Cortical and Subcortical Motor Systems and Disorders

Nancy L. Sicotte, M.D.
Director, Multiple Sclerosis Program
Cedars-Sinai Medical Center
Professor in Residence
Department of Neurology
David Geffen School of Medicine at UCLA
Overview

• Anatomy - Cortical
• Anatomy – Subcortical
• Upper versus Lower Motor Neuron Changes
• Syndromes
Fig. 53. Some external anatomical landmarks of the human brain.
Cortical Motor Areas
Major Cortical Motor Pathways

Fig. 60. Descending motor pathways of the human central nervous system.
Motor and Sensory Tracts Through the Brainstem

- Substantia nigra
- Corticopontine tracts
- PONS (Cranial nerves V to VII)
- Pontine nuclei
- MEDULLA (Cranial nerves VIII to XII)
- Spinothalamic tract
- Medial lemniscus
- Internal capsule
- Corticospinal tract
- Middle cerebellar peduncle
- Inferior cerebellar peduncle
- Olive
- Pyramid
- Decussation of pyramids (caudal end of medulla)

(Motortracts ascending to thalamus)
(Fibers descending from cerebral cortex)
Basal Ganglia

Corpus callosum
Head of caudate nucleus
Insula
Putamen
Globus pallidus
Lentiform nucleus
Third ventricle
Posterior limb of internal capsule
Thalamus
Tail of caudate nucleus
Temporal horn of lateral ventricle, with choroid plexus

Fig. 57. Horizontal section through the right cerebral hemisphere and midline structures.
Cortical/Subcortical Connections
For Motor control

Fig. 61. A general plan of neuronal circuitry for the control of movement.
Arterial Supplies to the Brain

Four arteries in the neck supply blood to the brain:

• two **internal carotid arteries** coming off the common carotid arteries.

• two **vertebral arteries** which also supply blood to the spinal cord.
The **Middle Cerebral Artery (MCA)** territory is most frequently involved in strokes of the anterior circulation.

This artery supplies the biggest territory in the brain and some of the most important brain structures reside in this territory.
Middle Cerebral Artery Territory

Full territory MCA strokes leave a person severely impaired.

Symptoms include paralysis, numbness, and blindness on the opposite side of the stroke. Left MCA strokes often leave the patient without ability to speak or understand language. Right MCA stroke leaves patient with inattention to the left side of the world and inability to recognize their own deficits.
Left Middle Cerebral Artery Stroke
Lacunar Syndromes

• Pure Motor Stroke – most common
  – Localization: posterior limb of internal capsule
• Ataxic Hemiparesis
  – PLIC, pons, coronal radiata, leg>arm (crural paresis)
• Dysarthria/clumsy hand
  – Pons (variant of ataxic hemiparesis)
• Pure Sensory Stroke
  – PLIC plus thalamus
• Mixed Sensorimotor Stroke
  – Larger PLIC plus thalamus
Lateral Medullary Syndrome (Wallenberg)
Fig. 51. A thoracic segment of the spinal cord, showing sensory and motor neurons and the connections of a paravertebral sympathetic ganglion.
### Upper Motor Neuron (UMN) vs. Lower Motor Neuron (LMN) Signs

<table>
<thead>
<tr>
<th>SIGNS</th>
<th>UMN Lesions</th>
<th>LMN Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Atrophy*</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Fasciculations</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Reflexes</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Tone</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
</tbody>
</table>

*Some atrophy may develop due to disuse*
Basal Ganglia
Neurochemistry of the Basal Ganglia
Connectivity diagram showing excitatory glutamatergic pathways as red, inhibitory GABAergic pathways as blue, and modulatory dopaminergic as magenta.
All Together Now..

Direct pathway lesions => Hypokinesia
Indirect Lesions => Dyskinesias
The Cerebellum
Histology of the Cerebellum
Single Folia
Cerebellar Connections
Motor Disorders

- Amyotrophic Lateral Sclerosis
- Multiple Sclerosis
- Parkinson Disease
- “Parkinson Plus” - PSP, CBD, Shy-Drager
- Huntington Chorea
- Tardive Dyskinesia
- Spinal Cerebellar Atrophy (SCAs)
- Benign Essential Tremor
ALS - “Lou Gehrig’s Disease”

- “Pure” Motor System Neurodegenerative disorder
- Affects Upper and Lower Motor Neurons
- Onset in late middle age, Men>Women
- Familial form (SOD mutation) accounts for 10% of cases
- Median survival = 5 years (3 years for bulbar forms)
- Cognitive impairment now recognized to occur
- Pathological laughing/crying
Multiple Sclerosis

- Autoimmune demyelinating disease of the central nervous system
- Age of onset 20-40, affects women: men - 2:1
- Wide spread white matter lesions
- Gray matter atrophy
- Relapsing-remitting course usually followed by progressive myelopathy
- Cognitive impairment/disinhibition common (la belle indifference)
MS Lesions: Axonal Changes

Courtesy of Rudick R
Basal Ganglia Connections
Parkinson Disease

- Neurodegenerative disease resulting in loss of pigmented neurons in the substantia nigra – mitochondria?
- Occurs in elderly men > women
- Environmental factors likely important (pesticides, MPTP)
- Difficulties with initiation of movement
- Tremor at rest
- Depression/cognitive impairment common
- Treatment: Dopamine agonists
- Deep brain stimulators/stereotaxic surgery
Parkinson “Plus”

- Share phenotype of tremor, stiffness, impaired initiation but with other features - many with Lewy bodies
- Progressive supranuclear palsy (PSP) - eye movement impairment, axial rigidity, personality changes
- Corticobasal degeneration (CBD) - present with unilateral (usually upper limb) apraxia, progressive motor/cognitive impairment, cortical lewy bodies
- Dementia with Lewy bodies (DLB) - may look like Alzheimer’s, frequent hallucinations, sleep disturbance
- Shy-Drager - like Parkinson disease, but severe autonomic involvement early
- Drug induced Parkinsonism - very common
Huntington Chorea

- Autosomal dominant disorder, first CAG repeat disorder described
- Symptoms begin in 40-50s.
- May present with psychiatric symptoms, depression, psychosis, mania
- Caudate atrophy
- Choreathetoid movements develop later
- Progressive decline in function over 10-15 years
- No effective treatment
Tardive Dyskinesia

- Develops after long term use of neuroleptics (dopamine antagonists)
- Frequently seen in patients with schizophrenia
- More likely with “high potency” forms ie Haldol
- Symptoms improve with use of offending agent - vicious cycle
Dystonia

- Abnormal, sustained contraction of muscles - (agonists and antagonists)
- Common forms - cervical, hand (writers cramp), can be generalized
- Cervical dystonia (torticollis) - “sensory tricks” sometimes work
- Some rare forms are responsive to dopamine agonists
- Cause not well understood ?traumatic, overuse?
- Can be caused acutely by certain drugs
- Most common treatment now is Botox
Spinocerebellar Atrophy

- Multiple genetic forms now recognized
- Many with triple nucleotide repeats
- Variety of phenotypes, many involving cognitive impairment
- Severe Cerebellar Atrophy
- Currently no effective treatments
Structural Imaging
Water Diffusion - Isotropic and Anisotropic

Diffusion along axons is anisotropic

**Figure 4.** A simplistic schematic of the longitudinal view of a myelinated axon. Myelin, the axonal membrane, microtubules, and neurofilaments are all longitudinally oriented structures that could hinder water diffusion perpendicular to the length of the axon and cause the perpendicular diffusion coefficient, $D(\perp)$, to be smaller than the parallel diffusion coefficient, $D(\parallel)$. Other postulated sources of diffusion anisotropy are axonal transport and susceptibility-induced gradients.

Diffusion gradients applied in 6 directions

Tensor Displayed as an Ellipsoid

Fig. 2. Ellipsoidal approximation of directional anisotropy. The ellipsoid surface represents the distance of molecule motion from the origin in a certain diffusion time.

Diffusion Tensor Imaging

Myelin Stain - Mid pons

FIBER ORIENTATION:
Red = right/left
Blue = dorsal/caudal
Green = anterior/posterior
Horizontal Gaze Palsy with Progressive Scoliosis (HGGPS)

Crisfield 1974
Dretakis & Kondoyannis 1974
Sharpe et al., 1975
MRI HGPPS Patient

Midpons - DTI

Control

HGPPS
Sagittal View - DTI

Control

HGPPS

Coronal View - DTI

Control

HGPPS

Tractography
Tract tracing with Diffusion Tensor Imaging (DTI)
Diffusion Tensor Imaging Metrics

- **Mean Diffusivity (MD)** - average of diffusion in all directions
- **Axial Diffusion (AD)** - 1st eigenvalue - parallel to tract
- **Radial Diffusion (RD)** - average of 2nd and 3rd eigenvalues - perpendicular to tract
- **Fractional Anisotropy (fA)** - dimensionless number ranging from 0 (isotropic) to 1 corresponding to the degree of preferential flow
Tract Based Spatial Statistics (TBSS) Skeletons
Group Differences: Fractional Anisotropy in RRMS vs Controls
fA group/correlation and with composite motor score

Controls vs. RRMS

Correlation with motor function
RD group comparisons and correlations with 9HPT

Radial Diffusivity controls vs. RRMS

Correlation with 9HPT
Corticospinal tracts
CSTs Rendered in 3D
DTT in Tumor Mapping

Presurgical fMRI in a patient with an astrocytoma

What task was the patient performing?
DTI of Motor Pathways: RRMS vs Controls

Kern et al. NeuroImage, in press
Radial Diffusivity in Callosal Pathways Predicts Worsening of Hand Motor Function in RRMS

Kern et al. NeuroImage, in press
Compensation or Disinhibition? fMRI during finger movements
Resting State fMRI: Default Network

Damoiseaux and Greicius  *Brain Struct Funct* 2009, 213:525-533
Altered DMN Activity in MS

Bonavita et al Mult Sclerosis epub Jan 2011
Sensorimotor Network

Human Connectome Project: http://humanconnectome.org
Conclusions

• Human Motor System is a complex network involving multiple cortical and subcortical areas

• Impairments in motor control are common in many neurodegenerative disorders

• Multimodal imaging approaches can be used to study changes in structural and functional integrity: in particular combined DTI/fMRI
Thank you for your attention!