

NEURAL MECHANISMS OF SLEEP (p.1)

1. Revisitation of Bremer's 1936 "Isolated Brain" Studies

Transected the brain:

a. Cut between the medulla and the spinal cord ("encephale isole")

Note: recall that in the 1930s the **"passive" brain** being driven into W was the major hypothesis

By cutting the CNS at this level, still have 4 of the 5 major senses still coming into the brain via cranial nerves

so...Cat's brain should still show what re. Sleep (REM&SWS) & Wake?
And, what did it show?

b. Cut between the inferior and superior colliculi ("cerveau isole")

By cutting the CNS at this level, would only have 2 of the 5 senses still coming into the brain via cranial nerves

so...Cat's brain should show what re. Sleep & Wake?
And, what did it show?

What was Bremer's (incorrect) interpretation of these data?

That indeed the brain was "passive", was driven into W by incoming sensory stimulation, w/o which brain lapses into sleep...

But what if there was another explanation?.....

What if there were a brain center just posterior to cut made in midbrain and just anterior to cut made in hindbrain, and what if that center generated wakefulness (and REM)?

2. Reticular Activating System

This structures generates wakefulness, alerting

Discovered in late 1940s by UCLA researchers Moruzzi & Magoun

Core of diffuse neurons lying midbrain+hindbrain

Receives information from many incoming sensory pathways

Sends axons to many areas of forebrain (incl. thalamus, basal ganglia, and basal forebrain)

If stimulate RAS while S is asleep ---?

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2. Reticular Activating System (cont.)

If stimulate RAS while S is awake ---?

If lesion the RAS ---?

What happens if you cut all the incoming sensory signals to the RAS but leave the RAS itself intact?

Thus, sleep and wake are active processes that are generated from within the brain itself, independent of (although affected by) sensory stimuli
Sleep and wake are not passive processes as once thought...

Why does RAS send so much output to:

Basal ganglia?

Thalamus?

Basal forebrain?

3. Raphe Nuclei

These are midline structures in the brainstem (near caudal RF)

Neurons are the major source of **5HT** in the brain

Serotonin seems to inhibit the RAS (and that seems to allow SWS to occur)

If lesion the Raphe Nuclei ---?

Give PCPA (parachlorophenylalanine) --- totally blocks synthesis of 5HT

What effect does it have on sleep?

If give S tryptophan (precursor to 5HT) ---?

4. Nuclei in Pons/Medulla that Control REM Sleep

If transect brain anterior to pons --- no REM

If transect brain posterior to pons --- still see REM (alternating with SWS)

PGO spikes precede the onset of REM sleep (Pons, lateral Geniculate nucleus, Occipital lobe)

Locus coeruleus (in pons regions):

If lesion just ventral to LC --- abolishes REM sleep

If stimulate LC --- induces/prolongs REM sleep

Neurons in LC are active only during REM sleep

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4. Nuclei in Pons/Medulla that Control REM Sleep (cont.)

Locus Coeruleus (cont.)

Neurons in this nucleus use **ACh**

Cholinergic agonists --- induces/prolong REM sleep (e.g. muscarine)

Cholinergic antagonists – reduce/block REM sleep (e.g. antidepressants)

Specialized nuclei in area of pons & medulla that control various aspects of REM sleep:

To generate PGO spikes

To produce cortical EEG desynchronization (**peribrachial area**)

To generate hippocampal theta waves (5-8 Hz)

To produce muscle twitches in face, extremities

To produce REMs

To produce skeletal muscle atonia (just ventral to LC)(**subcoerulear nucleus**)

To produce SNS arousal (cardiorespiratory irregularities)

If lesion **subcoerulear nucleus** --- abolishes muscle atonia normally seen in REM
Jouvet's cats got up and acted out their “dreams”(presumably)

If stimulate SN --- profound atonia (descending axons in spinal cord terminate on interneurons (Renshaw cells) that then inhibit alpha motor neurons --- skeletal muscle paralysis)

Note: this system uses **nor-epinephrine** as a NT

Peribrachial area sends axons to RF --- which, in turn, sends axons to basal forebrain (using ACh) --- desynchronous beta EEG in cortex

PB area also --- PGO spikes and REMs

PB area also --- activates the SN --- muscle atonia

5. Basal Forebrain Region

BFR and **anterior hypothalamus** are together implicated in initiating sleep

Tumors/lesions in this area --- difficulting initiating sleep

Neurons in this area are active only during sleep

Adenosine (peptide NT) levels increase with prolonged W; decrease with S

Adenosine inhibits cholinergic neurons of basal forebrain

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5. **Basal Forebrain Region** (cont.)

Adenosine (cont.)

Adenosine presumably --- drowsiness

Note: caffeine is an adenosine antagonist

Presumably there is a complex interaction between cholinergic (REM) and monoaminergic (noradrenergic and serotonergic) (nonREM) sleep controlling systems throughout the night's sleep

Anterior hypothalamus:

Patients with a sleep disorder called narcolepsy have great difficulty remaining awake and keep lapsing into sleep

They have normal neurons at birth (and do not exhibit narcoleptic symptoms until later in life, presumably after neurons in their anterior hypothalamus have begun to die off (possibly due to autoimmune effects))

These neurons use the NT **orexin/hypocretin** (is this a “wakefulness” NT?)

How does this NT interact with the NTs usually associated with arousal, such as norepinephrine, serotonin, and dopamine?

6. **Suprachiasmatic Nucleus of Hypothalamus**

area in brain of circadian timing mechanism

nucleus contains neurons that exhibit circadian cycles of electrical activity, metabolic activity, etc. (even when isolated from the rest of the brain)

neurons exhibit “endogenous” rhythm

Ss can be selectively bred to have shorter or longer rhythms

Transplant data

Receive major inputs from retina (signaling L&D), major zeitgeber is light

Note: SCN is not the only brain area that can do this circadian timing, because after lesioning the SCN Ss can still entrain to food or water availability (although can no longer do so to L/D)