from sleep to attention – lecture 20 – Nov. 29, 2010

attention deficit disorder

"Being ADD, when I read a book about marine life my mind allows me to travel with the fish and imagine life beneath the sea. Or I can read a book about astronomy and dance among the stars...I may not immediately comprehend that 3+4=7, but I may fully realize that n+26=51 and that the missing number is 25." - Matthew Kutz, age 13
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.

Theories as to the function of sleep nearly always suggest that the function pertains to the brain as opposed to the rest of the body.
themes II –

Neurally, attention is associated with either changes in the overall patterns of firing across a group of neurons (increased action potentials in response to the attended stimulus, and fewer to the unattended stimuli) and/or changes in the temporal firing patterns of neurons (neurons responding to attended stimuli fire in tune with a gamma rhythm). Such changes may, in part, be brought about by changing the subset of synpatic inputs to which a neuron responds most strongly.

Overall, attention appears to involve changes in the neural dynamics of multiple brain regions. Does this reflect the fact that the brain is extremely complex and best studied by considering the system as a whole, or does it reflect the fact that attention is defined in so many different ways?

Normally, we think of attention as altering the responsiveness of the cerebral cortex to different types of sensory input. That is, we think of attention as a sub-cortical process that impacts what happens in the cortex or thalamus. In the case of the parietal cortex and prefrontal cortex, we seem to have two systems of the cortex itself that regulate attention. Each of these structures is nevertheless impacted by subcortical inputs (e.g., from basal forebrain or locus coeruleus) and, remarkably, appear to impact activity in the same subcortical structures. Thus, attention is a cyclical process (i.e., a chicken-and-egg type process) that is continuous where what has been attended will affect, to some extent, what is attended to subsequently.

Depending on the requirements for success in an environment (i.e., the requirements of the experimental task), attentional processes invoked by different mechanisms (e.g., one versus another neuromodulatory system) may be beneficial or may negatively impact performance.
many brain disorders, particularly those associated with changes in attentional processing, are associated with DA dysfunction and/or prefrontal cortex dysfunction.

Brain rhythms are almost always produced as the result of activity within groups of interconnected GABA neurons.
what do we know so far (since midterm 2 material)?

the prefrontal cortex is, anatomically, perhaps the ultimate integrator of information in the brain – it collects inputs from vast number of cortical and sub-cortical structures

the prefrontal cortex is, anatomically, perhaps the ultimate controller of information utilization in the brain – it contains neurons capable of maintaining activity patterns across long stretches of time and projects to nearly all of the brain regions from which it gains inputs – it is perhaps not surprising, then, that working memory activity in other brain structures depends on prefrontal working memory activity

given the vast number of inputs it receives, it is perhaps not surprising that the prefrontal cortex can produce working memory activity not only for simple stimuli, but also for subtle aspects of the environment such as the duration of a stimulus or the category within which an ordered set of actions exists

schizophrenia is characterized by ‘negative’ symptoms such as flat affect and catatonia, but also ‘positive’ symptoms such as hallucinations

schizophrenia is accompanied by changes in attentional abilities

dysfunction in DA systems and GABA neuron numbers appear to be the primary changes in brain function in schizophrenics

attractors and cell assemblies refer to coordinated activity patterns existing among a group of neurons – it is thought that members of the same group enhance each others activity while inhibiting that of members of other groups - the ease with which it is possible to transition from one pattern to another can be termed the ‘energy barrier’

DA’s function in the brain is complex – for example, changes in DA release may also result in differential activation of D1 vs D2 DA receptors and these receptors produce different effects
what do we know so far (since midterm 2 material)?

The role of diminished GABA neuron numbers in schizophrenia remains to be determined, but could be related to the changes in gamma-frequency LFP rhythms observed in this disorder.
attention deficit disorder:

impacts 2-5% of the population

deficits in sustaining attention

increased distractability

increased impulsivity

increased ‘temporal discounting’ of reward

alterations in genes coding enzymes that regulate DA concentrations

treatment with drugs that primarily target DA systems
a word about the prefrontal cortex and distraction:

rats with lesions specific to the cholinergic system show deficits in responding to simple cues

the prefrontal cortex appears to have neurons whose activity changes tonically during sessions when detection of a signal cue is complicated by the presence of distractors

the prevalence of such neurons appears to depend in part on the presence of ACh inputs to the prefrontal cortex

Gill et al., J. Neuroscience, 2000
what do we really know about DA neurons? – mostly this:

DA neurons appear to be very sensitive to differences between expected and actual reward amounts

in experiments where environmental stimuli predict subsequent rewards, DA neurons respond initially upon presentation of the reward as it was unexpected – with experience, DA neurons respond to the cue that predicts reward as its appearance is unexpected – at the same time, responses to the reward itself diminish as its presentation is predicted by the stimulus

can focused thought come to signal reward in the same way as an environmental cue or is the role of DA in attention deficit disorder related to other, presently unknown, aspects of DA function?

\[ E = MC^2 \]
‘waiting for the big one’ - DA neurons are sensitive to reward delay:

Monkeys, like humans and rats, prefer immediate rewards, but will choose delayed rewards depending on the length of the delay and on the extent to which delay brings.

Temporal discounting refers to the measured effect of reward delay on subjective reward magnitude.

ADD patients tend to be ‘discounters’, preferring small immediate rewards over larger delayed rewards.

DA neurons are discounters as well as the duration of their response to a reward-predicting stimulus will depend on its associated prediction of delay.

cranking up DA in humans increases temporal discounting:

humans were treated with L-DOPA, a precursor to DA, to increase brain DA levels

under these conditions, they were more likely to choose smaller, immediate rewards over larger, delayed rewards (i.e., their ‘temporal discounting’ increased)

the degree of their temporal discounting correlated with changes in amygdala activity

so…boosting DA increased a symptom of ADD in normals, but alleviates that symptom in ADD patients

Pine et al., J. Neuroscience, 2010