

## NOTES BASED ON PIOTR NOTES :- [CH-4]

29th Oct

### 4.1 THALAMOCORTICAL NETWORK :-

- Objective of the thesis :-

→ To provide understanding of the EEG changes related to voluntary movements and absence seizures. (by means of computer modeling).

Therefore, the model has to be based on real anatomical & physiological data.

- Explanation of SEMATOSENSORY AND MOTOR PATHWAYS OF ARM :-

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- Motor commands are generated in the primary motor cortex;
  - Then targeted to the muscles;
  - Sensory Information from muscles, skin and joints ascends to the relay in the thalamus.
  - Then reaches primary Sensory cortex.

- DETAILED EXPLANATION :-

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- The stimulus to initiate and complete voluntary motor action is provided by the motivational (limbic) system → which acts on the motor system.

- a) The motor command goes through the brain stem to the motor neurons in the spinal

cond and from there to the muscles.



b) Sensory I/Ps from skin, muscles & joints ascend to the thalamus, relayed to the somatic sensory areas.



c) From there,

Somatosensory information is transmitted to the motor cortex and is used to modulate motor performance.

d) Role of Thalamus → is not restricted to relaying somatic Sensory signals.

• Distinct sensory thalamic nuclei receive I/Ps about sensory modalities (audition, vision)

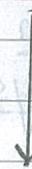


Therefore,

relay them to local regions of the cerebral cortex (auditory, visual)

Moreover,

• The motor nuclei of the thalamus transmit information from the cerebellum & basal ganglia to motor cortex.



[Part of the brain at the back of the skull which coordinates & regulates muscular activity]

[A group of structures

linked to the thalamus in the base

of the brain & involved in coordination of movement]

Therefore, the thalamus consists of not only of relay nuclei;

the other functional group are 'diffuse-projection nuclei'.



An example of the nucleus belonging to this group is Thalamic Reticular Nucleus (TRN)

→ it is critically involved in bringing out the rhythmic activities in thalamocortical nth.

#### • EXPLANATION OF CONNECTIONS BETWEEN TCR, RE & CORTEX :-

a) Each specific thalamic nucleus receives I/P from ascending specific afferents, then projects upon localized region of the cortex.

The cortex sends recurrent connections to both thalamic relay and reticular nuclei.

b) Thalamic relay cells send excitatory I/P to the reticular nucleus neurons.

The RE cells are connected to each other by means of dendrodendritic synapses and send back GABAergic inhibitory fibers to the TCR Cells.

c) Relay nuclei receive cholinergic modulatory IIP from the brain stem while,

Reticular nucleus receives cholinergic IIP from both the brainstem & basal forebrain.

NB :- In Diagram marked with pencil in Print Out.  
 [Explanation of Above Lines] →

NOTE :- P-21 [1st Para]

- Thalamus is the main relay station for sensory signals on the way to cortex.
  - ↓ it is also first station at which sensory signal can be blocked ⇒ when brain falls asleep or undergoes an absence seizure.

- The two functional modes ⇒ Relay and non-relay of the Thalamus :-

They are associated with 2 distinct modes of action potential generation by the thalamic neurons:-

a) Tonic firing (single Spike) Mode

b) Burst firing (oscillatory) Mode

a) Tonic firing mode is associated with the relay function of the thalamic cells.

↳ Because,

in this state, the incoming sensory information may be transmitted accurately to the context.

b) Burst mode is associated with synchronized oscillations in the thalamus.

↳ During which,

transmission of incoming sensory signals is depressed.

↳ These two modes of activity come from the properties of the specific ionic current.

#### 4.2 CELLULAR MECHANISMS :-

NB :- • Burst firing is present at hyperpolarized levels.

• Tonic firing at depolarized levels.

→ The firing pattern is being controlled by the level of membrane potential.

• Hyperpolarization is a change in a cell's membrane potential that makes it more negative.

→ It is the opposite of depolarization.

- Hyperpolarized state promotes burst firing.

and,

When a cell is relatively depolarized, it generates a train of single spikes (action potential) ↳ Tonic firing.

### IMPORTANT POINTS :-

- a) Single spikes are brought out by Sodium & Potassium Currents.

Burst consists of a calcium Spike (sometimes called a low threshold spike [LHS]) and 3 to 10 fast action potentials on top of it.

'LHS' is generated by activation of a  $\text{Ca}^{2+}$  current which is known as the low-threshold or transient ( $I_T$ ) calcium current.

→  $I_T$  calcium Current shows both activation and inactivation.

→ [It deals with halting of biological activity]

[To convert certain biological compound into biologically active derivatives.]

(It is a chemical substance derived from another substance either directly or by modification or partial substitution)

- In TCR cells activation occurs at membrane potentials  $\rightarrow$  positive to approx.  $-65\text{ mV}$

↳ Inactivation becomes complete at membrane potentials  $\rightarrow$  positive to approx  $-70\text{ mV}$ . and is removed at hyperpolarized levels  
 $\downarrow$   
 (Negative to  $-70\text{ mV}$ )

- Kinetics of inactivation  $\rightarrow$  Slow Activation  $\rightarrow$  Fast. (Relatively)

- a) If a cell is depolarized <sup>(+ve)</sup> from resting potential (around  $-70\text{ mV}$ )  $\rightarrow$  where  $I_T$  current is almost completely inactivated  $\Rightarrow$  Cell will respond with the fast Sodium-potassium Spikes.

- b) If a cell is hyperpolarized <sup>(-ve)</sup> first  $\rightarrow$  inactivation is removed.

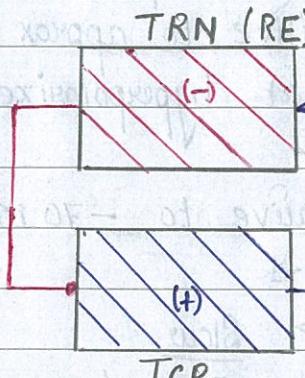
Release from  $\xrightarrow{\quad}$  Subsequent depolarization or hyperpolarization leads to Activation of  $I_T$  Current

$\downarrow$  which then slowly inactivates

$\downarrow$   
 Generating a low threshold spike with a burst of fast action potentials.

## 4.3 GENERATION OF THALAMOCORTICAL RHYTHMS :-

P-23 Explanation :- Generation of Thalamic Rhythms :-



- At freq around 10 Hz, Spindle waves are generated through interaction between GABAergic (RE) cells and TCR neurons.

- RE Cells inhibit (-ve GABA) ∵ inhibit the TCR cells.

which fire 'Hebound bursts' following GABA<sub>A</sub> IPSPs.

↓ (Inhibitory)

Post Synaptic Potential

These 'Hebound bursts' excite the RE cells and the cycle repeats itself.

Blocking GABA<sub>A</sub> Receptors results in disinhibition of the RE cells → which increase their discharges → and activate GABA<sub>B</sub> Receptors in Relay Neurons.

Consequently, N/W activity is transformed from 10 Hz to 3 Hz seizure like activity.

IMPORTANT POINTS:-

25th Oct

- 1) The low threshold  $\text{Ca}^{2+}$  spikes underlying burst firing in thalamic cells are essential for the rhythmogenesis of the activity in the alpha frequency range in the TCR-RE nW.
- 2) The TCR cells excite the RE cells with glutamatergic AMPA synaptic transmission.  
 RE Cells are inhibitory  
 and hyperpolarize the TCR Cells  
 by means of GABA inhibition.  
 This hyperpolarization is brought out mainly by the fast GABA<sub>A</sub> receptors in the TCR cells. ( $\because$  GABA<sub>B</sub> receptors have higher threshold for activation)
- 3) The GABA<sub>A</sub> receptor mediated hyperpolarization, enabling the TCR cells to fire 'tiebound bursts' which excite again the RE cells → the cycle repeats itself giving rise to rhythmic activity.
   
 The freq (7-14Hz) of the rhythmic activity is largely determined by time courses of both excitatory and inhibitory post synaptic potentials.
- 4) The role of the inhibitory connection between the RE cells is to control the discharges of those cells.

5) This can be put in evidence by application of the bicuculline that blocks GABA<sub>A</sub> receptors through which the RE-RE inhibition is mediated.

(Bicuculline is a compound that is a light sensitive competitive antagonist of GABA<sub>A</sub> receptors.)

↳ [a substance which interferes with the physiological action blocks of another)

It results in disinhibition of the RE cells and an increase of discharges of those cells.

Such prolonged discharges may activate GABA<sub>B</sub> receptors in the TCR cells.

→ GABA<sub>B</sub> receptor mediated hyperpolarizations (have longer duration)  
+ efficient in the removal of the inactivation of the I<sub>T</sub> current in the TCR cells resulting in larger bursts that excite the RE cells further.

ALSO,

the long duration of GABA<sub>B</sub> postsynaptic potentials is responsible for slowing down the oscillations from 10 - 3 Hz.

↳ leading to absence seizures.

(11)

6) It is observed that,

[a substance that fully activates the receptor that it binds to]

o injection of selective agonists of GABA<sub>B</sub>  
 Receptors → results in spike & wave discharges.

o GABA<sub>B</sub> receptor antagonists diminishes the occurrence of SW in dose dependent manner.

[is a substance that binds to a receptor but does not activate & can block activity of other agonists.]

NB :- Thalamocortical projections transfer thalamic activity to the cortical cells while, corticothalamic feedback plays a major role in synchronization of thalamic oscillations.

