Chapter: 5

The Neural Substrate for REM Sleep

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Sleep is biological state and occupies about one third of our life. We know since ages about two kinds of sleep but the scientific discovery of rapid eye movement (REM) sleep was made in 1953 by Aserinsky and Kleitman. Now we classify sleep as REM and non-REM sleep. REM sleep is also described as paradoxical sleep, desynchronized sleep, active sleep and dream sleep. Each of these terms reflects slightly a different emphasis on what its essential defining features are.

REM sleep in adult animals including human has vivid manifestation. The features of REM sleep are described below:

1. High frequency, low amplitude cortical EEG is present in both REM sleep and wakefulness making the identification challenging. These are also described as desynchronized cortical EEG.
2. The EEG of hippocampus is increased in size at a 4-10Hz (theta frequency). An absence of activity in antigravity muscles (muscle atonia) during REM sleep makes it distinct from NREM sleep and wake state. Only the diaphragm and extraocular muscles retain their tone during REM sleep. The atonia of REM sleep may be interrupted by muscle twitches and eye movements.
3. The rapid eye movements are distinguishing features of REM sleep. Singlet or clusters of REM are seen in electrooculogram (EOG) recording.

4. Another sub cortical phenomenon which is characteristic of REM sleep is ponto-geniculo-occipital (PGO) waves.

5. There are irregularities in respiration, heart rate, blood pressure and thermoregulation.
6. Penile erections are observed during REM sleep.
7. Most of the dreams occur during REM sleep.

The EEG, EMG and EOG signs of REM sleep can be explained in terms of changes in neuronal activity. The low voltage neocortical EEG results from the asynchronous activity of thalamocortical projection neurons. The theta rhythm is produced by CA1 pyramidal neurons, in the dentate gyrus and in the medial entorhinal cortex. This theta rhythm is primarily driven by the activation of specific cells in reticularis pontis. The loss of tone in antigravity muscles results from a cessation of discharge in the motor neurons supplying these muscles. Intracellular recording have demonstrated that this cessation is due to a hyperpolarization of the motor neurons. It is brought about by release of glycine onto the motor neurons. In addition to this there is disfacilitation of motor neurons by noradrenergic and serotonergic inputs The PGO waves are generated in the pons and project to lateral geniculate and other thalamic nuclei and to the cortex. PGO spikes are one of several phasic events of REM sleep. The neuronal population responsible for genesis of PGO waves are located in caudolateral part of the peribrachial area. Activation of REMs generating cells in the periabducens area stimulate oculomotor neurons in the abducens nucleus which activate oculomotor muscles to cause the expression of REMs associated with REM sleep.

Neural mechanism of REM sleep: The neural sites for the generation of REM sleep and its phenomenon have been studied using a wide variety of techniques which include transection, lesion, unit recording,

microinjection and molecular biology techniques. The transection studies have shown that the pons and caudal midbrain region are both necessary and sufficient to produce some of the basic phenomena of REM sleep. Electrolytic and subsequently chemical lesion studies have identified various discrete neuronal groups taking part in the generation of REM sleep and its features. Chemical natures of these neurons have been identified along with their connectivity. Single neuronal recording from these chemically different neuronal groups have shown different neuronal discharge pattern during REM sleep. The locus coeruleus (LC) neurons, the dorsal raphe neurons are silent whereas the cholinergic neurons are active during REM sleep. The identification of various neurotransmitters (acetylcholine, norepinephrine, serotonin, glutamate and GABA) and their interplay in the neuronal network is easing our understanding of REM sleep and its signs.

The generation and maintenance of REM sleep involves a complex system of neuronal interaction. Distinct neuronal groups within the brain stem are responsible for the expression of individual events that characterize REM sleep. The expression of REM sleep signs is a result of significant reduction in aminergic tone and a relatively high level of cholinergic tone. The induction of REM sleep is facilitated by two types of cholinergic cells in PPT and LDT. REM-ON neurons increase their firing rate during the transition periods from wakefulness to NREM and then to REM sleep. The second group of neurons wake-REM-ON cells increase their firing rate during both wakefulness and REM sleep.

Neurons in the LC and dorsal raphe have similar discharge patterns during sleep-wake cycle. During waking the discharge is quite regular, slows down during NREM sleep and cease during REM sleep. Lesion of LC neurons does not affect REM sleep. The minimal discharge rates suggest some gating role in REM sleep. These cells are often described as REM-

OFF neurons. The inhibition of these REM-OFF cells during REM sleep could be due to active inhibition by GABA. GABA amount has been shown to be increased in raphe and LC during REM sleep.

Much of the mechanisms that drive this very complex behavioural state of REM sleep are localized to the RPO nucleus of the pons and caudal midbrain. It should be emphasized that in the intact animals many brain areas other than the pontine structures participate in the control of REM sleep state. The role of non brainstem structures like cerebellum, frontal cortex, amygdala and septum can not be ignored in expression REM sleep. Therefore there exists a dynamic interaction between the forebrain and pons in molding and timing many phasic events of REM sleep like penile erection and dream.