INTRODUCTION TO NEUROLOGICAL DISEASE

LiR – Session #1

Winter 2018
Session Overview

• Introductions and Course Plan
• Intro to the brain
• Structure of the Nervous System
• Ventricular Systems and Meninges
• Brain Cells
  • General
  • Organization
• Major Functional Brain Regions
  • Cerebrum (aka cerebral hemispheres aka cerebral cortex)
  • Limbic System, Basal Ganglia, Brainstem, Cerebellum
Introductions/Plan

• Instructor (me!): Ashley Thompson
  • BSc, MSc, PhD Candidate

• How to get in touch with me:
  • Ashley.Thompson3@Carleton.ca

• This session:
  • Introduction to Neurological Disease
    • Introductory neuroscience
    • Selection of diseases/disorders
      • Symptoms
      • Causes
      • Pathology
Course Overview

• **Session 1** (today): Intro to Neurological Disease and Organization of the Brain

• **Session 2**: Communication in the Brain/Hormones and Stress

• **Session 3**: Epilepsy/Phantom Limbs

• **Session 4**: Stroke/Chronic Pain

• **Session 5**: Parkinson’s/Alzheimer’s

• **Session 6**: Brain Tumours/Split-Brain Patients
In this course, you can expect to learn...

- What the brain is, its major regions and their functions
  - Introductory level
- About brain cells and how they communicate with one another
- Clinical symptoms of a variety of neurological diseases
  - Biological, developmental, environmental, and experiential factors that contribute to disease
- Current and prospective treatments for neurological diseases
- The use of animal models of disease in research
Some Useful Terminology…

<table>
<thead>
<tr>
<th>Term</th>
<th>Meaning</th>
<th>Used to…</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIAGNOSIS</td>
<td>What disease is it?</td>
<td>Distinguish one disease from another</td>
</tr>
<tr>
<td>ETIOLOGY</td>
<td>What caused it?</td>
<td>Discuss the apparent causation and developmental history of an illness</td>
</tr>
<tr>
<td>PROGNOSIS</td>
<td>What are the short/long-term outcomes?</td>
<td>Forecast the probable course of a disease</td>
</tr>
</tbody>
</table>
Some Useful Terminology...

• **Incidence:** The number of new cases of a disorder in a given time period (usually a year)
  
  Ex. Approximately 6,200 new cases of Parkinson’s disease are diagnosed each year in Canada (OR 20 new diagnoses per 100,000 people)

• **Prevalence:** Percentage of the population that exhibits a disorder during a specified time period
  
  Ex. Over 100,000 Canadians are currently living with Parkinson’s

• **Lifetime Prevalence:** Percentage of people who have been diagnosed with a specific disorder at any time in their lives
  
  Ex. The lifetime risk of PD is 2% in men and 1.3% in women
How do we diagnose neurological disease?

• Historically, methods were...interesting to say the least
  • Most were very crude! Why do you think that was?

• Diagnosis for neurological disorders had to wait on a few things, which began to appear in the 19\textsuperscript{th} century:
  • Development of proper tools for clinical investigation
    • E.g. tendon hammers, syringes
  • Development of imaging techniques
    • X-rays, the electroencephalography (EEG)
  • After patients died, clinical neurologists compared their notes to those of the neuropathologist – made \textbf{correlations}
  • Eventually, as more note-keeping occurred, links were made between specific types of trauma and their consequences (ex. Stroke and hemiplegia)
How do we diagnose neurological disease?

- Even more numerous were the advancements made in the 20th century

<table>
<thead>
<tr>
<th>Advancements in Neurology</th>
<th>Improved Surgical Techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td>Information Sharing Between Scientists</td>
</tr>
<tr>
<td>Immunology (Vaccines)</td>
<td>Techniques for Visualization (e.g. microscopy, histology)</td>
</tr>
<tr>
<td>Diagnostic Imaging Techniques</td>
<td></td>
</tr>
</tbody>
</table>
Diagnosis Today

• Evaluating and diagnosing damage to the nervous system is very complex
  • Many symptoms occur in many disorders in different combinations
  • Many disorders do not have definitive causes or markers to test for

• In addition to a complete medical history and physical exam, there are a multitude of diagnostic procedures that may be used to investigate nervous system disorders:
  • E.g. MRI, EEG, lumbar puncture, evoked potentials
The Brain: Your Powerhouse
The Brain: Major Lobes

How did we find out which brain areas are responsible for certain functions (e.g. language, memory, decision-making)?
Cerebral Cortex

- Mediates most complex, higher-order processing
  - What most of us think of when we think of the ‘brain’
  - Like bark on a tree...
- Many bumps and grooves!
  - Bumps – gyri (sing. gyrus)
  - Grooves – sulci (sing. sulcus)
  - Deep grooves - fissures
- Prominent sulci and fissures separate brain regions
Longitudinal Fissure

- The longitudinal fissure separates the left and right ____________.
- What connects them?

http://library.med.utah.edu/WebPath/HISTHTML/NEURANAT/NEURANCA.html
Structure of the NS

- The nervous system is divided into the **central** and **peripheral** systems

  **Central**
  - Brain
  - Spinal Cord

  **Peripheral**
  - Somatic Nervous System
  - Autonomic (aka Visceral) Nervous System
Structure of the Peripheral NS

- Division of the PNS
  - Somatic Nervous System
    - Voluntary control
    - Spinal nerves that innervate skin, joints and muscles

- AFFERENT – “Arriving” - conducted TOWARD
  - Typically SENSORY and PROPRIOCEPTIVE input from periphery

- EFFERENT – “Exiting” - conducted AWAY FROM
  - Typically MOTOR commands from brain to periphery
Structure of the Peripheral NS

- Division of the PNS
  - Somatic Nervous System
  - Autonomic (aka Visceral) Nervous System
    - Outside voluntary control (e.g. blushing)
    - Smooth muscles: cardiac, intestines
    - Secretory functions: glands
    - Two divisions:
      - Sympathetic NS
      - Parasympathetic NS
Structure of the Peripheral NS

**REST AND DIGEST**

- **Eyes**
  - Parasympathetic: Constricts pupils
  - Sympathetic: Dilates pupils (enhanced vision)

- **Lungs**
  - Parasympathetic: Constricts bronchi
  - Sympathetic: Relaxes bronchi (increased air to lungs)

- **Heart**
  - Parasympathetic: Slows heart beat
  - Sympathetic: Accelerates, strengthens heart beat (increased oxygen)

- **Stomach, intestines**
  - Parasympathetic: Stimulates activity
  - Sympathetic: Inhibits activity (blood sent to muscles)

- **Blood vessels of internal organs**
  - Parasympathetic: Dilates vessels
  - Sympathetic: Contracts vessels (increased blood pressure)

**FIGHT OR FLIGHT**

Illustration from Kolb & Wishaw, An Introduction to Brain and Behavior, Sinauer, 2014
CNS – The Spinal Cord

• The spinal cord is segmented
• Responsible for reflexes (e.g. patellar reflex, withdrawal reflex)
• Forms a highway between the body and the brain for information that travels in both directions
• SC produces movement (mostly in response to signals from brain)
  • Exception: reflexes are autonomic, independent of brain’s involvement
The Brain’s Environment

- There isn’t a whole lot separating our brain from the outside world!
- There are a few things that keep it safe though...
  - What is the most obvious one?
The Meninges and CSF

- The brain and spinal cord are protected by three layers of membranes called **meninges**
  - **Dura mater** – ‘hard mother’
  - **Arachnoid** – ‘spider-web like’
  - **Pia mater** – ‘soft mother’
- It is in the sub-arachnoid space that we find the **cerebrospinal fluid (CSF)**
  - Surrounds brain and SC
  - Protects from trauma
  - Allows brain to float

Illustration from Kolb & Wishaw, *An Introduction to Brain and Behavior*. Sinauer, 2014
The Ventricular System

- **Ventricles**
  - Series of inter-connected fluid-filled spaces
The Ventricular System

- **Ventricles**
  - Series of inter-connected fluid-filled spaces

- **CSF**
  - Clear, colourless salt solution
  - Surrounds brain and spinal cord
  - Protects brain from trauma
  - Transports substances throughout NS
  - Removes metabolic waste
The Blood-Brain Barrier

- Not everything is allowed in, which is GREAT

Hey! We want in!

I'm sorry, but you are too highly charged, too large and not lipid soluble. You cannot enter the brain!

To the brain
The Brain – Big Picture
Brain Cells

Pyramidal neuron.
Santiago Ramón y Cajal – 1899
Brain Cells: 2 types

- **Neurons**
  - Aka nerve cells
  - Primary information processing units of the brain

- **Glia**
  - Supporting and modulate activity of neurons
  - The unsung heroes...sigh
  - They are **not** just background workers
  - Play a huge role in the development of the NS and in its function (and *dysfunction*) in the adult brain
Brain Cells: Neurons

• Just like body’s other cells in many ways, but neurons are specialized for their very important and very specific job!
Structure of a Neuron

- Cell body
- Nucleus
- Axon
- Dendrites
- Axon Terminals
- Myelin Sheath
- Synapse
Structure of a Neuron

- A neuron’s structure consists of:
  - **A Cell Body**: aka *soma*, has a nucleus, which contains neuron’s genetic information
  - Two set of **Processes**:
    - 1 – **Axon** - Transmits information from the neuron to other neurons (that it has connections with)
    - 2 – **Dendrites** - Receive messages from other neurons

The places where axons and dendrites connect are called “**Synapses**”
Neuron – Structure

- **Neurons** have specialized structures for their purpose (info transmission).
  - **Dendrites** – “tree (G.)”
    - Receive information from other neurons.
  - **Cell body**
    - Integrates information; decides whether or not to pass it on
  - **Axon hillock**
    - Junction of the cell body and axon, where the *action potential* begins (aka the point of no return)
  - **Axon**
    - Carries information to be passed onto other cells
    - No changing your mind now, neuron!
  - **Terminal button**
    - Knob at the tip of an axon that conveys information to other neurons.
    - Connects with dendrites of other neurons.
Neuron – Structure

- **Axons**, especially longer ones, are usually covered with a **myelin sheath**.

- **Myelin** is a fatty substance produced by **glial cells** (fatty nature gives **white matter** its colour).

- **Myelin** insulates the **axon**, increasing the speed and efficiency of electrical signal conduction.
Neurons – 3 types

- We discuss all 3 to understand this example of a **withdrawal reflex:**
  - **Sensory Neuron** – info from outside world to SC/brain
    - Fire hot!
  - **Interneuron** – connects sensory and motor neuron in SC
    - Fire hot, pass it on!
  - **Motor Neuron** – uses info to cause muscle contraction
    - Stop touching it then!
Neurons – 3 types

• OUCH!

• If a stimulus is too intense (like this example of a flame), tissue damage can result.

• We have specialized receptors called nociceptors (aka pain receptors) that are activated when this happens.

• They trigger protective reflexes (like quickly removing your hand from a hot stove) and create the sensation of pain (to hopefully remind us not to do this again).
Brain Cells - Organization

- Neuronal cell bodies can be organized in two main ways:

  **Layered** – such as in the cortex, where we see bands of cell bodies

  **Nucleus** (pl. nuclei) – where a distinct cluster of neural cell bodies form a functional group
Neurons form Networks

- Another way to look at organization of cell bodies...

- **Cortical networks**
  - Organization is uniform, grid-like
  - Most recently developed region of the brain (and of cities in analogy)

- **Sub-cortical and brainstem networks**
  - Sporadic, irregular organization
  - Older regions of the brain
  - Like city planners without foresight!
Axons: Tracts and Nerves

- Axons often cluster together to form a ‘wire’, connecting parts of the NS
- **Within the CNS, ‘wire’ = tract**
- **Outside the CNS, ‘wire’ = nerve**

**Example:**
The optic nerve and the optic tract
Grey matter & white matter

- It is the overall organization of cell bodies and axonal tracts that allows us to perceive grey VS white matter in the brain.
Grey matter & white matter

- **Grey matter**
  - Areas rich in cell bodies and blood vessels.
    - Ex. Cerebral cortex, subcortical nuclei
    - Nuclei (plural of nucleus): groupings of functionally similar cell bodies, densely packed in one area

- **White matter**
  - Areas rich in myelin (found on axons)
    - Ex. corpus callosum, sub-cortical tracts
Major Divisions of the Brain

- When you are new to neuroscience, learning the regions and divisions feels like this
Major Divisions of the Brain

Embryonic brain regions:
- Forebrain
  - Telencephalon
  - Diencephalon
- Midbrain
  - Mesencephalon
- Hindbrain
  - Metencephalon
  - Myelencephalon

Brain structures in child and adult:
- Cerebrum (includes cerebral cortex, white matter, basal nuclei)
- Diencephalon (thalamus, hypothalamus, epithalamus)
- Midbrain (part of brainstem)
- Pons (part of brainstem), cerebellum
- Medulla oblongata (part of brainstem)

Embryo at 1 month
Embryo at 5 weeks
Child
Major Divisions of the Brain

• Let’s break it down...
  • Forebrain, midbrain, hindbrain
  • Confusion arises when we realize some structures span more than one region
    • Ex brainstem
      • Consists of entire midbrain and hindbrain (less the cerebellum)

• So, depending on how we approach the brain (level of detail), we (neuroscientists) may discuss different divisions
Major Divisions of the Brain

Cerebrum
- ‘brain’
- largest portion of the brain
- controls voluntary process and cognitive activities

Brainstem
- deep structures of the brain which connects to the spinal cord
- controls involuntary processes required to sustain life (respiration, heart beat ...)

Cerebellum
- ‘little brain’
- predominantly involved in motor control
Major Divisions of the Brain

• Cerebrum
  • Consists of two nearly identical cerebral hemispheres
    • Some differences (aka specialization) of hemispheres, called lateralization
    • LEFT hemisphere controls right side of body
      • Particularly involved in language, math and logic*
    • RIGHT hemisphere controls left side of body
      • Particularly involved in emotion, spatial orientation, facial recognition, art/music
The corpus callosum

- Large fiber tract (bundles of axons)
- Nearly 200 million nerve fibers
- White or grey matter?
Major Divisions of the Brain

- Parts of the Cerebrum
  - Cortex
    - Neocortex (externally visible)
    - Cingulate cortex (deeper...why?)
  - Subcortical structures
    - Basal ganglia
    - Limbic System
Cortex – Two important gyri

- **Precentral gyrus** (frontal lobe)
  - AKA Primary Motor cortex (PMC)
  - Motor neurons from PMC send info to SC, which delivers motor commands to body

- **Postcentral gyrus** (parietal lobe)
  - AKA Primary Somatosensory cortex
  - Sensory map of body – receives sensory input

- **Homunculus** (pl. homunculi)
  - *Noun*, a very small human or humanoid creature
  - Essentially a ‘map’ – how much real estate different body regions take up
  - Looks strange...why?
Cortex – Two important gyri

- Precentral gyrus
- Postcentral gyrus
Cerebrum: Cerebral Cortex – 4 Lobes

- **Frontal Lobe**
  - Problem solving
  - Emotional traits
  - Reasoning (judgment)
  - Speaking
  - Voluntary motor activity

- **Parietal Lobe**
  - Knowing right from left
  - Sensation
  - Reading
  - Body orientation

- **Temporal Lobe**
  - Understanding language
  - Behavior
  - Memory
  - Hearing

- **Occipital Lobe**
  - Vision
  - Color perception

- **Cerebellum**
  - Balance
  - Coordination and control of voluntary movement
  - Fine muscle control

- **Brain Stem**
  - Breathing
  - Body temperature
  - Digestion
  - Alertness/sleep
  - Swallowing
Cerebrum – Cerebral Cortex – 4 Lobes

- All lobes also contribute to higher brain functions, including cognition
  - **Occipital lobe** – processing visual stimuli
  - **Temporal lobe** – recognizing stimuli
  - **Parietal lobe** – attending to stimuli
  - **Frontal lobe** – planning responses to stimuli, also personality, impulse control
Cerebrum: Basal Ganglia

- **Role**: control of voluntary movement, procedural learning, and habit formation

- **Components (3 main parts)**
  - Caudate nucleus (*tail, L.*) + putamen (*shell, L.*) = striatum
  - Globus pallidus (*pale globe, L.*): internal (GPi) and external (GPe)

- The **substantia nigra** (*black substance, L.*) is part of the midbrain
  - Concentration of dopaminergic neurons (project to striatum)
Cerebrum: Limbic System

- **Role:** emotional control; key site of learning and memory

- **Core components:**
  
  - **Cingulate cortex** (*encircling, belt, L.*)
    - Emotional processing and memory
  
  - **Amygdala** (*almond, G.*)
    - Fear, aggression, emotionally charged memories, decision-making
  
  - **Hippocampus** (*seahorse, G.*)
    - Site of learning and memory
      - Specifically important in converting short → long term memory (memory consolidation) and spatial navigation
Brainstem

- **Oldest** part of the brain – essential to sustain life
- Divided into 3 basic regions
  - 1 – Diencephalon (‘between brain’)
    - **Thalamus** – sensory relay station
    - **Hypothalamus** – controls homeostasis; regulates hormone release from pituitary gland
  - 2 – Midbrain
    - Small area, many important functions!
  - 3 – Hindbrain
    - **Pons** – connects cerebellum to brainstem
    - **Medulla** – controls breathing and heart rate

Illustration from Kolb & Wishaw, *An Introduction to Brain and Behavior*. Sinauer, 2014
Brainstem

- Midbrain (tectum and tegmentum)

  - **Tegmentum ROLE**: modulates activities like sleep, attention and reward
  - Contains various clusters of **nuclei** that use the same chemical messenger (ex. Substantia nigra → dopamine)
  - **All** groups send signals to cerebral hemispheres (ex. Substantia nigra sends dopamine to striatum)

- **Tectum ROLE**: Important in linking auditory and visual systems; controls orienting movements
  - Superior colliculi – vision
  - Inferior colliculi – hearing
Cerebellum

- Cerebellum – arises from roof of hindbrain
- Critical for timing/coordination of movements
- Maintenance of balance and posture
- Modifies motor commands to make movements more accurate
- 10% of brain’s volume → 50% of neurons in brain
  - Hence the name, ‘little brain’, is appropriate!
Summary - Organization

• Cerebrum
  • Neocortex aka cerebral cortex
  • Corpus callosum and other white matter tracts
  • Sub-cortical structures
    • Limbic System
    • Basal Ganglia

• Brainstem
  • Diencephalon: Thalamus and hypothalamus
  • Midbrain: Tegmentum and tectum
  • Hindbrain: Pons and medulla

• Cerebellum
Brain Organization – DONE