Learning Objectives

- Understand the anatomy of the brain, spine, and spinal cord
- Compare the incidence of spinal cord injury to TBI
- Distinguish between symptom patterns due to brain injury and syndromes in spinal cord injury
- Articulate the methods of neuroimaging which support diagnostic and treatment decisions when a patient has sustained either a brain injury or spinal cord injury

Skull Anatomy

- The skull is a rounded layer of bone designed to protect the brain from penetrating injuries
- The inside of the skull is rough with many bony protuberances
- These ridges can result in injury to the brain during rapid acceleration

Cerebrospinal Fluid

- Cerebrospinal fluid (CSF) is a clear liquid in the brain and spine
- It is produced within the ventricles of the brain and circulates throughout the brain and spine
- CSF fills the ventricles and meninges, supporting the brain inside the skull
- The ventricles are a series of reservoirs in the center of the brain
- The ventricles produce, store, and circulate CSF
The Meninges

- The meninges are layers of tissue that separate the skull and the brain.
- There are 3 layers:
  - Pia Mater
  - Arachnoid
  - Dura Mater

Essential Tip!

The Meninges P-A-D the Brain

Pia Mater

- Second layer of meninges
- Consistency similar to a spider web
- Below the Arachnoid layer is the subarachnoid space
- When there is a bleed in this space, it is called a subarachnoid hematoma

Arachnoid Layer

- Third layer of meninges
- Latin for 'tender matter'
- Molds around the sulci and gyri of the brain

Neurons are communicating cells
Glia cells are non-communicating cells supporting and nourishing neurons

The Brain is Composed of Discrete Cells: Neurons and Glia

Glia

Glia cells support and maintain neurons

Dura Mater

- Outer layer of the meninges
- Latin for "tough mother"
- A heavy cabbage-like covering
- Below the Dura Mater is the subdural space
- When there is a bleed in this space, it is called a subdural hematoma
Neurons Communicate with Each Other Via Synapses

- Neurons have processes that support electrochemical transmission.
- This allows them to communicate via an electrochemical process.
- Synapses are junctions between neurons where this electrochemical process takes place.
- The gap between an axon of one neuron and the dendrite of another neuron is the synapse.

A signal from the axon of Neuron A travels to the dendrite of Neuron B. An action potential then generates from the cell body of Neuron B, which sends a signal down the axon and passes that signal to the dendrite of Neuron C. The process proceeds forward as long as an action potential continues to generate and the needed neurotransmitters and other chemicals such as calcium and potassium, etc., are present.

Brain Stem Components

- There are 3 components:
  - Medulla
  - Pons
  - Midbrain

Midbrain

- The smallest part of the brain stem
- Involved in elementary forms of vision and hearing
- Plays a pivotal role in alertness and arousal
**The Pons**
- The pons is the rounded brainstem region between the midbrain and the medulla.
- The pons connects the cerebellum and the cerebral cortex.
- The pons is essential for facial movements, facial sensation, hearing, and coordinating eye movements.

**The Medulla**
- The medulla merges with the spinal cord creating the base of the brain stem.
- The medulla serves as a control center for involuntary reflexes such as breathing, heart rate, blood pressure, swallowing, vomiting, and sneezing.
- Involved in many basic living functions; injury to the medulla is life threatening.

**Reticular Activating System**
- A collection of nerve fibers and nuclei within the brainstem.
- Modulates arousal, alertness, concentration, and basic biological rhythms.
- Acts to activate/inactivate the brain with numerous connections to the cerebral cortex.

**Diencephalon-Thalamus**
- Sensory inputs pass through it to the higher levels of the brain.
- Sits at the top of the brainstem, just below the cortex.
- Many nuclei.
- All senses, except smell, relay their impulses through the thalamus.
- Injury causes a wide range of symptoms.

**Diencephalon-Hypothalamus**
- Controls the autonomic nervous system.
- Regulates body temperature.
- Regulates hunger and thirst.
- Controls endocrine system.
- Controls sleep/wake cycle.
- Controls emotional responses and behavior.
Limbic System
- It is a deep brain structure which sits on top of the brain stem and is interconnected with the diencephalon
- It is highly connected with other areas of the brain
- Involved in control of all internal and external responses and actions

Limbic System - Hippocampus
- Sits within the temporal lobe, with a structure on each side of the brain
- It is very susceptible to anoxia/hypoxia
- Associated with memory functioning
- Injury causes impaired short-term memory, problems consolidating short-term memories into long-term memory and difficulty organizing and retrieving stored memories

Limbic System - Amygdala
- Located near the hippocampus
- It is speculated that when a perception reaches the cerebral cortex it is transmitted to the amygdala and evaluated for emotional content
- It is tied to emotional memories and reactions, giving it the name the “fight or flight” structure

Basal Ganglia
- Receives input from the cerebral cortex, processes the information, and sends it back to the cerebral cortex
- Keeps on the alert for when something is not working the way it should and determines what behaviors to execute
- Regulates actions of the motor and premotor areas
- Handles physical movements by relaying information from the cerebral cortex to the brain stem and cerebellum
- Injury affects voluntary motor nerves causing slowness and loss of movement, tremor, and muscular rigidity

Cerebellum
- Located in the lower back section of the brain
- Coordinates and modulates all body movement
- Controls the direction, rate, force, and steadiness of movements
- Injury causes problems with fine motor movement, trajectory of movement, balance and proprioception
THE CEREBRAL CORTEX

- Two Hemispheres
- Four Lobes
- Interconnected

Cerebral Features

- Gyri – elevated ridges that wind around the brain
- Sulci – small grooves dividing the gyri
- Fissures – deep grooves, usually dividing large regions/lobes of the brain

Information Processing

<table>
<thead>
<tr>
<th>Right Hemisphere</th>
<th>Left Hemisphere</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holistic</td>
<td>Linear</td>
</tr>
<tr>
<td>Visual spatial</td>
<td>Verbal-analytic</td>
</tr>
<tr>
<td>Intuitive</td>
<td>Logical</td>
</tr>
<tr>
<td>Controls left side of body</td>
<td>Controls right side of body</td>
</tr>
<tr>
<td>Music, art, shapes</td>
<td>Speaking, reading, writing</td>
</tr>
</tbody>
</table>

LOBES OF THE CEREBRAL CORTEX

Frontal Lobe Functions

- Curves over the top part of the head
- Controls voluntary movement
- Injury causes weakness or paralysis on the opposite side of the body

- Located at the front part of the frontal lobes
- Evaluates options, predicts outcomes and decides the best course of action
- Influences ability to learn from consequences
- Injury causes difficulty making decisions, organizing and prioritizing, initiating and inhibiting actions, controlling emotions and interacting socially

Frontal Lobe

- Prefrontal Cortex
- Frontal Poles
- Primary Motor Cortex

Primary Motor Cortex

- Prefrontal Cortex
### Frontal Lobe Functions
- Planning
- Organizing
- Problem solving
- Judgment
- Impulse control
- Decision making
- Working memory

### Frontal Lobe Damage
- Changes in personality
- Poor self-awareness
- Reduced motivation/goal-directed behavior
- Impaired attention/short-term memory
- Poor judgment
- Inability to plan

### Prefrontal Cortex Injuries in Children
- Brain is not fully developed
- Effects not immediately apparent
- In their teens, deficits may become more apparent in teen
- May cause a wide range of poorly controlled behaviors

### Temporal Lobe Functions
- Memory
- Language
- Hearing
- Auditory processing
- New learning
- Understanding, storing, and retrieving new information

### Expressive Speech
**Broca’s Area**
- Located in the left frontal-temporal lobe area
- Responsible for speech production
- When damaged:
  - Broca’s Aphasia
  - Language expression is impaired
  - Speaks haltingly with few words
**Receptive Speech**

**Wernicke's Area**
- Located in the left temporal-parietal lobe
- Responsible for speech comprehension
- When damaged:
  - Wernicke's Aphasia
    - Language comprehension is impaired
    - Speaks fluently but does not make sense

**Speech Production & Understanding**

**Broca's Area**
- Left frontal-temporal lobe
- Speech Production
- Language expression is impaired
- Speaks haltingly with few words

**Wernicke's Area**
- Left temporal-parietal lobe
- Speech Comprehension
- Language comprehension is impaired
- Speaks fluently but does not make sense

**Occipital Lobe**

**Functions**
- Visual processing
- Interpret visual information
- Recognition of size, color, light, motion, dimensions, etc.

**Impairments**
- Cortical blindness
- Agraphia
- Field cuts
- Movement agnosia
- Visual agnosia

**Visual Pathway**

**Parietal Lobe**

**Primary Sensory Cortex**

**Somatosensory Cortex**
**Parietal Lobe**

**Primary Sensory Cortex**

- **Functions:**
  - Sensation and perception
  - Responds to touch, temperature and pain
  - Processes sensory information

- **Impairments:**
  - Difficulty identifying sensation
  - Location
  - Type
  - Temperature
  - Pain
  - Movement

**Somatosensory Cortex**

- **Functions:**
  - Sensory input integration
  - Spatial awareness and perception - awareness of body parts in space

- **Impairments:**
  - Agraphia
  - Acalculia
  - Anosognosia
  - Aphasia
  - Impaired attention
  - Neglect
  - Left-right disorientation

---

**Spinal Column**

- **Composition:**
  - 33 vertebrae (bones)
  - Each joined together with discs (cartilage) and ligaments (fibrous tissue)
  - Divided into 5 sections

- **Function:**
  - Supports muscles and organs
  - Protects the spinal cord

**Spinal Column Divisions**

**Cervical**
- 7 topmost vertebrae
- Built for flexibility
- 1st vertebra is the Atlas
- Supports the skull
- Movement up & down
- 2nd vertebra is the Axis
- Movement side to side

**Thoracic**
- 12 vertebrae
- Upper and middle back
- Built for stability

**Lumbar**
- 5 vertebrae
- Lower back
- Built for weight bearing

---
**Vertebral Bodies**
- Spinal Cord
- Disk
- Meninges
- Nerve Root
- Vertebra

**Spinal Cord**
- **Structure**
  - Passes through the foramen magnum into the vertebral canal
  - 31 pairs of spinal nerves branch off the spinal cord
  - Made of a core of gray matter surrounded by white matter
  - Has 3 levels of meninges

- **Function**
  - It sends messages to the brain through afferent nerve tracts
  - Receives message from the brain through efferent nerve tracts

**Spinal Cord Syndromes**
- **Central Cord Syndrome**
  - Cervical injury site; incomplete injury
  - Often the result of a fall in a person with neck arthritis or spondylosis
  - Presents as weakness and numbness in arms
  - Often accompanied by bowel/bladder incontinence

- **Brown-Sequard Syndrome**
  - Only one side of the spinal cord is injured
  - Loss of pain and temperature sensation on the same side
  - Loss of touch sensation on the opposite side

- **Anterior Cord Syndrome**
  - Loss of muscle control, pain and temperature sensation
  - No loss of proprioception and touch sensation

- **Posterior Cord Syndrome**
  - Presents with strength but no sense of where limbs are in space below the level of damage

**Neuroimaging**
**Computed Tomography (CT)**

- An X-ray procedure that combines multiple X-ray images with the aid of a computer to produce cross-sectional views and three-dimensional images of the internal organs and structures of the body.
- Useful for identifying gross anatomical changes.
  - Skull fracture
  - Hemorrhage
  - Blood clot
  - Swelling
  - Penetrating object

**Magnetic Resonance Imaging**

- Also known as MRI.
- Uses a magnetic field, radio frequency pulses, and a computer to produce detailed pictures of organs, soft tissues, bone, and other internal body structures.
- MRI provides better detail than CT.
- More sensitive to a variety of pathologies.
- Computer algorithms are used to create different forms of MRI, including:
  - Diffusion Tensor Imaging
  - fMRI
  - T2 Weighted

**Diffusion Tensor Imaging**

- A type of Magnetic Resonance Imaging which uses the rate at which water diffuses between cells to provide information about the internal structures of the body.
- Provides information about the connectivity and continuity of neural pathways (i.e., white matter).

**Functional MRI**

- The individual performs a task while in the MRI scanner.
- The scan measures and maps brain activity by detecting changes associated with blood flow.
- Changes in blood flow follow changes in neural activity.

**Brain Symmetry & Imaging**

- The brain in a normal state is symmetric.
  - See T1 and T2.
- Non-pathological brains and the structures that make up the brain should all appear similar to one another (i.e., from brain to brain).
  - See C and Flair.

**Mechanisms of Traumatic Injury**

### Categories of Brain Injury

**Focal**
- Contusions
- Lacerations
- Hematomas

**Diffuse**
- Diffuse Axonal Injury
- Hemorrhage
Mechanism of Injury

1. Rapid acceleration of the brain followed by rapid deceleration
2. Results in the shearing of axons and blood vessels throughout the brain, rendering white matter tracts (bundles of axons) non-functional
3. Predominantly Diffuse Axonal Injury, or DAI
4. White matter (the neuron's myelinated axons) and grey matter (the neuron's cell bodies, dendrites and axon terminals) have different densities
5. The junction between grey and white matter is where DAI is more frequent
6. The Corpus Callosum is often injured in this fashion


2. Results in the shearing of axons, and blood vessels throughout the brain, rendering white matter tracts (bundles of axons) non-functional
3. This is termed Diffuse Axonal Injury, or DAI

Mechanism of Injury: Intracranial Pressure

- The brain can bleed and swell when injured
- This can lead to pressure on brain tissue and blood vessels, depriving the brain of oxygen, leading to additional injury

Mechanism of Injury

- The bouncing of the brain in the skull can result in injury in two sites

Mechanism of Injury

Hypoxia & Anoxia

- Lack of oxygen causes brain cells to die
- When the cells die, they release chemicals that can cause further damage to the brain

Penetrating Injuries

- A penetrating injury results when an object penetrates the skull and enters the brain

Penetrating Injuries

- A penetrating injury results when an object penetrates the skull and enters the brain

Learning Objectives

- Be able to articulate the effects of brain injury and injury severity
- Understand the conceptions of neuroprotection, neuroplasticity, and neurodegeneration
- Be able to articulate the two main areas of the brain known to be sites of neurogenesis
- Be able to distinguish between rehabilitative training models appropriate for TBI and those for stroke
Neuroplasticity
Definition
- The ability of the nervous system to change itself, form new connections, and create new neurons in order to compensate for injury or adapt to changes in the environment.

Example
- The firing of Neuron A causes Neuron B to fire.
- The cycle repeats and chemical changes alter the connection and strengthen both neurons.

Early Research on Neuroplasticity
Seminal work by Merzenich and colleagues
- They mapped the sensory cortex of monkeys to see which areas responded to cutaneous inputs from each digit.
- They then surgically removed digit 3.
- As the monkeys used their hands post-amputation, they remapped the sensory inputs at various points in time.
- This resulted in no inputs registering in the area where D3 inputs were prior to amputation.
- The vacated receptors where D3 registered previously were then taken over by inputs from the adjacent digits, namely D2 and D4.

Experience Dependent Learning
- The previous slide showed that when inputs to the sensory cortex ceased in a particular area, adjacent inputs eventually took over those areas.
- It highlights just how valuable cortical space is, and justifies the saying “USE IT OR LOSE IT.”
- Merzenich and colleagues also researched this concept through mapping of the motor cortex.
- They trained monkeys on novel tasks that used only specific parts of their hands (digits, wrist, or forearm).
- They found that as monkeys used only that specific area of their hand, the size of the motor map increased for that area, and the size of the motor map for the other areas decreased (e.g., wrist and forearm).

Synaptogenesis
Definition
- The formation of synapses between neurons.
- The greater the numbers of synapses within a grouping of neurons, the greater the speed and efficiency with which those neurons communicate.
- There are many factors that impact synaptogenesis, but a key aspect of new synapse development is the dendrite.
- There are hundreds to thousands of dendritic spines on each dendrite; these structures contain neurotransmitter receptors and receive synaptic transmissions.
- The size and complexity of a dendritic arbor determine the volume of synapses.

Neuroplasticity Post-TBI
- Plasticity: the ability of the nervous system to change, grow or compensate for injury.
- Structural changes in the brain can occur in the area of the injury and remote areas connected to that area.
- Neuroplasticity may be modulated by experience.
Neuroplasticity Post-TBI:

Cortical Reorganization
- The brain's cortical map can change following injury
- The brain's cortical map can change through rehabilitation
  - Directed exercise
  - Constraint induced movement therapy

Neuroplasticity: TBI Research
- Following traumatic injury
  - The brain increases its own production of growth factors
  - There is a decrease in the amount of structural materials found in the brain

Neurogenesis
- Theory: the brain does not produce new neurons after development
- Research: neurogenesis occurs in the developed brain
  - Specific areas in the hippocampus
    - Subventricular zone
    - Dentate gyrus
  - Increases with exercise, decrease with stress
  - Cells may migrate to areas affected by the injury

Implications for Rehabilitation
- Spontaneous neuroplasticity in TBI does not appear to occur as it does in stroke
- Appears that TBI requires a more intense combination of rehabilitation therapies to improve function
- Further research is needed

Neuroprotection
- Reducing cell loss following injury leads to better function
- As a result, research has focused on ways to reduce cell loss including:
  - Using substances to prevent secondary injury cascade
  - How the brain reorganizes and adapts to injury
  - Rehabilitation
- Research focused primarily on stroke
  - Tissue plasminogen activator (tPA)
Biological Cascade Following TBI

- Primary Injury – direct damage to the brain
- Secondary Injury – causes additional damage
- Excitotoxicity
- Edema
- Apoptosis

Secondary Injury

- Excitotoxicity
  - Failure of neurons to maintain resting state
  - Sodium-potassium pump failure
  - Excitotoxic accumulation of sodium and calcium

- Edema
  - Swelling in cells
  - Increased Intracranial Pressure
  - Contributes to apoptosis

- Apoptosis
  - Cells surrounding the primary injury die as a result
  - This expands the size of the injury

Potential Neuroprotective Agents for TBI

- Neuroprotective agents limit neuronal death following injury and/or enhance recovery

<table>
<thead>
<tr>
<th>Neuroprotective Agent</th>
<th>Intervention Target</th>
<th>Animal Models/Showing Efficacy (Stroke)</th>
<th>Human Studies/Showing Efficacy (TBI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium</td>
<td>Increase Mg2 (decreased Mg2 results in excessive production of free radicals and mild inflammation)</td>
<td>✓</td>
<td>Failed</td>
</tr>
<tr>
<td>Progesterone</td>
<td>Decrease central edema</td>
<td>✓</td>
<td>Initial Efficacy/Follow Up</td>
</tr>
<tr>
<td>Nicotinimide</td>
<td>Reduce injury volume; decrease glial activation; reduce BBB breaches; reduce edema</td>
<td>✓</td>
<td>Unknown</td>
</tr>
</tbody>
</table>