PSL300 notes

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1 Introduction

2 membrane potentials

1. cell membrane is not rubber bag = composed of phospholipid bilayer
2. lipid soluble molecules and gases diffuse through readily
3. water soluble molecules cannot cross without help
4. impermeable to organic anions (proteins)
5. permeability depends on **molecular size, lipid solubility, and charge**

if substance can cross through membrane by any means, is permeable. concentration gradient -¿ high concentration - low concentration in MOLAR or mol/L

2.1 Simple Diffusion

small lipid soluble molecules and gases (O2, CO2, ethanol, etc.) either pass directly through phosoplipid bilayer or through pores. Involves brownian motion. movement of substance is down it's concentration gradient ([] gradient). Relative rate of diffusion is roughly proportional to concentration gradient. No energy input required.

2.2 Facilitated diffusion

needs assistance of carrier proteins (kinda like drawbridges, embedded in, but themselves don't cross). moves polar (sugar, amino acids, etc) molecules across cell membrane down the concetration gradient. energy comes from concetration gradient of solute. There are only so many carrier proteins, so it's not a continous process. one side opens, molecule enters, then opening closes, then the intracellular gate oopens.

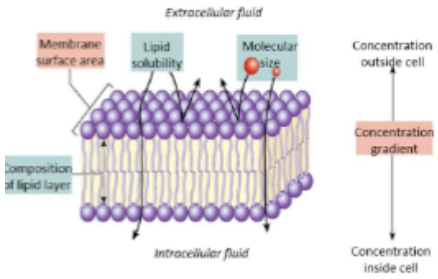

Figure 1: cell membrane

2.3 active transport

against concetration gradient. requires energy from ATP hydrologyg. goes agaisnt [] gradient. substance binds to protein carrier. MOst common example is Ion pumps.

2.4 secondary active transport.

rides the coattails of primary active transportation. sequential binding of substance. SAT is powered by chemical energy in substance diffusing down it's gradient (stored creates a delta, like a capacitor) and this is used to "push" some other substance against its [] gradient. Imagine an extroverted friend dragging an introverted friend into a party. An extrovert

2.5 channels

channels in a membrane 5-5 protein subunits crate central pore, lets specific ions difuse through. pores always open, not selective, channels usually gated, very selective. can be either ligand gated channel, or voltage gated channel.

2.6 Ligand gated channels

cell membrane receptors part of body chemmical signalling system. Binding of receptor with ligand triggers events at membrane, such as activation of enzyme.

2.7 voltage gated channel

some membrane channels are snestive to potential difference acrross membrane (e.g. depolirazation). Usually has negative voltage inside. Voltage sensing mechanism is in 4th transmembrane domain of protein, S4 segment (positively charged wings). Resting condition, -70mV for a neuron on the inside. wings are

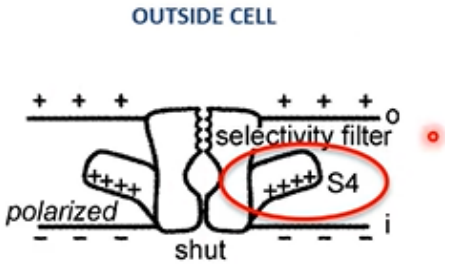

Figure 2: Enter Caption

in down position, pulls down, shut. With depolirazation, wings pull up.

3 endo/exocytosis

endo: inward pinching of membrane to create vesicle (pouch holding membrane) to capture protein from outside to inside. exo: fuses vesicles with cell membrane, trans membrane transport from in to outside exotyiss type 1: kiss and run, used for low rate signalling: vesicles dock at specific points: 'fusion pores', connect and disconnect multiple times. only some contents are emptied in one kiss, process repeates several times. type 2. full exocytosis. dumps everything all at once, compltely fuses vesicle with membrane. needed to deliver proteins and high level signalling. must be counterbalanced with endocytosis to stabilize membrane surface area, (kinda like saggy skin, need to pinch off a bit)

3.1 membrane potential

MP is potential difference across cell. all cells generate MP, if non negative on inside and MP is 0, cell is dead. neuron, -70 mV ish. need 2 conditions.

1. create concentration gradient, enzyme ion pump. ions move down that concentration gradient.

2. semi permeable membrane. allow certain ino species diffuse more.

all cell membrane have Na/K pumps. breaks down (hydrolyzes) ATP so that energy used to move ions against concetration gradient. for each ATP, 3 Na ions pumped out, 2 K ions pumped in, creates potential difference of -10mV. Consumes 1/3 of energy needs of body. in neurons, consumes 2/3rds of energy. PD means more negative on inside than outside.

3.2 resting membrane potential

in neuron, closer to -70mV. Due to existence of semi permeable membrane. K diffuses out of cell, down concetration gradeint. (goes from negative to positive but goes to where there is less potasium ions (pump). cations accumulate on outside of membrane, leaving net negativity inside membrane. at rest, very premeable to potassium until *electrochemical equilibrium* equilibrium, then closes. (when chemical force outwards (gradient) matches electomagnetic force inwards (postive charge) equal and opposite. membrane potential at equilibrium is determined by concetration gradient.

3.3 nernst equation

in an ideal situation, (only potassium ions move, can never really happen) Nernst equation: ln(x/y) positive ion, value is outside of cell (x) negative ion, inside is on top (ln(outside over inside). You get -90mV for equilibrium potential of K (what ptassium wants the membrane to be (if potasium channels were open and nothing else). Typical neuron is -70 to -80 mV. why??? but Na and Cl ions are diffusing a bit. actual membrane potential calculated from expanded nernst equation. inwards movement of sodium. goldman equation:

$$E_m = RT/Fln(outsideconcentration/insideconcetration \tag{1}$$

at rest, potassium ion is biggest contributor. if the membrane were more permeable to sodium, can use nernst equation. we know at rest, sodium channels not very open. what if too open? membrane becomes more positive on inside. diffuses along concetration gradient until membrane becomes positive on inside (when reache equilibrium. sodium is about +60 mV (should be positive). Closer to -70 bc more permeable (35-45x more) to potassium than sodium.

3.4 CL ions

No pump, but due to existence of negatively charged proteins in the molecule that can't get out unless exocitosis, concentrated on outside. creates concentration gradient

3.5 sodium channels

to generate action potential (signal), membrane increases conductance by opening a channel only permeable to Na+ ion (voltage gated). In normal resting MP, channel is shut. Need to make inside of membrane a little more positive. Moves the wings upwards allow passage of sodium from outside to inside. Closed at -70mV. Depolarize to about -55mV, Opens gate. That number is called the threshold potential. After that number, things happen very quickly. Positive feedback loop. There is an inactivation gate (kinda like a plug or a ball and chain) Half a milisecond after depolorzation. Without inactivation gate, should get to +60 (sodium equilibrium potential). Activation gate opens at threshold.

still open when inactivation gate is closed INactivation gate is time and voltage dependent. Closed until MP goes *below* activation potential. Action potential is an impulse, short lived change. Can only produce AP in membrane that has enough voltage gated Na channels. "excitable" membranes. When channels open, becomes closer to voltage equilibrium potential (60) never reaches because it closes 1/2 millisecond after. reaches maybe +30 mV. Only left with pottasium leakageas main current. We know we have more potassium inside than outside.

1. ¡15 mv subthreshold stimulus, opens some sodium channels, but not enouhg to overcome potassium outflow.
2. threshold stiumulus just enough
3. suprathreshold, more than enough, but still same level. all or nothing principle.

information is encoded in changes in frequency of action potential. 10 msec threshold stimulus, can generate 1 action potential. 20 msec can generate 2 APs.

3.6 refractory period

how long are channels inactivate for? absolute RP, none of the channels are reconfigured. no action potential generateed no matter what. frequnecy governmened by this relative refactory period, 2-5ms. some are open. could generate another AP, but smaller since fewer channels. could block membrane from produing AP. permanentaly depolarized. keep at +30 for example, permanently inactivatd. kill people -¿ add KCL, removes gradient. Potasium is no longer leaving the cell. membrane remains depolarized.

3.7 after hyper polarization.

K voltage gated channels opens up after threshold, has extra channels, becomes more negative, overshoots. AFTER the generation of AP. might repolarize to -80.

4 impulse conduction

in an AP. local reversal in potential temporarely goes from - to + on inside. propagates from origin to rest of cell. One AP, creates current, then creates AP in adjacent patch, etc. Most cells are not excitable bc they lack voltage gated Na channels. will conduct passive current, will not generate AP. Most cells won't carrry a signal any distance, wothout axon. axon is like a wire that carries AP to other location. Only neurons with long axons and muscle cells generate APs. tissue is poor conductor, lose about half of potential difference. due to capacitve property, becomes more traingular with rounded top rather than square (less magnitude too)

4.1 cable properties

λ length constant measures howfast potential difference decays to zero as a function of zero lambda increases with increasing diamater. less internal resistance. lambda is also increased with increasing membrane resistance, less curent leaked out, current forced down membrane **NOT INTUITIVE** $\lambda = \sqrt{R_m/(R_i + R_o)}$, but since $R_i >> R_o$, ignore that term Ri is internal resistance (decreases with increasing radius), Rm is membrane resistance. Ro is extracellular fluid resistance. λ is distance you can traveluntil voltage drops around 37% Want to increase as much as possible so that current spreads more. changing axon diameter is kinda hard to do physically. better to increase membrane resistance. (myelination). glial cells are kinda like a glue for the system. specialized glial cells **schwann in the PNS, oligodendrocytes in the CNS** wrap around an axon, myelin sheath 50-100 layers. reduces leackage outside membrane. increases lambda 25x say. only minority of axons are myelinated. schwann cells wrap around one axon, squeezes out cytoplasm. oligodendroctye is like an octopus, wraps around bunch of axons individually. **gap between adjacent glial cells -¿ node of ranvier** only place where AP can be generated, because only where voltage gated channels. You get MS if cell damaged (loss of mylenation). saltatory conduction (jumping) between nodes. in mylenated portion, no AP, just passively passes current. One node can generate enough PD for 5-10 nodes, will all be in different phases though. Only relevant one is last node down the line, becomes depolarizing force for next 10 or so nodes. If some nodes are damaged, still can work, need to destroy fair length of membrane.

5 unmyelinated axons

lots of leakage. both Na and K channels are mized. have some insulation. schwann cell/oligodendroctye engulf axon (5-30 axons) without winding -¿ remak bundle. improves membrane resistance. AP will be conducted until the end of the axon. still generated depolarizing current. AP cannot turn around because of refactory period, eventually dies out. only goes one direction.

5.1 synapses

functional association of neuron or effector organs. in electraical synapse, kinda like twisting two wires together. about 35 angstrom apart. transmitted from one cell to the next. bidirectional. bridged by connexin proteins.
chemical synapse. most common. transmitted (dopamine, etc) through snaptic cleft (gap) is about 200 A wide. very specialized space due to existence of post synaptic membrane. contain specific protein receptors which bind that transmitter molecule. axons end in boutons filled with vesicles (tiny organelles contain neurotranmistters, released into ECF). trigger for exocytosis is calcium ions. bouton membrane contains VG calcium channels, opens when depolarized by AP currents. AP depolarizes membrane, reaches threshold for opening VG CA channels (-50mV). Diffuses into bouton, triggers reactions which result in

vesicle exocytosis (kiss and run type = transient. or full fusion -¿ all transmitters released. Vesicles are lined up with membrane, calcium makes it fuse with membrane, makes it release contents into membrane.
chemical synapses are processing station. vesicle release is probabilistic. 1 AP has 10-90% chance of releasing 1 vesticle.

6 post synaptic receptors

what happens at the post synaptic cell does not depend on transmitter itself, but rather the receptor.

6.1 ionotrpic receptor

simplest -¿ ligand binding opens an ion channel. change in post synamptic membrane potential - ¿ PSP. 20-40ms (as long as transmitter present. Ion channel may be specific for cations, (Na, K, ¿ E(xcitory) PSP (depolarizing) or may be specfific for Cl or K¿ Inhibiotry PSP. Binding and channel opening is in one machinery (quicker). Ligands for ionotrpic receptors **(Acetylcholine, glutamate, GABA, glycine.** can also be metatrobic. GABA is commonly generated IPSP. becomes muscle relaxant. treats anxiety, etc. reduces communication to brain.

6.2 metabotropic receptor.

binding of ligand activates enzyme that is usually G protein coupled. either indcreased production or destruction of second messengers. Either cAMP, cGMP, or lnP3. then activates other enzymes. if you phosphorlate membrane proteins (i.e. ion channels, result in modulation of ion currents). ionotropic is much more immediate, opens directly. metabotropic takes time. might not have effect on MP. slower EPSP and IPSP, has to go through all enzyme activity first. example: beta receptor -¿metabilic receptor NA. binding activates adenyll cyclase via G protein alteration. AC increases production of cAMP (2nd messenger). cAMP then activates kinases which phosophorylate membrane Ca channel. increases Ca influx. possible ligands for metabotropic receptors

1. ACh
2. peptides
3. catecholamines
4. serotonin
5. purines
6. gases

PSPs are generated in inexcitable part of membrane (neuronal dendrites and cell bodies) not enough Na channels, cannot initate AP. instead, hve graded potential, which are lower the further away from stimulus (synapse). action potential **only in trigger zone**. EPSP must spread through membrane, hoping by the time you reach trigger zone, still have enough depolarization. Need lots of EPSPs too depolarize. Can sum graded potential (PSPs). either spatial summation. 10-30 synchronous EPSPs in each dendritic tree, from different synapses. temporal, few active snyapses, each generate a lot of EPSPs. Magnitudes add together. Have to overlap in time though. Temporal, takes time for EPSP to die out (30-40ms), can sum from same synapse. (staircase sorta effect). need high frequency of input. always a mixture of both irl.

6.3 IPSPs

preferntially located on soma, halfway between EPSP generation and trigger zone. can try to shunt/kill depolarizing EPSP current out of cell. need to make membrane more negative. IPSP opens CL channel, EP for CL is very close to -70, so opening channel brings it back when depolarized. inhibitory effect. IPSP are more important -¿ shape information, more precise and specific.

6.4 spike train

powerful post synaptic input, lasts up to 500 ms? you want a lot of APs. to generate spike train, need to hyperpolarize membrane, otherwise never generate spike train. after-hyperpolarization.

7 Receptor potential

change in MP due to receipt of signal from exterior sensory cue energy in environment reacts with proteins, will cause depolarization (similar to EPSP). receptor proteins will change shape, can either directly open ion channel. or activate enzyme with G protein coupling, leading to lots of 2nd messenger, amplifying signal. like metabotropic.
chemical stylmulus. activates G protein, activates adjacent enzyme (could be adynyl cyclase in olfactory for example), produces second messenger (cAMP), activates kinases, directly iteract with ion channels. 2 stages of amplification. G protein can activate a number of different enzyme molecules, each produces lots of 2nd messenger (cAMP).

7.1 transmission of signal

located at axon terminal, first patch of excitable membrane at branch point, receptor potential will have to travel and generate summation. generates receptor potential (graded). spreads into trigger zone, like you only have so many, kinda like nearest checkpoint or smth. other option

sensory cell releases vesicles when depolarized impulses generated in post synaptic neuron. if DP current produces NO AP, travel through membrane, at other end, depolarize membrane, influx of Ca ions and triggers exocitsis vesicles, sensory cell releases vesicles and not produces AP.

7.1.1 taste receptor

small cell, no AP, only RP. depolarizing ucrrent opens Ca voltage GP. 2nd order neurons create AP, bc otherwise brain wont get anything. can have differnt concentration.

7.2 adaptation

say continous pinch, you don't feel continously, original voltage is not sustained, drops over time. slow: always some receptor potential sustained as long as you maintain stimulus. square wave just becomes almost a triangle, slowly decays. trying to figure out overall magnitude.
rapidly adapting, potential elicited by change in stimulus energy, decays to zero when constant. interestd in velocity of stimulus (vibratory). pain does not adapt very well.

7.3 habituation

response to successive stimuli, (get used to) less and less voltage.

7.4 coding of stimulus intenstiy

greater intensity -¿ greater receptor depolirzation (graded potential) -¿ either increases AP freq or more transmitter released greater depolarization -¿ faster membrane will recover from hyperpolarization. if want to code above ceiling, recruit addiional neurons -¿ higher threshold, greater stimulus. (different types of receptors).

7.5 modality (labeled line strategy

pressing your eye hard, but you can also distringuish different properties. can **poulation code** RGB, instead of every colour of the rainbow. receptive field -¿ territory which you can activate a particular sensory neuron. $1-2cm^2$maybe receptive feilds are smaller in more sensitive area.

8 blood brain barrier

brain and spinal cord are protected. KCl injection ¿decreased gradient¿depolarization¿no more AP produced. cannot have neurotransmitter floating around for no reason. BBB is two fold entity. Between blood vessels and intersitial fluid and blood vessels and CSF fills cavities/ventricles in brain. between intersitial fluid

and CSF, basically free diffusion, very similar. MSG cannot cross BBB, but can activate glutamate receptors outside brain and PNS. Pituatary gland connected directly to hypothalmus, BBB purposely broken to allow release of hormones. in "circumventricular organs" third ventricle. BBB is broken is so neurons can sense specific chemical []. BBB is broken in areas that interact with endocrine system.

8.1 brain encasings

skull (duh) duramater very tough membrane, sac containing brain and spinal cord). arachnoid membrain (delicate tissue) pia matter (lies right on top of brain, tetherd to arachnoid by trabeculae) between the two, subarachnoid space (filled with CSF, brain floats to protect from mechanical stress. make up cranial or nervous emeninges. membranes surrounsing csf can bend. endothelial lining of general blood vessels contain large gaps through which molecules pass. in brain, cells are tightly bound -¿ no gaps.

8.2 ventricles

filled with CSF large curving Lateral Ventricle (LV) (first (right) and second (left) ventricles) inside each hemisphere, paired across midline. LV empties into 3rd ventricle (middle, deep under ccerebral hemisphere). 3rd ventricle communicates via "aqueduct of sylvius" to 4th ventricle. from 4th ventricle, have canal, connect to spinal cord. all ventricles have CSF, all connected.
CSF moves around through central canal, to outer parts of brain, then exits at top of brain (large venous sinus). 1/2 of CSF drains through arachnoid villi. -¿ out pouching of arachnoid tissue, through duramater into venous sinu, then drains into venous.

8.3 choroid plexus

CSF is produced from plasma by choroid plxus (lines all of the ventricles) CSF itself is bathing medium of brain, highly regulated ionic content, few macromolecules. eventually drains back into general blood circulation. Occurs without a pump, allows a cleansing mechanism. Some CSF is produced in brain capilaries. made up of epithlial cells connected by tight junctions. produces 550 ml a day of CSF. CSF fills ventricles and subarachnoid space. CSF has same osmolarity and [Na] as blood. A lot less K, Ca, Mg, concentration. avg person has about 215 ML of csf. cranial csf is 140 ml (25 ml in ventricles, 115 ml in subarachnoid space, 75 ml in spinal. most csf is a cushion. replaced about 3 times a day. spinal tap - collects CSF.

8.4 astrocytes

another type of glial cell. look like stars. they are end feet of flial cells. bridge between neurons and blood vessels. atrocytes are efficient at glycolysis, produces lactate as end product. Astroctyes lactch onto blood vessels. Can also help removing neurotransmitters, provide energy substrate. can regulate local blood flow. good spot to signal BV when to dialate/constrict. When lots of activity is happening, send signal upstream, to get more nutrients, etc. in response to glutamate being released (neurtransmitter), can b e dtected by MgluR receptor (in astroctye) Binds to glutamate, triggers calcuum release within atroctye. Wave of calcium travels to trhough astroctye to feet (touching blood vessel). triggers release of protograldin. (PGE2), causes vasodilation, increases blood flow.

9 endocrine

9.1 homeostasis

homeostasis is not equilibrium. steps for feedback control:

1. stimulus (something happens)
2. sensor/receptor (the body detects it somehow
3. afferent pathway (signal passes from sensor to control box via wire)
4. integrating center (decides what to do
5. efferent pathway (signal of what you need to do)
6. target/effector thing does what needs to be done
7. response (desired outcome)

can oscillate around set point, negative feedback only turns on outside of normal range.

9.2 negative feedback loop

stimulus, response, stimulus to get back to homeostasis, stabilizing
example, regulation of cortisol secretion. cortisol stimulated to be released. hypothamolous release CRH, stimulate antrior pituiatry, stimulate AACTH, stimulate adrenal cortex, release cortisol into target tissue. cortisol supresses release of both CRH and ACTH hormone.

9.3 positive feedback loop

stimulus, response, stimulus to get away from homeostasis (reinforcing), turned off by outside factor. for example childbirth. stretch, releases oxytocin, stretches, releases more and more until baby is released, NOT homeostatic.

9.4 intercellular communication

9.4.1 local control

gap junctions -¿ small ions and molecules through holes connecting cells (cardiac for example contact-dependent. changes in how cells touch. membrane protein to membrane protein autocrine. as molecules move through intersitial fluid - same cell taht produced signal. paracrine secreted by one cell diffused into adjacent cells.

9.5 neurohormones

neurotransmitters are chemicals secreted by neurons that diffuse across small gap to cell neurohormones are chemicals released by neurons

9.6 endocrine system

encodrine glands or cells release hormone through blood stream, only responds with cells of right receptors.

9.7 simple and complex reflexes

simple mediated by either nervous or endocrine complex mediated by both local control, just stimulus and response.

1. neural reflex terminates on sinlgle target cell or very local area
2. electrical through nerone, then chemical cell to cell
3. very fast and short, if need long, mediated by neuromodulators
4. identical in strength

1. endocrine, most cells exposed to hormone
2. chemical cells in blood
3. distribution of signal and onset of action much slower than in neural, last longer
4. inensity correlated with amount of hormone secreted

10 hormones

one hormone can act on multiple tissues, alter activity of target cells. should have negative feedback to maintain homeostasis. initial identification by AA berhthold -¿ remove gland, replace gland, find extract, etc. can also purify extract.

10.1 3 main types

1. hydrophilic hormones: water soluble, can disolve in plasma. not lipid soluble, cannot cross plasma membranes (lipid bilayer). peptides, proteins, catecholamines. **secreted by exoctyosis)** made in advance, stored in vesticles

2. hydrophobic (lipidphilic, do not disolve in plasma. steriod, thyroid, etc. almost all 99% are bound to a carrier protein to travel through blood stream (some free). secreted by diffusion only made on demand bc can't really be stored.

1. class 1 peptide/protein (3 or more amino acids) chains of amino acids. for ex, insulin

2. steroids (ALL derived from choleestrol (incl estrogen). only one thats hydrophobic

3. amines derived from single amines

10.2 peptide/protein hormones

most hormones, made in advance. synthesized like secreted proteins. short half life in plasma. first protein created to encode hormone has signal sequences. created in ER via ribosome. preprohormone has other stuff incl hormone, then cleaved off into prohormone then pinched off, proccesed in golgi complex, then cleaved off. eventually released by exoctyosis. original peptide can go through a lot of cleavages.
single preprohormone can contain multiple copies of same hormone. or diff types of hormanes. can have other peptide fragments too. for example, insulin is made alongside c peptide, so you can measure insulin levels by measuring c peptide levels.

10.3 steroid hormones

only synthesized from cholestrol. not stroed in vesticles, made on demand. bound to carriers in blood. long half life, diffuse into target cells, or endocytosis of carier proteins. can either find into cell or membrane

10.4 amine hormones

synthesized from trptophan (melatonin) can behave like both peptide or steroid secreted at night. govern biological clock. alo anti oxidant
or tyrosine catecholamines like peptides, numerous enzymes incolved in creating catecholamine, dopamine into adrenline. synthesized in adrenal medulla. (in cytosol). stored in vesicles. released via exocytosis. water soluble. bind to membrane receptors. snythesized from adrenal medula (middle). thyroid like steroids.

10.5 control of hormone release

stimulus can be metabolite, hormone, neurotransmitter/hormone. can be glucose for insuln. signal endocrine cell.
actual tgger. change in membrane potential. free cytosolic Ca, change in enzymatic activity. increase in transport of homrone substrates into cell. alter transcriptions of genes coding. promote survival/growh of endocryne cell. glucose stimulation. glucose opens GLUT2 channel. increases ATP/ADP ratio, binds ATP sensitive, blocks potassium channel. changes MP, cell depolarizes, opens up VG Ca channel, and Ca signals exocytosis. hormones released from hypothalamus pituitary axis regulate release of several hormones. hypothalamous sends hypothalamic hormone to anteriur pituitary, sends own hormone into peripherial endocrine gland, secretes own hormone into other targets. have negative feedback loop upwards typicaly. posterior pituitary cant create hormones, so not endocrine. anterior can.

10.6 hormone interaction

synergistic effects -¿ working together for greater effect (FSH and testoterone make good sperm) sum is greater than parts permissive. one hormone enhances target organs response to a second later hormone antagonistic -¿ one hormone opposes another. insulin vs glucagon.

11 receptors and signalling

hormones bind to receptor. changes conformation and activity of receptor. leads to synthesis or modification of proteins.

1. large protein
2. families
3. can be multiple receptors for one ligand variable number in target cell, 500-100 000
4. activated and inhibited
5. in cell membrane, cytoplasm, and nucleus
6. high affinity, saturable
7. specific and reversible

cell receptors are saturable (asymptotic), only so many receptors to bind to. intracellular receptors: bind lipid soluble hormones. cytosolic and nuclear directly alter gene transcription (genomic effect)

11.1 hormone receptors

petirde, cannot penetrate target cell steroid binds usually to nucleus, can take hours or days to show effect due to lag for protein syntehsis intracellular. hormone receptor complex binds to specific DNA sequence. receptors recruit corepressors to inhibit transcription. only genes with response elements will be activated/represed. membrane receptors: ion channels, change electrical properties of cell g protein coupled receptors (GPCR): membrane spanning proteins. have cytoplasmic tail linked to G protein. GPC adenyl cyclase cAMP system is signal transuction system for many hormones. use some lipid second pessengers, DAG, IP3, etc. when g protein activate, open ion channels, alters enzymes

11.2 Gq

stimulatory q subunit activates phospholipase C -¿ amplifier enzyme. activates DAG, stays in membrane, then activates PKC, which then phorphorylates downstream proteins. then activates IP3

11.3 Gi

inhibitory. inhibition of adenyl cyclase

11.4 flight or fight

epinephrine binds to different isofrms of adrenergic receptor for alpha receptor, constricts, beta 2, gets wider (dialates) Gas/i -¿ adenylyl cyclase-¿ cAMP-¿ PKA -¿ cell response GaQ -¿ PLC-¿ activates DAF (in membrane), PKC, IP3, Ca-¿ cell response

11.5 modulated

turn off by degradation, receptor down/upregulated desenitzation, breakdown of second messengers, modify pathway, or feedback.

12 calcium

critical for intracellular signalling, hormone secretion, blood clotting, neural excitability, build/maintain bone. most in extracellular matrix (bone) 0.1% ECF, 0.9 percent cells. can go in and out of ECF first (into intestine and also in/out of kidney). bone is mostly crytsals: hydroxyapatite.

1. osteoblasts (form cells)
2. osteoclasts break bone (much bigger than osteoblasts). attach to bone matrix like suction cup, ruffled. they secrete HCl, eats away at bone. also secrete proteases (enzyme) that desolves bone. ionized Calcium then enters blood stream. **carbon dioxide + water, catalyzed by CA**

(carbonic anhydrase) creates H ion and bicarbonate. free proton combines with chloride from bloodstream to create HCl.

3. osteocytes (osteoplasts surrounded by bone matrix, just maintain bone.

Bone dynamic (over 100 days). 3 weeks of osteoclasts break, then 3 months of osteoblasts replacing. osteoblasts promote osteoclast formation. osteoblasts has RANKL (rank ligand), and osteoclast precursor has receptor activator of nuclear factor kappa B (RANK). connects to rankL. but osteoprotegerin (OPG) is kinda like a condom, prevents RANKL from bonding with rank. after differentiating and fusion, get 3 nuclei osteoclast. denosumab mimics opg.

12.1 hormones controlling ionic calcium levels in plasma

1. parathyroid hormon (PTH) released by parathyroid glands (chief cells). increases plasma Ca concentraion. stimulated by low plasma Ca. very essential. As soon as calcum drops, jumps right away. uses Gq protein coupled receptor. inhibits Ca. increase vitamin D3 receptor. (MULTIPLE pathways). hormone released. on bone acts on osteoblasts. increases RANKL, decreases OPG. increases Ca into bloodstream. acts on kidneys, turns back around. PTH increases cAMP to increase RANKL. more osteoclasts are formed. if you want quick increase in plasma, increases phosphate release from bone, decreases phosphate reabsorption in kidney. any phosphate gets pissed away. kinda like emergency leak. prioritizes Ca.

2. calcitriol **active form! is a hormone** Vitamin D3. organs include skin, liver, kidney. from skin: 7 - dehydrocholestrol. goes into skin as cholecalciferol (vitaminD3). liver converts into 25 hydroxycholecalferol. PTH converts it into calcitriol. helps absorb Ca absorption from small intesite. also better from renal reabsportion. helps with supplements. binds to VDR (vitamin D nuclear receptor). diffuses through membrane. creates mRNA. mRNA becomes channels, transporters, help absorption. always have some. want to make bone, so increase abrosbtion by intestine and reabsorption in kidney. increased absorb too much vitamin D

3. calcitonin. secreted from C cells of thyroid gland. also have own Ca sensing receptors. peptide hormone. triggered by high plasma [Ca]. protect skeleton from Ca loss udring pregnancy and lactation. inhibits bone resporption. stimulates osteoblasts.inhibits calcium resorbtion of kidnes.

can go from intestine into plasma, and from plasma to/from kidneys and bones.

12.2 effect of calcium homeostasis misses

hypercalcemia (too much)

1. GROANS (constipation)

2. MOANS (fatigure, lethargy)
3. BONES bone pain
4. stones kidney
5. psychiatric overtones (depression

hypocalcemia (too little)

1. Convulsions
2. Arrhytmias
3. Tetany
4. Spasms, seizures, stridor

13 fluid balance

55 percent of person is water. 2/3rds is in cell (ICF). 1/3rd is ECF. 75 percent of that is intersitial. 25 percent is in plasma.
intake 2.2 L a day, produces like 0.3 L a day. piss away 1.5L a day. sweat, breath 0.9 L a day. not enough water -¿ less ecf, less blood pressure.

13.1 how is pee produced

blood goes into kidneys, filtered at nephrons. becomes urine. leaves throught the ureter. in nephron: 1500 litres a day blood comes in, filtered through some gets reabsorbed. some gets secreted. 180 L of filtrate formed. 1.8L of urina day (1 percent ish). Nephron is responsible for vitamin D (via PTH). also pH, electrolytes, etc.

13.2 urin hormones

vasopressin (ADH against pissing) increases synthesized in brain (hypothalamus) secreted from posterior pituitary. increases water reabsorption in kidneys, conserve body water. and also increases blood bolume and pressure. regulates premeability of kidney cells. **stimullus:** osmolarity. with high plasma osmolarity "saltiness", wants to dilute, so conserves water inside. or also triggered by low blood pressure., not as important as osmolarity though -¿ very potent huge increase outside of nromal range, gives you feelings of thirst. vasopressin in blood binds to receptor releases cAMP. signal cascade into aquaporin 2 water pores sitting in cells. then bind to inside of nephron. . into collecting duct lumen

13.3 aldosterone

steroid synthesized in adrenal cortex, regulates sodium. controlled by negative feedback stimulates by high [K] plasma, angiotensin 2. or decreased blood pressure inhibited by high osmolarity in ECF. 15 minute halflife.
diffuses into plasma membrane. only acts with cell with cytoplasmic receptor. initiates transcription in nucleus. transition of new channels. prevents degredation of apical Na channel increases expression of Na and K channels and NaK ATPase. kinda like a wall, gets more Na into blood
juxtamogelualr cells see BP. renin mixes with smth from liver. angiotensin then goes to lungs, cleaved into angiotensin 2 (active one). 450 amino acids to 8. stimulates hypothamolous, makes you thirsty. constricts blood vessels, elevates blood vessels. aldosterone secretes. retains salt and water.

13.4 natruetic peptides

ANP, BNP, CNP. secreted by secondary endocrine glands. ANP secreted by atria. increases K reabsorption. decreases Na and H20 reabsorption, low blood pressure (if too much pressure on heart (stretch)).

14 adrenal gland

2, one on top of each kidney from adrenal medula main hormone is epinephrine, controlled by peripheral nervous system (fight or flight response). epi pen.

14.1 adrenal cortex

outside, capsule. thin, connective tissue. see 3 zones. each zone creates different hormones. cholestrol can go to DHEA¡ androstenedione, testosterone, dihydrotestosterone

14.2 androgens

sex hormones, important in children, puberty, male prenatal development. in women, androgens maintain hair, etc. cortisol is important for stress, especially prolonged stress (corticotropin releasing hormones). released into anterior piteutiary, releases ACTH. can supress immune system, supresses immune system, breaks down proteins. can supress bone formation. also has two feedback loops, one to the hypothalmus.

14.3 addisons disease

adrenal insufficiency. hyposecreteion of adrenal steroid hormones. caused by destruction of adrenal cortex, hypotension, hypoglycemia. too much cortisonl -¿ too much sugar, salt, lyolysis skinnier limbs but face fat. if tumour, think negative feedback on healthy things.

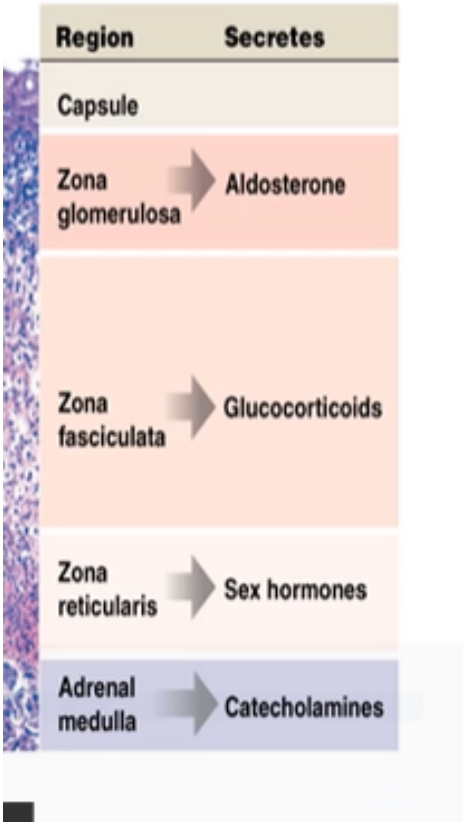

Figure 3: Enter Caption

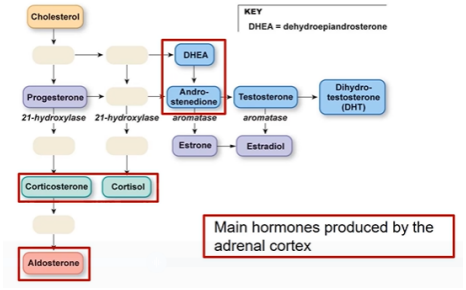

Figure 4: Enter Caption