Where is the proprioception first processed?
Thalamus vs. Cerebellum

Yoonju Cho, Jeff Pompe, Sung Soo Kim
Outline

• Traditional view of proprioceptive projection from the periphery to the cortex
  – Periphery to thalamus: Yoonju
  – Thalamus to cortex: Jeff

• A different paradigm of proprioceptive projection
  – Through cerebellum: Sung Soo
Traditional View

Peripheral receptors → Spinal Cord → Thalamus → Cortex

Golgi tendon (Aα)
Muscle spindles (Aα)
Joint receptors (Aβ)
# Peripheral Receptors

- 4 main receptors that are thought to be responsive to proprioceptive stimuli

<table>
<thead>
<tr>
<th>Afferent</th>
<th>Fiber type</th>
<th>Diameter</th>
<th>Conduction velocity</th>
<th>Type of responsive stimuli</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle spindle</td>
<td>A-alpha</td>
<td>12-20 um</td>
<td>72-120 m/sec</td>
<td>Muscle length</td>
</tr>
<tr>
<td>Golgi tendon</td>
<td>A-alpha</td>
<td>12-20 um</td>
<td>72-120 m/sec</td>
<td>Muscle force</td>
</tr>
<tr>
<td>Joint receptor</td>
<td>A-beta</td>
<td>7-12 um</td>
<td>42-72 m/sec</td>
<td>Joint position</td>
</tr>
<tr>
<td>Skin receptor</td>
<td>A-beta</td>
<td>7-12 um</td>
<td>42-72 m/sec</td>
<td>Skin stretch</td>
</tr>
</tbody>
</table>
Medial Lemniscus Pathway

Clarke’s nucleus to Dorsal spinocerebellar tract

External cuneate nucleus to Cuneocerebellar tract
Spinal Cord to Thalamus

- Nucleus Z, the Medullary Relay in the Projection Path to the Cerebral Cortex of Group I Muscle Afferents from the Cat’s Hind Limb
  - Landgren and Silfvenius (1971)
  - Electrical stimulation and recording in 17 anaesthetized cats
  - Cerebellum removed
Nucleus Z

• Just medial to cuneate nucleus and rostral of gracilis nucleus in medulla

• Known to relay proprioceptive information from body
Orthodromatic vs. Antidromatic
Results

• Electrical stimulation of Group I muscle afferents from the ipsilateral hind limb evokes responses in nucleus Z

• Antidromic discharges were evoked in nucleus Z by electrical stimulation of contralateral thalamus

• A lesion in nucleus Z eliminated responses in contralateral SI cortex
Thalamus

• Situated between midbrain and cortex
  – Location and Connectivity

• Generally thought to act as a relay between subcortical areas and cortex
  – Every sensory system (except olfaction) includes a thalamic nucleus the receives sensory signals and sends them to associated primary cortical area
Ventrobasal (VB) Complex

- VB is the major thalamic region linking somatic afferent pathways to the somatic sensory areas of cortex
- Composed of 2 parts with identical cytoarchitecture
  - VBex target of DCN
  - Vbarc target of Trigeminal
- Mode and Place specific modular groups of VB neurons
  - Unknown distribution within and projections from VB to cortex
  - Not known if the result of immutable connections or dynamic maintenance and modification
- Also projects to SII
  - May also project to motor areas

(Mountcastle and Henneman 1952)
Rod Organization of Thalamus

- Cells along a rod in VPL and VPM not only have overlapping receptive fields on the same part of the body, but are also activated by stimuli that affect the same class of peripheral sensory receptor.
- Basis for preservation of place and modality specificity in the relay of tactile information.
- Input to a place and modality specific column in cortex consists of a bundle of axons arising from an elongated, rodlike aggregation of relay cells extending through much of the AP length of the thalamic VB complex and receiving their inputs from a similarly elongated, place- and modality-specific aggregation of medial lemniscal axons.

(Jones, Friedman, Hendry 1982)
Thalamus to SI

(Jones and Friedman 1982)
Modality Segregation

(Sretavan and Dykes 1983)
Place Segregation

Depth of cingular sulcus

Depth of central sulcus

(Woolsey 1958)
Multiple Representation Hypothesis

(Kaas et al 1979)
However...

• On the other part of the world, there live people who believe that the main target of proproceptive information is cerebellum.
From spinal cord to cerebellum: Anatomy
Somatosensory properties of cuneocerebellar neurones in the main cuneate nucleus of the rat

Cerminara, Makarabhirom and Rawson
2003
The Cerebellum
• Projections from ECN and MCN to cerebellum (this study focuses on MCN)

• Targets of MCN: thalamus, cerebellum, inferior olive, prerectum, zona incerta, etc

• Some background.
  – ECN has been thought to be responsive to proprioception only.
  – Mouse study using genetically encoded GFP method shows that all proprioceptive afferents projects to ECN and all of them projects to cerebellum. (Nucleus Z might get information via axon collaterals from ECN. There is electrophysiological evidence, but no anatomical evidence.)
  – MCN has been thought to be responsive to cutaneous stimuli (modality-specifically).

• This study shows that neurons directly projecting to cerebellum from MCN is sensitive to joint and RA only. (other neurons in MCN may respond to other things)
• MCN neurons projecting to cerebellum (antidromic stimulation tests)

• Clear threshold
• Consistent latency
• Phase-lock in high freq.
• Collision
<table>
<thead>
<tr>
<th>Response</th>
<th>Number of Cells</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutaneous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>21</td>
<td>30.4</td>
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<tr>
<td>Hair</td>
<td>2</td>
<td>2.9</td>
</tr>
<tr>
<td>Deep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Joint</td>
<td>26</td>
<td>37.7</td>
</tr>
<tr>
<td>Muscle</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Convergence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin &amp; joint</td>
<td>10</td>
<td>14.5</td>
</tr>
<tr>
<td>Skin, joint &amp; hair</td>
<td>1</td>
<td>1.5</td>
</tr>
<tr>
<td>Not classified</td>
<td>9</td>
<td>13.0</td>
</tr>
</tbody>
</table>
• Cutaneous receptive fields are large

• Most of them are bound to joint area. They are responsive to joint movement.

• Large RF: not very responsive to puncture stimulation, but sensitive to larger probe, or finger running on the RF. probably responsive to a certain pattern of cutaneous input.

• All of them are RA. No SA, no PC

• cf) cerebellum receives SA-like information as well. This paper argues that MCN is not the relay of SA information to cerebellum. The caudal half of MCN projects to basilar pontine nuclei, which projects to cerebellum. So, it might be a candidate. (No direct evidence yet.)
• All of them are RA-like. None of them are SA-like.
- Also sensitive to the joint manipulation.
- Some of them are sensitive to multiple joints
Many of them are sensitive to the direction of movement.
• But they don’t show sustained response. → no joint angle coding
• They adapt in 2~4 seconds.
• They are highly sensitive to the small perturbation after steady position (or after adaptation period).
(neurons with sustained response in MCN, which encodes muscle extension, do not project to cerebellum.)
- Some are sensitive to both cutaneous and joint manipulation.

- RFs usually overlap. → strong association between joint movement and activation of cutaneous cells.
Summary

• MCN relays both proprioceptive and cutaneous information.

• Cutaneous information is exclusively RA-like.

• Proprioceptive information is exclusively from joint.

• No muscle stretch response, no SA-like response.

• For neurons sensitive to both tactile and joint stimuli, cutaneous RF and joint RF overlap.
Discussion

• Spinal cord → thalamic tract vs. cerebellar tract. Which is the main one?
• Steady vs. dynamic? (or object shape vs. object manipulation?)
  – Result of anatomy or plasitisity
• Are there separate pathways for sensory proprioception vs movement proprioception?
• Nonexistence of nucleus Z in mouse. → Redundant information to nucleus Z in other higher mammals?
• What is the function of modality and place segregation?
END
cf) Mouse spinal cord (difference over species?)

