from sleep to attention – lecture 9 – Oct. 13, 2010

the function of sleep IV – cortical homeostasis
Brain mechanisms for sleep and attention overlap extensively. For example, the cerebral cortex, where conscious perception is realized, undergoes radical changes in the patterning of synaptic potentials (as revealed by EEG/LFP recordings) between the lowest-attention state (stage ¾ non-REM sleep) and high attention states (waking, REM sleep).

Changes in sleep/wake state and attention are sometimes mediated by groups of neurons that are highly interconnected (brainstem reticular and thalamic reticular neurons).

The classroom can be very hot.

REM sleep appears to be associated with a maximal frequency of events associated with reorientation of attention (as in a startle response) while non-REM sleep is associated with a minimal frequency of such events. The frequency of such events in the waking state lies between the two sleep states. Oddly enough, a similar pattern is observed for brain metabolism.

Work attempting to uncover the function of sleep typically takes either a species-comparison approach, a sleep-deprivation approach, or an approach involving recording of specific neurobiological characteristics of sleep.
what do we know so far?

A definition for sleep that can be universally applied is difficult to come by. However, by combining the use of arousal thresholds, behavioral measurements (e.g., amount of movement or posture), and electrophysiological measurements a reasonably complete definition can be attained. Still, we end up with two very different forms of sleep which stand at opposite ends of the spectrum of attention.

At the core of changes in the form of cortical EEG/LFPs that accompany changes in sleep/wake state (wake, non-REM sleep stages 1-4, REM sleep), are changes in the activity of brainstem reticular and thalamic reticular neurons.

Changes in thalamo-cortical activity patterns (as measured through cortical EEG) are brought about by changes in the activity of brainstem reticular neurons and neuromodulatory neurons (ACh, NE, HA, DA, 5-HT, orexin).

Dreams occur primarily during REM sleep when cortical EEG patterns are most like those of waking. Dreams themselves appear to arise from repeated bursts of activity in brainstem reticular neurons that drive bursts of activity in the thalamus and cortex and that resemble responses seen during attentional reorientation in waking (e.g., startle responses). One hypothesis is that dreams reflect the outcome of the cortex attempting to make sense of the noisy inputs it receives in REM sleep.

The lack of conscious experience in non-REM sleep appears to result from the repeated interruptions of cortical activity associated with spindles and slow-waves. Thus, conscious experience (essentially equivalent to that to which we have attention), demands a continuity of cortical activity across time.
what do we know so far (page 2)?

Supporting arguments for metabolism as a function of sleep include the increased accumulation of adenosine (an ATP breakdown product) during sleep deprivation, the accumulation of ATP during non-REM sleep, and the effects of adenosine in inhibiting ACH neurons whose activity supports the waking state. Still, the savings in energy associated with sleep seem relatively minor and REM sleep is actually associated with greater utilization of energy.

Supporting arguments for development as a function of sleep are given by the association of neonatal and adult REM sleep increases with the degree to which a species is born with an immature brain.

Studies using sleep deprivation as a method to show a relationship between sleep and learning/memory yield inconsistent results and suffer from potential confounds due to stress effects and interference. Recently, however, studies examining brain activity in sleep reveal ‘reactivation’ of some recent memories during non-REM sleep and suggest that the extent of such reactivation is related to positively related to subsequent tests of memory.
potential/likely questions for midterm 1:

1. Describe 3 qualitatively different scientific approaches used to examine the function of sleep.

2. For 2 of the 4 potential functions of sleep discussed in class, describe how each is supported or not by work from the 3 scientific approaches of question #1.

3. Describe the steps by which dream content is realized according to the activation synthesis model.

4. List five major differences between REM sleep and waking and further specify the characteristics of each during non-REM sleep.
‘attention’ within sleep - sequences of hippocampal activity realized in waking are ‘reactivated’ during subsequent non-REM sleep

but…somehow…this effect fades rather quickly during the ensuing sleep period

O’Neill et al., TINS, 2010

Kudrimoti et al., J. Neuroscience, 2010
the need for sleep, thought to be necessary because of waking, has been modeled as a process, ‘S’, which builds during waking and is dissipated during sleep

but...what is process S? – Tononi proposes that it a net increase in strength of synapses during waking and that sleep is required to permit ‘synaptic down-scaling’

an overall bias of synaptic plasticity toward potentiation during waking is theorized to result in increased energy costs and decreased signal-to-noise ratios for neurons

during sleep, it is proposed that a wholesaled decrementing of synaptic strengths is realized and that this depends critically on the slow-waves associated with non-REM sleep

Tononi and Cirelli, Sleep Med. Rev., 2006
cortical homeostasis / synaptic down-scaling as a function for non-REM sleep – the basic notion

Axon terminals of 3 different neurons with input to cortical neuron’s apical dendrite

Early wake:
- Robust discrimination of inputs and lower energy usage

Late wake:
- Poor discrimination of inputs and higher energy usage

Early non-REM sleep:
- Activity during high-amp slow-waves causes LTD
- LTD results in fewer spikes to same input and low-amp slow-waves

Late non-REM sleep:
- Robust discrimination of inputs and lower energy usage

Cortical neurons

Spiking of cortical neuron

Spiking of input neurons (width = rate)

Cortical EEG/LFP
consistent with the ‘synaptic down-scaling’ / ‘cortical homeostasis’ theory of sleep function, markers for synaptic potentiation are indeed higher after a bout of waking than after a bout of sleep.

Vyazovskiy et al., Nature Neuroscience, 2008
consistent with the ‘synaptic down-scaling’ / ‘cortical homeostasis’ theory of sleep function, the size and frequency of miniature epsp’s are higher following a bout of waking and following sleep deprivation.
consistent with the ‘synaptic down-scaling’ / ‘cortical homeostasis’ theory of sleep function...cortical microinjection of BDNF, which can increase synaptic strengths, results in subsequent increases in slow-wave activity within non-REM sleep.