Functional Neuroanatomy and Physiology for Movement Disorders

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History of Surgery for Movement Disorders

- **Early 1900’**
  - **Target:** motor associated cortex
  - **Based on motor cortex somatotopical arrangement**
  - Cortical resection/ablation
    - Precentral gyrus resection for hemi-athetosis (Horsley, 1909)
    - Precentral-premotor cortex resection for incapacitating tremor (Bucy, 1937)
  - Limitation: operative mortality (up to 10%), motor weakness

- **1930~**
  - **Target:** spinal cord
  - Cordotomy
    - Extrapyramidal tract cordotomy in the high cervical anterior quadrant (Putnam, 1931)
History of Surgery for Movement Disorders

- **Middle of 20th century**
  - Target: *deep brain structure*
  - Based on the incidental experience
  - Anterior choroidal artery ligation for Parkinson’s disease (Cooper, 1952)
  - Limitation: motor weakness (11%), mortality (10%)

### Operation and Results

<table>
<thead>
<tr>
<th>Operation</th>
<th>No. patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exirpation of caudate head</td>
<td>1</td>
</tr>
<tr>
<td>Exirpation of caudate head, section of anterior limb internal capsule</td>
<td>11</td>
</tr>
<tr>
<td>Exirpation of caudate head, section of anterior limb internal capsule, removal of oral third of putamen</td>
<td>6</td>
</tr>
<tr>
<td>Exirpation of caudate head, section of anterior limb internal capsule, removal of oral third of putamen and oral pole of globus pallidus</td>
<td>4</td>
</tr>
<tr>
<td>Anotomy (section of pallidofugal fibers)</td>
<td>22</td>
</tr>
<tr>
<td>Anotomy, exirpation of caudate head, section of anterior limb internal capsule</td>
<td>10</td>
</tr>
<tr>
<td>Anotomy, exirpation of caudate head, section of anterior limb internal capsule, removal of oral third of putamen</td>
<td>3</td>
</tr>
<tr>
<td>Exirpation of caudate head, linear separation of motor and premotor cortex, undercutting of premotor cortex</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>58</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Results</th>
<th>No. patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Much Improved (tremor-free, some rigidity, no clinical neurological deficits)</td>
<td>11 (19%)</td>
</tr>
<tr>
<td>Improved (tremor and rigidity reduced, not abolished; if abolished, attended by some degree of postoperative dyspraxia, paresis, or spasticity)</td>
<td>25 (43%)</td>
</tr>
<tr>
<td>Unimproved</td>
<td>15 (26%)</td>
</tr>
<tr>
<td>Mortality</td>
<td>7 (12%)</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>58</strong></td>
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</table>
History of Surgery for Movement Disorders

- **1950’ ~present**
  - **Invention of human stereotactic surgery system**
    - (Spiegel and Wycis, 1947)
  - **Advances of neurophysiological monitoring**
    - Test electrical stimulation: Cooper (1954) and Narayabashi (1956)
    - Microelectrode recording for monitoring single neuronal activity
    - Intraoperative monitoring and electrical stimulation
  - **Advances in structural and functional neuroimaging**
    - Development of CT and MRI
    - Functional imaging: f-MRI, white matter tractography, PET
Movement associated Neural Structures

From Adam's and Victor's Principles of Neurology, 8th ed.
Anatomy and Physiology of the Basal Ganglia: Implications for Deep Brain Stimulation for Parkinson’s Disease

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FIG. 4. Indirect and direct pathways + added STN and GPe connections + midbrain and other thalamic structures. RT, nucleus reticularis thalami; CM/Pf, centromedian/parafascicularis thalamic nucleus; PPN, pedunculopontine nucleus; MEA, midbrain extrapyramidal area; Ach, acetylcholine; DA, dopamine; Glut, glutamate.
Basal Ganglia

Striatum (Neostriatum) → Caudate Nu.
  → Putamen
  → Globus pallidus (Paleostriatum)
  → Subthalamic Nu.
  → Substantia nigra

Lenticular nucleus

✓ The Nucleus accumbens and ventral pallidum can also be considered part of the basal ganglia.
✓ Amygdala and claustrum are usually excluded.
Basal Ganglia

- Putamen
- Globus pallidus (lateral part)
- Globus pallidus (medial part)
- Caudate nucleus
- Thalamus
- Subthalamic nucleus
- Substantia nigra

- Striatum: Caudate Nu., Putamen, Nu. accumbens
- Globus pallidus: external (GPe), internal (GPi)
- Subthalamic nucleus (STN)
- Substantia nigra: pars compacta (SNc), pars reticulata (SNr)
Connection around BG
Connection around BG
- **Gateway to cerebral cortex**
  - All that the cerebral cortex can do depends on messages pass through the thalamus

- **Receives projections from the cortical area to which it projects**

- **Virtually all sensory systems pass through**

- **Key link in the process of sensory perception of the world**
Subthalamic Nucleus
**Subthalamic Nucleus**

- **Anatomical position**
  - Ventral portion of thalamus
  - Medial part of IC
  - Medial side – hypothalamus

- **Subthalamic region**
  - Subthalamic Nu
  - Zona incerta
  - Nu of the tegmental field of Forel (Forel’s field H)
  - Passing fiber: ansa lenticularis, lenticular fasciculus(H2), thalamic fasciculus(H1), subthalamic fasciculus

Fig. 6 Schematic diagram of the subthalamic region, not drawn to scale. It shows the area in the caudal zona incerta where best clinical improvement was noticed and also the region in the prelemniscal radiation where some patients developed stimulation related speech and balance disturbance (cZI, caudal zona incerta).
Neural Connection of Cortical-Subcortical Structures

Connection between neocortex and basal ganglia circuit

(Trend in Neuosci. 33(10):474–484 (2010))
FIG. 3. The basal ganglia are somatotopically arranged in a fashion that mimics by and large the cortical representation of the body (homunculus). For all nuclei, the motor region lies posterolaterally with the leg dorsally, the face ventrally, and the arm in between. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
Somato-topical Arrangement

Coronal

Axial
Pathological Changes of Extrapyramidal Circuit

- **A** Normal situation
- **B** PD
- **C** PD + STN DBS
- **D** HD
- **E** (Hemi)ballism
- **F** Pallidal lesions

[Diagram showing different conditions of the extrapyramidal circuit]
Neurophysiological Monitoring

- **Purpose**
  - Detect **target and important neighboring structures**
  - **Limitation of current imaging technology** for visualizing whole subdivision of deep brain structures

- **Type of EPM**
  - **Local field potential (LFP):** EEG (scalp or ECoG), MEG, etc
  - **Microelectrode recordings (MER)**
  - **Semi-microelectrode recordings**
Neurophysiological Monitoring

- **LFP**
  - Scalp EEG can detect field (>6cm²) potential
  - Field potential consists of synchronized extracellular currents
  - Generator is layer V pyramidal cells
  - Not action potential, post synaptic potential

- **MER**
  - Recording single cell activities
  - Single unit action potential
  - Higher spatial resolution
  - Poor ability to identify nearby structures
Microelectrode Recording

Typically 150 - 750 μV

Cf. size of neuron: 4-100 μm
Microelectrode for MER

- Parylene insulated tungsten or platinum-iridium electrode
- Attaching to long stainless steel tubes insulated with kapton tubing etc

**Tip diameter:** 200 μm

**Tip exposure:** < 50 μm
Targets for Movement Disorders

- EPM for targeting *thalamic nucleus*
- EPM for targeting *subthalamic nucleus*
- EPM for targeting *GPI*

Ventral Intermediate (Vim) nucleus: Essential Tremor
Subthalamic Nucleus (STN): Parkinson’s disease
Globus Pallidus interna (GPI): Parkinson’s disease and Dystonia
Targets for Movement Disorders

**Frontal View**
- AC-PC plane
- Midline Brain
- VIM: (Z = 0, X = 13 to 15)
- STN: (Z = -3 to -6) X = 11 to 13
- Gpi: (Z = -3 to -7) X = 20 to 23

**Lateral View**
- AC
- PC
- VIM
- STN
- Gpi

Reference: MCP; (Z=0, Y=0)
AC – PC = 24-28 mm
VIM: (Z = 0, Y = -4 to -6)
STN: (Z = -3 to -6) Y = -1 to -3
Gpi: (Z = -3 to -7) Y = 0 to +3

**Inter-human variability = mm’s**
**N = 10,000’s of patients**
Target for Thalamic area

- **Indication**
  - **Tremor**: essential tremor, rubral tremor, Parkinson tremor, cerebellar tremor, etc.
  - **Pain**: central neuropathic pain syndrome, chronic nociceptive pain syndrome, etc.

- **Target nucleus**
  - **Vc**: responsive to light touch (tactile) to proprioception (joint capsule receptors)
  - **Vim**: passive movement and activation of muscle spindles, fire in synchrony with the pt’s tremor
  - **Vop**: active rather than passive movements
  - **Posterior subthalamic area**: prelemniscal radiation, caudal zona incerta, etc.
  - **CM-Pf**: Tourette’s syndrome, intractable seizure, etc.
Target for Thalamic area

- AP : 4 ~ 8 mm anterior to PC
- Lateral : 12 ~ 15 mm
- Depth : 0 ~ 2 mm above ICL

EPM: Thalamic area

- **Tactile area**
  - Ventrocaudal nucleus (Vc)
  - Medial lemniscus → sensory cortex
  - **Respond to superficial cutaneous stimuli**
  - Intraoral response: 11-12mm from midline
  - Foot response: 18-20mm from midline
EPM: Thalamic area

A. EMG from contralateral leg

B. EMG from contralateral arm

C. Output of window discriminator

D. Neural Activity

E. Rate Histogram

Touch mouth in ET patients
EPM: Thalamic area

- Kinesthetic (movement sensing) area
  - Just rostral to tactile area
  - Passive joint bending, deep tissue squeezing
  - Probably located in Vim (animal study)
  - Electrical stimulation:
    - Contralateral paresthesia at higher current
EPM: Thalamic area

A. EMG from contralateral leg

B. EMG from contralateral arm

C. Output of window discriminator

D. Neural Activity

F. Rate Histogram

Passive wrist extension
### Voluntary cells

- Probably into **Vop and Voa**
- Lie in the **terminal field of pallidal efferent**
- Spontaneous activity is less
- **Increased or decreased firing rates** occurring 200ms before contralateral voluntary movement
EPM: Thalamic area

A. EMG from contralateral leg

Active wrist extension

B. EMG from contralateral arm

C. Output of window discriminator

D. Neural Activity

E. Rate Histogram
Tremor cell

- Prominent features of recording in Vim
- Also found in GPi and STN
- Voluntary cell and kinetic cell also fire synchronously with tremor
- Relation or feedback mechanism of tremor cell and voluntary cell: unclear
- Best surgical target for tremor? : more dorsal vs. more ventral
EPM: Thalamic area

Spontaneous activity synchronized with tremor

A. EMG from contralateral leg

B. EMG from contralateral arm

C. EMG from ipsilateral leg

D. EMG from ipsilateral arm

E. Out of Window discriminator

F. Neural Activity
## EPM: Thalamic area

<table>
<thead>
<tr>
<th></th>
<th>Anterior</th>
<th>Posterior</th>
<th>Medial</th>
<th>Lateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caudate nucleus</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Anterior thalamus</td>
<td>Longer</td>
<td>Shorter</td>
<td>Longer</td>
<td>Shorter</td>
</tr>
<tr>
<td>Vop/Vim</td>
<td>Same or longer</td>
<td>Shorter: no tremor cell</td>
<td>Shorter: many tremor cell</td>
<td>Longer: many tremor cell</td>
</tr>
<tr>
<td>Vc</td>
<td>-</td>
<td>Early entry</td>
<td>Early entry</td>
<td>Late entry</td>
</tr>
<tr>
<td>End of tract</td>
<td>Zona incerta</td>
<td>Vc</td>
<td>Medial lemniscus</td>
<td>Zona incerta</td>
</tr>
</tbody>
</table>

*Movement disorder surgery: essential, Thieme, 2009*
Target for Pallidal Area

- **Optimal target site within GPi: lateral, ventral, and posterior portion**
  - Goal of targeting: to identify those structures to be avoided.
  - Optic tract, internal capsule, the GPe, and non-motor GPi
    → immediately dorsal to the OT and anterolateral to the IC.

- **Somatotopy**
  - Somatotopic organization of these neurons has relevance to optimal electrode positioning.
  - *Arm: ventral, lateral*
  - *Leg: dorsal, and medial*
Target for Pallidal Area

- AP: 2 ~ 3 mm anterior to MCP
- Lateral: 20 ~ 22 mm
- Depth: 2 ~ 6 mm below ICL
EPM: Pallidal Area

- **GPi**
  - Higher baseline rate (80+32 Hz),
  - Some of the cell fired with tremor
  - Lack of audible pauses

- **GPe: two populations of cells**
  - Pause cells (80-90%) – higher frequency discharge pattern (50±21Hz) broken by intermittent pause
  - Burst cells (10-20%) – lower frequency discharge pattern (18±12Hz) with irregular occurrence of high-frequency bursts

- **Border Cell**
  - Cell of the substantia innominata
  - Regular firing pattern (20-40 Hz)
EPM: Pallidal Area
EPM: Pallidal Area

F/51 with cervical dystonia
<table>
<thead>
<tr>
<th></th>
<th>Anterior</th>
<th>Posterior</th>
<th>Medial</th>
<th>Lateral</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Putamen</strong></td>
<td>Short</td>
<td>Short or absence</td>
<td>Absence</td>
<td>Long</td>
</tr>
<tr>
<td><strong>GPe</strong></td>
<td>Lower</td>
<td>Higher</td>
<td>Higher</td>
<td>Lower</td>
</tr>
<tr>
<td><strong>GPi</strong></td>
<td>Lower; SM=upper ext.</td>
<td>Higher; SM=lower ext.</td>
<td>Higher; SM=lower ext.</td>
<td>Lower; SM=upper ext.</td>
</tr>
<tr>
<td><strong>GPe/GPi</strong></td>
<td>$&gt;1$</td>
<td>$&gt;1$</td>
<td>$&lt;1$</td>
<td>$&gt;1$</td>
</tr>
<tr>
<td><strong>End of tract</strong></td>
<td>Ambient cistern, or basal forebrain</td>
<td>Internal capsule</td>
<td>Internal capsule</td>
<td>Ambient cistern</td>
</tr>
</tbody>
</table>

_Movement disorder surgery: essential, Thieme, 2009_
Target for Subthalamic Nucleus

- **STN**
  - Dorsolateral part of the nucleus: motor territory
  - Ventral part: association area
  - Medial part: limbic territory
Target for Subthalamic Nucleus

Schematic Axial picture

- AP: 2 ~ 3 mm posterior to MCP
- Lateral: 11-12mm from midline
- Depth: 4mm below ICL
MER: Subthalamic Nucleus

- 60° from the AC-PC plane → anterior part of the thalamus → zona incerta → STN

- thalamus: demonstrate bursting or non-bursting patterns, with mean discharge rates of 15±19Hz and 28±19Hz, respectively.

- ZI; very quiet background, characteristic of a scarcity of cells

- dorsal border of the STN: sudden increase in the background noise

- STN; high background activity, frequent multicellular recordings, and firing rates of 30 to 50 Hz

- between STN and SNr: decrease in background noise and sell density signals, 1-2mm acellular gap

- SNr: high-frequency(50-100Hz), relatively regular discharge
MER: Subthalamic Nucleus

- Bursting cell in Voa
- Bursting cell in zona incerta
- Upper border of STN
- High frequency bursting cell in STN
- Irregular bursting discharge in SNr
MER: Subthalamic Nucleus

Voa

STN border

STN tremor cell

SNr
MER: Subthalamic Nucleus

Sagittal view

- Paraesthesias
- Improvement in rigidity
- Tremor
- Akinesia
- Dyskinesias
- Autonomic symptoms
- Tetanic motor contraction ("fixed dystonia")
- Gaze deviation
- Eye deviation
- Dizziness

Coronal view

- Dizziness
- Improvement in rigidity
- Tremor
- Akinesia
- Dyskinesias
- Tetanic motor contraction ("fixed dystonia")
- Dysarthria
- Gaze deviation (contralateral to stimulation)
- Eye deviation (adduction, mydriasis)
- Paraesthesias
- Autonomic symptoms
**Conclusion**

- **Advancement of surgery for movement disorder**
  - Reinforced by technical innovation and development
    - **Diagnostic development**: neuroimaging and EPM technology
    - **Therapeutic development**: chemo-lesioning, RF lesioning, electrical stimulation, radiosurgery, ultrasound surgery

- **Neuroanatomy and physiology for movement disorder surgery**
  - Still under-investigation
  - Provide academic bases of these advancement
  - Rationale for therapeutic approach
  - Verifying treatment efficacy
감사합니다

- **Yonsei Parkinson Center**
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    - PA: EJ Kweon, SG Park
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    - Staff: YH Sohn, PH Lee, BS Yeh
    - Fellow: JJ Lee, YJ Lee
    - CRC: HK Woo
  - **Rehabilitation**
    - Staff: SR Cho