from sleep to attention – lecture 21 – June 8, 2012

aging

101 year-old smoker, beer drinker, …..marathon runner
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 ¼ 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.
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 synaptic 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.
themes III –

both aging and some brain disorders (Parkinson’s disease, ADD, and schizophrenia), 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 including sustained attention, working memory, and set-shifting

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

schizophrenics are also thought to be ‘hypofrontal’. for example, performance the Wisconsin Card-sorting task does not increase fMRI BOLD signals in schizophrenics, but does in normals
what do we know so far (since midterm 2 material)?

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.

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.

Expected uncertainty, as described in the Yu and Dayan publication (see resources page), refers to one’s understanding of stable variabilities in the environment. For example, one might know that lost car keys have a 70% chance of turning up in a coat pocket, but near zero probability of being found in the refrigerator. Attention can be expected to take advantage of such information.

Unexpected uncertainty refers to situations wherein one’s understanding of variability in the environment is challenged by new facts (e.g., the lost car keys start turning up in the refrigerator).

When one’s expected uncertainty is high (i.e., environmental variability is high, but stable), it is hypothesized that ACh release is increased to help distribute attention more broadly – NE is hypothesized to increase when unexpected uncertainty is high and thereby allow formation of new expected uncertainties appropriate to the current state of the environment.

As for schizophrenia, the main clue to neurophysiological explanation for attention deficit disorder is given by the main drug used to treat the disorder – a drug that alters DA release.
what do we know so far (since midterm 2 material)?

in attempting to link features of ADD to DA, current work examines the nature of ‘temporal discounting’ of reward in ADD patients, the response of DA neurons to delayed rewards, and the impact of DA-increasing treatments in humans on temporal discounting.

temporal discounting of reward is examined by measuring the tendency of subjects to choose immediate small rewards over larger, but delayed, rewards – with longer delays, the reward must be ever bigger else the subject will opt for the small immediate reward.

the prefrontal cortex appears to contain neurons that are tonically activated during time periods when attention to a desired signal is made difficult by the presence of multiple distractors.

aging is associated with a number of changes in the structure and function of the brain making it difficult to pinpoint what changes alter attentional abilities in adults.

the ability to shift attention to a new feature of the environment (e.g., odors instead of textures) in order to make correct choices is impaired in aging – this finding opens up a new way to examine attentional dysfunction in aging humans and rats and to relate such dysfunction to changes in the structure of the prefrontal cortex.
healthy aging is associated with a variety of changes in brain physiology and in cognitive abilities

- Auditory processing speed, memory, and ‘cognitive flexibility’ decrease with age – test yourself at: (www.positscience.com)
- Spatial memory impaired in aging – data from Morris water tank tests (path length to reach escape platform) – Yang et al., JNP, 2008
- The ratio of AMPA-type glutamate receptors to NMDA-type increases with age – Yang et al., JNP, 2008

- 9.8% decrease in substantia nigra DA cell numbers per decade
- 2-3% decrease in brain volume per decade
- Cortical cell numbers unchanged with aging
the ‘set-shift’ task reveals a specific extra-dimensional shift deficit in aged humans and humans with prefrontal damage.

circles = cups full of digging medium, some with reward at base  color of outer ring = digging medium (e.g., sand)
color of fill = odor (e.g., cinnamon)  star = correct choice (i.e., reward beneath digging medium)

initial learning (odor, not medium, is relevant)  intra-dimensional shift (i.e., odor still matters)

extra-dimensional shift (i.e., digging medium matters)  intra-dimensional reversal (i.e., correct odor switches)

Owen et al., Neuropsychologia, 2010
the ‘set-shift’ task reveals a specific extra-dimensional shift deficit in aged rats

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(i.e., odor still matters)
extra-dimensional shift
(i.e., digging medium matters)
intra-dimensional reversal
(i.e., correct odor switches)
initial learning
(odor, not medium, is relevant)

Barense et al., Learning and Memory, 2010
medial prefrontal cortex lesions impair performance on extra-dimensional ‘set shifts’

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intra-dimensional shift (i.e., odor still matters)

extra-dimensional shift (i.e., digging medium matters)

intra-dimensional reversal (i.e., correct odor switches)

Birrell and Brown, J. Neuroscience, 2000
medial prefrontal cortex lesions impair performance on extra-dimensional ‘set shifts’, but orbitofrontal lesions impair performance on intra-dimensional reversals

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intra-dimensional shift (i.e., odor still matters)

intra-dimensional reversal (i.e., correct odor switches)

Brown and Bowman, TINS, 2002
compared to young, healthy subjects (YHE) both healthy aged subjects (OHE) and Alzheimer’s disease (AD) patients have decreased volumes of medial and dorsolateral prefrontal cortex, but not orbitofrontal cortex.