

HYPOTHALAMUS & SLEEP:

- Homeostasis: keeping the internal environment within the normal range and this is the main function of the hypothalamus.
- Two regulatory systems that work on homeostasis:
1) Endocrine 2) Nervous system
- The major link between the endocrine and nervous system are the hypothalamus and pituitary gland
- The most important function of subcortical regions:
Internal reflexes

- **Hypothalamus function is related to :**

- 1)endocrine function 2)calorie balance
- 3)osmolarity balance 4) Thermal regulation
- 5)autonomic balance 6)somatic movements
- 7)Affective behavior 8)memory
- 9)Sleep.

- **Connections of hypothalamus:**

Hypothalamus is related to most area of the brain **especially** the subcortical and limbic system.

While talking about midbrain and reticular formation we confirm that there is control from hypothalamus over their functions.

Direct connection of hypothalamus to the cortex (telencephalon) doesn't occur frequently; but when it occur these connections happen through the Limbic system...But there is direct connection between hypothalamus and sub cortex.

- **Anatomy of the Hypothalamus:**

Located ventral to the dorsal thalamus
you can find it between midbrain and thalamus.

Hypothalamus subdivisions:

- 1) preoptic area

2) Periventricular zone

3) Medial zone

4) lateral zone

so in this section we can see the subdivisions From anterior to posterior.

***Preoptic area, which involve:**

- **Medial preoptic** : LHRH (luteinizing hormone releasing hormone)

(contain neurons that manufacture gonadotropic releasing hormone)

Medial preoptic is larger in females than males.

- **Lateral preoptic** : this part has inputs on motor cortex (directly, indirectly) to regulate our attention .

E.g: when you are hungry you will concentrate your attention and movement toward food

It controls motor movements for survival (Hunger and feeding) and non-survival skills, as well as emotional skills form limbic system and associated behavior.

From the Fundamental neuroscience book:

(The medial preoptic nucleus contains neurons that manufacture gonadotropin-releasing hormone (GnRH). GnRH is transported along the tuberoinfundibular tract to capillaries of the hypophysial portal system and thence to the anterior lobe of the pituitary gland, where it causes the release of gonadotropins (luteinizing hormone and follicle-stimulating hormone). Because gonadotropin release is continuous in males and cyclic in females, the **medial preoptic nucleus of males tends to be more active and consequently larger than that of females**).

- **Supraoptic region:** contains 4 nuclei
 - 1) **supraoptic part:** that release oxytocin and vasopressin (ADH)
 - 2) **Suprachiasmatic part:** that will take input from the retina and this nucleus mediate circadian rhythm (these being the hormonal fluctuations secondary to light-dark cycles).
 - 3) **Anterior nucleus:** involved in maintenance of body temperature
 - 4) **Paraventricular nucleus:** its neurons contain or release oxytocin and vasopressin (ADH) “like the supraoptic nucleus”

Main part of oxytocin and vasopressin will go to **posterior pituitary** through circulation and have peripheral effect. But, also it has central effect and can influence mood and behavior.

- When going posterior we have **Tuberal region**:

- 1) **Arcuate nucleus** : the primary location of neurons that contain releasing hormones either stimulatory or inhibitory on the anterior pituitary.
- 2) **Ventromedial nucleus**: considered as the satiety center of the brain, activation of this nucleus lead to satiety feeling and lesion or damage to this nucleus lead to seeking for food and excessive gain of weight.
- 3) **Dorsomedial nucleus** : related to anger and sham Rage (الغضب الشديد) which is an aggressive behavior... and lesion to this nucleus lead to decrease aggression.

- **The last part which is the Mamillary region**, which contain:

1) **Posterior nucleus**: for heat conservation

2) **Mamillary nucleus**: for learning and memory... contribute and help in the conversion of short term memory into long one.

- **prefrontal cortex function in two words**: plan for action (Plan center/social behavior center/ prediction center/ personality center/ inhibition for emotion) (all of these functions are under the function of planning)

-E.g.: when saying that this person is highly motivated, hard worker all this follow the plan action.

Another example, when comparing two personalities the first one is highly aggressive: there is fast activation of subcortical and emotional regions, and not good inhibition from cortex, prefrontal cortex doesn't plan..... While other person: if you try to irritate him he is calm so he has a good prefrontal cortex.

*planning and processing and predicting future consequences → prefrontal cortex

Functions of Prefrontal cortex :

1)planning

2)inhibition

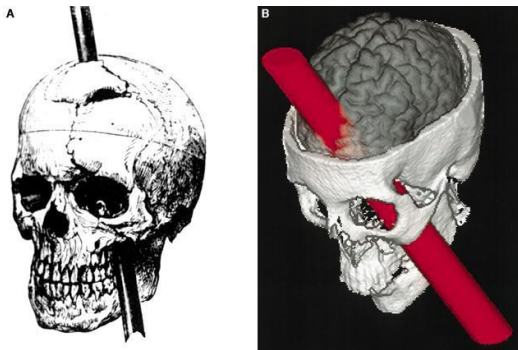
3)selectivity (I will do this\i will not do that)

- What helps the prefrontal cortex in the action of planning and prediction is the cerebellum.
- Note: cerebellum contributes in planning and memory.
- **Damage to prefrontal cortex:**

In **severe anxiety disorders** (like persons who are afraid from going out because of germs that might make them sick so they decide to stay at home) so in these cases we suggest to make a **surgical remove the prefrontal cortex**, but now drugs are substituted.

Phineas cage:

Phineas P. Gage (1823 – May 21, 1860) was an American railroad construction foreman remembered for his improbable survival of an accident in which a large iron rod was driven completely through his head, destroying much of his brain's left frontal lobe, and for that injury's reported effects on his personality and behavior over the remaining twelve years of his life—effects so profound that (for a time at least) friends saw him as "no longer Gage." (the dr said the same information, and I used Wikipedia, too).



- **Prefrontal cortex damage:**

- 1) Lack of foresight
- 2) Frequent stubbornness
- 3) Inattentive and moody
- 4) Lack of ambitions, sense of responsibility, sense of propriety (rude)
- 5) Less creative and unable to plan for the future
- 6) Impulsive behavior that can threaten their lives (they might think of jumping from the window and this result in paralysis)... pathological impulsive behavior

remember that misbalance in modulators and neurotransmitters (like ADHD → NE) also affect behavior !

***Sleep:**

- Why sleep is important?

To regenerate and reestablish and reorder the connections made before and consolidation of memory.

We actively go to sleep not passively.

That means that we don't go to sleep because we have no energy left, but to regenerate

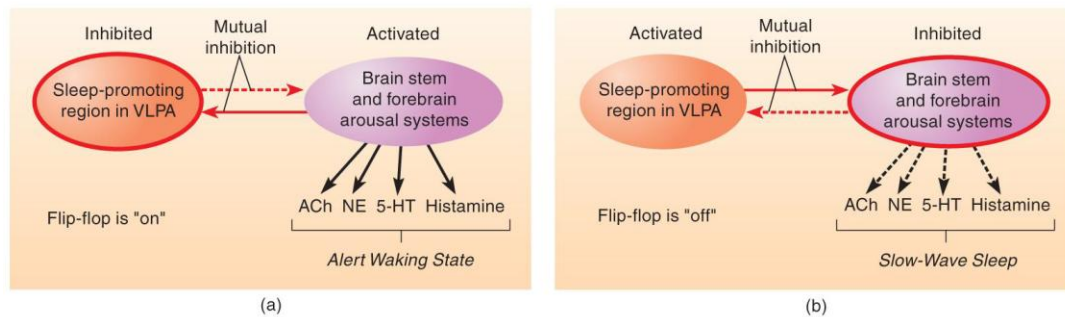
and reestablish and reorder the connections after collecting information all along the day. Some people says that sleeping also stores energy, but actually its not the main reason for sleeping.

Reticular activating system came from reticular formation and go to the cortex especially Diencephalon and cortex and activate it.

Amine neurotransmitters that stimulate Awake:

NE from locus coeruleus / Histamine/ Dopamine /Serotonin/ Ach from nucleus basalis & brain stem

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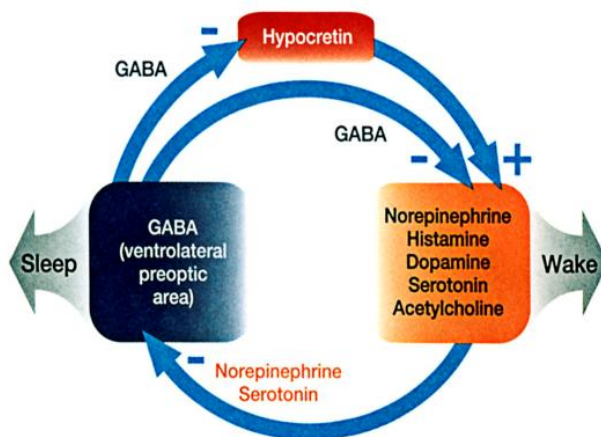


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Monoamine neurotransmitters are the main activating component . → awakening
 inhibitory component : GABA from **ventrolateral area**. → when inhibiting enough → sleep

Any Misbalance to the right : Awake and this can lead to **insomnia**

Any misbalance to the left side: lead to **narcolepsy**



Hypocretin :secreted centrally from the hypothalamus and it actively activate each center, increasing their firing.

also collaterals from other sensations helps in keeping you awake, such as walking, drinking water, etc.

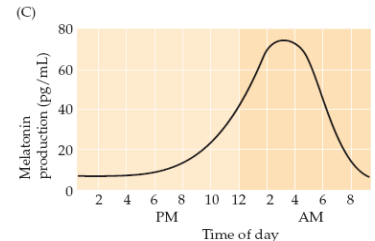
Melatonin:

pineal gland Neurotransmitter:

-Play a role in circadian and seasonal rhythm.

-Inhibitor for waking center and activating for sleeping center.
its written in the slides that :

((released at night-inhibited during the day (circadian regulation); initiates and maintain sleep; treat symptoms of jet lag and insomnia))



Pineal gland :

A gland attached to the dorsal tectum; produces melatonin and plays a role in circadian and seasonal rhythms.

- **function:** in addition to inducing sleep , its **major** function is in regulating circadian rhythm especially for a long time.

so increasing its concentration for a long time will not induce more sleep . It will help in the beginning in getting cercardean rhythm and has no further effect if we increase its concentration.

-**suprachiasmatic nucleus** of hypothalamus is concerned with circadian rhythm and normally it will send inhibitory signals to pineal gland... **when light fades** the activity of suprachiasmatic nucleus decrease and the activity of pineal gland increase and this increase melatonin level and this **induce sleep**.

-**when removal occur to suprachiasmatic nucleus...** person who sleep for 8 hours he will continue to sleep for 8 hours but the difference is that he become every now and then sleep every half an hour... what is the problem here that there is circadian rhythm but with 20 hour cycle ??

(Most sleep researchers consider the suprachiasmatic nucleus to be a “Master clock”. Evidence for this conclusion is that removal of the SCN in experimental animals abolishes their circadian sleep-wake cycle)

Note: Serotonin induces awakening ... so SSRI side effect is that it induces sleep.

Increase serotonin increase sleep load indirectly (the need for sleep increase).

Note that melatonin is synthesized from serotonin, so in some groups of people SSRI, which will cause an increase in serotonin levels, will increase melatonin levels. and in some groups, SSRI affect melatonin as they affect serotonin

***Effect of Coffee:**

-while working, break down for ATP occurs and this increase adenosine, and it has **A1 receptor (G-protein coupled receptor {Gi})** and it is **inhibitory for cAMP**. In brain stem A1 receptors are presented on Ach neurons and this inhibit Ach neurons and induce sleep.

-Caffeine and theophylline presented in *coffee* and *Tea* are **A1 receptor antagonist**.



***Q) is sleep voluntary ??**

you Can not to sleep, but remember that it's a balance !! you can train yourself to stay awake up to a certain limit, then the load increase and then you can't prevent sleep.

In Animals; if we prevent sleeping

- 1)loss of memory
 - 2)then they start to loose weight despite that they are eating more
 - 3) then they die
- rats die within 7-8 days, while horses die within 10 days.

Many people tried not to sleep, and the Guinness Record is 18 days and 17 hours (449 hours)

(used wikipedia to get the actual number)

Please refer to the slides.

Good Luck :D