Clinical Neuroanatomy for PG4s

**PG4 Core Curriculum**

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Revisiting neuroscience & neuroanatomy in the PG4 curriculum

- Integration with clinical experience
- Fill potential knowledge gaps
- Prepare you for changes in psychiatry during your professional years, in
  - Diagnostics (?descriptive -> pathophysiologic?)
  - Therapeutics (?global -> specific brain regions?)
  - Theories & conceptual framework

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CNS Building Blocks

CNS Components Parts

- CNS contains
  - Neurons - ~100 billion*
  - Glia (“glue”) - ~1 trillion [much of neuropil]
- Gray matter
  - Cortical regions & Nuclei
- White matter
  - Tract, fasciculus, funiculus, lemniscus, peduncle

* Global population ~6.5 billion humans as of 9/26/06 (www.census.gov)
CNS Macro Components

- White vs Gray matter vs structural changes (periventricular hyperintensities shown here)
- More on this during later lectures on neuroimaging

Cook et al., Arch Neurol 2002

Neurobiology: Functional aspects

- Synthesis - primarily in cell body
  - Enzymes, structural proteins, membrane components, transmitters
  - Need transport systems to convey to other parts (microtubules provide cytoskeleton and transport system)
- Any disorders come to mind?*

* Michaelis “Cytoskeletal Integrity as a Drug Target.” Curr Alzheimers Res 2005

Neurobiology: Functional aspects

- Energetic demands
  - Brain uses 20% of body’s energy
  - No major storage - must depend on an uninterrupted arterial supply (gluc & O₂)
  - Energy is primarily used to maintain the electrochemical gradients *
  - PET, SPECT, fMRI depend on coupling of neuronal activity to energy use to glucose uptake and to blood flow


In general, information flows electrically down the axon, then chemically across synapse. Multiple types of synapse are depicted.

Nolte The Human Brain... 2002
Neurobiology: Dendritic Spines

Dendritic spines on pyramidal cells (arrows).

Correlations:
* enriched environment
* antidepressants and Li

Human Cerebral Cortex

- Most cortex is neocortex (95%)
  - Neocortex - nearly all visible surfaces
  - Paleocortex - base of telencephalon
  - Archicortex - hippocampus
- Pyramidal cells
  - most numerous neocortical neurons
  - principal neocortical output neurons
  - nonpyramidal cells - principal interneurons
- Neocortex has six layers (lamina)
  - Each with distinctive connections

Laminar Organization of Cortex

Layers vary from region to region: motor ctx gives rise to many long axons, and II-IV have abundant pyramidal cells, few stellate ("granule") cells [granular ctx]; I sensory ctx has short projections, and layers II-IV have more small cells [granular ctx or koniocortex]

Cortical inflow and outflow

- Afferents from cortical or subcortical areas
  - Thalamic relay nuclei - IV
  - Intralaminar nuclei - VI
  - From other cortical regions - II, III
  - Specialized subcortical nuclei (locus ceruleus)
- Efferents go to cortical or subcortical areas
  - Cortico-cortical fibers - III
  - Cortico-striate and to brainstem/cord - V
  - Cortico-thalamic fibers - VI
- Laminar pattern may related to disease/deficits
  - Reduction in cell number in layers II and IV in early AD in entorhinal ctx, same layers where NFTs first appear

Gomez-Isla J Neurosci 1996
White Matter Association Tracts

Long association bundles connect cortical areas and support network processing. “Disconnection syndromes” may underlie some cognitive and affective disturbances (Geschwind Brain 1965; Leuchter Brain 1992; Cook Arch Neurol 2002; Kumar & Cook Dev Neurosci 2002).

Nolte The Human Brain: an introduction to its functional anatomy 2002: fig 22-10

Bridging to the Macroscopic

Hemispheric Landmarks

Specific mental functions have been related to activity in specific brain regions.

Theories, diagnostics, and treatments of the future may depend on these relationships.

Haines. Neuroanatomy: an atlas of structures, sections, and systems. 2004

Somatotopic Organization

Penfield & Rasmussen. The Cerebral Cortex of Man. 1950.
**Brodman’s Cytoarchitectural Map**


**Brodman Areas II**

Brodman areas (BA) are frequently used in fMRI and other functional neuroimaging reports.


**Talaraich Stereotaxic Coordinates**

The coordinate system developed by Talairach and Tournaux (1988) provides a common space for comparing or combining data on individuals.

MRI and PET datasets often are transformed or “warped” using this system, though some limitations have been acknowledged.


www.neuro.xpc.org/talaraic

www.mrc-cbu.cam.ac.uk/Imaging/Common/brodmann_areas.shtml

**Cerebral Circulation (macro level)**
Circulation & Watershed Infarcts

The distal branches of the anterior (green), middle (blue) and posterior (red) cerebral arteries overlap to create border zones ("watershed areas") which are susceptible to hypoperfusion-based infarcts.

Connections at the synapses

Electrical & Chemical Synapses

- Chemical synapses - molecules cross
- Electrical synapses - "gap junctions" connexin proteins form connexons to create aqueous pore, small molecules and currents pass directly.
  - Rare in adult mammalian CNS
  - Horizontal cells of retina
  - Charcot-Marie-Tooth disease - gap junction channelopathy

Small Molecule* Neurotransmitters**

<table>
<thead>
<tr>
<th>Category</th>
<th>Example</th>
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<tbody>
<tr>
<td>Amines</td>
<td>Acetylcholine</td>
</tr>
<tr>
<td></td>
<td>Monoamines</td>
</tr>
<tr>
<td></td>
<td>Catecholamines (dopamine, norepinephrine)</td>
</tr>
<tr>
<td></td>
<td>Serotonin</td>
</tr>
<tr>
<td></td>
<td>Histamine</td>
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<tr>
<td>Amino Acids</td>
<td>Glutamate</td>
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<tr>
<td></td>
<td>GABA (γ-aminobutyric acid)</td>
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<tr>
<td></td>
<td>Glycine</td>
</tr>
<tr>
<td></td>
<td>Aspartate, homocysteine, taurine</td>
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<tr>
<td>Others</td>
<td>Nitric oxide</td>
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<tr>
<td></td>
<td>ATP</td>
</tr>
<tr>
<td></td>
<td>Adenosine</td>
</tr>
</tbody>
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* namely, < 10 carbons
** Neurons can employ endocytotic vesicle recycling for these
# Neuropeptide* Neurotransmitters

<table>
<thead>
<tr>
<th>Category</th>
<th>Peptides</th>
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</thead>
<tbody>
<tr>
<td>Opioid peptides</td>
<td>Enkephalins, Endorphins</td>
</tr>
<tr>
<td>Posterior pituitary</td>
<td>Oxytocin, Arginine vasopressin</td>
</tr>
<tr>
<td>Tachykinins</td>
<td>Substance P, Neurokinins</td>
</tr>
<tr>
<td>Other</td>
<td>Angiotensin II, Neuropeptide Y, Corticotropin-releasing factor, Vasoactive intestinal peptide</td>
</tr>
</tbody>
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* Peptidergic neurons generally do not employ endocytotic recycling.