ATP

TEAM

6.3 Glial Cells

* half of the cells in the human CNS.
* glial cells → glia "glue".
* Glial cells surround the soma "cell body", axon and dendrites of neurons and provide them with physical and metabolic support.
* Many CNS tumors actually originate from glial cells.
* several different types of glial cells found in the CNS.

→ one type :- oligodendrocyte

Function :- forms the myelin sheath of CNS axon.

→ second type :- astrocyte → function :-

- Composition of the extracellular fluid in the CNS by removing Potassium ion and neurotransmitters around synapses.
- stimulate the formation of tight junction between the cells that make up the walls of capillaries found in the CNS

- blood-brain barrier, selective filter for exchanged substances than is present between the blood and most other tissues.
- sustain the neurons metabolically
  ex: → Providing glucose and removing ~~amonia~~ ammonia.

→ Three type:- Microglia
- Specialized macrophage.
- Perform immune functions in the CNS
- Contribute to synapse remodeling (إعادة تشكيل/بناء) and plasticity. (اللدونة)

→ forth type:- ependymal cells:-
- line the fluid-filled cavities within the brain and spinal cord
- regulate the production
- flow of cerebrospinal fluid.

6.4 Neural Growth and Regeneration.

* growth cone :- forms the tip of each extending axon and is involved in finding the correct route and final target for the process.
* soluble neurotrophic factors :- in the extracellular fluid surrounding the growth cone or its distant target.
* A surprising aspect of development of the nervous system occurs after growth and projection of the axons.
* plasticity :- involves both the generation of new neurons and remodeling of synaptic connections and is stimulated by exercise and by engaging in cognitively challenging activities.

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6.5 Basic Principles of electricity.

* The Predominant solutes in the extracellular fluid are Sodium and Chloride ions.
* The intracellular fluid Contains high Concentration of Potassium ion
* distribution of these charged particles occur at the [1] Cell's plasma membrane and [2] play a significant role in signal integration and [3] cell-to-cell Communication.
* Separated electrical charges of opposite sign have the potential to do work ... allowed to come together This potential ⇒ electrical potential.
determined by the difference in the amount of charge between two points (Potential difference)
* electrical potential are Volts.
* measured in millivolts. (1mV = 0.001 V)
* Current :- The movement of electrical charge
* The electrical Potential between charge tend to make them flow, Producing a current
* Current bring them toward each other

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* Current depend on the potential difference between the charge and on the nature of the material or structure through which they are moving.
* hindrance to electrical charge movement is known as resistance .(R)
* I = Ohm's law :- $I = \frac{V}{R}$
* material that have a low resistance allow rapid current flow and are called conductors
* water good conductor because the ions can carry the current
* lipids , contain very few charged groups and cannot carry current
* Lipid layers of the plasma membrane are regions of high electrical resistance - separating the intracellular fluid and the extracellular fluid

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6.6 The Resting membrane Potential

* the inside of the cells negatively charge with respect to the outside.
* resting membrane potential varies from about -5 to -100 mV ⇒ depending upon the type of the cells.
* in neurons ⇒ in the range of -40 to -90 mV
* The resting membrane potential exists because of a tiny excess of negative ion inside the cell and an excess of positive ion outside.
* excess charge (ions) collect in a thin shell right against the inner and outer surfaces of the plasma membrane.
* The bulk of the intracellular and extracellular fluid remains electrically neutral.
* Table 6.2
* Na^+ and K^+ ⇒ generally play the most important roles in generating the resting membran potential
* Na^+ and Cl^- conc. are lower inside the cells than outside.
* K^+ conc. is greater inside the cell.

* the pumps Na^+ out of the cells and K into it.
* Cl^- ⇒ varies between cell types
* The magnitude of the resting membrane Potential depend mainly on two factors:
  1- differences in specific ion Con. in the intracellular and extracellular fluid
  2- differences in membrane permeabilities to the diffient ion
* reflect the number of open channels for the different ion in the plasma membrane
* fig 6.10
* equilibrium potential for an ion there is no net movement of the ion because the opposing fluxes the equal
* magnitude of the equilibrum potential (in mV) depend Con. gradient for that ion across the membrane.
* Equilibrum potential for one ion species can be different in magnitude and direction from those for other ion species, depending on the concentration gradient

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between the intracellular and extracellular compartments for each ion.

* Nernst equation :- describs the equilibrum potential for any ion species.

$$E_{ion} = \frac{61}{Z} \log\left[\frac{C_{out}}{C_{in}}\right]$$

Z: constant value — temperture 37° — Faraday constant

* $E_{Na} = +60$, $E_{K} = -90$ mV

* Goldman-Hodgkin-Katz (GHK) equation :-
  ↳ Can be used to determine the resting membrane Potential.

$$V_m = 61 \log \frac{P_K[K_{out}] + P_{Na}[Na_{out}] + P_{Cl}[Cl_{in}]}{P_K[K_{in}] + P_{Na}[Na_{in}] + P_{Cl}[Cl_{out}]}$$

* Sitting the Permeabilities of two ions to that the Cl^- Conc. are reversed as Compared to Na^+ and K^+
* inside Conc. ⟶ numerator
* Outsid Conc. ⟶ denominator
* Cl^- is an anion and its movement has the opposite effect on the membrane potential
* in mammalian neurons the K^+ permeability may be as much as 100 times greater than that for Na^+ an Cl^-

* The resting potential is generated across the plasma membrane largely because of the movement of K^+ out of the cells down its Conc. gradient through Open K^+ channel ⇒ called Leak K^+ channel
* Leak K^+ channel :- makes the inside of the cell negative with respect to the outside.
* K^+ flux has more impact on the resting membrane potential than does Na^+ flux.
* The resting membrane potential, ion channels allow net movement both of Na^+ into the cell and K^+ out of the cell.
* Conc. of intracellular Na^+ and K^+ ion does not change → becaeies of the action of the Na^+/K^+ - ATPase Pump.
* the Na^+/K^+ - ATPase pump not only maintains the Conc. gradient for these ion but also helps to establish the membrane potential
move directly,
* Na^+/K^+ - ATPase pump → move three sodium ion out of the cell → two potassium ion that they bring in

~~Pump~~ Pump move net charge across the membrane and contributes directly to the membrane potential →
→ electrogenic pump.

* electrogeinic Contribution to the membrane potential is quite small.
* electrogenic pump is indirect Contribution to the membrane potential? becaus it maintains the conc. gradients.
* fig 6.13
* Cl^- diffusion into the cell Contributes to the excess negative charge inside the cell

6.7- Graded Potential and action Potential

* Such channel give a cell the ability to Produce electrical signal that can transmit information between different region of the membrane ⇒ excitability. ((excitable membrane))

* cells of this type include all neurons and muscle cells, some endocrine, immune, and reproductive

* The electrical signal occur in two forms:

1- Graded Potential

2- action Potential

* graded Potential :- are important in signaling over short distances

* action Potential :- long distances signals that particularly important in ① neuronal and ② muscle cell membrane.

* Depolarizing, repolarizing, hyperpolarizing and overshoot changes in membrane potential relative to the resting potential.

* Depolarized :- its potential becomes less negative the resting level

* Overshoot :-

* Overshoot :- reversal of the membrane potential polarity -- the inside of a cell becomes positive relative to the outside.
* repolarizing :- membran potential has been depolarized is returning. returning toward that resting value
* hyperpolarized :- When the potential is more negative than the resting level
* gated channel in a membrane may be opened or closed by mechanical, electrical or chemical stimuli.
* Graded Potential :- are important signaling.
* Graded Potential :- Change in membrane potential that are confined to a relatively small region of the plasma membrane.
* Graded Potential produced when some specific change in the Cell's environment.

* graded potential act on a specialized region of the membrane.
* graded potential → receptor potential
  Synaptic Potential
  Pacemaker Potential
* Table :- 6.3
* graded potential occurs charge ~~pot.~~ flows between the place of origin of this potental and adjacent regions of the plasma membrane.
* Small region of a membrane has been depolarize by transient application of a chemical signal.
* Fig 6.15
* Depolarization and graded potential caused by chemical stimulus
* decremental is local current.
* Summation is add to the depolarization from the first stimulus

Action Potential:

* different from graded potential.
* action potential :- They are large alterations in the membrane potential.
* Vary rapid (as brief as 1-4 millisecond)
* Voltage-Gated ion channel :- Na^+ + K^+
* ligand-gated channel ⇒ open in response to the binding of signaling molecules.
* mechanically gated channel :- open in response to physical deformation
* ligand and mechanically-gated channel is graded potential that can serve as the initiating stimulus for an action potential.

Fig 6.18

* Action potential mechanism :

The membrane potential depends upon the conc. gradients and membrane permeabilities of diffirant ion ⇒ Na^+ and K^+

Fig 6.19

* Na^+ ⇒ depolarizes the membrane
* K^+ ⇒ repolarizes the membrane

* Fig 6.20
* Na^+ → Channels exert positive feedback on membrane Potential.
* K^+ → channels exert negative feedback.
* number of ions that cross the membrane during an action potential is extremly small compared to the total number of ion in the cells.
* Cellular accumulation of Na^+ and loss of K^+ are prevented by the Continuous action of the membrane Na^+/K^+ – ATPase Pump.
* not all membrane depolarization in excitable cells trigger the positive feedback process that leads to an action potential.
* action potential occur only when the initial stimulus
* stimuli that are just strong enough to depolarizatio the membrane to this level are threshold stimuli

Fig 6.21
* Threshold is not indicated becaus it varies from cells to cell.
* Weak depolarization are called subthreshold potentials, subthreshold stimuli

* action potential :- either occur maximally or the do not occur at all.

((action potential are all-or-none))

* The generation of action potential is prevented by local anesthetics such as → Procaine (Novocain) and Lidocaine (Xylocaine) these drugs block voltage-gated Na^+ channels.

* ~~Pufferfish~~ Pufferfish → Produce an extremely potent toxin, terodotoxin.

* Refractory Periods :-

* Fig 6.22

* absolute and relative refractory periods of the action potential determined by a paired-pulse protocol.

* relative refractory period :- interval during which a second action potential can be produced.

→ Last 1 to 15 msec

* Some but not all of the Voltage-gated Na^+ channel have returned to a resting state and some of the K^+ channel repolarized & the membrane are still open.

new stimulus to depolarize the membrane.
Refractory periods contribute to the separation of these action potentials so that individual electrical signals pass down the axon

Action potential Propagation:-
Fig 6.23
one way propagation of an action potential.
local current from the opening of ligand-gated ion channels in the cell body.
dendrites causes an action potential to be initiated in region(1), ~~depo~~ depolarizes (2) refractory (1)
Voltage-gated Na^+ channel located there open
action potential propagation:- Producing yet another action potential at the next site along the length of the membrane.
(action potential not move:-)
new action potential in the region of the axon just ahead of it. Because each regeneration of the action potential depend on the positive feedback cycle of a ~~me~~ new group of Na^+ channel.

* action potentials do not decreases in magnitude with distance like graded potentials.
* the only ~~direction~~ direction of action potential propagation is away from a region of membrane that has recently been active.
* action potential are initiated at one end of the cell, and propagate ~~to~~ toward the other end.
* The velocity with which an action potential propagates along a membrane depends upon fiber diameter and whether or not the fiber is myelinated.
* The larger the fiber diameter the faster the action potential propagates.
* Conc. of voltage-gated Na^+ channels in the myelinated region of ~~axon~~ axon is low.
* action potential occur only at the nodes of Ranvier
* propagation is called saltatory conduction

* action potential dose not in fact jump from to region but rather is regenerated at each ~~node~~ node
* Propagation via saltatory conduction is faster than propagation in nonmyelinated fibers of the same ~~axon~~ axon diameter.
* Pacemaker Potential

Table 6.4.