Neuroanatomy, Neuroscience Methods and Technology

Thomas A. Woolsey, MD

Thursday - June 3, 2010

Background and Approaches

History, Technologies, Disciplines, Time Lines

Leonardo da Vinci (ca 1490's)  Brunschwig (ca 1525)

(Covaci, 2002)
**Terms**

- *per curiam*  
  "by the court"

- *qui tam*  
  *(qui tam pro domino rege quam pro se ipso in hac parte sequitur)*  
  "[he] who sues in this matter for the king as [well as] for himself"

- *corpus callosum*  
  "big body"

- *superior colliculus*  
  "upper hill (bump)"

- *amygdala*  
  "almond"

- *hippocampus*
Tech Time Lines

Anatomy
Histology
Physiology
Radiology

Vesalius
Preservations
Microscope
Neuron
Synapse
Stimulation
AP
CBF

1500
1600
1700
1800
1900
2000

Main Features
Divisions, Components, Environment

Magnetic Resonance Image (MRI) of head and neck at the midline.

Organ

Weight
2-3% of body

O₂ Consumption
20% of total

Brain Energy (Glucose) Utilization
20% of total

Brain Blood Flow
20% of heart output at rest
Peripheral (PNS - outside the skeleton)
- Sensory (sensation)
- Motor (movement)
- Autonomic ("involuntary")
- Enteric (gut)

Central (CNS - inside the skeleton)
- Spinal Cord (Spine)
- Brain (Skull)

Views of the human spinal cord and lower brain stem.
LEF - Left lateral (side) showing segments and spinal nerves.
MID - Anterior (front) view of spinal cord without showing enlargements.
RIG - Posterior (back) view of spinal cord with roots, ganglia and nerves.

Spinal Cord Segment

The different regions of the brain from the lateral (side) and median section (middle) human brain. These brain regions are discernible in all vertebrates and in early embryos.
- (pallidum = gold; thalamus = blue/purple; midbrain = orange; pons = purple; cerebellum = blue; medulla = red/orange; spinal cord = green)
**Gray Matter**
- Cortex, Nuclei or Ganglia (groups of nerve cell bodies and neuropil) generally of similar function
- Neuropil - neuronal processes, synapses and glia

**White Matter**
- Bundles (groups of myelinated axons [see below] that course in the same direction)
- Tracts (also groups of axons (myelinated and unmyelinated but indicates origin, destination and therefore function)

**Anisotropy - Diffusion Tensor Imaging**

**Cerebrospinal Fluid (CSF)**
The brain and spinal cord are bathed in a colorless fluid called cerebrospinal fluid (CSF). The fluid is made in chambers in the brain called ventricles (blue). It circulates between all the cells and their processes and in the space between a membrane on the brain surface (called the pia mater) and a membrane that is next to the skull or spine (arachnoid mater) called the subarachnoid space (gold).
Other

- Blood Vessels (arteries, capillaries, veins and venous sinuses)
- Coverings - meninges (dura mater (tough mother), arachnoid (spider web like), pia (tender/affectionate))
- Cerebrospinal fluid (CSF - ventricles, canals, intercellular space, subarachnoid space)

Cells of Nervous System

Neurons, Contacts, Support, Function

Neurons

- Parts: cell body (soma), dendrites (input processes), axon (output process)
- Types: local circuit (90%), projection (10%)
- Variations: stellate (star like); pyramidal (conical/triangular); famous guys - Purkinje, Betz, Cajal, Retzius, Mauthner…
- All variations are correlated to particular functions.
**Glia (glue) or Supporting Cells**

- Parts: cell body (soma) and "short" processes
- Types: astrocytes (star-like); oligodendrocytes (fewer (oligo) branches (dendrites)); microglia (small ones)
- Variations: fleshy, fibrous (stringy), myelinating, non-myelinating
- All variations relate to specific functions.

---

Cajal’s drawing of “glia” in the spinal cord.

- **A Ependyma** (lining of the central canal of the spinal cord)
- **B Oligodendrocytes** which myelinate axons in fiber tracts
- **C Astrocytes - Protoplasmic** (fleshy) in gray matter
- **D Astrocytes - Fibrous**
Physiology of Nervous System
Conduction, Transmission, Reflexes

Dermatome =
The region (slice) of skin innervated by a single spinal or posterior (dorsal) root ganglion
Mixed spinal nerve

Periphery (skin, muscle, etc.)

Segmental nerve: (posterior (dorsal) root = sensory - touch; anterior (ventral) root = motor - movement; spinal or posterior (dorsal) root ganglion = sensory nerve cell bodies)

Axon diameters differ in motor and sensory nerves

Cross section of human muscle (motor) nerve – myelin stain

Cross section of human sensory nerve – myelin stain

Axon diameters differ in motor and sensory nerves

Segmental Nerves

Spinal or Posterior (dorsal) Root, Ganglion Cells & Sensory Nerves

(axons inn from posterior (dorsal) root ganglia)

Dermatomes

Anterior (ventral) Root & Motor Nerves

(axons out from motor neurons)

Motor Units

Segmental Nerves

Spinal or Posterior (dorsal) Root, Ganglion Cells & Sensory Nerves

(axons inn from posterior (dorsal) root ganglia)

Dermatomes

Anterior (ventral) Root & Motor Nerves

(axons out from motor neurons)

Motor Units

Axons diverge to multiple spinal targets

motor neurons: c, interneurons: c, spinal cord: b, and brain: a

Spinal or Posterior (dorsal) Root Ganglion Cells

Pseudo-Unipolar Neurons

(neurons start as bipolar cells and become "unipolar" during development)

Single sensory endings

light & crude touch, pain, temperature and muscle senses

Axons diverge to multiple spinal targets

motor neurons: c, interneurons: c, spinal cord: b, and brain: a

Axon diameters differ in motor and sensory nerves

Cross section of human muscle (motor) nerve – myelin stain

Cross section of human sensory nerve – myelin stain

Axon diameters differ in motor and sensory nerves

Segmental Nerves

Spinal or Posterior (dorsal) Root, Ganglion Cells & Sensory Nerves

(axons inn from posterior (dorsal) root ganglia)

Dermatomes

Anterior (ventral) Root & Motor Nerves

(axons out from motor neurons)

Motor Units

Axons diverge to multiple spinal targets

motor neurons: c, interneurons: c, spinal cord: b, and brain: a

Spinal or Posterior (dorsal) Root Ganglion Cells

Pseudo-Unipolar Neurons

(neurons start as bipolar cells and become "unipolar" during development)

Single sensory endings

light & crude touch, pain, temperature and muscle senses

Axons diverge to multiple spinal targets

motor neurons: c, interneurons: c, spinal cord: b, and brain: a

Segmental nerve (posterior (dorsal) root = sensory - touch; ventral root = motor - movement; spinal or posterior (dorsal) root ganglion = sensory nerve cell bodies)

Periphery (skin, muscle, etc.)

Spinal cord
Motor Units, Motor Neuron Pools & Somatotopy

Spinal Motor Neurons

- Multipolar
- Output Diverges to -
  several or many muscle cells: motor unit
- Input Converges from –
  spinal or posterior (dorsal) root ganglion cells
  spinal interneurons
  long tracts from from brain
- Integrate
- Map
  flexors, extensors, proximal, distal

Motor Unit - A motor neuron and the muscle fibers it innervates.

Motor neuron pools (nuclei) are organized systematically according to the body plan - somatotopically

“Knee Jerk”
Stretch Reflex & Antagonist Inhibition
When the knee is struck...

Ia muscle afferents fire...

there is monosynaptic activation of the extensor α-motor neuron...

and the (agonist) muscle(s) contracts.

...which inhibit motor neurons to the flexor (antagonist) muscle.

The knee extends.

Glycinergic (inhibitory) interneurons are also activated...

Brain Pathways

Organization, Geography, Function

Path Finding

• Loss of a particular function after damage (lesion)
• Stimulation (natural/electrical) with recording
• Pathology - degeneration of cells and axons with secondary loss of myelin
• Experiments - special stains and tracers that take advantage of physiological processes

Conventions

• Subserve a particular function
• Axons travel together in specific locations (i.e., tracts) in a particular order (topography)
• Always consider: cell body (soma) location, axon course, synapses and side relative to origin and destination
• Nomenclature often origin and target, i.e., Cortex-Spinal Tract = from cortex to spinal cord

• Related to whole brain through “sections” – gross, histological, imaging
• Related to fiber bundles (fasciculi; i.e., lateral columns, internal capsule, corpus callosum)
• Related to nuclei, ganglia, areas, layers
• Related to transmitters and effects: excitatory, inhibitory, modulatory, fast, slower, slow
Dorsal Column/Medial Lemniscus (a ribbon) Pathway
This pathway carries fine discriminative and active touch, body and joint position, and vibration sense.

Corticospinal (Pyramidal) Pathway
This is the direct connection from the cerebral cortex for control of fine movements in the face and distal extremities, e.g., buttoning a jacket or playing at trumpet.
For Review

Use the Bio 3411 Work Sheet 082809 (handout and posted on the course web site) to get comfortable with the neuroanatomy.

It’s neither rocket science nor is it neurosurgery, it just takes a little practice!
After the pyramid was cut (lesioned) the opposite hand (the right hand) was used to try to get food from a well but all fingers were used. The monkey could not get food from the smallest well.

The hand opposite the normal pyramid (the left hand) was used to get food from the small well by opposing the thumb and forefinger. The monkey got the food from the smallest well.

Cut Pyramid

<table>
<thead>
<tr>
<th>Electrical stimulation of different points in motor cortex with small currents (thresholds) causes different movements</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.4 0.6 1.5 1.6 1.8</td>
</tr>
<tr>
<td>1.0 1.0 1.8</td>
</tr>
<tr>
<td>2.1 0.4 2.1</td>
</tr>
<tr>
<td>1.0 1.0 1.2</td>
</tr>
</tbody>
</table>

Normal Pyramid

<table>
<thead>
<tr>
<th>After the pyramid was cut the movements were coarser and the currents required to produce them were larger.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 0.2 0.3</td>
</tr>
<tr>
<td>0.7 0.4 0.2</td>
</tr>
<tr>
<td>1.2 0.3 0.5</td>
</tr>
<tr>
<td>0.4 0.8 1.0</td>
</tr>
</tbody>
</table>

A neuron in the motor cortex of an awake behaving monkey fires when the wrist is extended (red arrow in diagram above). It fires more when more force is required (flexors loaded) and not at all if no contraction is needed to extend the neck (extensions loaded).

A neuron in the motor cortex of an awake behaving monkey fires in relation to the direction of the movement (see "tuning" curve - left).

Sources of Descending Pathways for Movement Control

1. Forebrain (Cortex)
2. Midbrain (Red Nucleus & Superior Colliculus)
3. Pons (Reticular Formation)
4. Medulla (Reticular Formation and Vestibular Nuclei)
Descending systems from the brain influence cells in the spinal cord to create movements. The cerebellum and the basal ganglia indirectly influence movements as indicated schematically here.

Relative Size of Different Brain Parts in Phylogeny - The forebrain becomes relatively larger as new pathways (functions) are added.

Why are brain pathways “crossed”? Ramón y Cajal suggested that brain pathways are crossed to preserve the appropriate relationships after optical inversion by the lens as indicated schematically by the arrows in the uncrossed (left) and the crossed (right) visual pathways.

Brain Blood-flow/Function
Anatomy, Physiology, Imaging

Arteries of the brain from the lateral aspect (side view). The sources and destinations of these vessels are hidden by the convolutions of the cerebral cortex.

Axial slice of the brain, MRI at the same level and a map of the vessel territories. The arrow indicates the region supplied by the middle cerebral artery.
Magnetic Resonance Image (MRI) after a stroke (blocked blood vessel) in the territory of the middle cerebral artery (arrow).

Sensors for recording the EEG from an awake normal volunteer.

During an operation for treatment of seizures the patient is awake. This patient had a seizure which is a burst of abnormal action potentials in the right lateral postcentral gyrus. The active cortex got redder when blood flow increased.

Video clip of the brain surface under a fluorescence microscope showing movement of labeled red blood cells through the vessels. When the brain is stimulated the numbers and velocity of these cells increase.

Dr. Marcus Raichle (here in his youth) and colleagues at Washington University pioneered the use of positron emission tomography (PET also developed here) to study complex behaviors such as language. Here he injects tracers into a volunteer. The volunteer’s head is in an early device to monitor regional changes in radioactivity.
Definitions

- **-phasia**: to speak
- **aphasias**: disorders of speech “content”
- **prosody**: stress, intonation, patterns of utterances in speech
- **aprosodias**: disorders of speech “affect”
Strokes from blocking different branches of the middle cerebral artery have different effects on language function (aphasias).

<table>
<thead>
<tr>
<th>Type</th>
<th>Verbal Out</th>
<th>Sentene</th>
<th>Compre-</th>
<th>Naming</th>
<th>Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Broca’s</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓+</td>
</tr>
<tr>
<td>Wernicke’s</td>
<td>Fluent</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Conduction</td>
<td>Fluent</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Global</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Anomic</td>
<td>Fluent</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Trans-cortical</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Motor</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Sensory</td>
<td>Fluent</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>

PET scans show activation of different areas with different “speech” related activities.

Pathways for Prosody: Expression in response to a written or spoken question.
<table>
<thead>
<tr>
<th>Type</th>
<th>Area</th>
<th>Aphasia</th>
<th>Aprosodias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global</td>
<td>MCA</td>
<td>Comprehension</td>
<td>Comprehension</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Speech Production</td>
<td>Gesture Production</td>
</tr>
<tr>
<td>Sensory</td>
<td>Wernicke’s</td>
<td>Speech</td>
<td>Gesture</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Comprehension</td>
<td>Comprehension</td>
</tr>
<tr>
<td>Conduction</td>
<td>Angular</td>
<td>Word</td>
<td>Gesture</td>
</tr>
<tr>
<td></td>
<td>Gyrus</td>
<td>Repetition</td>
<td>Repetition</td>
</tr>
<tr>
<td>Motor</td>
<td>Broca’s</td>
<td>Speech</td>
<td>Gesture</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Production</td>
<td>Production</td>
</tr>
</tbody>
</table>

**Music**

Musician with perfect pitch

Musician without perfect pitch

**Genius**

Albert Einstein – “for my scientific thinking”

...“words do not seem to play any role”

...but there is “associative play” of “more or less clear images” of a “visual and muscular type.”
Development and Plasticity

Embryology, Refinement, Wiring, Learning

http://embryo.soad.umich.edu/

THE BRAIN ATLAS, 3rd ed, p. 10

**Human Brain Areas**

(Area 17, the visual cortex also called striate cortex is on the banks of the calcarine fissure.)

**Labeled axons from visual thalamus to visual cortex in monkeys of different ages**

Axons related to left eye are red and those related to right eye are blue.
**Both Eyes Open From Birth** - projections from one eye labeled

**One Eye Closed From Birth** - expanded projections from open eye labeled

**Thalamocortical axons related to Open Eye**

**Thalamocortical axons related to Closed Eye**

---

**rs-fcMRI**

*Spontaneous Default Network Activity*

---

**Left**
*Fair et al., 2008*

**Right**
*Fair et al., 2008*
Summary for “Late” bilinguals - in the ANTERIOR (Broca’s Area) and the POSTERIOR Wernicke’s Area. There is overlap of activity for language interpretation but not for language production.


Donald O. Hebb
1904-1985
Speech, FOXP2 and the human–chimp divide

...
5th Grader's ceramic of the brain showing "language" cortex.

Michelangelo's Creation of Adam in the Sistine Chapel at the Vatican

"Damn it, I'm a brain surgeon, not a rocket scientist!"

(Scalman, 2006; Woolsey et al., 2008)