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Bio Psych 302

October 11th

Sleep (continued)

Neural control of arousal

-neuro modulators

-ACh from the pons and basal forebrain, behavioral activity levels correlate with ACh levels. Desynchronize the EEG. Controls neural excitability. ACh high in REM sleep.

-NE from the locus coeruleus: vigilance, attention, amphetamines, produces arousal

-5HT from the Raphe nuclei (in pons)" correlates with sleep stages. Active during transitions out of REM sleep

-Histamines(tuberomammilary, nucleus, and hypothalamus): activate the cortex directly and indirectly(through basal forebrain ACh) Anti-Histamines promote drowsiness

-orexin: excitatory projections to cortex and many neuromodulatory centers. Wakefulness promoting. Indirect arousal effects, narcolepsy when damaged

Neural control of sleep

What makes us go to sleep?

-Adenosine hypothesis: adenosine accumulation during the awake period. Adenosine as a sleep promoting substance

Awake state

Astrocytes-(Glycogen fuel) ->Neurons

Astrocytes-(Adenosine) ->Neurons

Glycogen depletion->Increase in adenosine-> progressive increase in general inhibition-> increase in sleep tendency

Sleep state

Glycogen-> Astrocytes

Neural bases of sleep: SWS

Ventral lateral Preoptic Area (vLPOA)

Destruction->No sleep-> death

Stimulation-> drowsiness and delayed sleep

Mutual inhibition: vLPoA sends inhibitory projections in histamine, Ne, 5HT, ACh systems, and these systems in turn inhibit the vLPOA

Flip flop circuitry

On: Inhibited: Sleep promoting region in vLPOA-> activated: brain stem and forebrain arousal (alert waking state)

Off: Activated: Sleep promoting region in vLPOA-> inhibited: brain stem and forebrain arousal system(slow wave sleep

Turning the flip-flop on: orexin neurons

-orexin neurons active during awake state and project to the arousal system

ON: motivation to remain awake, stimulus driven, mediated by external signals, biological clocks, hunger signals

Neural control of sleep: SWS

Turning the flip-flip off: the adenosine hypothesis

-active state: glucose consumption from blood

-when blood glucose not sufficient, use glycogen

-glycogen-> (locally) glucose adenosine (nucleoside transmitter)

-Adenosine accumulate in those parts of the brain that were the most active

-Adenosine is inhibitory-> decrease brain stem activity-> increase vLPOA-> SWS

Off: also related to food consumption: satiety signals inhibit orexin neurons

Therapeutic manipulations of SWS

Prolonged total sleep deprivation leads to loss of body weight, temperature deregulation and eventually death

However 1 night sleep deprivation (total or 2nd half of the night) has antidepressant effect

Neural control of sleep: REM

-dreams=windows to the psyche, 65% sad, angry 20% happy excitement 1% sexual

Executive mechanism (switch, flip-flop)

-ACh levels are high during REM(and awake) from pons

REM Flip flop

-mutual inhibition: sublaterodorsal nucleus(SLD): ventrolateral PAG (vlPAG)

SLD projections can explain the normal features of rem

-Cortical Activation: Thalamus (dream content), Medical Pontine Reticular Formation (dream intensity)

-REM: Tectum (superior colliculi)

-Genital Activity: lateral Preoptic area (sexual preparedness)

-Atonia: medulla, prevents the acting out of dreams

-Lesion of paralysis neurons (in medulla) yield REM without atonia

When orexin neurons are damaged: emotional stimuli take over (cataplexy)

Amygdala and Hypothalamus

Biological rhythms

-internal clocks

 -Infradian (less than 1 day)

 -circadian (one day): sleep/wake cycle- 25 hours free running

 -supradian (more than one day): menstrual cycle

 -Circannual(one year): hibernation

-Suprachiasmatic Nucleus: Circadian/Supradian

 -time scale day-> month

-Small (8600 cells) within the hypothalamus

-Reset by light (retina-hypothalamic tract)" melanospin in special retinal ganglion cells projecting to SCN. LIGHT IS A zeitgeber (giver of time)

-Intrinsic and network rhythmic phenomena: SCN neurons by themselves or as a group in a dish have a circadian rhythm

-transplantation studies indicate the SCN uses chemical non-synaptic connection to affect its targets

SCN sends inputs to the SWS flip-flop. Inhibits vLPOA (decrease drowsiness), excite orexin neurons (promote wakefulness)

-SCN tickling= slow production of a self-inhibiting protein

-Normal sleep onset: 10-11pm, Average length 8 hours

-Advanced sleep phase syndrome: sleep onset 6-7pm, wake up 3-4am. Genetic mutation

-Delayed sleep phase syndrome: sleep onset 2-3am, wake up 10-11 am, genetic mutation

-> Normal genetic variations may explain normal variations in sleep onset time and sleep duration

Pineal Gland: circadian/Circannual

-in the midbrain (near cerebellum) secretes melatonin (during night)

-Melatonin: highest levels just before bedtime

-melatonin helps jet-lag(take before adjusted bed-time) side effects: depression, low sec drive, weight loss

-melatonin helps blind people to sleep better