Gage was fitful, irreverent, indulging at times in the grossest profanity (which was not previously his custom), manifesting but little deference for his fellows, impatient of restraint or advice when it conflicts with his desires, at times pertinaciously obstinate, yet capricious and vacillating, devising many plans of future operations, which are no sooner arranged than they are abandoned in turn for others appearing more feasible. A child in his intellectual capacity and manifestations, he has the animal passions of a strong man. Previous to his injury, although untrained in the schools, he possessed a well-balanced mind, and was looked upon by those who knew him as a shrewd, smart businessman, very energetic and persistent in executing all his plans of operation. In this regard his mind was radically changed, so decidedly that his friends and acquaintances said he was ‘no longer Gage’. – Dr. John Martyn Harlow
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.
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.
what do we know so far (since midterm 1 material)?

Neural mechanisms for attention fall into 3 basic categories. 1) changes in signal-to-noise ratio. Here differences in the selectivity for firing responses of neurons are accentuated, in one or another form, by attention; 2) changes in the temporal coherence of neurons. Here, attention increases the degree to which neurons fire with temporal relation to a gamma frequency. 3) changes in the functional anatomy of neurons. Although neurons usually have thousands of synaptic inputs, they are not always ‘listening’ to all of them. Even synapses that are strong (more depolarizing when activated) can be depressed temporarily.

Acetylcholine and norepinephrine appear to be intimately involved in both altering the strength of responses of neurons to stimuli when they are attended and in altering, dynamically, the ‘strength’ of different synaptic inputs to a neuron.

The ‘hemineglect’ syndrome arises from damage to the right parietal cortex and impacts the left side of not just egocentric frames of reference (e.g., the left visual field or left side of the body), but also the left side of objects (i.e., in an object-centered frame of reference).

The ‘hemineglect’ syndrome could conceivably arise because the parietal cortex serves as that brain area where a ‘spatial representation of the world’ is laid out or because the parietal cortex serves to regulate spatial aspects of attention.
what do we know so far (since midterm 1 material)?

Locus coeruleus NE neurons impact attention in a rather ‘global’ fashion as their axonal projections may be, even from the same neuron, to multiple regions of the brain. As NE neurons are clustered into primarily one nucleus, they appear to operate as a unified group to impact widespread regions of the brain simultaneously. High NE seems to result in a greater breadth of attention (i.e., searching behavior) which can present as an inability to maintain focus on some one feature of the environment. Low NE may induce a different attentional deficit, namely an inability to move attention away from what is currently attended.

The basal forebrain appears to be much more complex than the locus coeruleus. There are at least three types of cortically-projecting neurons and these neurons group into different nuclei whose axonal targets are more restricted than those for LC neurons. As such, they are poised to control aspects of attention in a more fine-tuned, region-specific manner (e.g., heightening attention to visual as opposed to touch stimuli).

Both NE and basal forebrain neurons ‘learn’ fast in that they exhibit rapid changes in their responses to stimuli when the novelty or relevance of those stimuli has changed.
questions for midterm 2

we discussed three types of neurophysiological change that appear to accompany attention. Name and describe each. Feel free to draw, but be sure to add labels.

recall two pieces of evidence that suggest that hemineglect can occur not only for egocentric space, but also for object-centered space

compare and contrast the basal forebrain and locus coeruleus in terms of their anatomical projections. Based on what was discussed in class, what types of attention might be enhanced under the following three conditions: high ACh; high NE; low NE

BONUS – reprise the anatomical connectivity between two sensory systems, the prefrontal cortex, and the basal forebrain that can result in attention being selectively incremented in one versus another sensory cortex – in what way is this system ‘recursive’
the role of the prefrontal cortex in the control of attention was perhaps made most obvious by the case of Phineas Gage whose behavior changed radically following prefrontal damage.

It appears that prefrontal cortex can be roughly divided into 3 sub-regions (not shown here) – these are dorsolateral (the ‘inclusionary’), orbitofrontal (the ‘exclusionary’), and the medial (‘the intensive’).

Prefrontal anatomy is truly remarkable – it receives input from structures whose neurons contain very different forms of information (e.g., parietal spatial representation vs. temporal object representation vs. hypothalamic satiety information vs. olfactory bulb odor information).

Prefrontal sends output to essentially all areas providing it input – this includes output to all major neuromodulatory systems which, in turn, can impact a wide array of structures.
prefrontal cortex not only contains ‘working memory’ type activity, but appears to be responsible for its appearance in other brain structures.
prefrontal cortex neurons form responses to complex ‘categories’ of stimuli – and thus could conceivably guide attention according to them

**TASK:** monkey observes a four-item sequence wherein three buttons (push, pull, turn) are lit in different combinations – monkey must remember the sequence and then perform it

**PREFRONTAL NEURONS:** have delay activity that corresponds to one of three ‘categories’ of action sequence (AABB, ABAB, AAAA)

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Shima et al., Nat. Neuro., 2007
tracking time – PFC neurons appear to have the requisite properties to guide attention across time

Mita et al., Nat. Neuro., 2009
the timing of attention – a role for prefrontal mapping of time intervals?

task: monkey is instructed to pay attention 1 of 4 regions of the visual field – when orientation of stimulus in that region changes, the monkey releases a bar

timing aspect: the probability that the orientation will change varies across time

activity of single neurons in visual cortex (area V4) responding to a visual stimulus fire more if their response field (RF) overlaps the region of the visual field that must be attended (‘attend in’ vs. ‘attend out’)

subtracting the ‘attend out’ from the ‘attend in’ firing rate curve yields the ‘attention index’, which measures the difference in response to the stimulus due to attention

the ‘attention index’ changes in accord with the probability that the stimulus will change orientation – that is, attention has a temporal component