# NERVOUS SYSTEM

2018

## Organization of nervous system :

rapid

### (A) Histological

**Neurones**

Basic unit

- Human CNS : $10^{11}$ neurones
- Each neurone : 2000 synapses
- → $2 \times 10^{14}$ synapses

Static

**Glial cells** (Neuroglia)

Supporting cells

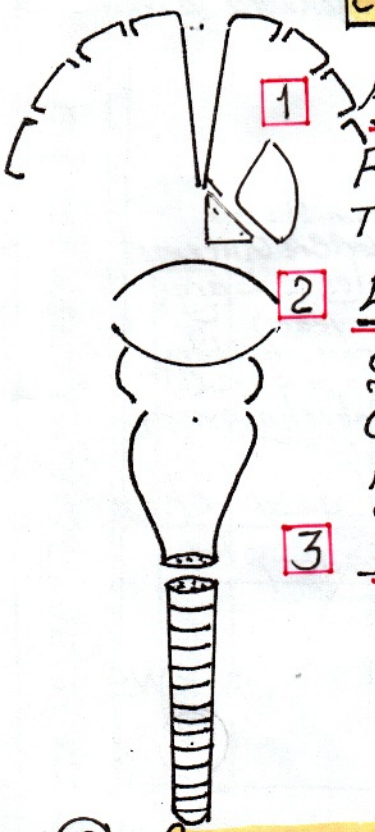
10 - 50 times number

3 types :

a. Microglial : phagocytic cells
b. Oligodendrites : Myelin sheath
c. Astrocytes : Maintain $K^+$ ! BBB

### (B) Anatomical and Functional

**CNS**



1. Higher brain (cortical) level.
   Fine motor & sensory
   Thinking, Memory, learning & Speech.
2. Lower brain (subcortical) level
   Subconcious activities
   CVS, Resp & GIT control.
   Posture & equilibrium
   Emotional reactions, Wakefulness
3. Spinal cord level
   Immediate autonomic activities.
   Withdrawal reflexes,
   Walking movement Suppor. rections.
   Bladder & Rectal evacuation.

**PNS**

1. Sensory (Afferents)
2. Motor (Efferents)
   - (a) Somatic to SK m
   - (b) Autonomic to
     - glands < exocrinal, endo
     - muscles < cardiac, smooth

### (C) Sensory division

Thalamus

sp. cd. & CC

RF of brain stem

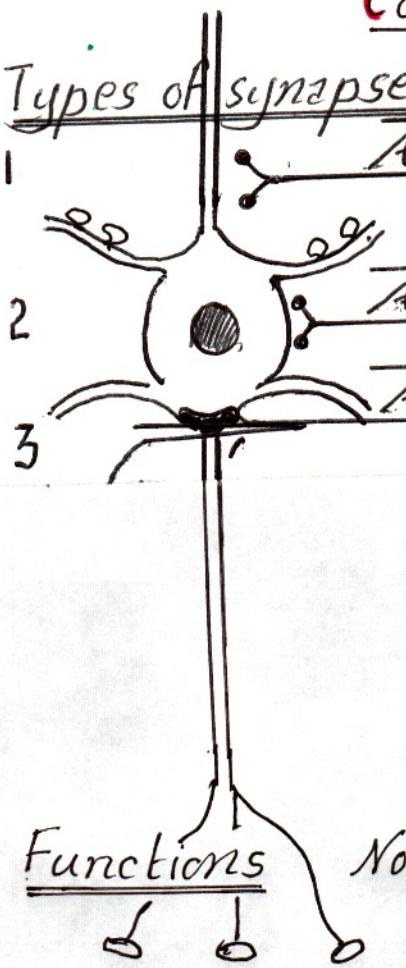
### Motor division

1

Basal ganglia

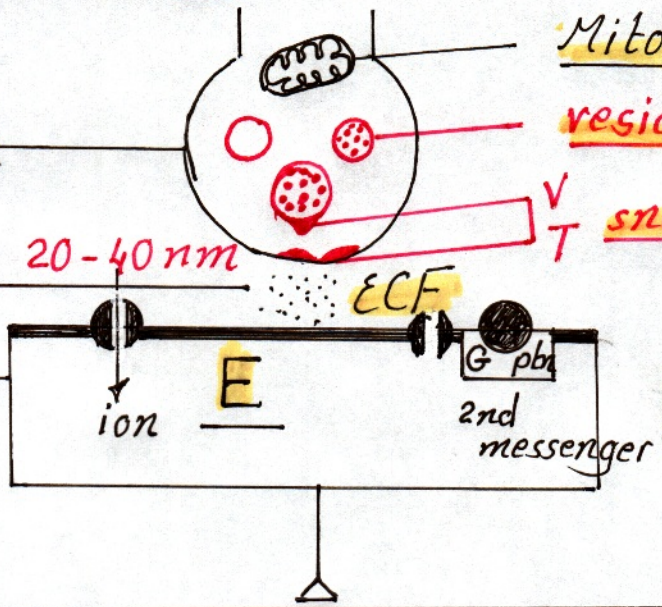
# Synapses

- **Definition** — Site of junction between 2 neurones
  Axon terminal of presynaptic & postsynaptic ,,
- **Transmission**
  conjoint
  1. Electric = Gap Junction — Rare — Short latency
  2. Chemical — Chemical transmitter — Long latency
     Common — Controlable — One way
- **Types of synapses** — sp.cd Cortex < Cerebral / Cerebellar
  1. Axo-dendritic — 80-98% — least excitable
  2. Axo-somatic
  3. Axo-axonic — Most excitable
     Lowest threshold
     More voltage gated $Na^+$ ch. ?
     Site of generation of A.pot
     Adjacent to Axon hillock
     Spreads forwards & backwards



- **Functions** — Not electric simple transmission but chemical complex
  Allow Grading & Adjustment
  1. Facilitating transmission
  2. Amplification of ,,
  3. Blocking ,,
  4. Changing on repeated stim.
  5. Distribution of information
  6. Integration of information
  7. Storage of information.

## Functional anatomy



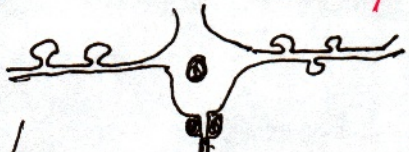

## Vesicles

| | Small clear | Small dense | Large (dense) granular |
|---|---|---|---|
| 1 | ACh<br>Glycine GABA<br>Glutamate | Catecholamines | Neuropeptides |
| 4 | Short term 1ms or less | | Long term min., H, days or more |
| 2 | Axon terminals (boutons) | Formed in | Cell body |
| 3 | Near synaptic cleft | Release | All parts of presynaptic terminal |
| | exocytosis release via small holes | $Ca^{++}$ | |
| 5 | endocytosis refill locally | Exocytosis | Small amount<br>Not recycles |

Kiss & run discharge

Notes: usually [ One neurone secretes ONE type of ch. trans.
Excitation or Inhibition depends on Receptor

Functions of dendrites:

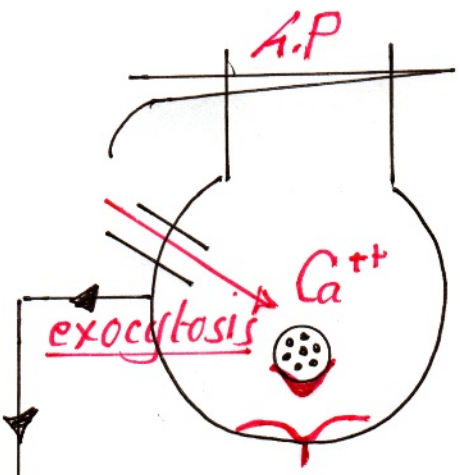


1 Expand area of integration
2 Some initiate A potential
3 Dendritic spines appear disappear or change in min or H.
import. for motivation, learning & long term memory

# Mechanism of synaptic transmission.

1 **Release**

A pot. opens voltage gated $Ca^{++}$
Migration of vesicles to active zone
Fusion of V & t snare
Release of ch. tr. by Exocytosis

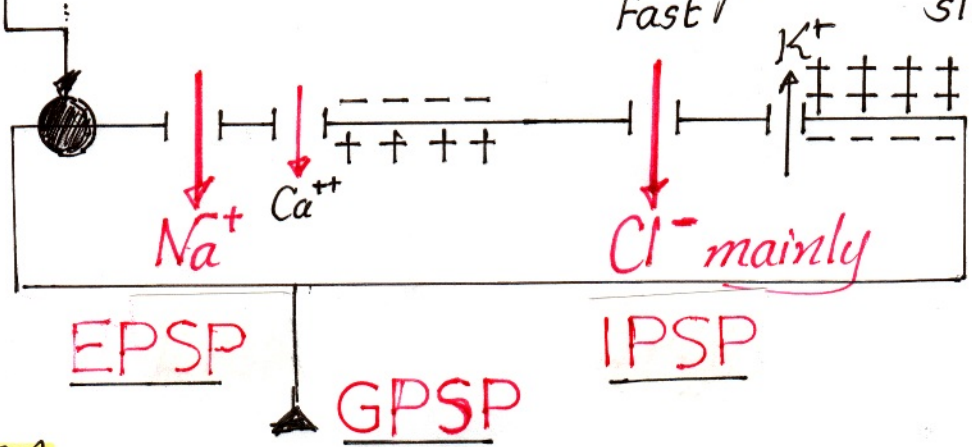



Exocytosis $\propto Ca^{++}$

2 **Binding**

Ch tr with specific receptor
ionotropic or metabotropic
fast slow

3 **Generation of**




EPSP IPSP

GPSP

4 **Inactivation**

a Presynaptic : Active reuptake.

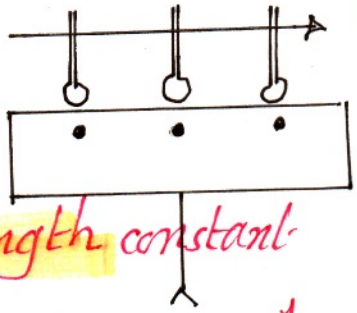
b Cleft : Diffuse away in ECF.

c Postsynaptic : Inactivation.

d Microglia : Removal.

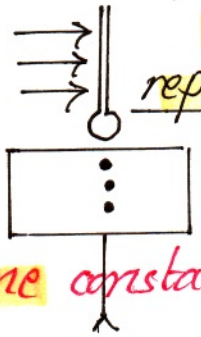
| | EPSP | | IPSP |
|---|---|---|---|
| 1. | Depolar. | Transient \| localised \| Partial | Hyperpolar. |
| 3. | Fast or slow | Time begins 0.5 msec | Fast |
| | | peak 11.5 msec | |
| | | lasts 15 msec | |
| 2. | ↑ | Excitability | ↓ |
| 4. | opening of $Na^+$ mainly $Ca^{++}$ | Ionic basis | opening of $Cl^-$ mainly $K^+$ (slow IPSP) |
| 5. | | Characters: Graded, Summated | |

**SPACE** Spatial — Many Simultaneously



Length constant — Depends — Number of Knobs $\propto \frac{1}{L}$

**TIME** Temporal — One repetitively



time constant — Frequency of S $\propto \frac{1}{T}$

Notes: Slow postsynaptic potential

Latency: 100–500 ms — Lasts Several seconds

Site: Autonomic ganglia. Cortical neurones

Smooth ms Cardiac muscles

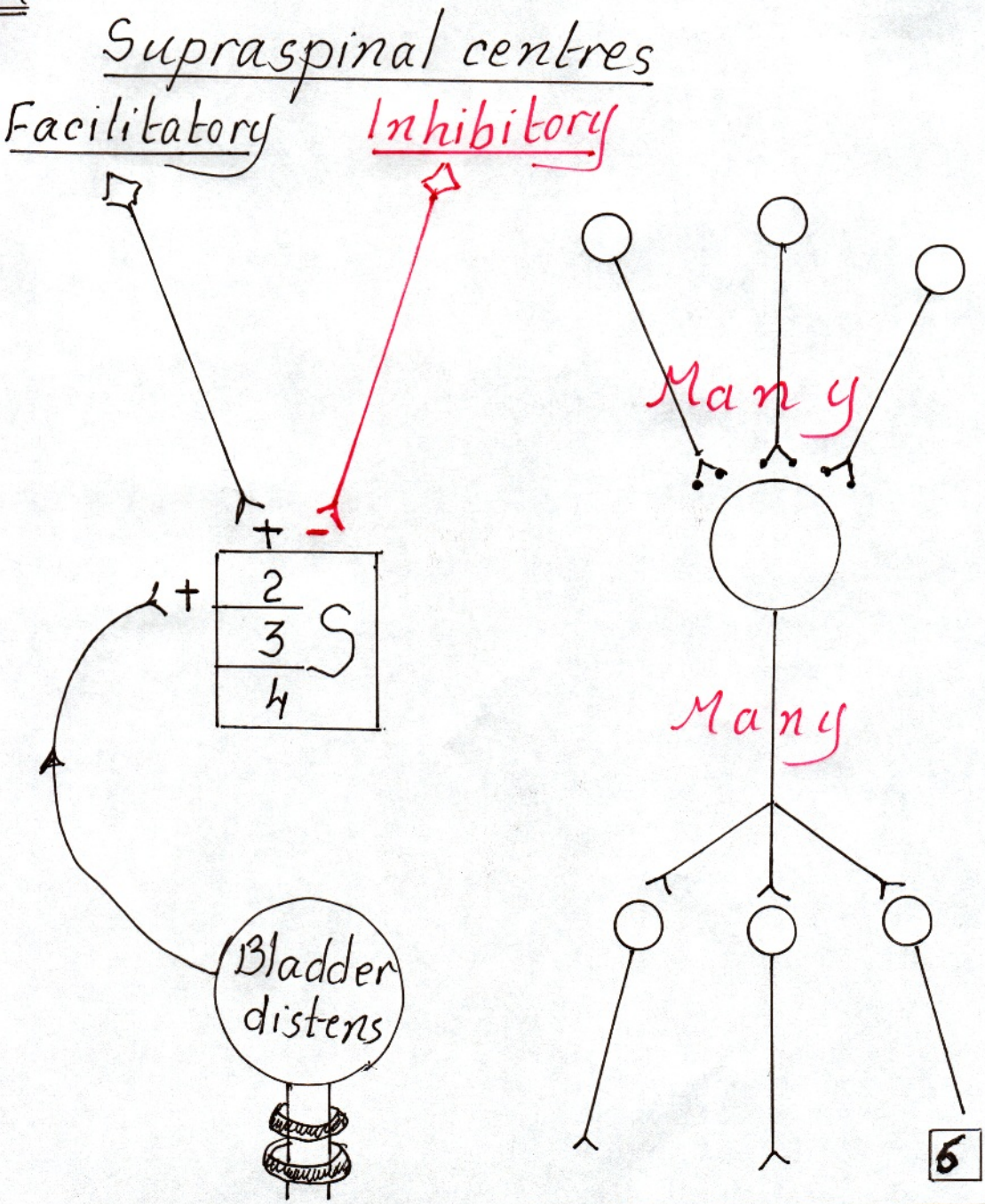
Slow EPSP ↓ $K^+$ conductance ↑ Slow IPSP

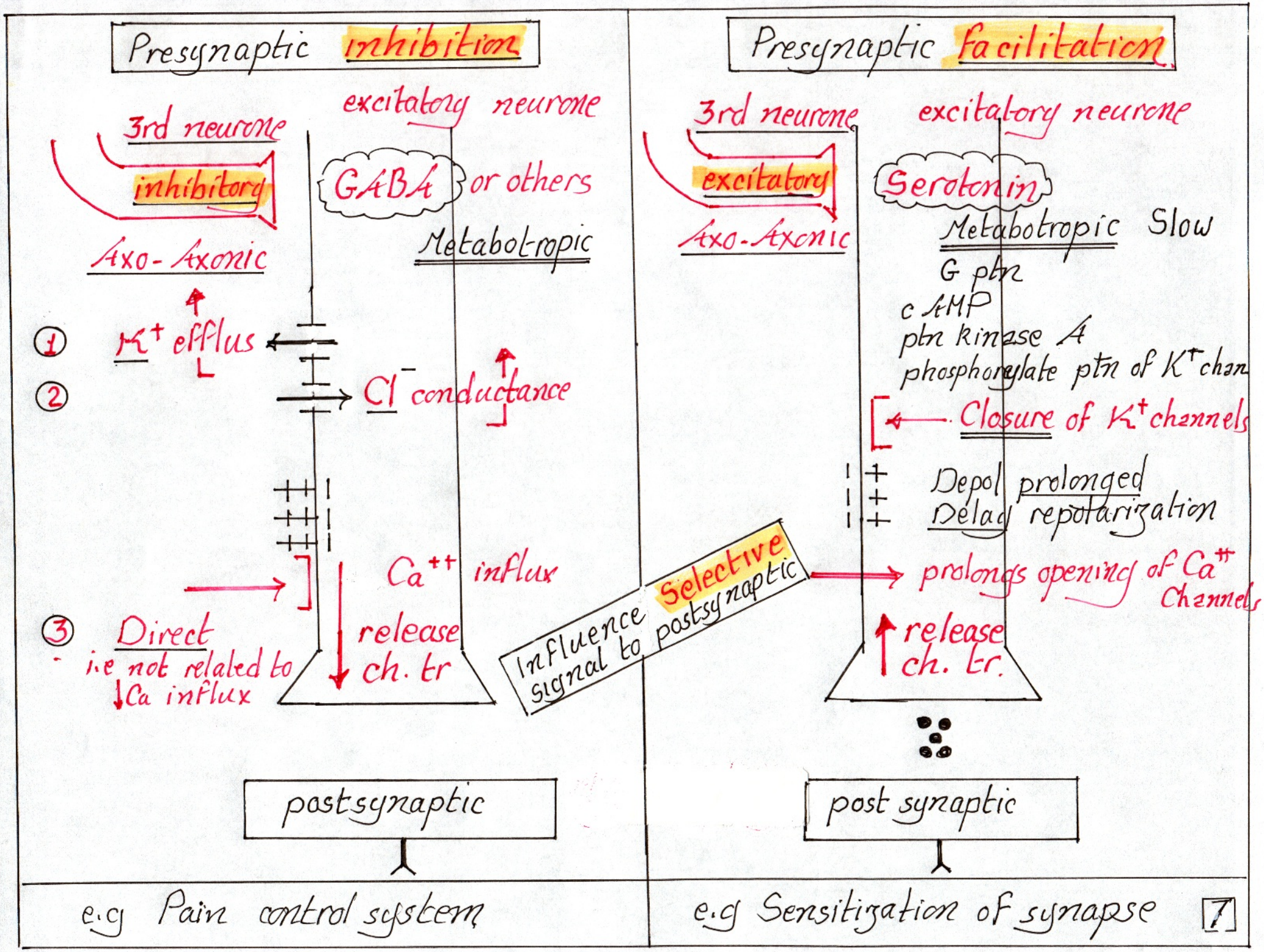
Notes • GPSP Algebric sum of EPSP & IPSP
At one neurone

Results Inhibition, Excitation, A pot or no changes

- In motor neurone Axon hillock most excitable
  lowest threshold 1st to fire in Both directions
  Down Axon Antrograde
  Back to s.oma i.e retrograde to wipe electrical activity of cell for new activity

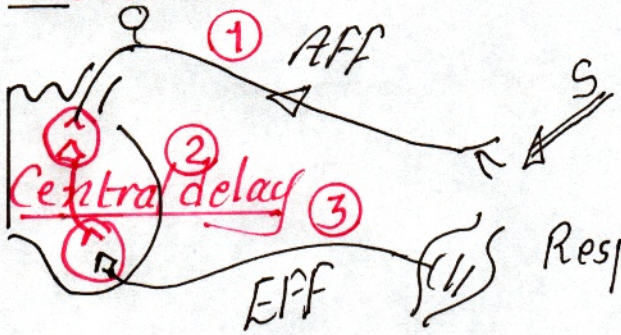
e.g Micturition




Presynaptic inhibition
3rd neurone
inhibitory
Axo-Axonic
excitatory neurone
GABA or others
Metabolotropic
① K+ efflus
② Cl− conductance
③ Direct
i.e not related to
↓Ca influx
Ca++ influx
release
ch. tr
postsynaptic
e.g Pain control system
Presynaptic facilitation
3rd neurone
excitatory
Axo-Axonic
excitatory neurone
Serotonin
Metabotropic Slow
G ptn
c AMP
ptn kinase A
phosphorylate ptn of K+ chan
Closure of K+ channels
Depol prolonged
Delay repolarization
Influence Selective
signal to postsynaptic
prolongs opening of Ca++
Channels
release
ch. tr.
post synaptic
e.g Sensitization of synapse
7

## Characters of synaptic transmission:

1. **Forwards direction** from Pre to post
2. **Synaptic delay** 0.5 msecond




Number of synapses = Central delay

Number of interneurones = Synapses − 1 (0.5)

3. **Fatigue** Cause: Rapid Repeated stim.

Mechanism: presynaptic / postsynaptic ↓ ch. Tr / R response (exhaustion / inactivation)

Importance: prevents overexcitation of CNS e.g epileptic fit

4. **Synaptic plasticity** 1966

Ability of change | strengthened weakened | short or long

According to demands

Based on past experience

ⓐ Short term
- inhibition of (habituation)
- Post tetanic Potentiation
- Sensitization

ⓑ Long term
- Potentiation LTP
- Depression

Discuss
- presynaptic
- post synaptic
- stimulus
- response
- mechanism
- example (Importance)

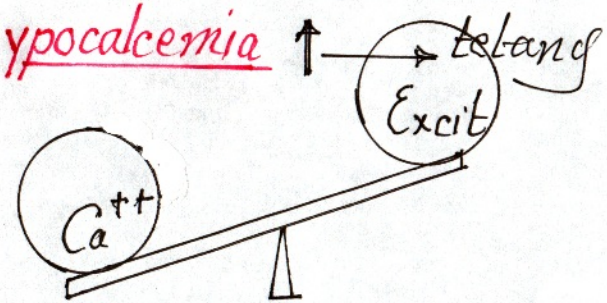
Presynaptic
Postsynaptic
Ionic bases

# Factors affecting synaptic transmission

## A Composition of internal environm. (4)

P

- Ions
  - Alkalosis ↑ → convulsion
    - due to -- $Ca^{++}$
    - e.g Hyperventilation
  - Acidosis ↓ → coma
    - due to ++ $Ca^{++}$
    - e.g DM
- Hypoxia
  - 3-5 second → coma
  - prolonged → brain damage
- Hypoglycemia ↓ → coma
  - Glucose only brain fuel.
- Hypocalcemia ↑ → tetany




## B DRUGS (3)

theophyline ↑
theobromine
caffeine

Analgesic
Hypnotic
Anesthetic

↓ synthesis, release & uptake

Strykrnine ↑
- competes with inhibitory ch. tr at postsynaptic
  - → convulsions, spasm & death
- used hoarse racing

## C Diseases (2)

### Neurotoxins

Tetanus toxins

Blocks release of GABA & Glycine

→ Spastic paralysis

lock jaw Arched back

prevention tetany toxoid vaccine

### Botulism toxins

Blocks release of Ach

→ Flaccid paralysis

ptosis, diplopia, dysarthria dysphagia fatality 5-10%

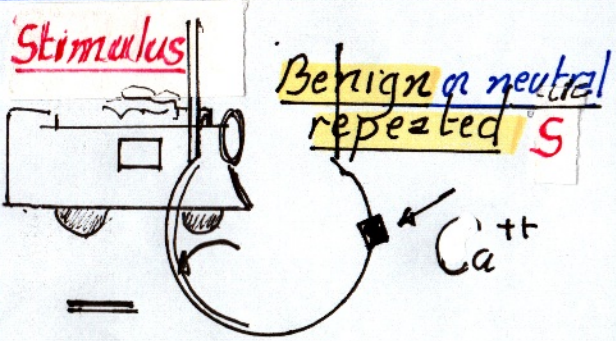
ttt antitoxin

Theraputic uses of Botox

- Facial ms to remove wrinkles.
- achalasia of esophag sphincter

## Short term

### Short term inhibition ("habituation")




**Response**

Gradual loss of response

**Ionic basis**

gradual Inactivation of $Ca^{++}$ channels

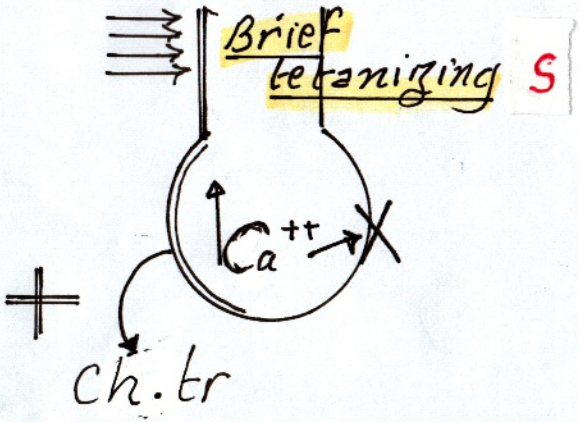
→ −− $Ca^{++}$ in presynap

→ −− release ch. tr.

**Importance**

Noises

### Posttetanic Potentiation (PTP)




Continues to discharge few seconds or min. after

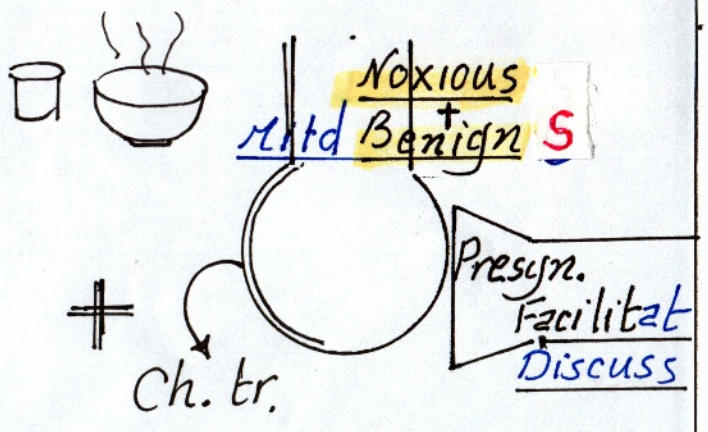
Weak $Ca^{++}$ pump

→ ++ $Ca^{++}$ in presynaptic

→ ++ release ch. tr.

**Immediate** memory

### Sensitization



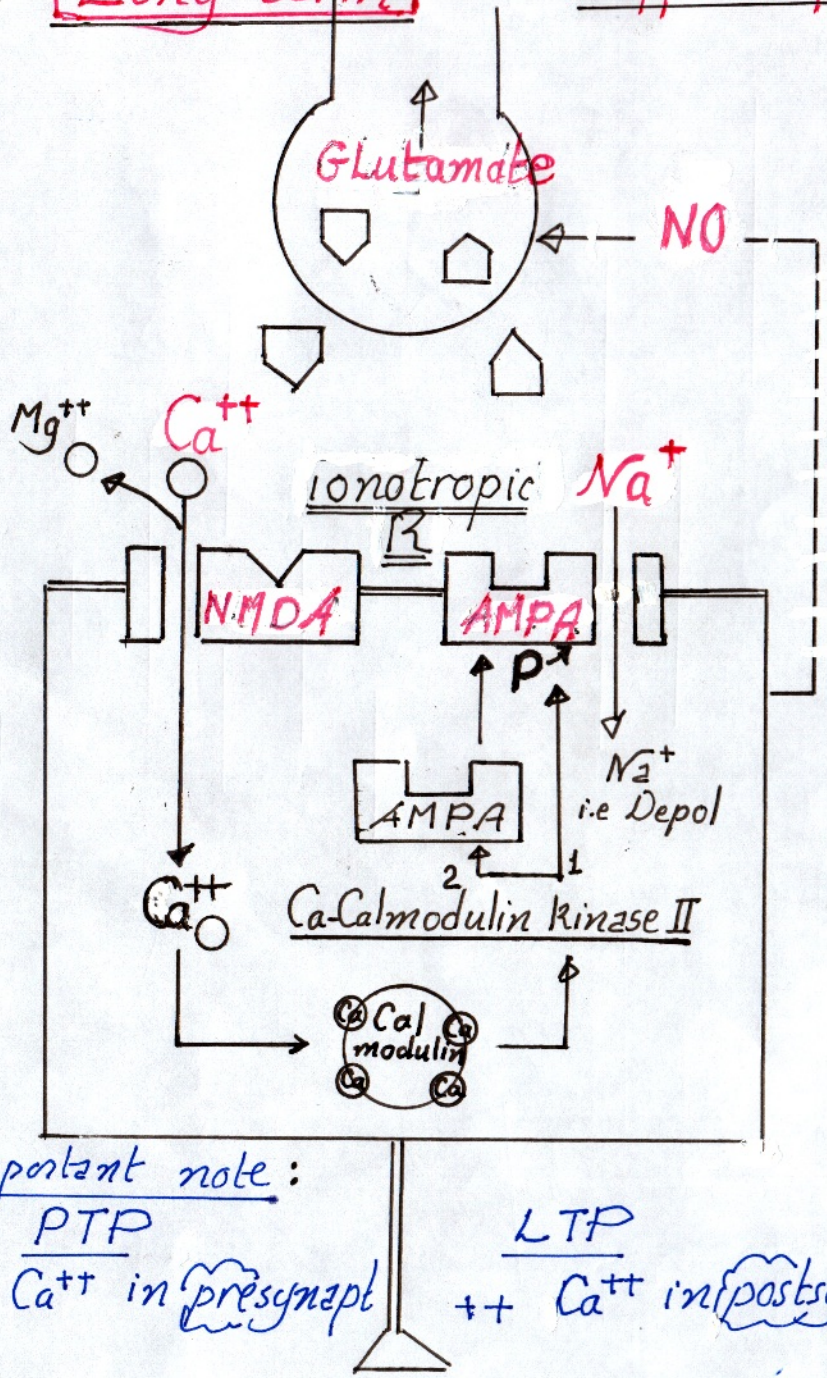

Prolonged augmented response

Presynaptic Facilitation

i.e prolonged opening of $Ca^{++}$ channels

**Short term** memory

# Long term — Hippocampus




Important note:

PTP

++ $Ca^{++}$ in presynapt

LTP

++ $Ca^{++}$ in postsynapt

Persistant strengthening of synapt connection

**Long - Term potentiation** LTP

Glutamate released from presynaptic neurone binds to AMPA & NMDA receptors on postsynaptic membrane leading to

Activation of AMPA receptors → Depol. which:

removes $Mg^{++}$ block on NMDA receptors channels

→ $Ca^{++}$ entery

→ $Ca^{++}$ calmodulin

→ activates $Ca^{++}$/ calmodulin Kinase II

which, in turn,

1. phosphorylates AMPA receptors increasing its conductance to $Na^+$
2. moves more AMPA receptors into the synaptic membrane.

Persistent weakening of synaptic connection

**Long term depression**

Ionic bases $Ca^{++}$ enters via NMDA -- AMPA receptors in postsynapt mem.

e.g Hippocampus الذعر

AMPA Adenosine MonoPhosphate/Adenylate

NMDA N Methyl - D Aspartate.