Neurophysiology

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Lecture Content

- Membrane physiology
- Synaptic transmission
- Reflexes: segmental and suprasegmental control of movement
- Sensory receptors and perception
- Cerebral blood flow
- Special senses
- Autonomic nervous system
- Reticular formation
- Cerebellum
- Pathophysiology of pain
- Memory and hippocampus

Membrane Physiology
Neurophysiology

**Resting Membrane Potential**

Nernst Eqn
\[ E_K = \frac{RT}{F} \ln \left( \frac{[K^+]_o}{[K^+]_i} \right) \approx -70 \text{mV} \]

Goldman Eqn
\[ p[K+i/o] + p[Na+i/o] + p[Cl-/o] \]

**Temporal Summation of Excitatory Postsynaptic Potentials**

Electrotonic conduction

Temporal summation of epsp’s

**Spatial Summation of Excitatory Postsynaptic Potentials (epsp’s)**

**The Action Potential (AP)**

Critical Features
- All or none
- Rapid depolarization
- Na channel inactivation
- K+ conductance
- Absolute refractory
- Relative refractory
- Afterhyperpolarization

Resting membrane potential

Afterhyperpolarization

Depolarization

Refractory period

Threshold

Action potential
Neurophysiology

AP Conduction Velocity

- Unmyelinated axons
dia. 0.5-2um
Conduction velocities 1-10m/s

- Myelinated axon
dia. 2-5um
Velocity 10-100m/s

Synaptic Transmission

Presynaptic Neurotransmitter Release

Review Physiology of Synaptic vesicles
Docking proteins
Ca2+ triggered release
Postsynaptic receptors

Synaptic Transmission:
Summation of Excitatory and Inhibitory Inputs

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2 major categories of postsynaptic receptors:

1) Ionotropic
2) Metabotropic receptors

Metabotropic Receptors (cAMP)

Activate ion-channels indirectly through second-messengers

Metabotropic Receptors (PKC, Ca2+)

Metabotropic Receptor (GirK)

G-protein coupled receptors and ion channel conductance (GirK)

GABA-B receptors
Neurotransmitter Metabolism

Glutamate Metabolism

GABA Metabolism

Reflexes
Segmental and Suprasegmental Control of Movement

Overview of Motor System
Reflexes

- Fundamental of neural circuits
- "Hard-wired" of motor functions
- Stable input-output functions
- Do not require volition
- Important part of neurological-uninfluenced by patient's subjective reporting (sensory) or level of effort (motor)
Review of Muscle Spindle Control

Myotatic Reflex and Reciprocal Inhibition

Hoffmann Reflex
Flexor Reflex/Crossed Extensor Reflex

Myotactic Reflex and Reciprocal Inhibition
Sensory Receptors and Perception

Sensory Innervations of Skin

- Free (naked) nerve endings
- Merkel cell neurite complex (pressure sensors)
- Follicular endings

Cerebral Blood Flow

Blood Brain Barrier (BBB)

Endothelial tight-junctions

Endothelial cells >tight-junctions >pericytes >astrocyte foot processes
Special Senses

Hearing, Auditory System
- Sound transduction
- Tympanic membrane
- Pressure waves
- Basilar membrane
- Hair cell depolarization
- Activate afferent nerve terminals
- Bipolar spiral ganglion cells

Vision
- Retina—8 layers
- Photoreceptors
- rods (dim light). Hyperpolarized by light, activate ON/OFF ganglion cells
- cones (sensitive to color, fovea), 3 types, (sensitive red, blue, green)
- Horizontal cells, inhibit bipolar neurons
- Amacrine cell, modulate transmission (Ach, DA, serotonin) enhance movement detection, contrast

Olfactory System
- Piriform cortex
- Olfactory tract
- Mitral cells
- Bipolar neurons

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Parasympathetic Nervous System

1. 4 cranial nerves
2. Sacral (S2/3/4)

Sympathetic Nervous System

Critical Elements
- Hypothalamus and brain stem
- Preganglionic neurons (T1-L5)
- Sympathetic chain
- Postganglionic fibers

Parasympathetic Nervous System

- Oculomotor n. pupil
- Facial n. lacrimal > nasal
- Glossopharyngeal n. parotid gland
- Vagus n. heart > lungs > small intestine > colon

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Neurotransmission in ANS

- All preganglionic neurons are cholinergic
- Acetylcholine activates nicotinic receptors on postganglionic neurons
- Sympathetic postganglionic neurons release noradrenaline (except innervation of sweat glands-cholinergic)
- Parasympathetic postganglionic neurons are all cholinergic
- Activate muscarinic receptors (M1-M5)
- M1, M3, M5 are excitatory, M2 M4 inhibitory

Reticular Formation

- Polysynaptic network
- Brainstem
- Diffuse rostro-caudal projections
- Complex networks, modulates sleep-wake cycle, mood, cognition, etc,
- Median reticular formation (midline raphe) a major network of serotonergic projections located in raphe nuclei of mid-brain, pons and medulla
- Paramedian reticular formation. Magnocellular neurons (dopaminergic) of the lower pons/medulla project to the thalamus
- Parvocellular reticular formation

Median Reticular Formation (Midline Raphe): Major Network of Serotonergic Projections
Anatomy and Principal Functions of the Cerebellum

- Evaluate disparity between “intention and action” of the motor system
- 10% of brain weight, 50% of all neurons
- Vestibulocerebellum (median strip, vermis); inputs from visual, auditory, vestibular. Outflow >fastigial nucleus >brainstem >gaze control >1 proximal muscles of the trunk and limbs
- Spinocerebellum (paramedian); inputs from limbs, projects to interposed n. (globose and emboliform nucleus), projects to corticospinal, rubrospinal systems, control distal muscles, gait
- Cerebrocerebellum; input from cerebral cortex, projects >dentate >motor, premotor and prefrontal cortex

Cerebellum: Microscopic Anatomy

- Molecular layer; axons from granule cells, dendrites of purkinje cells; also contains inhibitory interneurons (stellate cells, basket cells)
- Purkinje cells; large neurons, principal outflow of the cerebellum. Project to deep cerebellar nuclei, exclusively, inhibitory (GABA). Inhibited by stellate cells and basket cells
- Granule neurons; principal afferent relay for (mossy fiber) inputs from spinal cord, brainstem and cerebral cortex. Axons project into the molecular layer and purkinje cells

Afferent Pathways

- Trunk, limbs >post. spinocerebellar and cuneocerebellar t. >inferior cerebellar peduncle (ipsilateral)
- Spinal reflexes >ant. spinocerebellat t. >via sup. cerebellar peduncle
- Tectocerebellar fibers (special senses, auditory, visual, vestibular) >sup. cerebellar peduncle
- Pontocerebellar t. >middle peduncle
- Reticulocerebellar fibers >inferior peduncle
Cerebellar Lesions
- Midline lesions > tumors (medulloblastoma)
  - Trunkal ataxia
  - Nystagmus
  - Scanning eye movements
  - Decreased postural muscle tone
- Ant Lobe > ataxia (chronic alcohol abuse)
- Neocerebellum, dentate, superior peduncle
  - Incoordination of fine movements
  - Impaired rapid alternating movements
  - Intention (action) tremor
  - Speech, explosive, scanning

Pain Fibers
- Unmyelinated (type C) fibers or thinly myelinated (Adelta)
- Polymodal (temp. press. Irritants)
- Dorsal root entry zone (DRZ) lat. tract for Lissェur
- Visceral pain fibers, travel w sympathetic fibers > same spinal segment
- Allodynia, injury > inflammatory substances (bradykinin, histamine, sub.P, etc) > sensitize free nerve ending > lower threshold spontaneous activation

Ascending Pain Pathways
- Spinothalamic tract (important)
  - LI, II, V, project to cont. SC > ventroposterior lateral (VPL) and ventroposterior medial (VPM) thalamus
- Spinoreticular tract L
  - VII, VIII, ant.lat. SC > mesencephalic, periaqueductal gray
- Spinomesencephalic tract
- Cervicothalamic tract
Pathophysiology of Seizures

- Seizure focus: increased excitability (ischemia, blood, tumor cells)
- Paroxysmal depolarization (DPS) overcome rectifying currents (K+, Cl-) + inhibitory (GABA-B) synapses
- Spread involves normal cortical circuits (Jacksonian march)
- Generalization >corticothalamic tracts > synchronization
- Drugs Rx. Enhance GABA-A mediated inhibition. Block voltage gated NA-channels (phenytoin, carbamazepine)

Hippocampus Circuitry

- Hippocampus (H) formation comprises, > entorhinal cortex > granule n. > dentate gyrus >(mossy fibers) >CA3 > Schaffer collaterals >CA1 > septal area, ant hypothalamus, mammary body ant. nucleus thalamus, which projects to the cingulate (Papez circuit)

Mechanisms of Memory

- Long-term potentiation (LTP), brief (1 – 2 sec) high frequency (10–20Hz) stimulation of hippocampus afferents (perforant pathway) causes enhanced synaptic transmission that can persist for hours (NMDA-R activation)
- Development of new synaptic connections (presynaptic boutons/dendritic spines)
Questions and Answers