CENTRAL NERVOUS SYSTEM

- ○ Handout
- ● Sheet
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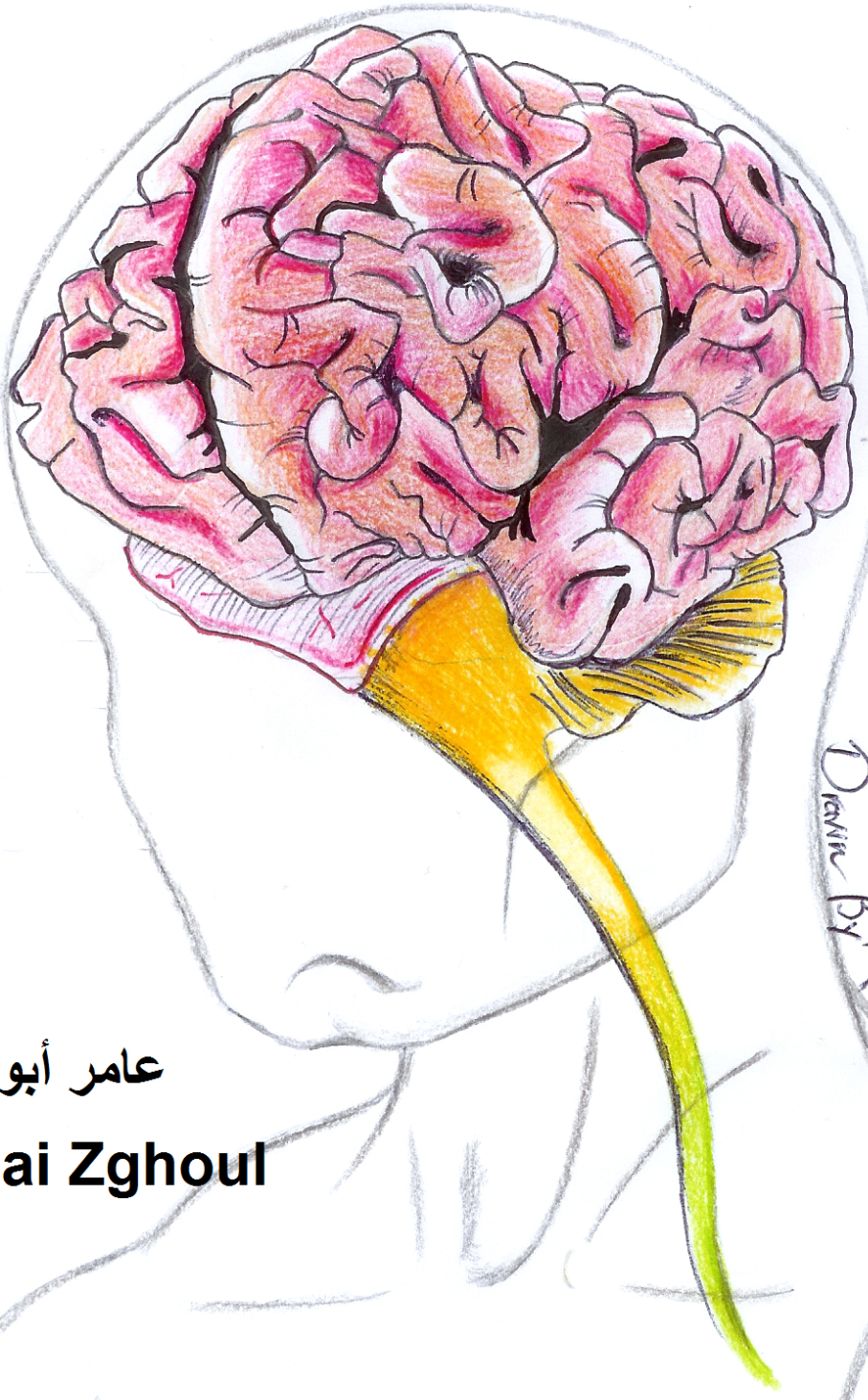
- ○ Anatomy
- ● Physiology
- ○ Pathology
- ○ Biochemistry
- ○ Microbiology
- ○ Pharmacology
- ○ PBL



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GENERAL PHYSIOLOGY

السلام عليكم ويعطيكم العافية, بدايةً فصل بيسك أخير جميل وممتع ان شاء المولى للجميع, هاد الفصل مو سهل وبدو فهم كثير وحفظ كثير وتعب كثير وبعده راحة لمدة 52 يوم أتوقع كافية لترد الحياة لطالب الطب الجميل.

عكل حال, أسامة بالشيت الأولى عرفكم وحكالكم كيف تقدرو "تفهمو" المادة, وانا هسا راح احكيلك كيف ممكن تدرس المادة لغرض الجامعة "العلامة" وبالاخير القرار الك :)

وهذا ما جرى بيني وبين الدكتور

"انا : مرحبا دكتور, يعطيك العافية

الدكتور : اهلا اهلا, الله يعافيك

انا : دكتور عندي سؤال, دكتور اعتبر حالك طالب طب سنة ثالثة فصل ثاني, وبدرسك الدكتور الفاضل لؤي الزغول مادة الفسيولوجي للـ سِ ن سْ , فشو راح تعتمدلو كمصدر للدراسة ؟؟

الدكتور : انا السنة الماضية حكيت للطلاب كلمة والتزمت فيها, حكيتلهم ادرسو فقط سلايداتي مع كلامي (يعني شيتاتي) وهاد راح يكون كافي للإجابة على كافة الأسئلة, طبعاً هاد السنة الماضية, اما السنة هاي لانو اضفت بعض الشغلات وعدلت بعضها فما راح اغطي كل المادة بالمحاضرة فلازم الطالب يرجع للكتاب مع سلايداتي.

انا : جميل دكتور, بس في ثلاث شغلات, الأولى انو الطلاب اللي اكبر منا حكولنا انو ما قدرو يحلو اسألتك بالرغم من انهم دارسين الشيتات والسلايدات ؟ والثانية شو رأيك انت بالكتاب, مو طويل دكتور؟ والثالثة اذا كان الكتاب هو مصدر الأسئلة فما في داعي الواحد يهتم كثير بالمحاضرة والشرح فيها (الشيتات يعني),صح ؟

الدكتور : نعم صحيح انو في طلاب ما عرفو يحلو الأسئلة بس في طلاب تانيين جابو علامة كاملة بأسئلتي, وغير هيك انا بعد الامتحان حليتلهم الأسئلة وفرجيتهم انها كلها من المحاضرة, اما السنة فغير. بالنسبة للكتاب فهو ككل طويل بس فعلياً احنا ما راح نوخدو كلو, بالعكس احنا راح انبلش من تشابتر 17 لانو قبل هيك اناتومي (طبعا انا الكتاب اللي معتمدو هو اديشن 4), اما بالنسبة للمحاضرة فهي اشي ضروري لانو في شغلات ما بشرحها وفي شغلات بحكي مو مطلوبة او مو حفظ وفي شغلات تانية بركز عليها كثير وبحكي انها جاي بالامتحان وفي شغلات من خارج الكتاب أصلا, فلازم الطالب يعرف هاي الشغلات وكمان في شغلات بشرحها بطريقة غير عن الكتاب واسهل منو.

انا : يعني دكتور كمحصلة شو راح تُدرس ؟؟

الدكتور : راح ادرس كتاب مع سلايدات مع شيتات :) :) :) :) :)"

رابط الكتاب: https://goo.gl/XmBl0u

والكرة الآن بملعبكم .....

ملحوظة مهمة 1: اول 3 محاضرات مو موجودين بمكان معين بالكتاب واصلا مو من الكتاب فمصدر دراستهم الوحيد للغرض الجامعي هو السلايدات مع الشيتات.

ملحوظة مهمة 2:جميع الكلام ومعظم الصور اللي موجودين بالسلايدات لهاي المحاضرة انا اضفتهم على الشيت هون فمافي داعي ترجع للسلايدات الا لبعض الصور اذا بدك.

ملحوظة مهمة 3: الدكتور 75% من شرحولهاي المحاضرة كان باللغة العربية, يعني هاي الشيت عبارة عن ترجمة + تفريغ ريكورد + شوية شرح إضافي للفهم, عدا اني اعدت ترتيب كثير كثير شغلات عشان يتناسق الشرح.

Let's start our nice lecture:

Definitions:

1-**Membrane potential** (MP) = the difference in the net charges around the cell membrane; hence, between inside the cell (the cytoplasm) and outside it.
Wiki def. of MP = is the difference in electric potential between the interior and the exterior of a biological cell.

2-**Resting membrane potential** (RMP) = the difference in the net charges around the cell membrane during rest. (At rest means when there is NO excitation). And it measures between -60 to -70 mVs.

3-**Threshold** = the MP at which the cell fires (continues its depolarization) spontaneously without further need of a signal.

4-**Action Potential** (AP) = A momentary change in electrical potential on the surface of a cell, especially of a nerve or muscle cell, that occurs when it is stimulated resulting in the transmission of an electrical impulse.

Goldman Equation:

Goldman Equation

$$V_m = \frac{RT}{F} \log \frac{P_K[K^+]_o + P_{Na}[Na^+]_o + P_{cl}[Cl^-]_o}{P_K[K^+]_i + P_{Na}[Na^+]_i + P_{cl}[Cl^-]_i}$$

We use this equation in order to **measure the resting membrane potential for any cell**. We do **NOT** have to know, memorize, or work on it, but we have to know what do the differences in the RMP mean. **SO what is the difference between RMP= -70 and RMP= -80 and what effects does this value have on the cell?**

Answer: As each cell determines its RMP, it also determines its specific threshold. This means that if the RMP is changed, the cell may become farther or closer to the threshold and this affects the probability of the cell getting excited. These changes also affect the **velocity** and the **frequency** of the action potential.

So the most important ions that affect the MP are: (those in the equation)
1- Na+ 2- K+ 3- Cl-
If there is a **change** in one or more of the **previous ions**, the **RMP is going to change** and the cell membrane becomes either hyperpolarized or hypopolarized. Don't forget that **the threshold and the excitability of the cell may also change**. So due to these changes in the RMP, threshold and excitability of the cell the entire functions of the CNS and the muscles would get altered and modified.

RMP is different from one cell type to another. There are **factors that determine it**:

1-**The cell proteins**> it gives about -10 to -15 negative charges (consider it -10)

2-**Sodium/potassium pump**> which pump 3 Na+ to the outside and 2 K+ to the inside > by this the cell loses some +ve charges > becomes more -ve >> it gives about -50 negative charges

3-**The potassium leakage** (from inside to outside) and this depends on the difference of K+ conc. between inside and outside (specifically the conc. of K+ outside because it's affected easily by factors like increased potassium intake)

Other factors also affect and control the RMP like temperature and cell type.

Now, let's go through the ions changes and their effects on the cell one by one:

<u>The effect of K+ changes:</u>

1- **Hyperkalemia**

- **Definition:** high conc. of potassium outside the cells

- **The effect:** the RMP of the cells became less negative, so the cell becomes easier to excite and this affects the CNS. (since the hyperkalemia is generalized)

- **Mechanism:** more K+ outside > less leakage of K+ from inside to outside (because there is some kind of resistance due to high +ve charge outside)> more K+ stays inside the cell > the cell becomes more +ve (less negative) > the RMP becomes closer to the threshold > more excitable cell ☺

- **Signs and symptoms**:

  a- General weakness in the muscles

  b- Ascending paralysis: it means that the weakness and the paralysis starts at the lower limb (from the lower feet) and then ascend up to the body

  c- Cardiac arrhythmias: the cells are easier to excite > more excited cardiac cells

2- Hypokalemia

- **Definition**: low conc. of potassium outside the cells

- **The effect**: the RMP of the cells became more negative, so the cell becomes harder to excite and this affects the CNS.

- **Mechanism**: the dr. didn't mention it but it is opposite to the previous one. So less K+ outside > more leakage of K+ from inside the cell to outside (low +ve charge outside)> less K+ stays inside the cell > the cell became less +ve (more negative) > the RMP gets farther from the threshold > less excitable cell ☺

- **Signs and symptoms:**
  a- General weakness in the muscles.

  b- General fatigue: remember that the RMP becomes more negative and the cells are harder to excite.

  c- Motor paralysis.

  d- Myopathies (muscles pain): like Myotonia. As we know K+ is responsible for the relaxation and due to the low conc. of K+ there would be delay in the relaxation.

The effect of Na+ changes:

We have to remember that the permeability of the cells to Na+ is minimal and so the effect on the RMP is little. In addition to that the effect on the action potential here is shown mostly by the velocity and width of the action potential. So the effect of Na+ changes is called combined because it affects both the RMP and the action potential itself.

1-Hypernatremia

- **Definition**: high conc. Of Na+ outside the cells

- **Mechanism**: high Na+ outside > high osmolarity > the extracellular fluids and the blood became hypertonic > by this the water moves to outside of the cells > shrinking of the cells > and this affects the RMP and the excitability of the cells.

- **Signs and symptoms:**
  a- Nausea and vomiting (N&V)

  b- Altered mental status

  c- Confusion

  d- Neuromuscular excitability and hyper-reflexia (because Na+ conc. outside is high, when the sodium channels open large number of Na+ ions would get inside the cell leading to faster action potential > excitability and hyper-reflexia

  e- Irritability

  f- In serious conditions > coma (due to shrinkage of CNS cells). In chronic conditions there would be shrinkage of the CNS as a whole, and the brain and the brain stem descend down out of the foramen magnum to fill the space that has been left behind by the shrunken cells. This causes more pressure on some foramens leading to coma, seizures and death.

  Clinical note: when doctors correct hypernatremia they have to be very carful to NOT correct it rapidly, simply because rapid correction of hypernatremia may cause rapid filling of the cells leading to either cells bursting or swelling large enough to apply even more pressure on the surrounding foramens, in addition to the pressure already applied by the descended brain and stem. This also leads to many other problems like: brain edema, brain hemorrhage, seizures, permanent brain damage or even death. So we do correction BUT SLOWLY. The hypernatremia is corrected by **HALF NORMAL SALINE (0.45)**.

2- Hyponatremia

- **Definition**: low conc. of Na+ outside the cells

- **The effect**: they are minimal because, as we said, the cell membranes have low Na+ permeability. The effect of hyponatremia on action potential is on the width and the speed of it (NOT the length).

- **Mechanism**: low Na+ outside > low osmolarity > the extracellular fluids and the blood become hypotonic > by this the water moves to inside the cells > swelling of the cells > and this affects the RMP and the excitability of the cells by mechanisms we do NOT have to know.

- **Signs and symptoms** :
  a- Weakness

  b- Lethargy

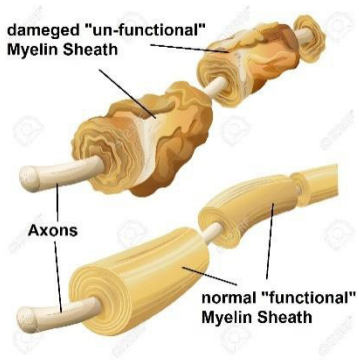
  c- Confusion

  d- Muscle cramps

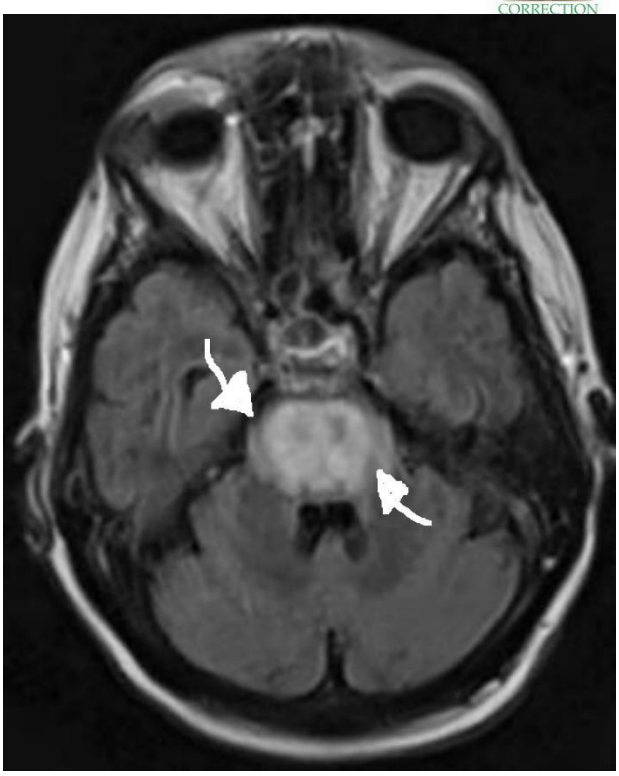
  e- Nausea and vomiting (N&V)

  f- In serious conditions > coma (due to pressing of some swelled cells on nearby cells) > seizures > death

-**Clinical note**: hyponatremia is a serious condition, however the most important and most common serious problem associated with it is the correction of it. Usually, when a patient with hyponatremia (and severe diarrhea) comes to the ER room, the doctor gives him/her **NORMAL SALINE (0.9)** in order to correct the situation and replace the fluids. In this procedure the doctor must be cautious about the RAPID correction of hyponatremia by normal saline, which can lead to death! This occurs either directly or more commonly through central pontine demyelination of nerve axons.



Pontine = pons ☺☺



In this MRI image we can see the brain stem and the pontine. The white thing in the center of the Pons (pontine) is the demyelination of the axons found in the pontine (these axons, as we took with Dr.faraj, come from the cortex to the stem to the pontine and then descend to supply the body). So due to this demyelination, the function of these axons would be disrupted and they don't work very well, and this may result in: paralysis and other symptoms.

The mechanism is complex and not needed from us, but one explanation of this disorder states that because the myelin around the axons depends on the axons to stay alive, during hyponatremia the cells get swelled, and by rapid correction the axons shrink faster than the myelin sheath that surrounds them; so they get separated. Then myelin dies and the nerve fiber is no longer functional and the white color appears on the MRI.

(IMPORTANT NOTE: please please please take care about each single MRI we're going to take in this course)

When we became clinical students, 2n sha2 allah, they will tell us that one of the most important things is fluid replacement and we have to be very carful when we treat hyponatremia. To avoid the death of patients you should always remember that the symptoms of hyponatremia affect the brain, and the treatment of it should happen very slowly. Very slowly means we supply the patient with 1mMol/liter/hour of sodium or on average 8 to 12 mMol/liter/day.

The effect of Ca+ changes:

In the books version of the equation, there is NO Ca+, BUT in the real equation we can find Ca+ and that's because it has an effect on the RMP. Its effect is because it competes with Na+ on its ions channels. So when sodium channels open, the Na+ ions do NOT pass rapidly because Ca+ competes with it on its channels, and this affects RMP as well as the velocity of the action potential.

1- Hypercalcemia

- **Definition**: high conc. of Ca+2 outside the cells
- **The effects**: less excitable cells
- **Mechanism**: high Ca+ outside > as we said Ca+ compete Na+ on its channels > high Ca+ would lead to high competing of Na+ > less Na+ enter the cell when Na+ channels open > less excitability
- **Signs and symptoms**:
  a- Headache

  b- Lethargy: due to less excitable BRAIN cells

  c- Anxiety and depression: this happens when the brain tries to increase its excitability a little more because it is already decreased due to high Ca+

  d- In serious cases > coma

  e- Insomnia الارق

  f- Cognitive dysfunction مشاكل في الادراك

2- **Hypocalcemia** (more common than hypercalcemia)

- **Definition**: low Ca+2 outside the cells
- **The effects**: more and faster cell excitability (esp. muscle and CNS cells)
- **Mechanism**: (NOT mentioned by the Dr.) low Ca+ outside > as we said Ca+ compete Na+ on its channels > low Ca+ would lead to low competing of Na+ > higher Na+ enter the cell when Na+ channels open > more excitability
- **Signs and symptoms**:
  a- Irritability: due to easy excited CNS cells

  b- Hyper-reflexia

  c- Seizures

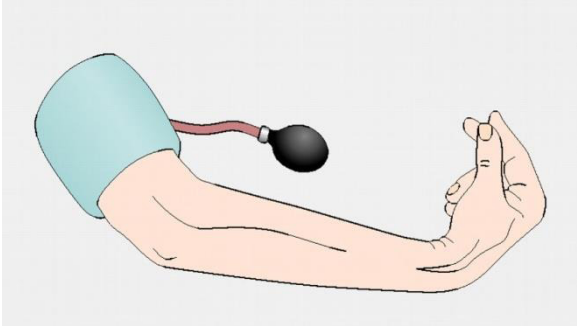
  d- Psychosis

  e- Hallucination

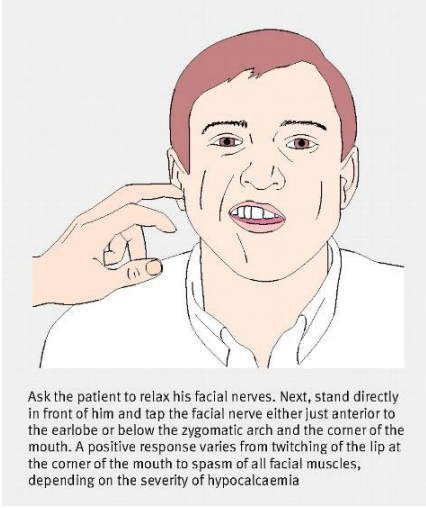
  f- Tetany

-Tests OF Hypocalcemia:

I- **Trousseaus sign**: if we reduce the amount of ATP and O2 supplied, there would be excitation of the cells because they are easier to excite. If we tie the patient's arm by a glove or a pressure cuff so less blood flows in the hand, this will lead to excitation and contraction of the hand muscles. (As in this picture)



II-**Chvosteks sign**: as we said, in hypocalcemia the nerves and the muscles are easy to excite, so if the doctor taps on one of the nerves then the nerve and the corresponding muscle would be excited and it contracts. So if the doctor taps on the corner of the cheek there would be excitation in the facial muscles.



Ask the patient to relax his facial nerves. Next, stand directly in front of him and tap the facial nerve either just anterior to the earlobe or below the zygomatic arch and the corner of the mouth. A positive response varies from twitching of the lip at the corner of the mouth to spasm of all facial muscles, depending on the severity of hypocalcaemia

The effect of Cl- changes:

Even though it is included in the equation, BUT changes in it have minimal effect on both the RMP and action potential. Toxicity of Cl- could happen in infancy and young adult but the mechanism is complex and we will NOT go through it now.

NOW, lets move to action potential topic:

This picture shows normal action potential (AP). Notice the following:

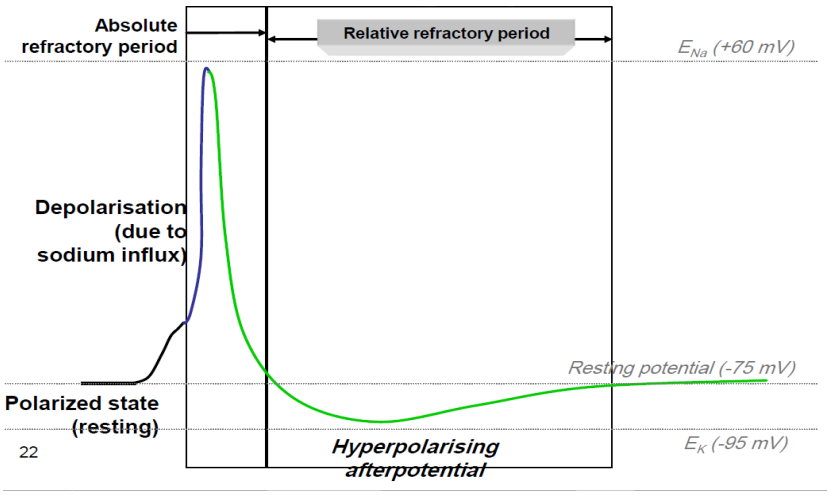
1- RMP (resting membrane potential)

2- Threshold

3- Raising phase

4- Falling phase

5- The hyperpolarization area

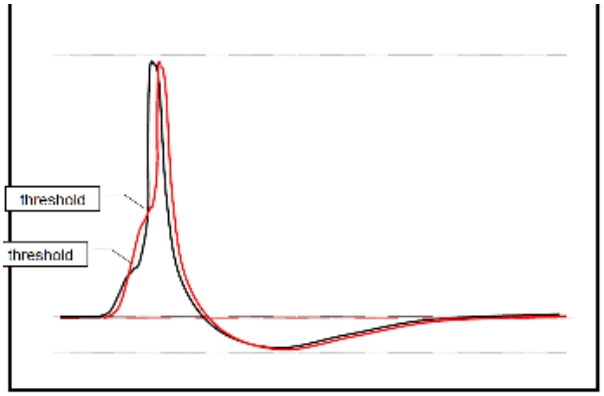


As we know,

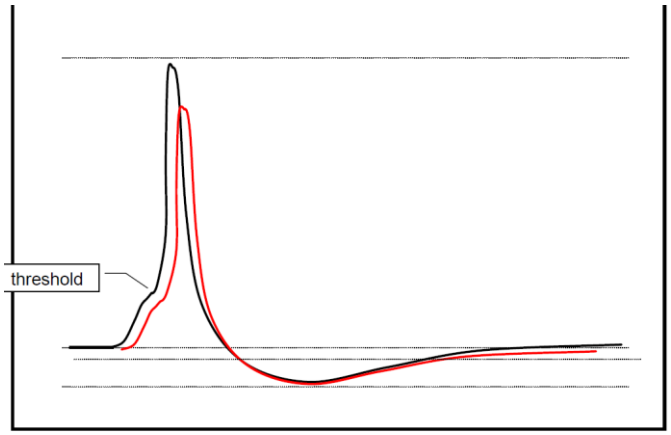
- the general AP shape is somewhat constant (for the same cell type),
- it follows "All or None" rule,
- if the Membrane potential reaches the threshold, an action potential would be the result,
- RMP, AP and threshold are different between cells, for eg. The threshold could be (-50, -20, -60, ...) and what determines the threshold is: the VOLTAGE GATED SODIUM IONS CHANNELS. This channel has many versions; each one has its own threshold. Once the Membrane potential reaches this specific threshold, the corresponding voltage-gated sodium ion channel version would open, Na+ gets inside the cell and an action potential is formed.

Now let's take some examples showing some differences between different types of cells:

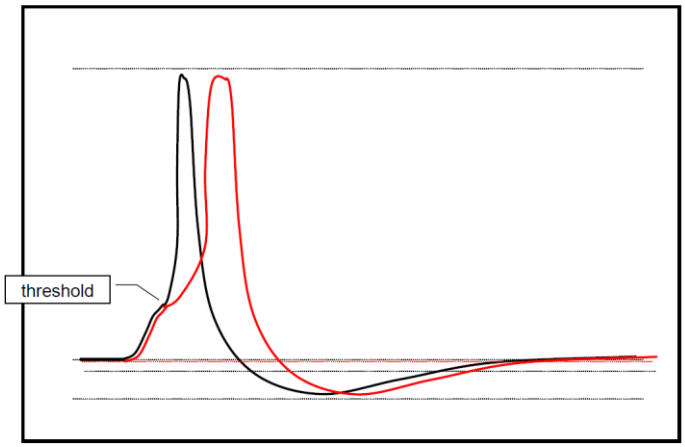
1-in this diagram, we can see 2 action potentials with different "thresholds". We said that the threshold is mainly determined by the type of the Na+ channels expressed on the cell.



2- In this diagram we can see 2 action potentials with different "altitudes", let's say one reach +30 and the other reach +20. The cells can manipulate this also by the type of the sodium channel and depends on when does this channel open or close (different types of channels have different values). Notice that we can NOT find a cell that has 2 different types of channels.

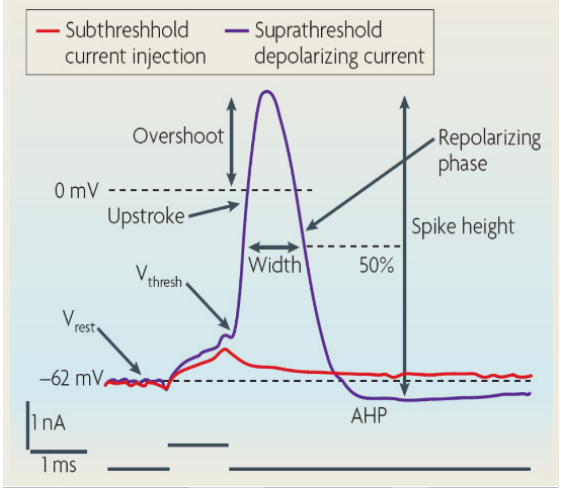


3- In this diagram we can see 2 action potentials with different "velocities" which affects the width of the AP. So in both APs the same amount of Na+ enters, BUT one of them (the left one) need less time than the other one (the right one). And again, this is because these 2 cells have different channel versions. One important note, is that the width (the velocity) also determines the frequency of the AP (logic ☺).



(did you notice somthn?????? Yes, all of the differences are controlled by the **Na+ channel type**)

The AP does NOT change its height in the same cell type because it follows all or none rule. So how can we change the stimulus in order to produce different responses of the same cell type?? This could be achieved by changing the frequency of the stimulus NOT the magnitude of it. By changing the frequency, we can control the relative information that is carried by the stimulus.



Extra explanation: if we decrease the magnitude of the stimulus > NO action potential is going to happen (remember all or none rule). And if we increase the magnitude of the stimulus > the cell is going to fire an action potential once it reaches the threshold and we will get an action potential with the same height of normal stimulus (No benefit from the increase in the stimulus magnitude). BUT if the width of the AP is increased > the frequency of the stimulus decreases and the number of AP per unit of time would be less. On the other hand if the width of the AP decreases > the frequency of the stimulus increases and the number of AP per unit of time would be more. So there is an effect if we change the frequency of the stimulus but there is NO effect if we change the magnitude of the stimulus.

So, what determines the width (hence, the frequency) of the action potential ?

1- **The conc. of the sodium (Na+) around the cell** (as we saw before☺☺).

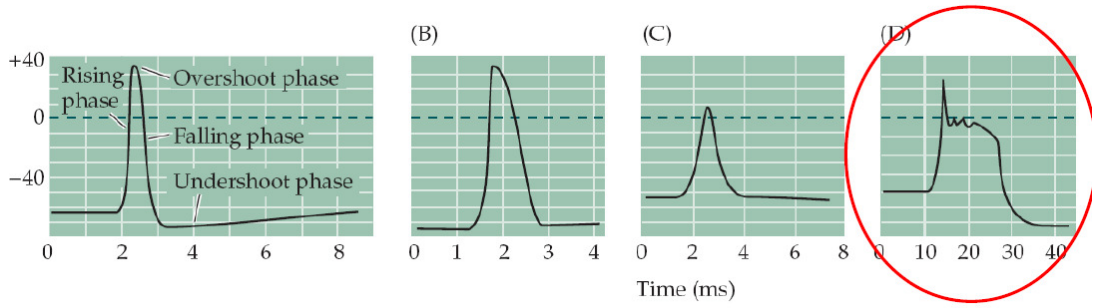
-High conc. Of Na+ > once the voltage gated sodium channels open > huge amount of Na+ enters the cell within a short time > high velocity > small width > high frequency of AP.

-Low conc. Of Na+ > once the voltage gated sodium channels open > small amount of Na+ enters the cell within a unit of time > low velocity > large width > low frequency of AP.

2- **The number of** VOLTAGE GATED SODIUM IONS CHANNELS.

Now, have a look at the following diagram and notice the different types of AP shapes in different cell types. Remember that the AP shape is constant in the same cell type but could be different in different types of cells and this is dependent on:

- The function of the cell
- The differences between the dendrites and the cell bodies and other cell part organizations
- The type of ion channels the cell has on its surface and how it spliced the genes coding for those channels in order to specify their function



In figure (D) in the previous diagram you can see an AP of the **inferior olive cells** in the brain stem of the brain. (Yes, its resembles cardiac cell AP)

We already talked about the importance of the channels in the process of the AP. So any **genetic mutation in one of these channel lines would** cause a loss of function of those channels. These are called **Channalopathies.**

Mutations in one or more ion channel genes change the function of the ion channels due to changing their shape, and this happens mainly in:

1-Na+ channels and K+ channels **(most common two)**

2-Cl- channels and Ca+ channels

In some disorders (like epilepsy or seizures), the doctors failed to determine the cause of the disorder until they tested the patients genetically and found that they have some genetic mutations in their ion channel producing genes. These mutations usually affect the splicing of the ion channels leading to a change in function **by changing the threshold, width, or other characteristic**s.

To be more specific

1- **Most channelopathies that affect "peripheral" channels** (in the **limbs and the muscles**) > the net result changes are **neuromuscular effects** like:

Hyper-reflexia	Myotonia
Hypertonia	Periodic paralysis
Fatigue	Pain
Myasthenia	Erythema
	Fetal akinesia

And they also can affect the **sensory neurons** producing something called ataxia. (**Note**: Ataxia is typically defined as the presence of abnormal uncoordinated movements)

2- **Most channelopathies that affect "central" channels** (in the **spinal cord and the brain**) > the net result changes are different **central effects** including:
-mood effects eg. depression
-seizures effects
- ataxial effects

Some specific central effects include:

Epilepsy (brain effect)	Ataxia (spinal cord effect)
Migraine (brain effect)	Hyperexflexia(spinal cord effect)

IMPORTANT NOTE: there are many tables that show the channelopathy disorders and the affected channel in each one, BUT we do NOT have to memorize any of these tables except those in page 84 and 85 of "neuroscience 3rd edition by Dale Purves" (not the same as our recommended book). There are yearly questions on these pages so study them well.

And here are the two pages:

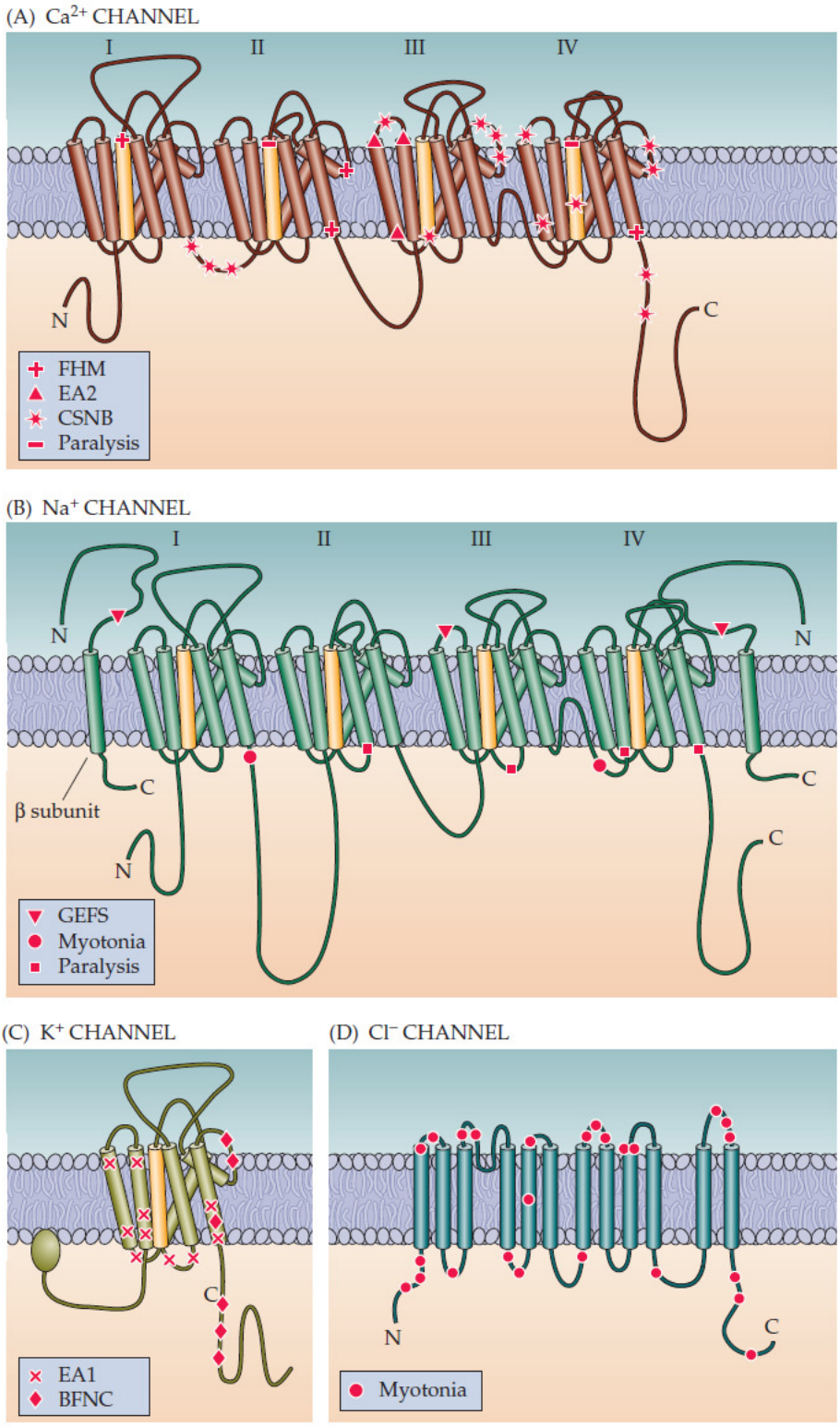
Box D

Diseases Caused by Altered Ion Channels

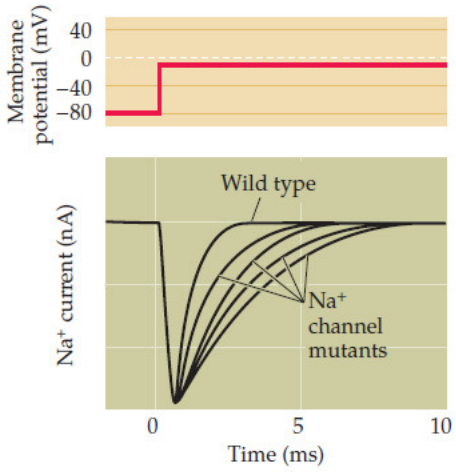
Several genetic diseases, collectively called *channelopathies*, result from small but critical alterations in ion channel genes. The best-characterized of these diseases are those that affect skeletal muscle cells. In these disorders, alterations in ion channel proteins produce either myotonia (muscle stiffness due to excessive electrical excitability) or paralysis (due to insufficient muscle excitability). Other disorders arise from ion channel defects in heart, kidney, and the inner ear.

Channelopathies associated with ion channels localized in brain are much more difficult to study. Nonetheless, voltage-gated Ca^{2+} channels have recently been implicated in a range of neurological diseases. These include episodic ataxia, spinocerebellar degeneration, night blindness, and migraine headaches. *Familial hemiplegic migraine* (FHM) is characterized by migraine attacks that typically last one to three days. During such episodes, patients experience severe headaches and vomiting. Several mutations in a human Ca^{2+} channel have been identified in families with FHM, each having different clinical symptoms. For example, a mutation in the pore-forming region of the channel produces hemiplegic migraine with progressive cerebellar ataxia, whereas other mutations cause only the usual FHM symptoms. How these altered Ca^{2+} channel properties lead to migraine attacks is not known.

Episodic ataxia type 2 (EA2) is a neurological disorder in which affected individuals suffer recurrent attacks of abnormal limb movements and severe ataxia. These problems are sometimes accompa-



Genetic mutations in (A) Ca^{2+} channels, (B) Na^+ channels, (C) K^+ channels, and (D) Cl^- channels that result in diseases. Red regions indicate the sites of these mutations; the red circles indicate mutations. (After Lehmann-Horn and Jurkat-Kott, 1999.)



Mutations in Na^+ channels slow the rate of inactivation of Na^+ currents. (After Barchi, 1995.)

nied by vertigo, nausea, and headache. Usually, attacks are precipitated by emotional stress, exercise, or alcohol and last for a few hours. The mutations in EA2 cause Ca^{2+} channels to be truncated at various sites, which may cause the clinical manifestations of the disease by preventing the normal assembly of Ca^{2+} channels in the membrane.

X-linked *congenital stationary night blindness* (CSNB) is a recessive retinal disorder that causes night blindness, decreased visual acuity, myopia, nystagmus, and strabismus. Complete CSNB causes retinal rod photoreceptors to be nonfunctional. Incomplete CSNB causes subnormal (but measurable) functioning of both rod and cone photoreceptors. Like EA2, the incomplete type of CSNB is caused by mutations producing truncated Ca^{2+} channels. Abnormal retinal function may arise from decreased Ca^{2+} currents and neurotransmitter release from photoreceptors (see Chapter 11).

A defect in brain Na^+ channels causes *generalized epilepsy with febrile seizures* (GEFS) that begins in infancy and usually continues through early puberty. This defect has been mapped to two mutations: one on chromosome 2 that encodes an α subunit for a voltage-gated Na^+ channel, and the other on chromosome 19 that encodes a Na^+ channel β subunit. These mutations cause a slowing of Na^+ channel inactivation (see figure above), which may explain the neuronal hyperexcitability underlying GEFS.

Another type of seizure, *benign familial neonatal convulsion* (BFNC), is due to K^+ channel mutations. This disease is characterized by frequent brief seizures commencing within the first week of life and disappearing spontaneously within a few months. The mutation has been mapped to at least two voltage-gated K^+ channel genes. A reduction in K^+ current flow through the mutated channels probably accounts for the hyperexcitability associated with this defect. A related disease, episodic ataxia type 1 (EA1), has been linked to a defect in another type of voltage-gated K^+ channel. EA1 is characterized by brief episodes of ataxia. Mutant channels inhibit the function of other, non-mutant K^+ channels and may produce clinical symptoms by impairing action potential repolarization. Mutations in the K^+ channels of cardiac muscle are responsible for the irregular heartbeat of patients with long Q-T syndrome. Numerous genetic disorders affect the voltage-gated channels of skeletal muscle and are responsible for a host of muscle diseases that either cause muscle weakness (*paralysis*) or muscle contraction (*myotonia*).

References

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In short, ion channels are integral membrane proteins with characteristic features that allow them to assemble into multimolecular aggregates. Collectively, these structures allow channels to conduct ions, sense the transmembrane potential, to inactivate, and to bind to various neurotoxins. A combination of physiological, molecular biological and crystallographic studies has begun to provide a detailed physical picture of K^+ channels. This work has now provided considerable insight into how ions are conducted from one side of the plasma membrane to the other, how a channel can be selectively permeable to a single type of ion, how they are able to sense changes in membrane voltage, and how they gate the opening of their pores. It is likely that other types of ion channels will be similar in their functional architecture. Finally, this sort of work has illuminated how mutations in ion channel genes can lead to a variety of neurological disorders (Box D).

We said that the genetic mutations produce channelopathy disorders, and now we add the **environmental factors**. Environmental factors can change the ion channel function. **One example of such factors is TOXINS**, so some toxins can block certain ion channels affecting their ability to work, and this affects the nervous system.

One of the **commonest toxins is TETRATOXIN**, which is a sub-sort of toxins found **in jellyfish and scorpions**. It **blocks VOLTAGE GATED SODIUM IONS CHANNELS**, so by this blockage **NO more action potential can be generated**, resulting in **paralysis**.

We, as doctors, are going to use some sub-types of these toxins in **ANESTHESIA** procedures during surgery (specifically local anesthesia). One of the sub-types we use is **LIDOCAINE** (we took it with Dr.Muneer if you remember) which can block the voltage gated sodium ions channels "**temporally and locally**" preventing their induction during surgeries.

And that's it,

I know it was such a long sheet, BUT as I said in the beginning, this is CNS ☺☺

This sheet is dedicated to A & S & R

Best of luck all, and always remember,

(وَابْتَغِ فِيمَا آتَاكَ اللَّهُ الدَّارَ الْآخِرَةَ ۖ وَلَا تَنْسَ نَصِيبَكَ مِنَ الدُّنْيَا ۖ وَأَحْسِنْ كَمَا أَحْسَنَ اللَّهُ إِلَيْكَ ۖ)

Yours Sincerely,

Amer ABU Shanab