Arterial Blood Pressure

Burst Frequency (Hz)

Rectified & Integrated Lumbar SNA

Raw Lumbar SNA

*Data generated using DSI Telemetry System
Analysis of Sympathetic Nerve Activity

- Raw Signal – Spike or Action Potential Frequency (less common)
- Rectify & Integrate (subtract noise) – Normalize to baseline (100%) & report voltage
- Burst Frequency & Amplitude (Caution – for increases in SNA in rodents)
- Normalization to Nasopharyngeal Reflex
Analysis of Sympathetic Nerve Activity

- Raw Signal – Spike or Action Potential Frequency (less common)
- Rectify & Integrate (subtract noise) – Normalize to baseline (100%) & report voltage
- Burst Frequency & Amplitude (Caution – for increases in SNA in rodents)
- Normalization to Nasopharyngeal Reflex (might depend on nerve)

Results – Water Deprivation

- **Arterial Blood Pressure**
  - Baseline
  - 48 hr Water Dep
  - 1-Day Post Water Dep
  - TC=2 s
  - TC=10 ms

- **Rectified & Integrated Lumbar SNA**
  - Burst Frequency (Hz)

- **Raw Lumbar SNA**
  - 20 µV

- **Heart Rate (bpm)**
  - 300
  - 400

- **Mean ABP (mmHg)**
  - 80
  - 90
  - 100
  - 110
  - 120

- **Lumbar SNA (%)**
  - 80
  - 100
  - 120
  - 140

- **Time (days)**
  - D1
  - D2
  - D3
  - D4
  - D5

- **n=7  *P<0.01**

*Data generated using DSI Telemetry System*
Telemetry Research versus Data Sciences International

<table>
<thead>
<tr>
<th>Feature</th>
<th>Telemetry Research</th>
<th>Data Sciences International</th>
</tr>
</thead>
<tbody>
<tr>
<td>Battery life</td>
<td>12 hr (continuous)</td>
<td>2 months (continuous)</td>
</tr>
<tr>
<td>*rechargeable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample Rate</td>
<td>8000 Hz</td>
<td>5000 Hz</td>
</tr>
<tr>
<td>Size</td>
<td>15 g (33x9x23mm)</td>
<td>12.5 g (5.5cc)</td>
</tr>
<tr>
<td>Lead Length</td>
<td>25 cm</td>
<td>12 cm</td>
</tr>
<tr>
<td>Animal weight</td>
<td>&gt;200 g</td>
<td>&gt;200 g</td>
</tr>
</tbody>
</table>

12 cm
**Telemetry Research versus Data Sciences International**

- **Advantages**
  - Record from multiple animals in 1 cage
  - Rechargeable transmitter
  - Integrate with existing DSI equipment
  - Different probes for different uses

- **Disadvantages**
  - Difficult to integrate charging pads with unconventional cages (ie metabolic)
  - Signal drop-out
  - Charging pads generate heat
  - Refurbishment costs
## Cost Comparison – Telemetry Research vs Data Sciences

<table>
<thead>
<tr>
<th>Telemetry Research</th>
<th>Data Sciences</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ TR46SP – BP and SNA Transmitter</td>
<td>➢ PA-C40 BP Transmitter</td>
</tr>
<tr>
<td></td>
<td>$1,750</td>
</tr>
<tr>
<td>➢ TR802 – Wireless Charger</td>
<td>➢ F50-W-F2 SNA Transmitter</td>
</tr>
<tr>
<td></td>
<td>$595</td>
</tr>
<tr>
<td><strong>Subtotal ($2,345 x 6) = $14,070</strong></td>
<td><strong>Subtotal ($3,765 x 6) = $22,590</strong></td>
</tr>
<tr>
<td>➢ TR162 SUB – SNA Sub Receiver</td>
<td>➢ RPC-3 Receiver</td>
</tr>
<tr>
<td></td>
<td>$2,995</td>
</tr>
<tr>
<td><strong>Subtotal ($2,995 x 5) = $14,975</strong></td>
<td><strong>Subtotal ($995 x 6) = $5,970</strong></td>
</tr>
<tr>
<td>➢ TR162 – SNA &amp; Master Receiver</td>
<td>➢ DL11 for F50-W-F2 (converter)</td>
</tr>
<tr>
<td></td>
<td>$8,995</td>
</tr>
<tr>
<td><strong>Subtotal ($8,995 x 1) = $8,995</strong></td>
<td>➢ R11CPA (Analog Adapter)</td>
</tr>
<tr>
<td></td>
<td>$1,100</td>
</tr>
<tr>
<td></td>
<td><strong>Subtotal ($2,245 x 6) = $13,470</strong></td>
</tr>
</tbody>
</table>

**Total Cost = $38,040**

**Total Cost = $42,030**

*Six animal system to record continuously

*Prices are approximate – package depends on end-user

**Neither system includes Data Acquisition Platform (~$8000 using ADInstruments or Cambridge Electronic Design Spike2)
## The “Materials”

<table>
<thead>
<tr>
<th>Item</th>
<th>Supplier</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>7-0 vicryl suture</td>
<td>veterinary supply company Anchoring leads to muscle</td>
</tr>
<tr>
<td>2.</td>
<td>4-0 ethilon</td>
<td>veterinary supply company suturing muscle and/or incision sites</td>
</tr>
<tr>
<td>3.</td>
<td>Isoflurane</td>
<td>veterinary supply company Ideal anesthetic for clear activity in various sympathetic nerves (~2% in 100% oxygen)</td>
</tr>
<tr>
<td>4.</td>
<td>Bupivacaine*</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Lidocaine*</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Carprofen*</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Ampicillin *</td>
<td>*veterinary supply company analgesic, pain, and infection</td>
</tr>
<tr>
<td>8.</td>
<td>Digital Oscilloscope</td>
<td>Newark Electronics See nerve signals and noise</td>
</tr>
</tbody>
</table>
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<tr>
<th>Item</th>
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<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Adson forceps</td>
<td>Fine Science Tools (Cat#11006-12)</td>
<td>general surgery</td>
</tr>
<tr>
<td>2. Wound clip applicator</td>
<td>Fine Science Tools (Cat#)</td>
<td>wound closure</td>
</tr>
<tr>
<td>3. Vanna/Micro Scissors</td>
<td>Fine Science Tools (Cat#91500-09)</td>
<td>cut sutures</td>
</tr>
<tr>
<td>4. General Scissors</td>
<td>Fine Science Tools (Cat#14078-10)</td>
<td>general surgery</td>
</tr>
<tr>
<td>5. MicroNeedle Holder</td>
<td>Fine Science Tools (Cat#12060-01)</td>
<td>suturing</td>
</tr>
<tr>
<td>6. Graebe forceps</td>
<td>Fine Science Tools (Cat#11052-10)</td>
<td>Dissection of vena cava and connective tissue</td>
</tr>
<tr>
<td>7. Scalpel Handle</td>
<td>Fine Science Tools (Cat#10007-12)</td>
<td>general surgery</td>
</tr>
<tr>
<td>8. Sliding Retractor</td>
<td>Fine Science Tools (Cat#17003-03)</td>
<td>Retracting vena cava and muscle to expose lumbar nerve</td>
</tr>
<tr>
<td>9. Absorbent spears</td>
<td>Fine Science Tools (Cat#18105-03)</td>
<td>Cut into little pieces – absorb fluid from electrode/nerve</td>
</tr>
<tr>
<td>10. Retractors</td>
<td>Various</td>
<td>General retraction of intestines</td>
</tr>
<tr>
<td>11. Dumont forceps</td>
<td>Fine Science Tools (Cat#11254-20)</td>
<td>Dissect nerve from connective tissue</td>
</tr>
<tr>
<td>12. Cotton Applicators</td>
<td>Various</td>
<td>General dissection</td>
</tr>
<tr>
<td>13. KWIK-SIL</td>
<td>World Precision Instruments (Cat#KWIK-SIL)</td>
<td>Silicone Adhesive to insulate nerve and electrode</td>
</tr>
</tbody>
</table>