

PHYSIOLOGY 2

Effect of K Ions on the RMP

INCREASED (Hyperkalemia):-hyperpolarized because of more incurrent K^+ , SO the RMP will be at new level further from the Threshold, so the probability to have an Action potential is less. This will affect the heart and muscles in general, weakness, ascending paralysis, and if untreated cardiac arrhythmias.

DECREASED (hypokalemia):-Weakness, fatigue, motor paralysis, Myopathies (Myotonia:delay relaxation or continuous spasm after voluntary contraction).

Effect of Na Ions on the RMP

Hypernatremia:-generally change of sodium doesn't affect RMP, The permeability of it is low, so Na will accumulate (more distribution) extracellularly, this sodium if doesn't influx to the cell will cause shrinking to the cell-**this mostly affect the brain**-shrinking to the brain, nausea, and vomiting, altered mental status, confusion, neuromuscular excitability and hyperreflexia, irritability, seizures, and even coma or death.

*how to correct this?? we give the patient water or Hypotonic solution, if the patient has not showed neurological effects yet we give him isotonic or almost non-hypotonic solution, but if there are neurological effects this mean that there is shrinking in the brain so if we give him rapid infusion of hypotonic solution or water this will cause brain edema or hemorrhage, so usually the infusion is half the isotonic 0.45% NaCl slowly. Less common than Hyponatremia.

Hyponatremia:-more common than hypernatremia, swelling and edema in the CNS will cause lethargy, confusion, weakness and muscle cramps, nausea and vomiting, and would finally lead to a coma. So whether the cells enlarged (edema) or shrunked will cause Neurological effects.

If you have a patient with Hyponatremia and you give him rapid infusion > this will cause shrinking and Osmotic demyelination syndrome (central pontine myelinolysis), it can affect any part of the nervous system, may be so severe may cause death or may be subtle paralysis in one limb > quadriplegia > coma > seizure. Correction: - 1mMol/L/Hour.

Effect of Cl Ions on the RMP

The effect of Cl ions on neurological is not specified, especially in adults. However, some new studies show effects on infants.

Effect of Ca Ions on the RMP

Ca^{++} competes with Na so if there is more Ca^{+2} this means more blocked channels so less Na influx and less depolarization, but when Ca^{++} is low so the competition is less and Na influx increased and so the depolarization.

Hypercalacemia:-Headache, and lethargy. Anxiety, depression, and cognitive dysfunction insomnia, coma.

Hypocalcaemia: Irritability, hyperreflexia, Seizures, psychosis and hallucination (depression in very rare cases) and the hallmark is neuromuscular irritability and tetany in the periphery, like:-

Trousseau's sign (75-85 % of cases): continuous spasm (contractions) in the hand or fingers. The doctor played this video <https://www.youtube.com/watch?v=Ry5Rh3wO8Sw> . More common than *Chvostek's* which is only found in about 25-30% of the cases.

Chvostek's sign: over excitation when you tap on the corner of the mouth starting with spasm in the lip to spasm in the whole face. 25-30% of cases.

It is possible to find a hypocalcaemia patient doesn't have neither of the signs above.

The neurological effects happen in the sever cases.

THE ACTION POTENTIAL -AP-

RMP → Threshold → open Na⁺ gated channel → Na influx → depolarization → open K⁺ channels → K⁺ efflux → falling phase (Hyperpolarization) → RMP

The goal of AP is to transfer information.

AP is (all or none) SO if started must complete.

The shape of AP is the same to the cell , but differs from cell to another :-

1. AP depends on Threshold which depends on the voltage gated Na⁺ channels so if the channels open on -55 so the threshold is -55, and this channels differ from cell to cell. But the cell itself will always have the same Threshold.
2. Amplitude peak depends mainly on The opening of K⁺ channels, put it could be on the Inactivation of the Na⁺ channels mainly there is no cell the rising phase of it reach the resting of the Na, if the resting of the sodium is +60 the rising phase must be less than 60+.
3. The amount or length of hyperpolarization which determines the latent period and the relative refractory period.

In slide 29 shape D :- it is not the cardiac AP but the inferior olive nucleus.

Why it is important to know the shape of the AP? It will affect the transfer of the Information, how ??

A) The refractory period, so if the AP potential is narrow so the maximum frequency of the neuron is differ from a wider AP.

B) The amplitude OR duration when AP reach the synapse will change to chemical information by induce ca⁺⁺ influx so if the depolarization of the AP takes 2 ml second so the

calcium will keep influx within 2 ml sec , the number of the receptors neurotransmitter will be higher if I have small and narrow AP.

*so each cell during the development form its AP to suite its function, except if the we have one of the two following problems:-

1. Ion in manner that affect the RMP or some of the properties of the AP, like that mentioned before.

2.the most common, more clinical Channelopathies.

Channelopathies: genetic modification or mutation in one of the genes that goes for Ion channels which cause change in its characteristic , like a change in the opening time , or opening period , or change in the function like loss of the function or gain another, as a result the electrical activity and the AP, usually will accompanied by clinical symptoms.

But if there is a mutation in gene, this doesn't mean that the effect will appear in all of cells of the body because it depends in the characteristic... so if there is a mutation in the Na gated channels so it is not important that all the Na channels will affected.

Divisions of the Channelopathies according to the site:-

1. Central nervous system 2.neuromasclar and motor peripheral 3.sensory.

If the effect is in the motor nerves the symptoms will be in the muscles hyper exciting or hypo, weakness or paralysis. And if the channel in the muscle itself so a disease *MYASTHENIA GRAVIS*.

IF the symptoms in the sensory it will cause *ATAXIA*: is a general term mean abnormal and irregular movement in the muscles.

If the problem is in the central Nervous system, epilepsy or seizure or form of migraine.

The tables in the slides not for memorize, just the Pages 84 & 85 in Neuroscience 3rd edition Dale Purves is required.

There are some drugs and toxins can affect the channels like Ion Channel Neurotoxins.

Some bacterial toxins can block the synapses ,other can cause spasm and degradation to the Ach.

Some toxins cause complete block to the Na⁺ channels can block the AP so a paralysis can appear , if this paralysis happens in the diaphragm this can cause a serious problem. Other toxins cause modification to the channels.

Na can affected by tetratoxins which is very common, and some blocks K⁺ but less common.

A clinical use for tetratoxins is the Lidocine (anesthesia) which blocks the Na channels so no AP.

SYNAPSES:A specialized site of contact, and transmission of information between a neuron and an effector cell.

1. Electrical synapses : more common in the cardiac and almost not exist in the CNS.

2. Chemical synapses: AP → Change terminal → release Ca^{++} → induce NT release → release NT by activated channels → activate the receptor and affect the post synaptic.

The activity of the synapses is mostly controlled by the type of the receptor, not by NT or Ca^{++} channels .

Any activity of the neuron increase the probability of AP called Excitatory, and any decrease is Inhibitory neuron

Types of receptors:-

1. Ion channels, NT bind to receptor and open the ion channels.
2. 2nd messenger (G protein):-
 - A) G receptor → G Protein → activates c AMP → open ion channels... if Na → depolarization , if Cl or K → Hyperpolarization
 - B) Alter some enzyme that excite or inhibit the cell or activate internal cascades and activate gene transcription, the most common cascade is the c AMP (RECEPTOR increase or decrease it) or less common the c GMPG-protein-- activates PLC-- generates DAG and IP3 –induce Ca^{++} release.

The calcium either by IP3 or opening of Ca^{++} gated channels Or by activations the genes will alter the calcium level ... Ca^{++} is the 2nd messenger and very important for the neuron.

So: c AMP or Ip3 or the channels will alter the Ca^{++} levels and it could work as 2nd messenger.

The tyrosine kinase coupled receptor is important in nervous system..usually it is activity work through two induced growth and survival .

The details are not important, the important is the end results , all the 2nd messengers including the Ca^{++} can affect the transcription and the survival or the characteristic of the cell,, the best characteristics differ between the 2nd messenger and the voltage gated channels are signal amplification and response; the response through ion channels will directly make excitation and cause AP in the post synaptic neuron but the response of 2nd is slower.

