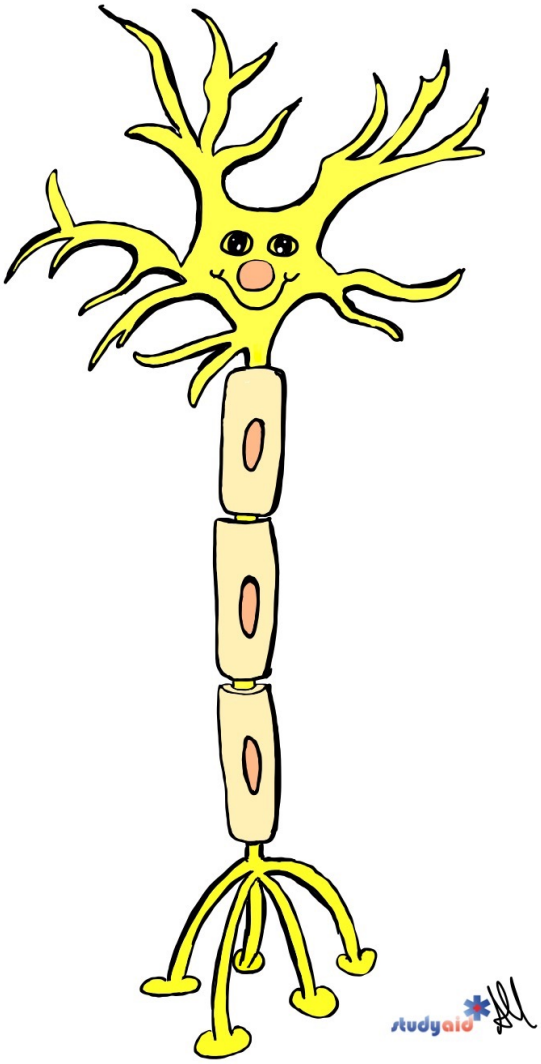

Neurophysiology

Second edition

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Booklet Disclaimer

Although the authors have made every effort to ensure the information in the booklet was correct at date of publishing, the authors do not assume and hereby disclaim any liability to any part for any information that is omitted or possible errors. The material is taken from a variety of academic sources as well as physiology lecturers, but are further incorporated and summarized in an original manner. It is important to note, the material has not been approved by professors of physiology.
All illustrations in the booklet are original. This booklet is made especially for students at the Jagiellonian University in Krakow by tutors in the StudyAid group (students at JU).
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About StudyAid

StudyAid is a student organization at the Jagiellonian University in Krakow. Throughout the academic year we host seminars in the major theoretical subjects: anatomy, physiology, biochemistry, immunology, pathophysiology, supplementing the lectures provided by the university. We are a group of 25 tutors, who are students at JU, each with their own field of specialty. To make our seminars as useful and relevant as possible, we teach in an interactive manner often using drawings and diagrams to help students remember the concepts. In addition to most seminars we create booklets, on which the seminars are based to aid the students in following the presentations. If you have any questions, do not hesitate to contact StudyAid at www.studyaid.no, we are always happy to answer any questions you may have academically related or not.

Using this Compendium

This work is intended as a supplement for students during the neurophysiology portion of the Physiology course. It summarizes the vast majority of the lectures, drawing on the original "Neurophysiology bible" while additionally compiling high yield information from Ganong, FA, and other resources.

Students may notice some discrepancies between things found in this compendium and in other leading resources - this is due to the ever-changing research in the field of neurology and varying sources used. Utmost care was taken to preserve the content of the lectures (which is typically seen on examinations) while attempting to balance in new, factual information.

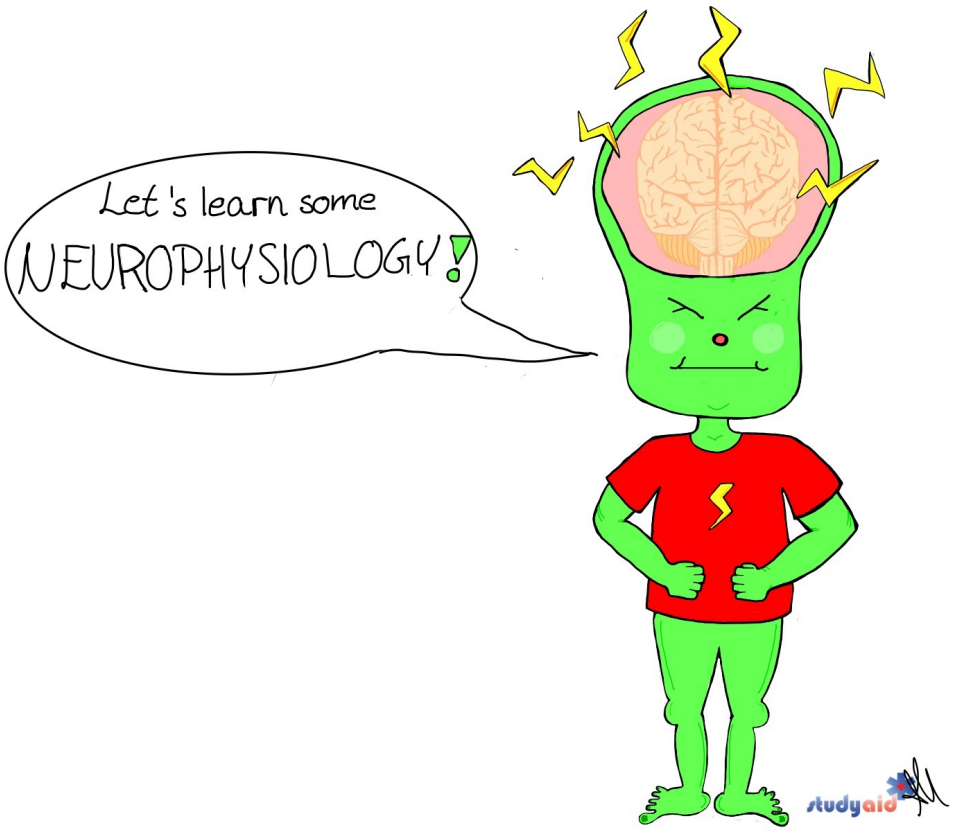
We recommend that students do not use this independently, but in addition to a suggested textbook (e.g. Ganong) with a provided reading list to yield the best results in not only preparing for the midterm, but also to gain knowledge in the most important concepts of neurophysiology.

Several students in StudyAid have participated in revising and editing this booklet.

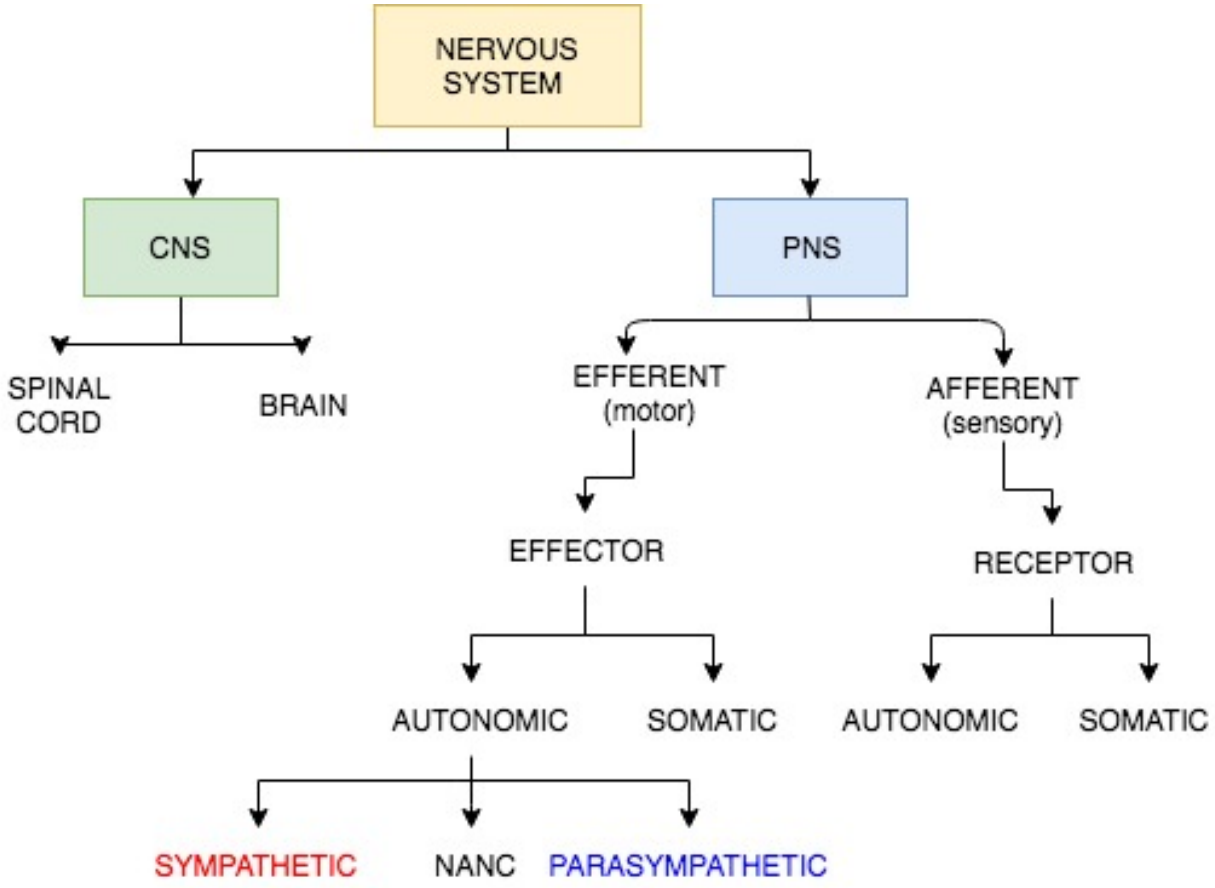
Table of contents

There are 7 chapters in this compendium, and each contains what studyaid considers high yield for the exam. At the end of each chapter, you will find a page where you can write in your own notes, and also a couple of review questions so that you can check your own knowledge. There is not provided an answer sheeth to these questions, but all the information needed is in the compendium.
If in doubt, ask a tutor.

We wish you the best of luck on your exam, and happy studying!



Divisions of the Nervous System



Section 1 – General Neurophysiology

I. The nervous system consists of three different types of tissue:

1. Neurons
   - Signal transmitting cells of the nervous system
     - Dendrites – receive input
     - Axons – send output
   - Permanent cells - do not divide in adulthood

2. Glial Cells
   - Non-neuronal cells that maintain homeostasis
   - Macroglia
     - Astrocytes
       - Located all over the nervous system
       - Make up 20-40% of all glial cells
       - Physical Support, K+ and Ca2+ metabolism,
       - Remove excess neurotransmitters
       - Component in Blood-brain barrier
       - Involved in scar formation/repair
     - Ependymal cells
       - Present in cerebral ventricles
       - Produce the cerebrospinal fluid (CSF)
     - Oligodendrocytes
       - Myelinate the axons of neurons in the ***CNS***
       - Predominant type of glial cell in white matter
       - Each oligodendrocyte can myelinate around 30 axons
     - Schwann cells
       - Each Schwann cell myelinates only 1 ***PNS*** axon
       - Promote axonal regeneration

   - Microglia
     - Microglial cells – macrophage like cells
       - Phagocytic scavenger cells of the CNS
       - Activated in response to damage of tissue and inflammation
       - Present in the vicinity of blood vessels
       - Hypothesized to produce Interleukins
       - Can produce neurotrophins
       - Hyperactive cells can damage other neurons

3. Blood vessels
   - Provide nutrients for all cells within the nervous tissue

II. Mirror neurons

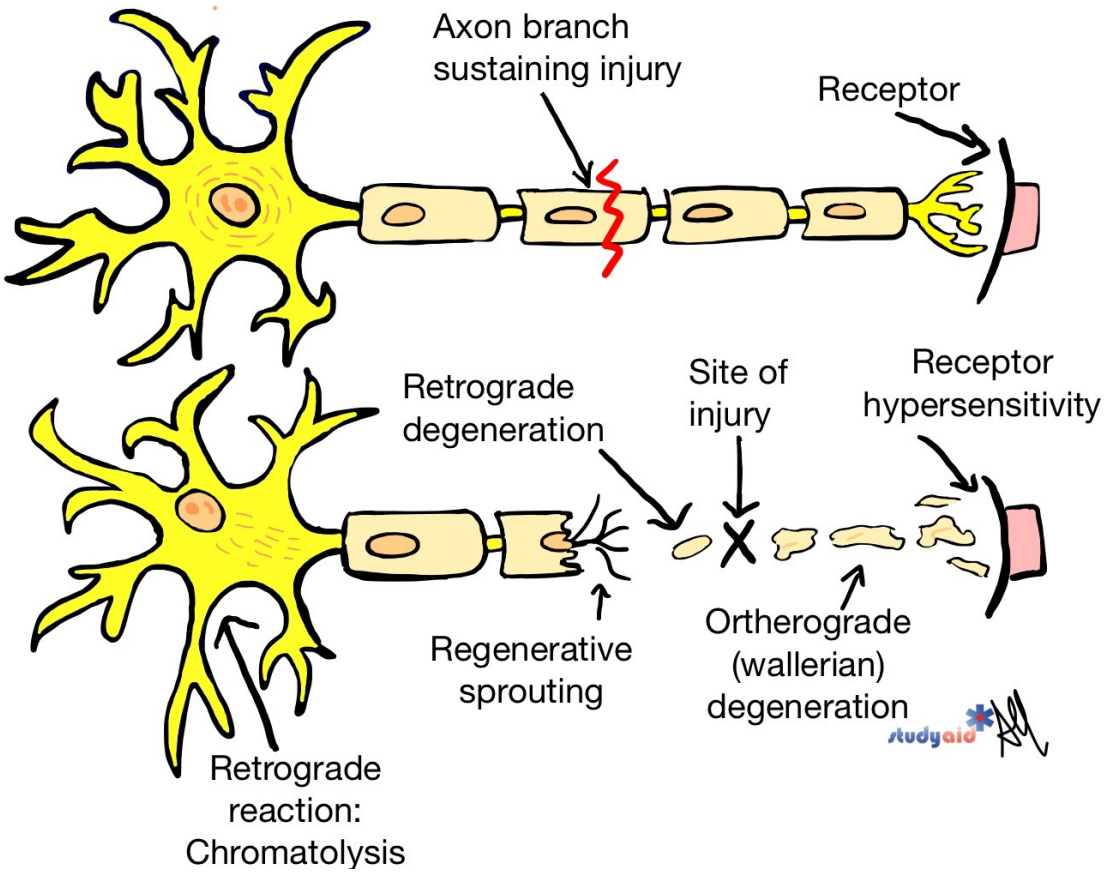
- Present in frontal and parietal lobe
- Neurons fire both when the person performs the activity itself, and also when the person observes the activity being done by others.
- They are responsible for empathy, recognition of emotions and also for learning skills by imitation.
    - Important for social function
- It is hypothesized that dysfunction can lead to autism

III. Neuron Degeneration

- Chromatolysis – reaction of neuronal cell body to axonal injury
    - Dissolution of the Nissl bodies in the cell body of a neuron
    - Cellular edema
    - Displacement of the nucleus towards the periphery
    - Happening together with Wallerian degeneration

- Wallerian Degeneration
    - Degeneration distal to the injury
    - Axonal retraction proximally
    - Allows for possible regeneration (if within the PNS)
        - Macrophages remove debris and myelin

- Trans-synaptic Degeneration
    - Occurs when a neuron is overstimulated by a neurotransmitter, causing nearby synapsing neurons to be driven into metabolic deficit
    - Degeneration of the neuron which synapses with the injured neuron



IV. Denervation Hypersensitivity

- Interruption of innervation to an organ (denervation)
    - As a result, the synaptic receptor becomes extremely sensitive to neurohumoral agents
        - Muscle denervated → Stronger response to ACh → Repetitive contractions
- Also called the Cannon-Rosenberg Law of Denervation

V. Regeneration (applies to PNS only)

- Assuming less-extensive damage, the proximal axons are able to regrow as long as the cell body is intact
    - Start with regeneration tube via Schwann Cells
    - Secretion of NGF (nerve growth factor) by Schwann Cells
    - Guidance of axon to destination
- Can take weeks to months

1.1 – Neurotrophins

- Small proteins that maintain the function and growth of neurons
- Secreted by target tissue (muscle cells, glial cells, etc)
- Capable of signaling particular cells to survive, differentiate, or grow
- Also induce differentiation of progenitor cells to form neurons
- Receptors for neurotrophins can be either p75 or TrK family

Four main Neurotrophins are:

Nerve Growth Factor (NGF)	Brain Derived Neurotrophic Factor (BDNF)	NT-3	NT-4
- Regulates the growth and up-keeping of sensory and sympathetic neurons - Alpha, Beta, Gamma subunits	- Located in the brain and the periphery - Helps to support existing neurons - Encourages the growth and differentiation of new neurons and formation of synapses	- Closely related to NGF and BDNF - Hypothesized to maintain cutaneous mechanoreceptors	- Another neurotrophic factor

Other Factors that can affect the Nervous Tissue

- Ciliary neurotrophic factor (CNF)
    - Promotes the survival of neurons (for example, during inflammation) e.g. spinal cord
- Glial cell-line derived neurotrophic factor (GDNF)
    - Promotes the survival of dopaminergic and motor neurons
- Leukemia Inhibitory Factor (LIF)
- Fibroblast Growth Factor (FGF)
- Transforming Growth Factor (TGF)

- Platelet Derived Growth Factor (PDGF)

1.2 – Cerebrospinal Fluid

- Approximately 500-600 mL of CSF produced daily
- Produced in cerebral ventricles by the ***choroid plexus*** and ***ependymal cells***
- CSF passes through the interventricular foramina to the 3rd ventricle, then to the 4th ventricle
- The fluid then passes through openings to enter the subarachnoid space

Composition

- A few lymphocytes (typically less than 5/microliter)
- No red blood cells
- pH of 7.33
- 60-65 mg/dL of Glucose
- 15-50 mg/dL of Proteins (avg. 35)

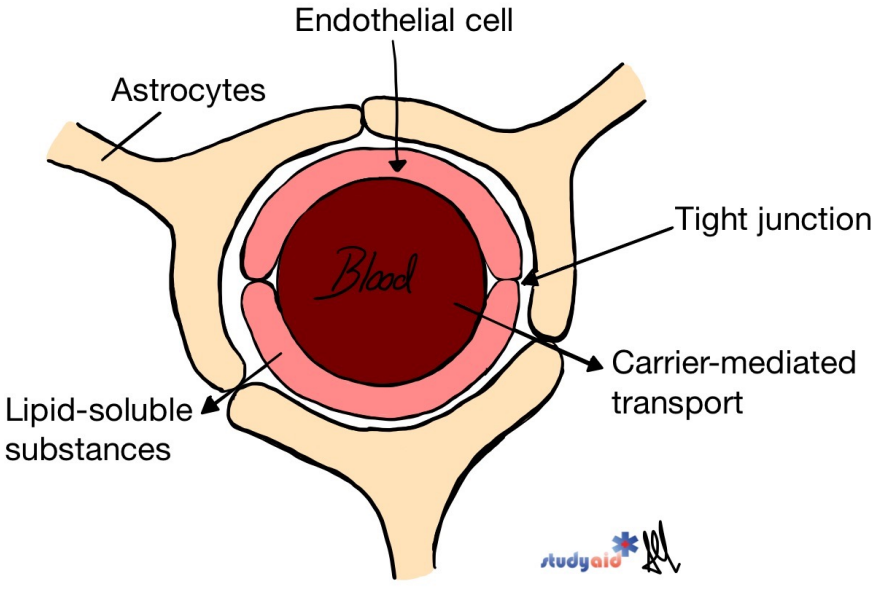
- Reabsorbed from subarachnoid space to dural venous sinuses
- Only about 100-160 (avg. 150ml) present at a time due to reabsorption
    - Pressure is 8-15 mmHg if patient is lying down, increases to around 18 mmHg when patient is standing

Significance

- Facilitates exchanges of nutrients, materials between different parts of Brain
- Protects nervous system against mechanical injury (trauma)
- Decreases the weight of the brain (neutral buoyancy)
- Analysis of the CSF (collected via a lumbar puncture) can give clues to etiologies of diseases
    - Changes in white blood cells and proteins can be indicative of inflammation
    - Along with glucose and differentiation of various WBC levels, etiology of infection may be deduced
    - RBCs present may detect bleeding (e.g. a subarachnoid hemorrhage) or be a result of a traumatic spinal tap

1.3 – Blood-Brain Barrier

- Formed by three structures
    - Tight junctions between endothelial cells of blood capillaries
    - Basement membrane
    - Astrocyte processes
- Nonpolar/lipid soluble substances pass with ease via diffusion
    - O2, lipids, steroid hormones, CO2 etc.
- Glucose and amino acids can cross through the membrane via carrier mediated transport



- Poorly permeable for protein and high molecular weight substances
- Hypothalamus influences blood-brain barrier permeability

1.4 – Sympathetic versus Parasympathetic – the Characteristics

Characteristic	Sympathetic	Parasympathetic
Origin of Preganglionic Nerve	Nuclei of Spinal Cord segs T1-T12, L1-L3	Nuclei of CNIII, VII, IX, X Spinal Cord S2-S4
Length of Preganglionic n. Axon	Short	Long
Receptor type in ganglion	Nicotinic	Nicotinic
Neurotransmitter in ganglion	Acetylcholine	Acetylcholine
Length of Postganglionic nerve axon	Long	Short
Effector Organs	Smooth + cardiac muscle, glands	Smooth + cardiac muscle, glands
Neurotransmitter in effector organs	Norepinephrine (ACh in glands)	Acetylcholine
Receptor types in effector organs	A1, A2, B1, B2, B3	M1, M2, M3

Non-adrenergic Non-cholinergic System

- Autonomic system typically deals with Acetylcholine, Epinephrine, and Norepinephrine
    - If a neurotransmitter is not one of those three, it belongs to a classification of being NANC
    - Examples include GABA, 5-HT (serotonin), dopamine, NO, substance P

Functional Levels of the CNS

Spinal Cord level

- Automatic function
    - Information entering the spinal cord produces an "automated" response
        - Reflexes are based on this principle

Lower Brain level

- Control of subconscious reactions
- Blood pressure, heart rate, breathing
- Appetite control

Higher brain level

- Processing and storing information
- Perception of information

- Voluntary actions
- Memory

NOTES:

Review questions general neurophysiology:

1. What is the function of astrocytes?

2. Why are mirror neurons important?

3. Cerebrospinal fluid produced in _____ by the

   _____.

4. What are the 4 main neurotropins, and what is their function?

5. What does not need carrier mediated diffusion to pass through the blood brain barrier?

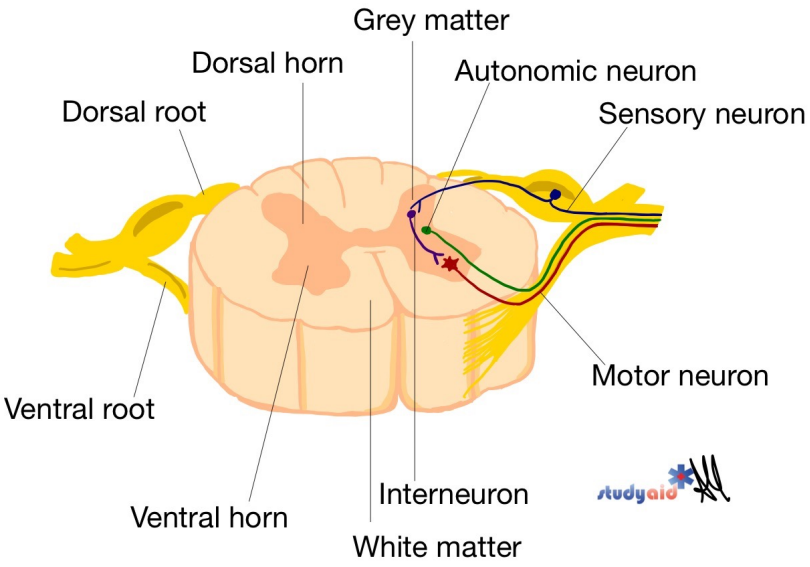
6. Explain when and how a neuron can regenerate:

Section 2 – Spinal Cord

2.1 – The Spinal Cord

The functions of the spinal cord include

- Connecting nerve pathway segments
- Forming the pathway for reflexes
- Transmitting signals of voluntary movement
- Transmitting sensory information



Spinal Cord extends to the lower border of L1-L2 border

- Subarachnoid space (with CSF) goes to lower border of S2
    - Cauda Equina typically around L3 by adult age
- Lumbar puncture, to sample CSF, can be performed between L3 and L4 or L4 and L5

· Spinal Cord contains gray and white matter

- The grey matter is made of cell bodies
    - Forms a butterfly-shaped area in the center of the spinal cord
- White matter is made of axons of nerve fibers that carry the spinal tracts

Grey matter can be divided into three sections

1. Ventral horn (motor area)
    - Alpha fibers have great diameter with higher conduction velocity
    - Alpha motor neurons - alpha nerve fibers
        - Innervate extrafusal muscle fibers
        - Stimulate skeletal muscle to contract
    - A single alpha motor neuron and all of the fibers it innervates is called a motor unit
    - Beta motor neurons - beta nerve fibers
        - Innervate intrafusal nerve fibers
    - Gamma motor neurons - gamma nerve fibers
        - Innervate intrafusal nerve fibers

2. Intermediate horn
    - Centers of autonomic nervous system)

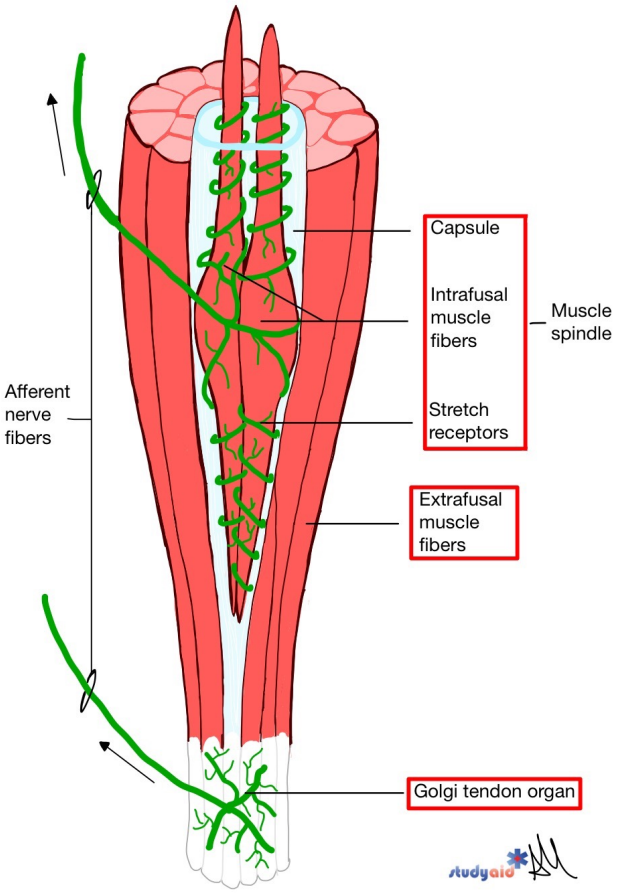
3. Dorsal horn (sensory area)

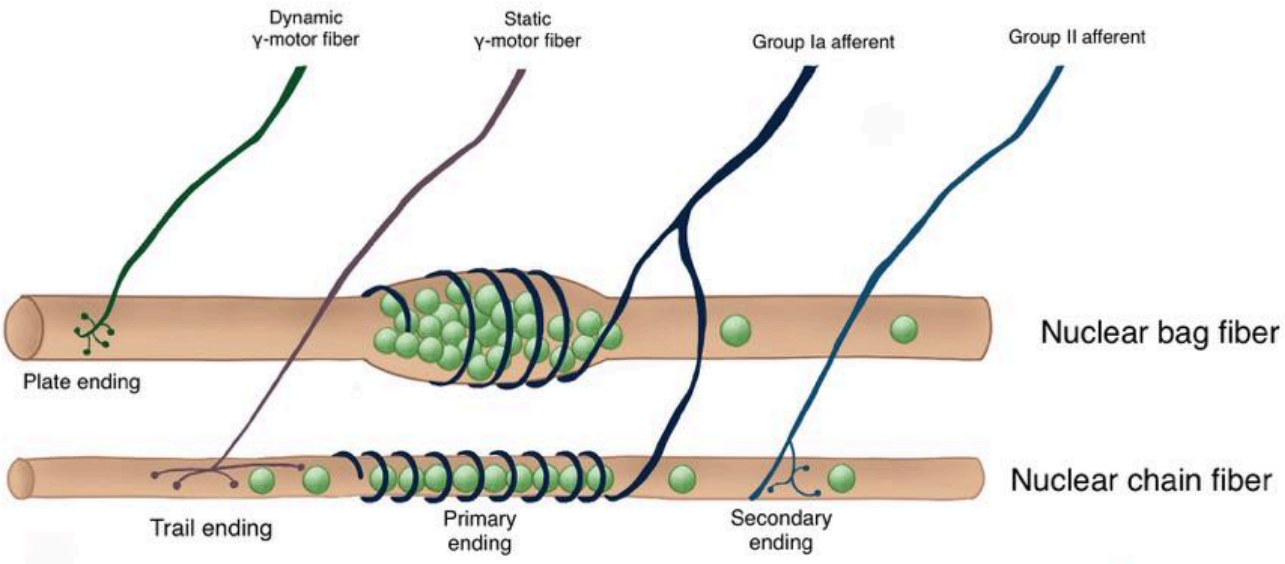
Bell-Magendie Law

- Sensory impulses enter the spinal cord via dorsal roots and motor impulses leave the cord via ventral roots
- Impulses are thus conducted in only one direction

2.2 – Intrafusal Fibers

- Skeletal muscle fibers that serve as specialized sensory organs that can detect the quantity and rate of change in length of a muscle
- Constitute the "muscle spindle"
- Consist of two axons - one sensory, one motor
- Walled off from other fibers with connective tissue
- There are two types of intrafusal fibers
- Nuclear bag
    - Lies in the center of a muscle spindle
    - Has a large number of nuclei concentrated in "bags"
- Nuclear chain fibers
    - Half the size of the nuclear bag fibers
    - Nuclei in a "chain" (in a row)
-





2.3 – Reflexes

- Subconscious effect produced in response to the stimulus applied to the receptor
    - Specifically, an involuntary reaction in direct response to a stimulus, transmitted through integration centers in the CNS.
        - Most include some form of stretching/contraction

- Elements of a reflex
    - Receptor (to detect stimuli)
    - Afferent pathway of sensory neuron
    - Integration (via interneurons, to motor neuron)
    - Efferent pathway of motor neuron
    - Effector

Clinical Significance of Reflexes

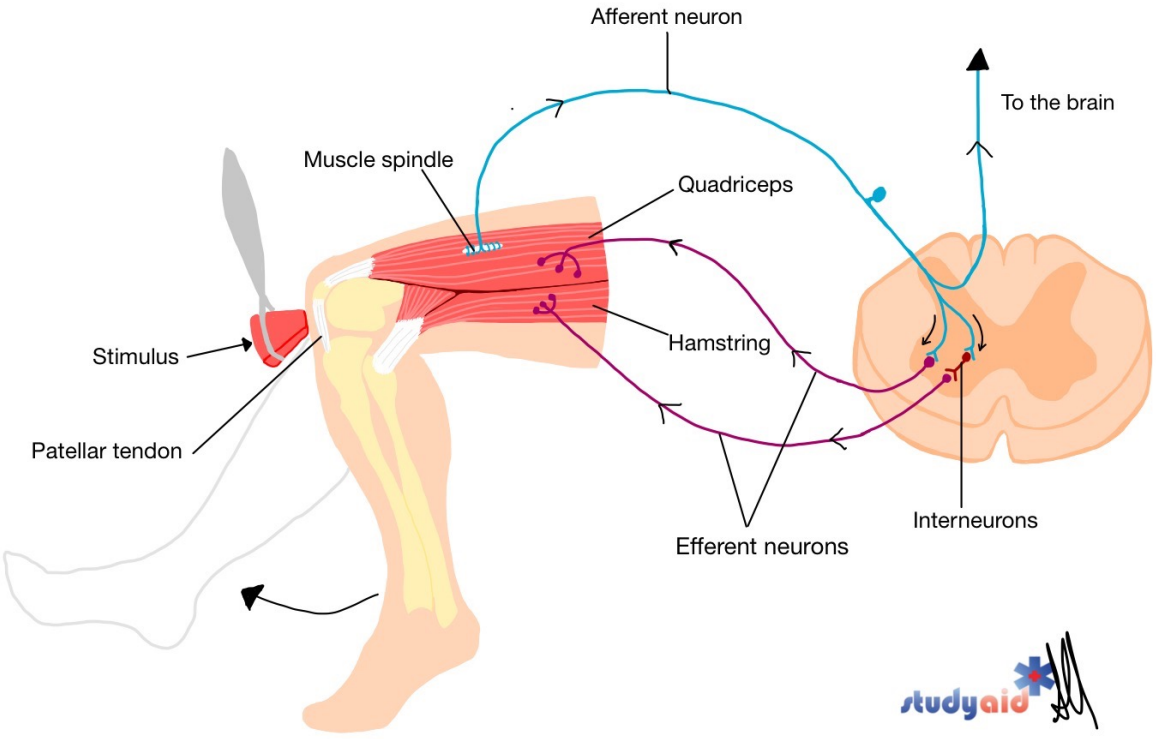
- Assessment of deep tendon reflexes (e.g. knee-jerk) can be helpful in determining lesions within the CNS
    - Diminished reflexes can be a sign of a lower motor neuron lesion
    - Hyperreflexia can be a sign of an upper motor neuron lesion
- Presence or absence of reflexes can also be helpful to determine viability of different spinal cord levels, for example (but not limited to)
    - Biceps reflex mediated by C5 and C6 roots
    - Triceps reflex mediated by C7 and C8 roots
    - Abdominal reflexes mediated by T8-T12
    - Ankle jerk reflex mediated by S1 and S2
    - Presence of these reflexes indicates functional viability of transmission at this level of the spinal cord

Stretch Reflex

Stretch reflex – reflex arc	
1. Receptor	Muscle spindle – stretch of muscle spindle with intrafusal fibers
2. Afferent neuron	Ia myelinated fibrs (120 m/s)
3. Center (integration)	Monosynaptic – Single synapse to motor neuron
4. Efferent neuron	Motor axon (ventral root, via motor axon)
5. Effector	Extrafusal fibers of stretched muscle

Physiological role of Stretch Reflex

- Maintain muscle tone (static response)
- Adapting muscle tone to increased load
- Dynamic Response
    - Receptor - primary endings on nuclear bag fibers
    - Rapid discharge → rapid muscle contraction
- Static Response
    - Receptor – primary endings on nuclear chain fibers
    - Slow stretching → maintain the muscle tone



Inverse stretch reflex

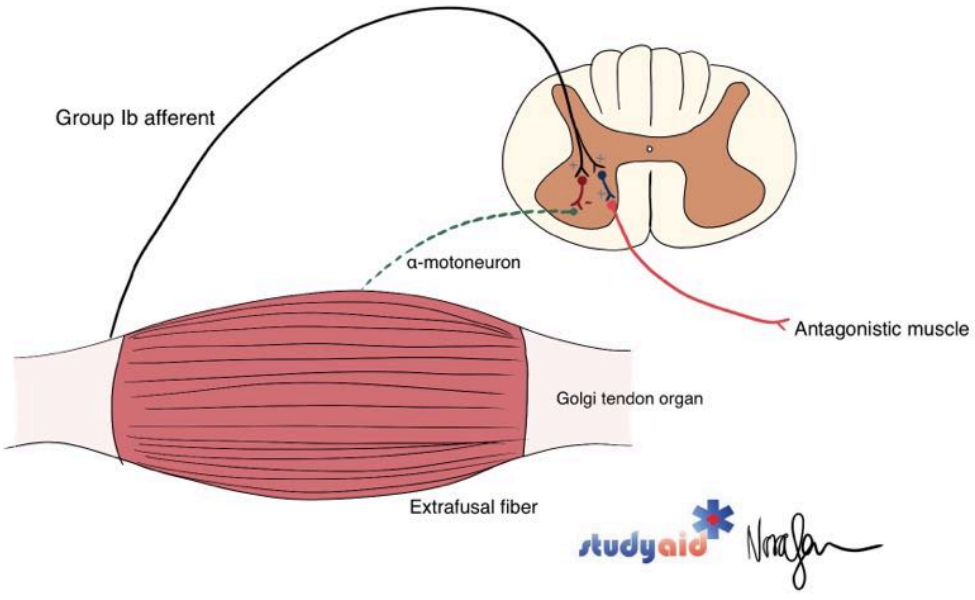
Inverse Stretch reflex – reflex arc	
1. Receptor	Golgi tendon organ
2. Afferent neuron	Ib myelinated fibers - rapidly conducting
3. Center (integration)	Polysynaptic – (inhibitory interneurons =IPSP) Inhibition of motor neuron of contracted muscle, stimulation of antagonist muscle (fx. hamstring is inhibited, and quadriceps is stimulated)
4. Efferent neuron	Motor axon – to antagonist muscle
5. Effector	Contracted muscle = relaxed Antagonist muscle = contracted

Relaxation in response to strong stretch is called the **inverse stretch reflex**

- When the tension of muscle contraction becomes great enough, contraction suddenly ceases and the muscle relaxes

Physiological Significance

- Prevention of direct muscle damage or separation of the tendon from the bone
- Maintaining the muscle tone
- Clasp-knife reflex
    - During neurological exam, stretch reflex present with a rapid decrease in resistance when attempting to flex a joint
    - Like a pocket knife that is difficult to open at first, but gets easier as you go
        - Can suspect an upper motor neuron lesion



Withdrawal Reflex

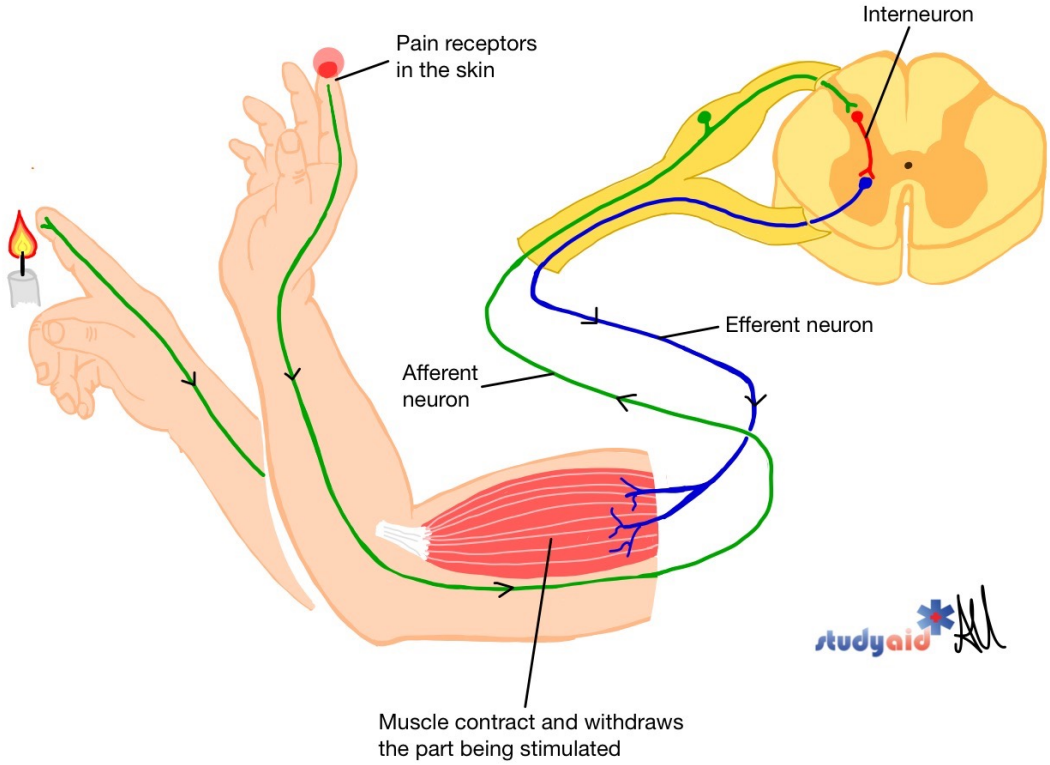
Withdrawal reflex – reflex arc	
1. Receptor	Naked (free) nerve endings
2. Afferent neuron	Type II, III nerve endings
3. Center (integration)	Polysynaptic – (inhibitory interneurons, motor neurons) Inhibition of neurons of extensors, stimulation of neurons of flexors
4. Efferent neuron	Motor axon
5. Effector	Flexors = contracted Extensors = relaxed

Reflex that occurs in response to a noxious stimulus to the skin

- Response is flexor muscle contraction and extensor muscle inhibition
    - Stimulated body part is withdrawn from dangerous stimuli

Physiological significance

- Protection of the body from danger
- Contribution to locomotion



Crossed Extensor Reflex

- Is a withdrawal reflex
- Flexors in the withdrawing limb contract and the extensors relax
    - The opposite occurs in the other limb
    - E.g. Stepping on glass, the leg that is stepping on the glass pulls away, the other leg balances and maintains the weight of the whole body
- Also contributes to locomotion

2.4 – Spinal Shock

- During transection of the spinal cord, all functions below the point of transection are immediately blocked
- Possible effects
    - Loss of BP
    - Loss of some thermoregulatory actions
    - Loss of spinal, sacral reflexes
    - Loss of sensation (depending on the level of transection)
    - Loss of voluntary movement (depending on the level of transection)
- After 2-5 weeks, some functions of the spinal cord may be restored
    - Neurovegetative reflexes may return
    - Muscle tone becomes spastic
    - Spinal reflexes may return in hyperactive form
    - Sacral reflexes may return (must be "trained" – e.g. urination, defecation)

Decerebrate rigidity

- A complete transection of the brainstem between superior and inferior colliculus (aka at the superior border of the pons), causes cerebrate rigidity. The transection permits the brainstem pathways to act without input from higher structures as this lesion stops all input from the cortex and red nucleus.
- The reticulospinal tracts remain intact, and dominance from ascending sensory tracts to the excitatory reticulospinal pathway leads to hyperactivity of extensor muscles in all four exteremities. In other words, the extensor muscles will stretch out the arms and legs, wrists will be pronated and feet will be plantarflexed due to the contraction of the extensor muscles.

Decorticate rigidity

- Removal of the cortex (due to e.g. hemorrhage or infarction) causes decorticate rigidity.
- Flexion of the upper extremities at the elbow and extensor hyperactivity in the lower extremities, aka the elbows are bent and legs are stretched.

2.5 – Renshaw Inhibition

- Example of negative feedback
- Renshaw cells are inhibitory interneurons found in the spinal cord
- Lateral inhibition - inhibits neighboring motor neurons
    - If alpha-motor neuron is stimulated, Renshaw cells inhibit gamma and beta motor neurons
- “Sharpens” signal
- Receive an excitatory signal from the alpha neuron's axon
    - Know how vigorously that neuron is firing.
    - When required, send an inhibitory axon to synapse with the cell body of the initial alpha neuron

NOTES:

Review questions Spinal cord:

1. What different parts of the muscle does the alpha, beta and gamma motor neurons innervate?

2. What is the reflex arc of the inverse stretch reflex?

3. The Bell-Magendie law states that:

4. What is the function of intrafusal fibers?

5. What is the physiological role of the stretch reflex?

6. Decerebrate rigidity will occur when:

7. Explain the function of the renshaw inhibition:

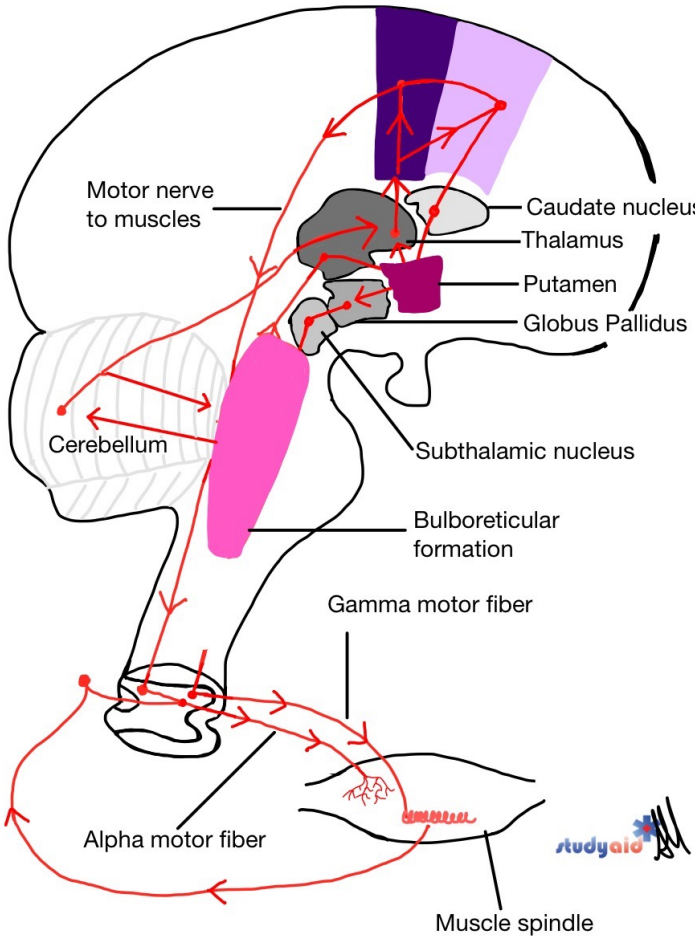
Section 3 – Motor Axis

Elements needed for control of movement

- Cerebral cortex
- Basal Ganglia
- Cerebellum
- Reticular Formation
- Spinal Cord

Body Movement

- Voluntary movement - Pyramidal tract (corticospinal + corticobulbar) + motor cortex
- Involuntary movement - Basal ganglia



3.1 – Motor Cortex

- Primary motor cortex - Brodmann area 4
    - Sends impulses to the spinal cord and controls the execution of movement
- Premotor cortex - Brodmann area 6
    - Planning of coordinated, complex movements
- Supplementary motor area - Part of Brodmann area 6
    - Planning of movement, series of movements
- Suppressor Strip to area 4 - Brodmann area 4S
- Posterior parietal cortex (Brodmann area 7)

Plasticity of Motor Cortex

- The motor cortex changes with experience
- E.g. Lesions can lead to rearrangement of “muscle representative areas”

Contralateral representation

- Motor area of the left hemisphere coordinates the movement of the muscles of the right side of the body
- Motor area of the right hemisphere coordinates the movement of the muscles of the left side of the body

3.2 – Corticospinal Tract

- Descending tract is responsible for voluntary movement of contralateral limbs
- Starts in cortex, then divides into two tracts (lateral + anterior)
    - The first order neuron is an upper motor neuron
        - Begins in motor cortex, descends ipsilaterally through the internal capsule, most fibers undergo pyramidal decussation (at caudal medulla)
            - Continue descent on contralateral side
            - **Anterior corticospinal tract fibers do NOT decussate in the medulla** (responsible for voluntary movement of trunk)
    - The second neuron is a lower motor neuron at the cell body of the anterior horn of the spinal cord. **The anterior corticospinal tract will decussate at this level.**
    - Destination is a neuromuscular junction
- Decussation is why the "left brain controls right side of the body" and "right brain controls the left side of the body"

Tract	1st and 2nd order neuron	Decussation	Function/transmission
Lateral corticospinal (80-90% of fiberS)	***1st*** **-** Giant cells of Betz of precentral gyrus (upper part) and anterior paracentral lobule (Brodmann area 4) **2nd -** Motor nuclei of anterior horn of spinal cord	Fibers decussate in the pyramidal decussation and descend contralaterally.	Transmission of motor function to **distal** musculature on the **contralateral side**
Anterior corticospinal (10-20%)	***1st*** **-** Giant cells of Betz of precentral gyrus (upper part) and anterior paracentral lobule (Brodmann area 4) **2nd -** Motor nuclei of anterior horn of spinal cord	Fibers remain in the ipsilateral anterior white column. These remaining fibers decussate in white anterior commissure of spinal cord at the level of the LMN they innervate.	Transmission of motor function to **axial** musculature of the **contralateral side**

3.3 – Upper and Lower Motor Neurons

- Since the corticospinal tract is transmitted via two successive neurons, we can divide the tract into upper motor neurons (between the motor cortex and the spinal cord) and lower motor neurons (the neuron that runs from the anterior horn to the motor unit of the muscle)
- Depending on whether the UMN or LMN is destroyed, muscles will present different signs (e.g. spasticity, atrophy, hyperreflexia, fasciculations, etc.)
- Observation of these signs allow you to determine where the lesion lies, and clues you into what the disease process might be
- Some diseases, e.g. ALS, may have signs of both UMN and LMN lesions

I. Upper motor neurons

Motor neurons that start in the motor cortex or in the brain stem

- Carry motor information down to the lower motor neurons
- Lesions are anywhere between the motor cortex and synapse to anterior horn, e.g. a stroke in the cerebral hemisphere

Upper Motor Neuron (UMN) lesions will show

- Muscle weakness
- Increased muscle tone → spasticity (difficult to manipulate the patient's muscles)
- Increased reflexes (e.g. increased knee jerk)

Signs of Upper motor lesions	
Positive Babinski sign	Scratching the bottom of your foot normally causes all the toes to plantarflex. In an UMN lesion, the big toe will extend (go the other way) while the other toes plantarflex – this is a **positive** Babinski sign.
Positive Rossolimo reflex	Stimulating the tips of the toes causes flexion of the toes
Positive Oppenheim sign	Extension of the toes induced by scratching inner side of leg

II. Lower Motor Neurons

- LMNs are motor neurons located in the:
    - Anterior grey column (ventral horn) (innervating muscles of the body)
    - Spinal lower motor neurons
    - Cranial nerve nuclei of the brainstem (innervating muscles of head and neck)
- All voluntary movement relies on spinal lower motor neurons
- Three different types of neurons: alpha, beta, and gamma

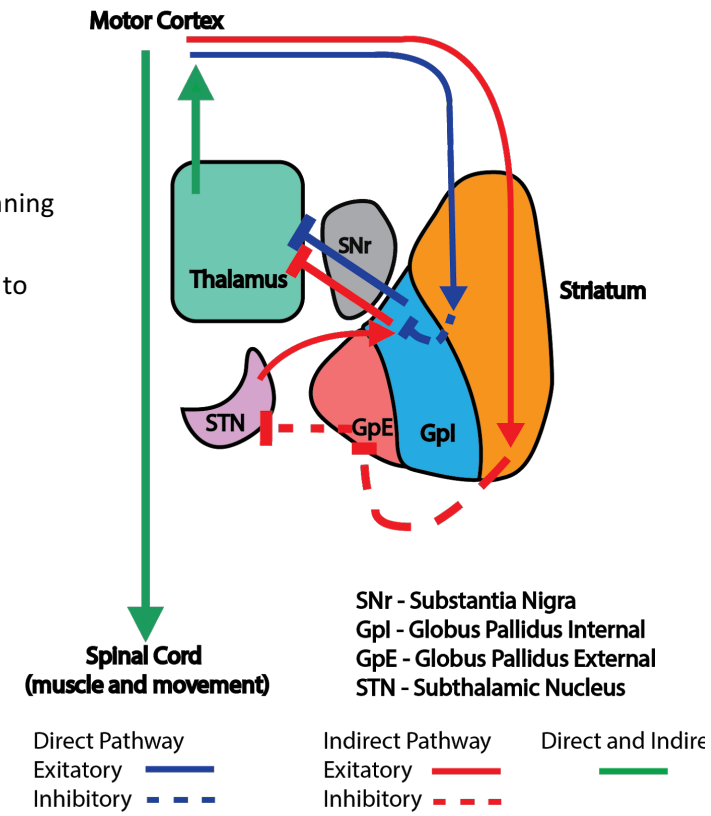
Lesion of Lower Motor Neuron (LMN) – "Everything will be **lowered** with a lesion in the **lower** motor neuron"

Lesion can for example be caused by atrophy of the anterior gray column, or a cut motor neuron between the spinal cord and muscle. This will show signs of:

- Decreased muscle strength
- Decreased reflexes
- Decreased muscle tone
- Flaccid Paralysis
- Muscle atrophy
- Fasciculations (small spontaneous muscle twitches that can especially be triggered tapping muscles)
- **Babinski sign** will be negative (normal plantarflexion of all toes)

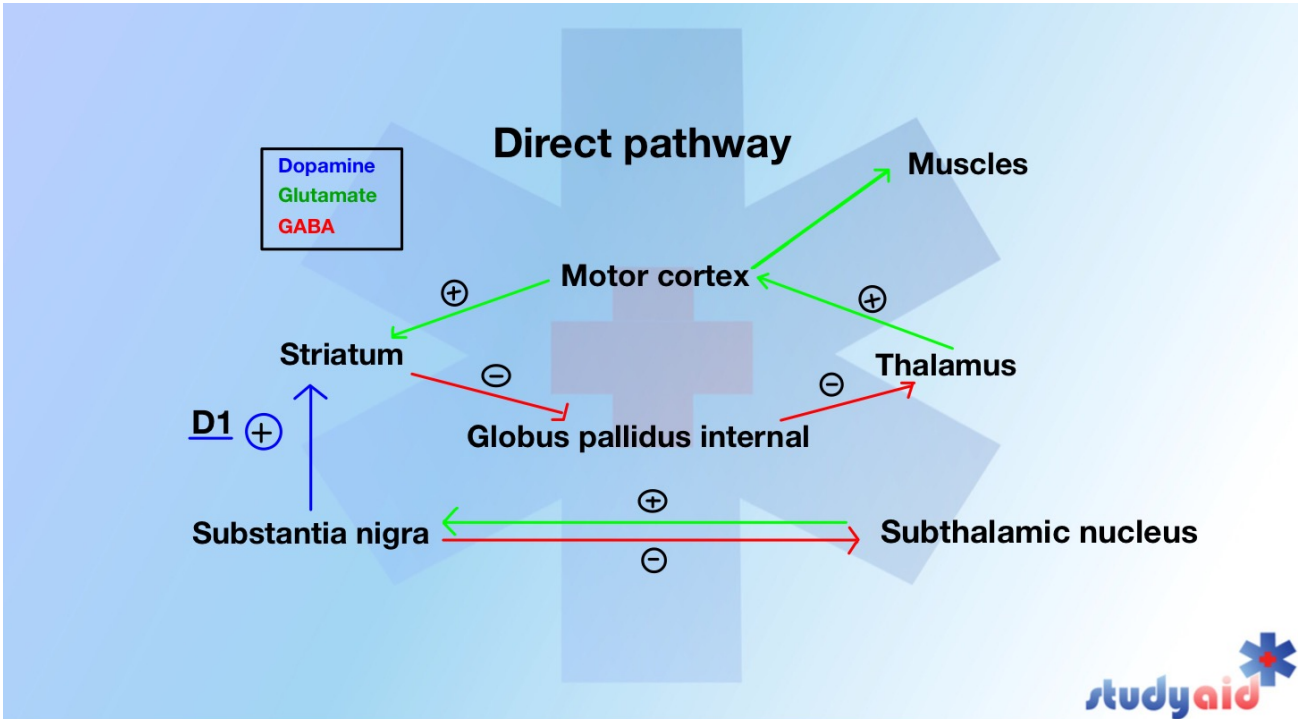
3.4 – Basal Ganglia

- Important in voluntary movements and making adjustments in posture
    - Control scale of movement, combining planning with movement
- Receives cortical input, provides negative feedback to cortex for adjustments
- **Five key components**
    - Caudate nucleus
    - Putamen
    - Globus pallidus (internal and external)
    - Subthalamic nucleus
    - Substantia Nigra
- The basal ganglia receives signals from all over the cortex, the thalamus, substantia nigra.
- **Striatum** = putamen + caudate nucleus
- **Lentiform** = putamen + globus pallidus



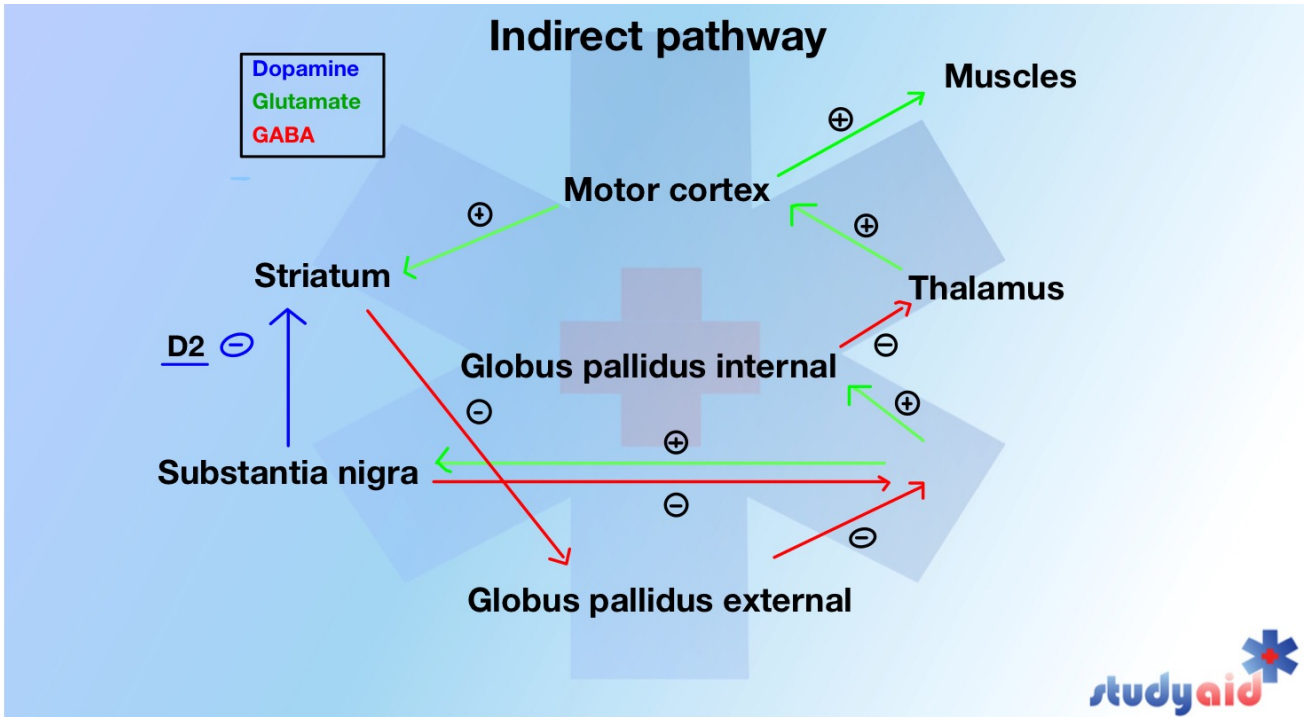
Direct Pathway

- Facilitates movement
- Motor cortex stimulates striatum → Inhibits GpI/SNr complex → Less inhibition of thalamus → More stimulation of cortex → More stimulation of muscles (hyperkinesia)



Indirect pathway

- Inhibits movement
- Motor cortex stimulates striatum → Inhibits GpE → Less inhibition of Subthalamic Nucleus → More stimulation of GPI → More inhibition of Thalamus → Less stimulation of cortex → Less stimulation of muscles (hypokinesia)



Dysfunction of the Basal Ganglia

Parkinson's disease

Loss of dopaminergic neurons in the pars compacta region of the substantia nigra

Symptoms: **TRAPS**

- **T**remor (at rest)
- **R**igidity (high muscle tone on assessment)
- **A**kinesia (or bradykinesia – patient has difficulty initiating movements)
- **P**ostural instability
- **S**huffling gait

Huntington's Disease

Genetic defect on chromosome 4

- Trinucleotide repeat (**CAG**)
- Autosomal dominant inheritance
- Repetitive/rapid movements (called chorea), decreased muscle tone
- Aggression/depression/dementia
- Due to loss of Cholinergic and GABAergic release, increased dopamine
- Loss of GABA to external palladium releases inhibition, allowing for rapid/repetitive movements
    - **C**audate loses **A**Ch and **G**ABA (**CAG**)

3.5 – Cerebellum

The cerebellum is involved in the planning, coordination, and modification of motor activities

Anatomic division

- Anterior lobe
- Posterior lobe
- Flocculonodular lobe
- Vermis

Roles in Movement

- Controls muscle tone
- Controls posture
- Controls muscle contraction
- Assists in planning/sequence of movement

Voluntary Motor Control

- Feedback connects cortex and cerebellum
    - Assist cortex in coordinating and planning a sequence of movement
- Cerebellum compares intention of movement with what is actually occurring
    - Cerebellum informs cortex about current muscle tone, position
    - Cortex makes changes to the plan using information from the cerebellum

Afferent Connections

Superior Peduncle	***Ventral spinocerebellar tract*** - Proprioceptive and exteroceptive impulses from the body - Control of fine movement of the limbs
	Tectocerebellar tract - Hearing (inferior colliculus) and visual (superior colliculus) impulses
	Cuneocerebellar tract - Proprioceptive impulses (emphasis on head, neck)
Middle Peduncle	***Pontocerebellar tract*** - Signals from motor and other parts of cerebral cortex
Inferior Peduncle	***Dorsal spinocerebellar tract*** – - Proprioceptive and exteroceptive reception - Control of fine movement of the limbs
	Olivocerebellar tract - Proprioceptive input from the body
	Vestibulocerebellar tract - vestibular input from labyrinths - Control of posture and equilibrium

Deep Nuclei

- Deep nuclei from lateral to medial - "**D**on't **E**at **G**reasy **F**oods"
    - **D**entate
    - **E**mboliform
    - **G**lobose
    - **F**astigial

Input

- Contralateral cortex through middle cerebellar peduncle
- Ipsilateral proprioceptive information from spinal cord through inferior peduncle

Output

- Sends information to contralateral cortex to regulate movement
- Purkinje cells → deep nuclei of cerebellum → contralateral cortex through superior cerebellar peduncle
- **Control of Equilibrium**
    - Cerebellum controls balance between agonist and antagonist muscles
        - E.g. if bicep flexes, triceps will extend
    - Signals inform how rapid movement is and in what direction it is moving
    - Signals from effectors (e.g. muscles) inform about its position, tone
    - Signals from cortex relay planned sequences of movement
        - Cerebellum can determine where a part of the body will be a few miliseconds ahead

Cerebellar Lesions

Dysmetria	Impaired coordination, overshoot or undershoot movements (can't determine intended position). Seen as difficulty in performing finger to nose test.
Ataxia	Lack of coordination due to errors in rate, force, direction of movement. Seen as generalized difficulty in coordination.
Dysdiadochokinesia	Unable to perform rapidly alternating (opposite) movements. For example, the patient can't quickly perform pronation, followed by supination.
Dysarthria (ataxic)	Slurring of speech (don't confuse with an aphasia!)
Intention tremor	Tremor which worsens when reaching end of planned movement. If the patient is asked to do finger to nose, his finger will progressively zig-zag as he gets closer.
Nystagmus	Rapid, involuntary movement of the eyes ("beating" of the eyes").

NOTES:

Review questions of Motor Axis:

1. What does “Plasticity of the motor cortex” mean?

2. What is the 1st order neuron in the corticospinal tracts? _____.

3. At what level does the lateral corticospinal tract decussate?

4. Babinski sign will be positive with a lesion in _____.

5. What are characteristic signs for a lower motor neuron lesion?

6. What is the cause of Huntigton’s disease?

7. What does the patient have difficulty with if he/she has ataxia?

8. Explain the pathway and function of the direct pathway of the Basal ganglia:

Section 4 – Sensory Axis

4.1 – Functional components of the cranial nerves

A nerve can have different fibers depending on what type of information they process. Therefor the nerve fibers can be categorized by these 3 elements

Firstly:

- Special – For vision, taste, smell, hearing.
- General – For general sensation of pain, touch, pressure etc.

Secondly:

- Visceral – The name of the nerve fibers with axonal endings in the viscera[1], glands and vessels: Pain and distension of viscera. Otherwise you can see these as autonomic fibers.
- Somatic – "Refers to the body opposed to the mind". For information about body position and movement, and contact with external factors. Impulses are intentional.
- Can be divided into:
    1. Exteroceptive:
        - Receptors in skin. Gives information about external environment, perception of touch, superficial pain, temp.
    2. Proprioceptive:
        - Receptors in joints. Gives information about body position and movement.

Thirdly:

- Afferent = impulses coming back to the brain (sensory)
- Efferent = impulses going to the tissues - e.g. muscle, (motor)

Combining these three words you can tell a lot about the fiber type in nerves, and one cranial nerve can have more than one type of fibers, as they have more than one function

General somatic afferent (GSA)	E.g. fibers from the skin and striated muscle
General visceral afferent (GVA)	E.g. fibers convey impulses from the viscera and blood vessels
General visceral efferent (GVE)	E.g. fibers innervate smooth muscle in viscera, intraocular muscles, heart, salivary gland etc.
General somatic efferent (GSE)	E.g. fibers innervate striated muscle.
Special somatic afferent (SSA)	Fibers conduct from the retina and auditory and vestibular apparatus
Special visceral afferent (SVA)	Fibers conduct impulses from the taste buds of the tongue and from the olfactory mucosa
Special visceral efferent (SVE)	Fibers innervate muscle derived from the brachial arches (branchogenic efferent's and branchogenic muscles.

[1] Viscera = internal organs in the main cavities of the body, e.g. intestines.

Classifying receptors based on their location

Interoceptors or visceroceptors	Receptors within the body. • Information about the events in the viscera ex. Blood pressure, glucose levels.
Exteroceptors	Receptors in skin. • Information about the external environment (touch, temperature, tickling, itching)
Proprioceptors	Receptors in joints, tendons, ligaments, muscles. • Information about body position and movement.

4.2 – Specific High Yield Receptors

Type	Responds to	Found in	Adaption
Free Nerve Endings	Pain/Temperature	Skin/some viscera	Slow/Quick
Meissner Corpuscles	Fine/Light Touch	Hairless skin	Quick
Merkel Discs	Pressure	Fingertips/Superficial Skin	Slow
Pacinian Corpuscles	Vibration/Pressure	Deep Skin/Joints	Quick
Ruffini Corpuscles	Pressure/Skin Stretch/Joint Angle Change	Fingertips/Joints	Slow

Receptor specificity

- Receptors are able to respond to form of energy different than typical stimulus but the threshold for such a sense is higher
    - E.g. If you close your eyes and press them, you initiate mechanical stimulation and the colors change

Muller Law

- Principle that each type of sensory nerve cell normally responds to only one specific stimulus and gives rise to one sensation
    - A cell may be excited artificially by other forms of stimuli (eye rubbing above), but the sensation evoked will be the same
- More simply put - sensation triggered is dependent on the kind of stimulated receptor, not on the energy applied to the receptor

Law of Projection

- The conscious sensation produced is referred to the location of the receptor
- Independent of where the pathway was stimulated
    - E.g. phantom limb (patient feels pain in a limb that was amputated)

Sensory Transduction

- Stimulus finds itself at sensory receptor
    - E.g. light hitting rod/cone, sodium receptor on the tongue
- Membrane conduction changes (allows current to flow, depolarization)
    - Exception: Photoreceptor, hyperpolarization
- If these changes are large enough, and membrane potential exceeds the required threshold, action potential continues down sensory neuron
    - Receptor potential is recorded from receptors
        - Amplitude is directly proportional to the intensity of the stimulus
    - Action potential is recorded from sensory nerves
        - Frequency of action potential is proportional to the intensity of stimulus

4.3 – Sensory Adaptation (desensitization)

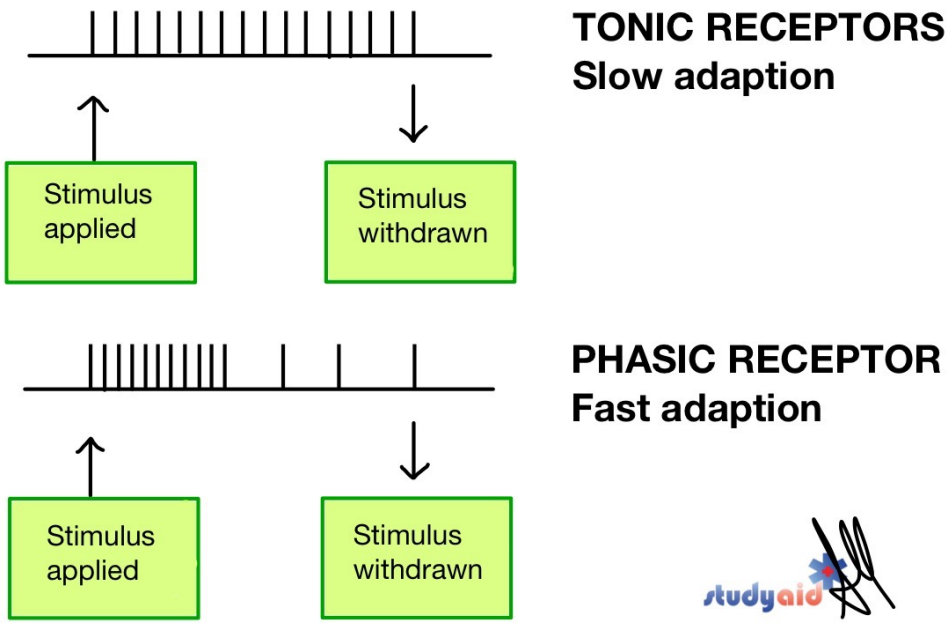
Continuous application of stimulus to a receptor leads to decreased frequency of action potentials in the sensory nerve. The degree to which adaptation occurs depends on the type of sensory receptor.

Phasic Receptors

- E.g. touch receptors
- Adapt **rapidly**
    - Registration of the start and of the end of stimulation
    - Registration of the rate of change

Tonic Receptors

- E.g. Proprioceptors
- Adapt **slowly**
    - Sometimes non adaptive
    - Continuous registration of receptor activation
    - Plays active role in homeostasis due to constant update in registration



4.4 – The Sensory Unit

- Sensory axon with all its peripheral branches
- Receptive field is the area innervated by a single sensory unit
- Recruitment of sensory units depends on the strength of the stimuli
    - Weak stimulus → activation of a receptor with the lowest threshold
    - Stronger stimulus → activation of receptors with higher threshold
        - Results in increased frequency from the unit
    - Stronger stimulus → more units fire → more afferent pathways transmit the information to the brain
        - Brain interprets this as an increase in stimulus intensity
- Two Point discrimination
    - Answers the question: how far apart do two separate points on the skin need to be before they are perceived as two points rather than one?
        - Depends on the location on the body, directly relating to density of receptors
            - E.g. Fingers are more receptor dense, skin on the back is less receptor dense, stronger two-point discrimination on the finger than on the back

4.5 – Processing of information

Role of thalamus

- Information from different parts of the body is processed here, further directed to different parts of the sensory cortex
    - Destruction of thalamic nuclei (e.g. a thalamic stroke) results in loss of sensation on the contralateral side of the body

High Yield Thalamic Nuclei

- VPL - Ventral posterolateral
    - Input - spinothalamic and dorsal column/medial lemniscus
    - Information transmitted - pain, temperature, proprioception, touch, pressure, vibration
    - Export to somatosensory cortex
- VL - Ventral lateral
    - Input - Basal ganglia, cerebellum
    - Information transmitted - motor
    - Export to motor cortex

Somatic Cortex

- "Decodes" the sensory signals
- *Somatosensory area I - postcentral gyrus (parietal lobe 3, 1, 2)*
- *Somatic sensory cortex II – superior wall of sylvian fissure*
- Plasticity of sensory cortex
    - Ability to change the representative area of the cortex by experience
        - "Rewiring" axons, dendrites of neurons
    - In general, sensory unit connections to cerebral cortex became stronger with usage, weaker with a lack of usage

4.6 – High yield pathways

Tract	1st, 2nd & 3rd order neuron	Decussation	Sensation
Anterior spinothalamic - Ascends in anterior white column	***1st*** **-** Dorsal root ganglion (no synapse here) ***2nd*** **-** Nucleus in dorsal horn of spinal cord ***3rd*** **-** Ventral Posterolateral nucleus (thalamus) **Ends in primary sensory cortex (areas 3,1,2)**	Decussates in anterior white commissure and ascends as anterior spinothalamic	Crude touch and pressure *Sensation reaches consciousness*
Lateral spinothalamic - Ascends in lateral white column	***1st*** **-** Dorsal root ganglion (no synapse here) ***2nd*** **-** Nucleus Proprius and/or Substantia Gelatinosa of dorsal horn of spinal cord ***3rd*** **-** Ventral Posterolateral nucleus or reticular formation (thalamus) **Ends in primary sensory cortex (areas 3,1,2)**	Decussates in anterior white commissure toward <u>contralateral</u> lateral white column of spinal cord, and ascends as lateral spinothalamic.	Pain Itching Temperature *Sensation reaches consciousness*
Dorsal Column-Medial Lemniscus (Spinobulbothalomocortical) *"C comes before G in the alphabet, therefore Cuneate have the fibers from above T4"*	***1st*** **-** Dorsal root ganglion (no synapse here) ***2nd*** **-** Cuneate (from above T4) & Gracile nuclei (from under T4) ***3rd*** **-** Ventral posterolateral nucleus **Ends in primary sensory cortex (areas 3,1,2,) and posterior paracentral lobule**	Decussates in the brainstem Decussate as **internal arcuate fibers** in the medulla then becomes **medial lemniscus**	Fine touch (2 point discrimination) Pressure Vibration Proprioception *Sensation reaches consciousness*

4.7 – Pain

- Protective mechanism for the body to remove dangerous stimuli
- Receptors for pain are ***free nerve endings***
    - Detect thermal, chemical, and mechanical noxious stimuli
- Pain can be arbitrarily (for the purposes of this course) divided into two types

Fast pain	Slow pain
- A delta fibers (6 - 36 m/s) - Glutamate - Fast, sharp - Mechanical and thermal stimuli - Localization very exact when stimulated together with tactile receptors - Transmitted to thalamus (ventrobasal complex) then to SII and SI	- C fibers (0,5 - 2 m/s) - Substance P - Weak burning pain - Poor localization - 75 – 90 % of fibers terminated in on Reticular Formation (RF)

Analgesic System

- Refers to the system which reduces pain
    - Gate Control Theory
        - When fibers larger than the pain fibers fire, they close the paingate. Leading to the pain transmission not reaching the CNS
        - Analgesic nerve fibers produce endogenous opioids substances e.g. enkephalins, endorphins, dynorphin. These inhibit pain transmission.
            - Signals from raphe nuclei → interneurons release endogenous opioids → pain gate closes

- Neuromodulators of pain
    - Serotonin (of the raphe nuclei)
    - Enkephalins, endorphins, dynorphins

I. Other Types of Pain

- Visceral Pain
    - Poorly localized and frequently are accompanied by sweating and changes in BP
    - Associated with autonomic sensations (nausea, vomiting)
    - Receptors for pain in the viscera are similar to those in skin
        - No proprioceptors in the viscera
        - Few temperature and touch receptors
        - Nociceptors are present, although not very well distributed

- Referred Pain
    - Discomfort of a visceral organ frequently produces pain that is felt in a structure that can be distant from the actual location of pain
        - When pain is referred, it is usually to a structure that developed from the same embryonic segment as the structure in which the pain originates
            - Also known as the dermatome theory
            - E.g. heart and arm came from the same segment, during a myocardial infarction, pain is often felt in the left arm
        - Alternate theory - convergence of somatic + visceral pain fibers to the same neurons in the dorsal horn that project to the thalamus and then to the sensory cortex

- Parietal Pain
    - Typically occur as a result of irritation of visceral membranes
    - Described as sharp, strong pain
    - Typically; well localized

4.8 – Thermal Sensation

- Thermal receptors
    - Cold receptors react between $5 - 40$ ℃
        - Pain fibers stimulated by cold at <10 C
    - Warmth fibers react between $30 - 50$ ℃
        - Pain receptors stimulated by heat > 45 C
        - Warmth receptors typically begin to fail around 45 degrees Celsius, at which point nociceptors (pain receptors) begin to kick in
    - Overlap exists at midrange temperatures

- Transduction of warm temperatures involves transient receptor potential (TRP) channels
    - There are many - e.g. vanilloid receptor 1 (VR1) and VRL-1
    - These channels are also activated by substances from the vanilloid class (e.g. capsaicin found in hot peppers)
- Transduction of cold temperatures involves a different class of TRP channels (e.g. TRPM8)
    - Cold and Menthol sensitive receptor
- Transmission of thermal sensation via the anterolateral pathway
    - Through reticular formation → thalamus → sensory cortex

NOTES:

Review questions sensory axis:

1. Meissners corpuscles are found in _____and responds to _____.
2. The Muller law states that:

3. Phasic receptors adapts _____, and tonic receptors adapts_____.
4. Anterior spinothalamic tract decussates in _____.
5. What sensations are transmitted by the lateral spinothalamic tract?

6. _____ fibers transmits the slow pain, and this pain is characterized by _____.
7. Which tract is responsible for the transmission of proprioception?

8. Explain the pathway and sensory information transmitted by the Dorsal Column Medial Leminiscus:

Section 5 – Activation of the Brain and Sleep

I. Awareness

- Two types
    - Relaxed awareness
    - Awareness with concentrated attention

II. Reticular Formation (RF)

- Located in the central portion of the medulla and midbrain
    - Contains the cell bodies and fibers of many systems.
        - Contains many areas associated with regulation of heart rate, blood pressure, and respiration (basic life necessities)
        - Connections from ascending sensory tracts, trigeminal, auditory, olfactory, visual systems, descending motor tracts
    - Upper Reticular formation
        - State of brain activity
    - Lower Reticular formation
        - Regulation of muscle tone and spinal reflexes
            - Facilitatory area - increases muscle tone, controls reflexes
                - Spontaneous neuron discharge
            - Inhibitory area - reduces tonic signals, decreases muscle tone
                - Driven by higher neural centers

III. Reticular Activating System

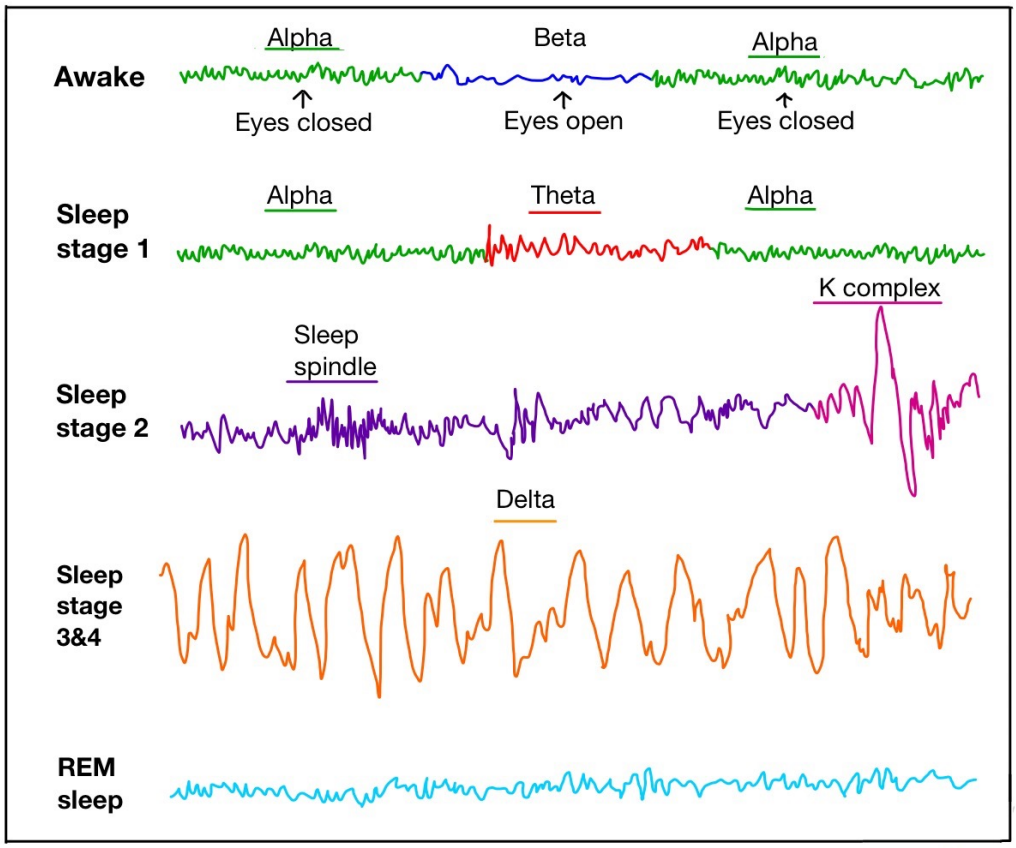
- Controls levels of consciousness
    - E.g. if you are sleeping, the RAS determines whether stimulus around you is important enough that you wake up
- Pathway arising from the brain stem RF and hypothalamus
- Connections to the intralaminar and reticular nuclei of the thalamus
- Non-specific system
- Anesthetics and RAS
    - Anesthetics decrease conduction in RAS by blocking parts of synaptic connections → result in loss of consciousness

5.1 – Electroencephalogram (EEG)

- Used to measure the electrical activity of the brain (from superficial layers, noninvasive)
- Measures of the summation of dendritic postsynaptic potentials (not action potentials)
    - Dendrites of the cortical neurons are a forest of similarly oriented, densely packed units
- As excitatory and inhibitory endings on the dendrites of each cell become active, current flows into and out of these units
    - Cell body–dendrite relationship is therefore that of a constantly shifting wave
    - When the sum of the dendritic activity is negative relative to the cell body, the neuron is depolarized and hyperexcitable
    - When it is positive, the neuron is hyperpolarized and less excitable
- This process is continuous, and so provides the grounds of an EEG recording
- EEG activity always reflects the sum of the synchronous activity of thousands or millions of neurons that have similar spatial orientation
- Synchronization
    - Observed when large groups of neurons fire at the same time
    - Example of spatial summation
- Desynchronization
    - Decreases in oscillatory activity are referred to as event-related desynchronization
        - Simultaneous unrelated neuron events lead to cancelling each other out

5.2 – Possible states of the Brain

Alpha Rhythm	- Observed at rest, awake, eyes closed - Most observed in the parietal and occipital lobes - Associated with decreased levels of attention
Beta Rhythm	- Alert, active mental concentration, eyes open - Highest frequency, lowest amplitude - Mostly observed in the frontal leads - Also occurs during REM sleep (see below)
Theta Rhythm	- Light sleep, occurs during stage N1 - Hypothesized for memory consolidation
Delta Rhythm	- Low Frequency, high amplitude - Seen during stage N3 of sleep - Deepest non REM sleep - Associated with sleepwalking, night terrors
Seizure	Seizure - occurs when there is a sudden abnormal discharge of electrical activity in the brain. It is characterized by synchronized, high frequency neuronal firing. - EEG is useful in finding the defective area of the cortex.



5.3 – Sleep

- Sleep is regulated by circadian rhythms
    - Controlled through **Suprachiasmatic Nucleus** of hypothalamus
        - Regulated by levels of light
    - Two stages of sleep
        - Rapid eye movement (REM) - also called paradoxical sleep
        - Non rapid eye movement (NREM)

Phases of sleep cycle - Entire cycle takes between 90-120 minutes in average adult	
Awake (eyes open)	*Beta Waves*
Awake (eyes closed)	*Alpha Waves*
Non REM sleep	
Stage N1 (shortest)	*Theta waves* Light sleep, very slow eye movement sometimes noted. During transition into this sleep, hypnic jerks can be observed.
Stage N2 (longest)	Characteristic with sleep spindles and K complexes Sleeper easily awakened
Stage N3	*Delta waves* Deepest Non REM sleep Right before REM sleep, PGO spikes sometimes noted
REM sleep – occurring every 90 minutes, duration increases through the night	
	Theta waves *Beta waves* In REM sleep: - There is loss of motor tone - Increased brain oxygen consumption - Increased and variable pulse and blood pressure Dreams from this state can be recalled As age increases, amount of REM sleep decreases Sleep, especially REM sleep, is necessary for learning and **memory consolidation.**

- **PGO** spikes
    - Seen right before transition from NREM to REM
    - Waves begin as electrical pulses from the **P**ons
    - Move to the lateral **G**eniculate nucleus residing in the thalamus
    - Finally end in the visual cortex of the **O**ccipital lobe

5.4 – Circadian Rhythm

- Controls night release of ACTH, prolactin, melatonin, norepinephrine
    - Mediated via the Suprachiasmatic nucleus (SCN)
    - SCN → norepinephrine release → pineal gland → melatonin
    - Regulated by light hitting/not hitting the retina
    - Light inhibits the pathway of production of melatonin (not produced during the day whilst exposed to sunlight)

NOTES:

Review questions from Activation of the Brain and Sleep

1. The longest phase of NREM sleep is _____.

2. Suprachiasmatic nucleus is responsible for regulating _____.

3. In sleep phase _____ it characteristic with sleep spindles and K complexes.

4. What is the function of RAS (Reticular Activating System)?

5. What does the EEG show us?

6. Decribe the different characteristics of the 4 types of brain rhythms:

7. Explain what happens with the body during REM sleep and why is it important?

Section 6 – Hypothalamus and the Limbic System

6.1 – Hypothalamus

- Center of complex mechanisms that maintain the homeostasis of the body

Structures	• Anterior Hypothalamus • Tuberal Hypothalamus • Posterior Hypothalamus • Lateral area • Ventromedial area
Afferent connections from	• Limbic system • Brain stem • Thalamus
Efferent connections to	• Thalamus • Brain stem • Pituitary gland

I. Role of the Hypothalamus ("TAN HATS")

- **T**hirst and water balance (osmolarity control)
- **A**denohypophysis control
    - Regulation of anterior pituitary
- **N**eurohypophysis releases hormones produced in the hypothalamus
- **H**unger regulation
- **A**utonomic regulation
- **T**emperature regulation
- **S**exual urges

II. Relationship with the Pituitary gland

The posterior pituitary is a collection of axonal projections from the hypothalamus that terminate behind the anterior pituitary

- Also called the neurohypophysis
- Serves as a site for the secretion of neurohypophysial hormones (oxytocin and vasopressin)
- Hypothalamic–neurohypophyseal system
    - Consists of the hypothalamus (specifically the paraventricular nucleus and supraoptic nucleus), posterior pituitary, and axonal projections

III. Lateral Area of the Hypothalamus

- Responsible for hunger
- Destruction leads to anorexia (never feeling hungry) "**L**ateral injury makes you **L**ean"
- Chronically active (only temporarily inhibited by the ventromedial area (satiety)
    - Stimulated by
        - B-endorphins
        - **Neuropeptide Y**
        - **Orexins A and B**
        - Agouti related peptide
        - **Ghrelin**
        - Melanin-concentrating hormone
    - Inhibited by **Leptin**

IV. Ventromedial area of the Hypothalamus

- Responsible for satiety (feeling full)
- Destruction makes you "**V**ery **M**assive" (leads to hyperphagia, always hungry and always eating)
- Stimulated by (still experimental + theorized, bolded ones are high yield)
    - **Leptin**
    - **CCK**
    - POMC
    - CART
    - CRH
    - Bombesin
    - Glucagon
    - GLP-1, GLP-2
    - Neurotensin
    - Oxytocin
    - Somatostatin
    - PYY

V. Regulation of Food Intake

- Three hypotheses exist at the time of writing of the Neurophys lectures
- These inhibit signals for food intake, causing satiety
        - Thermostatic - increased temperature
        - Glucostatic - increased glucose available
        - Lipostatic - fat and leptin
            - Leptin synthesized by white adipocytes
                - Production of proteins of OB gene
                    - Receptor encoded for by db gene
                    - *Long form of ob receptor similar to IL-6 receptor*

VI. **Regulation of ECF osmolarity and volume**

- Hypertonicity occurs → osmoreceptors activated → signal to hypothalamus → increased thirst
- Hypovolemia occurs → baroreceptors activated → Release of Angiotensin II (pathway) → ADH
    - Water retention by renal system

VII. **Hypothalamus and Stress**

- Regulation of hormone release
- Control over autonomic system
    - Heart rate, BP, respiration etc.

6.2 – Temperature Adjustment

I. **Anterior hypothalamus** is responsible for cooling the body (responding to heat)

- Parasympathetic actions
- Mechanisms of action
    - Sweat
    - Increased rate of respiration
    - Cutaneous vasodilation
    - Decreased rate of physical activity, muscle relaxation
    - Decrease in appetite
    - Increased thirst

II. **Posterior hypothalamus** is responsible for heating the body (responding to cold)

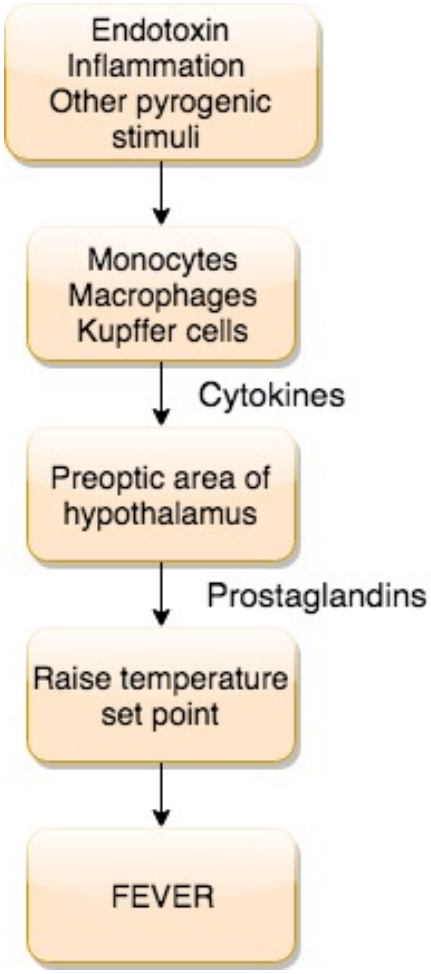
- Also sympathetic actions
- Mechanisms of action
    - Shivering
    - Cutaneous vasoconstriction
    - Increased muscle movement (e.g. shivering)
    - Horripilation response (“goose bumps”)
    - In babies, brown adipose tissue activation

III. **Regulated changes of body temperature**

- Lowest levels around 4 a.m. and the highest in the late afternoon
- Menstrual cycle increases the body temperature ever-so-slightly
- Physical activity (activation of muscles) increases body temperature

IV. Fever

The mechanism of fever is summarized in this picture, but shortly the endotoxins work on monocytes, macrophages and Kupffer cells (Type of macrophages in the liver) to produce cytokines (e.g. IL-1, IL-6, TNF-a) this reaches the OVLT of the hypothalamus which then activates the Preoptic area. Via release of prostaglandins (e.g. PGE2) the temperature set point is raised, and you have fever in the body.



V. Benefits of Fever

- Inhibition of bacterial growth
- Stimulation of antibody production
- Decrease of tumor growth

6.3 – Limbic System

- Collection of neural structures involved in emotion, long term memory, behavior modulation (e.g. motivation, addiction), ANS function, sexual behavior, olfaction
- Structures include
    - Allocortex, Hippocampus, Parahippocampal gyrus, Cingulate gyrus, Olfactory bulb, Orbitofrontal part of frontal lobe, **Amygdala**, Septal Nuclei, Hypothalamic Nuclei
- Hypothesis of Emotional states
    - Two systems related to hypothalamus and limbic system
        - System promoting rage, system promoting placidity
            - Emotional state depends on the balance between rage and placidity
- The remaining part of the limbic system lecture is still highly theorized and under research, but there will most definitely be questions about it so here is what is presented during the lectures

Amygdala

- Important structure of the limbic system
- Believed to be responsible for strong (negative) emotions such as rage and fear
- Stimulation of amygdala for example causes
    - Rage reaction
    - Pain
    - Punishment

Klüver-Bucy syndrome

- Caused by destruction of amygdala
- Symptoms are:
    - Loss of fear
    - Extreme curiosity
    - Increased sex drive
    - Tendency to put everything into the mouth

6.4 – Reward and punishment system

- Reward involves Dopaminergic system
    - Nucleus accumbens (key)
    - Ventral tegmentum
    - Dorsal brain stem
- Punishment involves cholinergic system
    - Posterior hypothalamus
    - Dorsal midbrain
    - Entorhinal cortex

Addiction

- Repeated compulsive use of a substance despite of its negative effects (opiates, drugs, alcohol, nicotine etc)
    - Each affect the brain in different ways, but all increase the quantity of dopamine available to bind with D3 receptors in the nucleus accumbens.

Dopaminergic systems (noted associations)	Serotonergic System

- Nigrostriatal system
- Mesocortical system (n. Accumbens)
- Tubero-infundibular system (PRL secretion)
- Interohypothalamic system
- Dopaminergic receptors overstimulation
  - D2 – role in schizophrenia
  - D3 – role in addiction
	- Key neurotransmitter of the body
	  - Decreases in its concentrations of the body can lead to anxiety, depression
	- Produced in the Raphe nuclei (pons, midbrain, medulla)
	- Receptors for serotonin are called 5-HT
	- Mediate the effects of serotonin
	- Bind a broad range of pharmaceutical and hallucinogenic drugs.
	  - Drugs that primarily affect 5HT2 receptors
	  ▪ LSD, Psilocin, Mescaline

NOTES:

Review questions from Hypothalamus and the Limbic System

1. Name the functions of the hypothalamus:

2. The area of the hypothalamus responsible for hunger is the

   _____, and the are area responsible for

   satiety is the _____.

3. Which structure is responsible for cooling of the body, and what is the mechanisms of action?

4. The addiction center of the brain is located in the _____.

5. What are the cause and symptoms of Kluver Bucy syndrome?

6. What is the mechanism of fever?

Section 7 – Higher Function of the Brain

Learning and memory

- Learning - the ability to replicate, change, or modify behavior as a result of experience
- Memory - the retention and storage of information

7.1 – Types of Memory

I. Declarative (explicit)

- Associated with consciousness (or awareness) - dependent on hippocampus
- Two types
    - Episodic - memory of events, facts
    - Semantic - memory of words, rules of language, etc

II. Non-declarative (implicit)

- Does not involve awareness, or processing in the hippocampus
- Skills and habits
- Associated learning
    - Classical
    - Operant
    - Imprinting
- Nonassociative learning

Brain Structures associated with memory

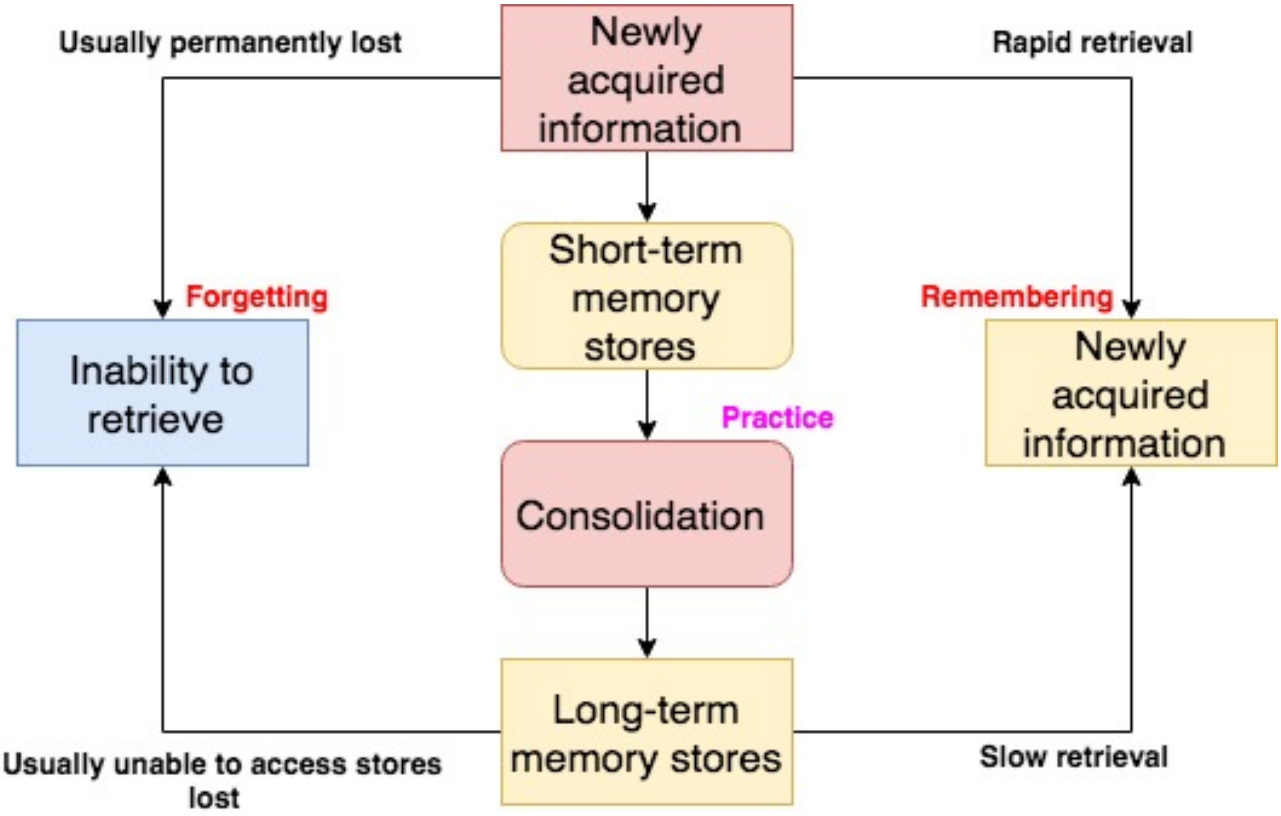
Declarative memory	Temporal lobe, diencephalon
Skills and habits	Striatum
Priming	Priming
Non-associative learning	Reflex pathways (spinal cord)

III. Working Memory

- Keeps information available for short period of time (decision on what to do with it)
    - Involves hippocampus

IV. Long Term Memory

- Persists for years
- Information is stored in neocortex
    - Visual, auditory or olfactory areas
    - Can be recalled by different associations
    - Associations are proportional to quantity and strength of neural connections
        - Repetition-repe-repetition



V. Reflexive Memory

- Associative learning (skills, habits, conditioned reflexes)
    - Person learns about the relation of one stimulus to another
- Non-associative learning
    - Person learns about a single stimulus

VI. Habituation

- Single stimulus is repeated many times
- Decrease in responsiveness to stimulus
- Organism is “habituated” and begins to ignore stimulus

VII. Sensitization

- Enhancement of a behavioral response to a stimulus
    - Occurs when coupled to a novel stimulus

VIII. Conditioned Reflexes

- Unconditioned stimulus (US) is a stimulus that normally evokes a specific response
- Conditioned stimulus (CS) is a neutral stimulus that did not previously produce a response
    - The CS and US have to be paired countless times until eventually the (now) conditioned stimulus is evoked during propagation of the unconditioned stimulus
        - If the CS is presented without the US enough, there is extinction, which means that the conditioned reflex disappears
        - External inhibition - in the presence of external stimuli the organism is disturbed and the reflex may not occur

7.2 – Mechanisms for Learning and Memory

(for the purposes of Neurophys midterm)

- Short term sensitization
- Involvement of facilitatory (5HT) interneurons
- Greater influx of calcium → more neurotransmitters releases
- Long term sensitization
    - Activation of RNA transcription and protein synthesis
    - Movement of axons → new neuronal connections, strengthen memory, make new associations

7.3 – Amnesia

Retrograde amnesia

- Inability to recall former events
    - Typically resulting from brain damage

Anterograde amnesia

- Inability to form new long-term memory
- Typically resulting from neurodegenerative disease, senile dementia

7.4 – Language Disorders

- Dysarthria - Inability to produce words (motor problem, e.g. due to cerebellum lesions)
- Dysphonias - Inability to produce sounds
- Dysphasia/Aphasia - higher-order inability to speak

Dysphasia/Aphasia	Lesion
Broca	Non-fluent with intact comprehension (patient understands what you're asking him, but can't express himself)
Wernicke	Fluent with impaired comprehension and repetition ("word salad" – there are words, but they're not in the right order or don't make sense)
Conduction	Poor repetition but fluent speech, comprehension intact
Anomia	Consistent inability to produce words for things desired to talk about

7.5 – Prefrontal Association Area

- Region of the brain characterized by the following responsibilities
    - Planning for voluntary movement, the future
    - Consideration of consequences of actions before following through
    - Predictions
    - Solving logical/math problems
    - Self-control in regards to social, moral, ethical laws and norms

7.6 – Parieto-occipito-temporal area

- Work between the somatosensory, auditory, and visual cortex
    - Responsible for the following
        - Analysis of spatial coordination
        - Area for language comprehension
        - Area for visual language (reading)
        - Area for associating vision with memory

7.7 – Categorical Hemispheres

- For the typical (right handed) human, each of the two hemispheres is divided into specific ranges of processes
    - **Left hemisphere** (dominant side)
        - Analytical processes
            - Sensation/movement of the contralateral side of the body
            - Mathematical/logical problem solving
            - Analysis and Conclusions
            - Language
        - Lesions: language disorders, depression
    - **Right hemisphere** (nondominant side)
        - Spatio-temporal relations
            - Sensation/movement of the contralateral side of the body
            - Creativity/Artistic qualities
            - Identification of form of objects, emotions

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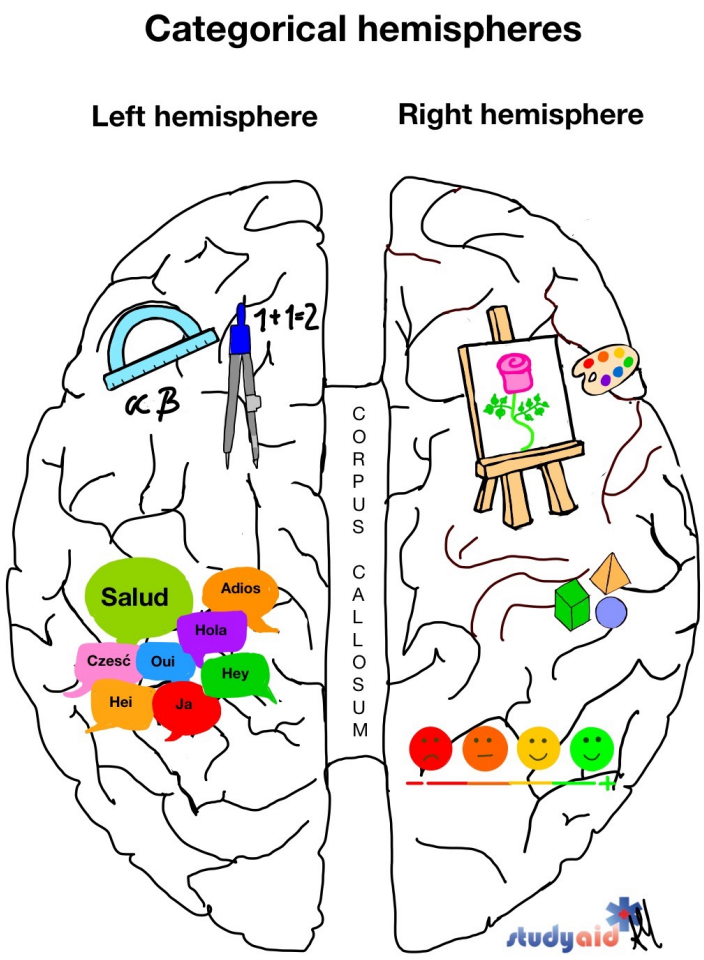

NOTES:

Review questions for Higher Functions of the Brain

1. What is the difference of declarative and non-declarative memory?

2. Long-term memory is stored in _____.

3. Explain the term “habituation”

4. Retrograde amnesia is defined as _____

   _____, whilst anterograde amnesia is defined as_____

   _____.

5. With a lesions in Wernickes area you will experience:

6. Explain what a conditioned reflex is

7. A lesion in the left hemisphere will most likely impair abilities tied to:

8. Prefrontal association area is responsible for: