

3 Functional Zones of Neuron - *CORRECT ANSWERS* -1) Input - cell body w/ dendrites (leads to graded response)

2) Relay - axon (info travels as AP)

3) Output - terminal of neuron (info passed to target cell)

2 major types of neuron signals - *CORRECT ANSWERS* -graded potential & action potential

Graded Potential vs. Action Potential - *CORRECT ANSWERS* -Graded Potential:

- decays with distance
- can be inhibitory or excitatory
- amplitude proportional to duration & magnitude of stimulus
- no refractory period

AP

- no decay (self-regenerative)
- depolarizing
- triggered by net graded potential
- has threshold
- all-or-none
- refractory period

Funny Na current - *CORRECT ANSWERS* - Na channels activated when cell is hyperpolarized (instead of depolarized)

SNS on heart rate - *CORRECT ANSWERS* - released noradrenaline which increases Na & Ca²⁺ influx & increases HR

PSNS on heart rate - *CORRECT ANSWERS* - releases Ach, increases K⁺ conductance & decreases Ca²⁺ conduction & decreases HR

GPCR structure/function - *CORRECT ANSWERS* - 7 transmembrane alpha-helices, inactive when GDP bound

when NT binds, GDP is released & GTP binds, alpha subunit dissociates from beta-gamma subunit

cAMP pathway - *CORRECT ANSWERS* - norepinephrine binds B1 receptor, G-alpha stimulates adenylyl cyclase to catalyze synthesis of cAMP. cAMP activates PKA by binding to regulatory subunits. PKA phosphorylates calcium channels to increase calcium release (increases HR, & can also phosphorylate SERCA to decrease relaxation time)

How do G beta-gamma subunits activate K⁺ channel? How do we know this? - *CORRECT ANSWERS* - ACh binds to muscarinic GPCR on cardiac tissue, activated B-gamma subunits interact directly with K⁺ channels to increase efflux which hyperpolarizes SA node & decreases HR. Gi (alpha inhibitory) subunit also inhibits adenylyl cyclase activity to minimize Ca²⁺ influx.

Know this by inside-out patch clamp (place in bath with beta-gamma subunit & observed K⁺ conductance)

inositol phospholipid pathway - *CORRECT ANSWERS* -Gq (alpha) activates phospholipase C (PLC) which cleaves PIP₂ which leads to the production of DAG & IP₃

What does IP₃ do? - *CORRECT ANSWERS* -Triggers release of Ca²⁺ from SR

What does DAG do? - *CORRECT ANSWERS* -activates PKC

Calcium-induced calcium release (CICR) - *CORRECT ANSWERS* -low cytosolic [Ca²⁺] increases opening of IP₃-gated channels (calcium moves into the cell and stimulates release of calcium from the SR)

Negative feedback of calcium release - *CORRECT ANSWERS* -high [Ca²⁺] inhibits IP₃-induced Ca²⁺ release (IP₃ receptor has Ca²⁺ binding sites)

Calcium blips - *CORRECT ANSWERS* -Ca²⁺ release from SR by SINGLE IP₃ receptor calcium channel (occurs in response to low IP₃ levels)

Calcium puffs - *CORRECT ANSWERS* -Ca²⁺ release through CLUSTERS of IP₃ receptor calcium channels

DHPRs & RYR - *CORRECT ANSWERS* -DHPRs are L-type Calcium channels (long lasting voltage-gated) in T-tubule membrane. When depolarized, DHPR is activated which causes opening of its own Calcium channel and causes conformational change to open RYR channel on SR membrane

Calcium sparks - *CORRECT ANSWERS* - Ca^{2+} release through CLUSTERS of RYR channels (faster & smaller than puffs, equal to blips)

Cannabinoids - *CORRECT ANSWERS* - cannabinoids are produced by hydrolysis of phospholipids containing arachidonic acid during increases intracellular $[\text{Ca}^{2+}]$

cannabinoids bind to CB₁ (GPCR) receptors which inhibit NT release in nervous system, and SR Ca^{2+} release from skeletal muscle.

Overall leads to muscle weakness & fatigue

Nitric Oxide (NO) pathway - *CORRECT ANSWERS* - ACh acts on muscarinic AChR in IP₃ pathway (calcium activates calmodulin which leads to NO synthase)

NO diffuses through membrane to activate guanylate cyclase which stimulates cGMP production which activates PKG

Causes muscle relaxation & vasodilation

Regulated by PDEs (phosphodiesterases) which degrade cGMP

Viagra - *CORRECT ANSWERS* - developed for hypertension by targeting PDE₅ for inhibition (would increase cGMP), PDE₅ was believed to be found in all blood vessels but is predominantly in lungs and penile tissue.