Synaps: Communication region between two neurons or neuron with effectors (muscle or glandular cell)

* information is transmitted in CNS in form of AP

the impulse may be (called synaptic function of neuron)

- Blocked
- changed into reptitive impulses
- integrated with another

types of synaps

- chemical synaps (most one in the CNS)
  - * contain secretion of neurotransmitters in nerve ending
    - → excite, inhibit, modify sensitivity of neuron
    - → act on receptor protein in the membrane of next neuron
  - * it is one-way presynaptic → postsynaptic
  - * used for direct signal to specific goals and specific function
  - * presynaptic terminals has two internal
    - transmitter vesicles contain neurotransmitter which inhibit or excite the postsynaptic neurone
    - mitochondria to provide ATP which supply the energy to produce new neurotransmitters
  - * presynaptic membrane has Voltage gated Ca^{2+} channel

    So when AP depolarize the presynaptic neuron the Ca^{2+} enter and

    Ca^{2+} ion ∝ neurotransmitter released
- electrical synaps (direct connected with gab junction) as
  - Smooth muscle
  - Cardiac muscle
  - * and it is Biderictional

    advantages of Biderictional
    - faster communication
    - Synchronization and increasing neuronal sensitivity of connected neurons

* 0.5 mSec is delay of transmission of neural signal by
- → discharge of transmitters by presynaptic
- → diffusion of transmitter to post synaptic neuron
- → action of the transmitter on membrane receptors
- → action of membrane receptor on permeability
- → inward diffusion of Na^+ to rais EPSP

On post synaptic neuron the receptor activation of ion channel by
- → gating ion channel directly (ionotropic receptor)
- → activating second messenger (metabolic receptor)

ion channels on post synaptic

anion(−) ← → Cation(+)

which allow Cl^- mostly but allow some time other anions
⇓
inhibitory transmitter

which allow Na^+ mostly but can allow often K^+ and Ca^{2+}
⇓
excite the neuron
so transmitter called Excitatory transmitter

* the open and closed of channels on post synaptic neuron called rapid control of post synaptic neurons

* process of memory need changes to stay for long time (prolonged)
so these channels does not compitable with it because it close rapidly (with millisecond)

here the role of second messenger come (for prolonged excitation or inhibition)

So the second messenger is chemical substance in the postsynaptic neuron itself cause prolonged effect (G-protein as an example)

* Excitation of post synaptic neuron

① opening of Na^+ channel

② depressed conduction of K^+, Cl^- channels

change in internal metabolizm to excite cell to increase more excitatory membrane receptors or decrease inhibitory receptors

the inhibition of post synaptic neuron is opposite of above

Types of synaptic transmitters

Small molecules (rapidly acting transmitter) which caused most of responses such as sensery signals to brain and motor signals to muscles

neuropeptids used for prolonged actions as long-term changes in number of neuronal receptors, long-term opening or closing channel or long-term of changes of number or size of synapses

* Small molecule, Rapidly acting transmetter

① it is mostly synthesis in cytosol of presynaptic terminal and by active transport to transmitter vesicles, so each time AP reaches the presynaptic neuron few vesicles only release thier transmitters into synaptic cleft and this actions occure in millisecond and the action of postsynaptic neuron is also take millisecond or less

and mostly the effect is to increase or decrease conductance in ion channels

and vesicles that release transmitter is recycled and used again So the vesicles fuse with synaptic membrane and it's membrane will become a part of synaptic membrane, After the release of transmitter it will invaginate back and pinches off to form new vesicles and still have appropriat enzyme and transport protein to

concentrating transmitters in vesicles ↔ synthesis neurotransmitter

Examples :- ① Acetylcholine (Ach) (in pre synaptic terminal)

Acetyl Coenzyme A
choline
} choline acetyltransferase → Acetylcholine —transported to→ specific vesicles —then released to→ synaptic cleft —split to By cholinesterase→ acetate + choline

Areas of Acetyl Choline of the NS

① terminals of pyramidal cells of motor cortex
② different type of basel ganglia
③ motor neuron innerate skeletal muscle
④ pre ganglionic neurone in ANS and post ganglionic in parasympathetic and some of sympathetic

* mostly Ach is excitatory except some locations as inhibition of the heart by vagus Nerves

② Norepinephrine (NEP) : secreted by neurons located in locus cerules in pons in brain stem and hypothalamus and these neuron send nerve fibers widespread areas of the Brain to help overall activity and mood of the mind, such as increasing level of wakefulness * mostly excitatory but in few areas it is inhibitory

* also NEP is secreted in postganglionic neurons in SNS and exeite some organs and inhibite others.

(3) Dopamine: Secreted from neuron which originate from substantia nigra and terminate in striatal region of basel ganglia. And it is usually inhibitor

(4) Glycine: secreted in synaps in spinal cord and always is inhibitory neurotransmittor.

(5) GABA: (gamma-Amino Butyric acid) secreted By nerve terminals in spinal cord, cerebellum, basel ganglia and many Areas of the cortex, Always cause inhibition.

(6) Glutamate: secreted By presynaptic terminal in many senseroy pathway entering CNS and many Area of cerebral cortex and it is always excitatory.

(7) Serotonin: Secreted By nuclei that originate from median raphe of Brain stem and spinal cord Areas especially to the dorsal horns of spinal cord and to the hypothalamus it is inhibite the pain pathway (and because it is inhibitor action of high region of NS it is thought to cause sleep and help control the mood

finally (8) nitric oxide: secreted By nerve terminals in Brain for long term behavior and memory

it is different than the small molecule in formation mechanism and action on post synaptic neuron

* does not stored in vesicels but synthesised as needed and diffuses out

* in post synaptic neuron it usually does not change membrane potential but do changes intercelluler metabolic function for modify neuronal excitability for second or minute or longer

SUM UP

Small rapid molecule (transmitter)

- inhibitory
  - Dopamine from neuron in substantia nigra and termination in striatal region in basal ganglia
  - Glycine in synaps of spinal cord
  - GABA terminals of spinal cord, cerebellum and basal ganglia and areas of cortex
  - Serotonin nuclei originate from Brain stem in median raphe and spinal cord in dorsal horns and to the hypothalamus inhibitory of pain and cause sleep ....
  - Nitric oxide: by nerve terminal for long-term memory and it is different than others, not stored in vesicels and cause metabolic rxn in the cell
- excitatory
  - Glutamate in prisynaptic terminals in CNS and many area of cerebral cortex
  - NEP By neuron terminals in hypothalamus and brain stem and SNS
  - Ach

* Neuropeptids: synthesised different and have actions that are usual slow.

* it is synthesised in cell body by ribosome as integral part of large-protein molecule.

So the protein molecule enter the space inside the ER and then enter golgi complex where two changes occur:

① the neuropeptid-forming protein is split into smaller fragment some of which are either the neuropeptid or precursor of it

then ② the golgi package it into minute transmitter vesicels and release it into the cytoplasm.

then the transmitter vesicles traveled all the way to the tips of nerve fiber by axonal streaming of the axon cytoplasm and it is travelling at slow rate (few centimeters per day)

* However after releasing the neurotransmitter as a response to AP the vesicle is Autolyzed and is not reused

* as you see the method is hard so fewer transmitter released compared by small molecule transmitter.

* But the main difference between them is the neuropeptid is thousand more times as potent (power) as small molecule transmitter. and it causes more prolonged actions

- prolonged closure of Ca channel
- " changes in metabolic pathway
- " " in activation or deactivation of specific gene
- prolonged Alterations of number of excitatory or inhibitory receptor

Fatigue of synaptic transmission

the main mechanism of fatigue is exhaustion or partial exhaustion of transmitters stores in presynaptic terminals

* excitatory terminals in many neurons can storage enough transmitters for 1000 AP and can be exhausted in only few seconds - minutes in rapid stimulation.

other factors of fatigue

- progressive inactivation of many of postsynaptic membrane receptors (يعني المشكلة بالمستقبلات)
- depletion of transmitter stores
- slow development of abnormal conc. of ion inside postsynaptic neuron

* Alkalosis effects the synaptic transmission

Most neurons highly responsive of pH of the interstial fluid

So Alkalosis increase the excitability of neuron and cause cerebral epileptic seizures

So if this person with epileptic seizures has hyper ventelation $\longrightarrow \uparrow O_2 \downarrow CO_2 \uparrow pH$ so he will have epileptic attack

and vice verca so acidosis greatly depressed neural activity so lowering pH may cause comatose state

* in very sever diabetic or Uremic acidosis, coma always develops

Effect of Hypoxia (lack of oxygen)

* neuronal excitability is highly depand on adequate supply of oxygen so cessation of oxygen can cause inexcitability of some neurons, so if Brains of the Blood flow is interrupted for 3-7 second the person become unconscious

last thing is about the drugs

increase excitability

Caffeine in Coffee

Theophylline in tea

Theobromine in Cocoa

By lowering the threshold of neurons

decrease excitability

⇓

most anesthetics increase the threshold

⇓

decrease synaptic transmission

* Some of anesthetics are lipid-soluble so some of them might change the physical charastaristics of neural membrane making them less responsive for excitment