from sleep to attention – lecture 10 – April 30, 2012

neural mechanisms for attention I – controlling the signal-to-noise ratio

themes –

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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.

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.

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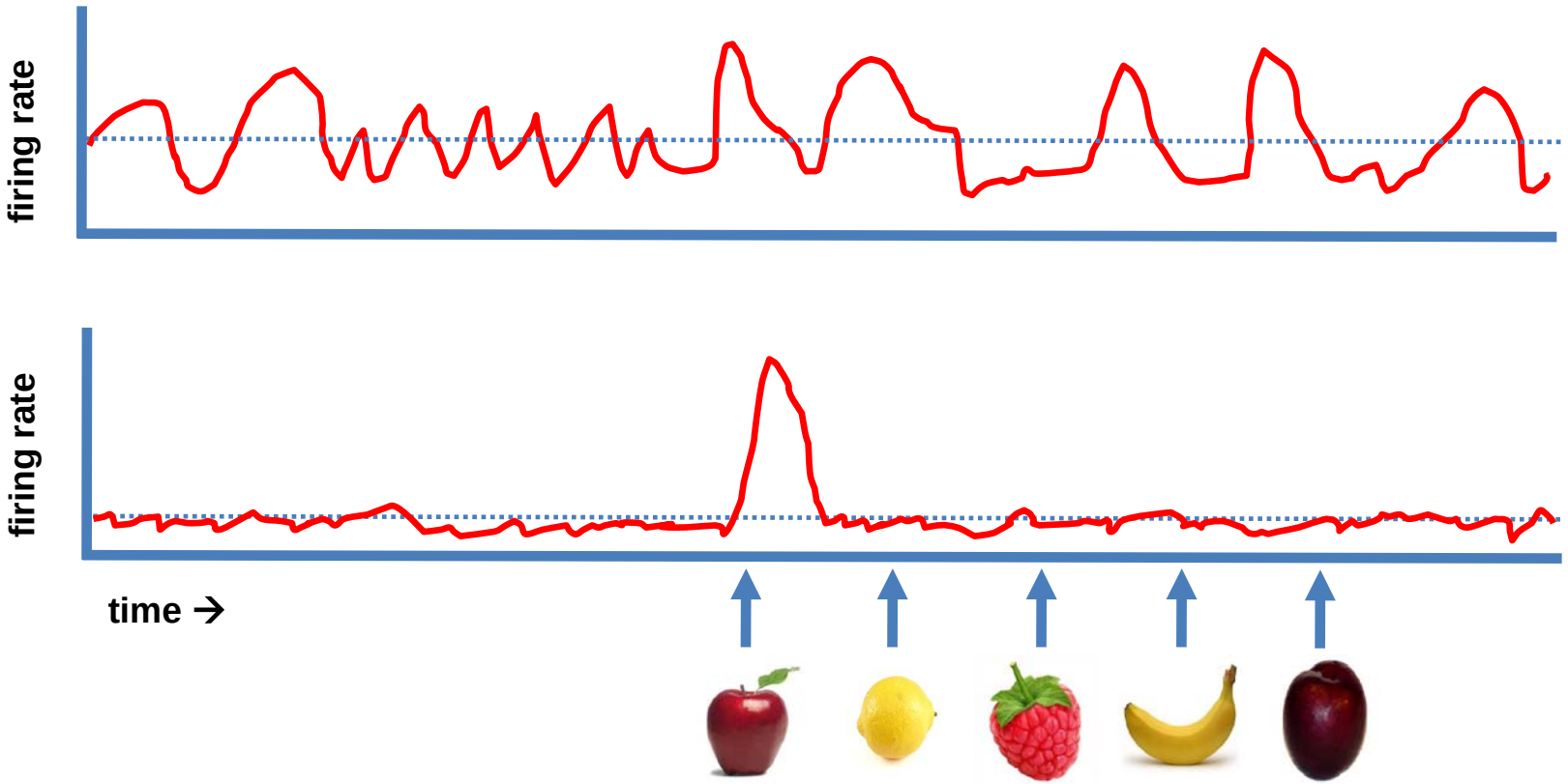
Recent work suggests that waking periods are associated with a net increase in the strength of synaptic connections between cortical neurons. Non-REM sleep may function to down-scale the strength of all synapses such the signal-to-noise ratio of cortical neurons is enhanced and energy is saved.

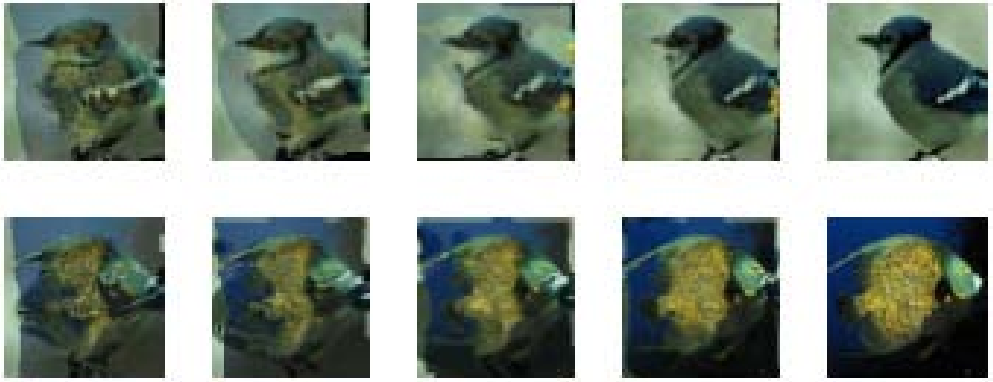
signal-to-noise (i.e., making a distinction between some one thing and everything else)

- activity rate of the neuron in the top trace is highly variable in the absence of visual stimuli and the neuron responds with moderate increases to 4 out of 5 visual stimuli

– activity rate of the neuron in the bottom trace is low and stable in the absence of visual stimuli and the neuron responds with robust increases to only 1 of the visual stimuli

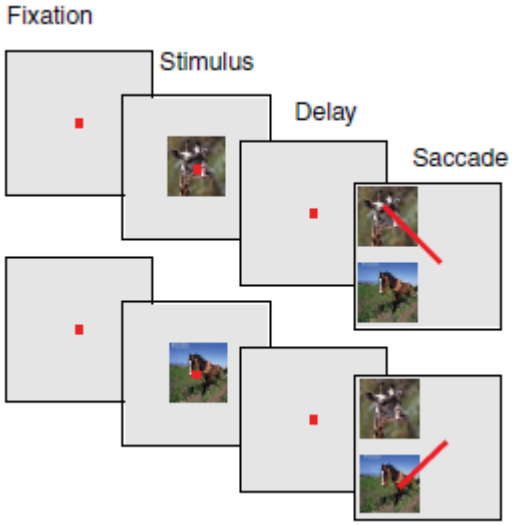
- thus, compared to the top neuron, the bottom neuron's responses have higher signal-to-noise ratios when considered according to comparison of stimulus response rate (signal) to baseline rates (noise) and when considered according to comparison of its best visual stimulus response to its response to all visual stimuli



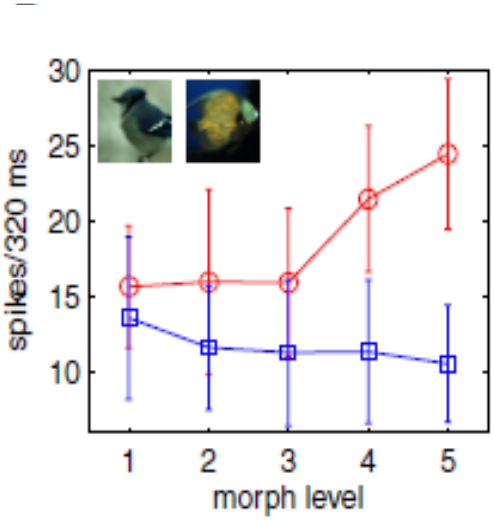


experimenter identifies pairs of pictures which, when 'morphed-together' to different degrees, appear more or less similar

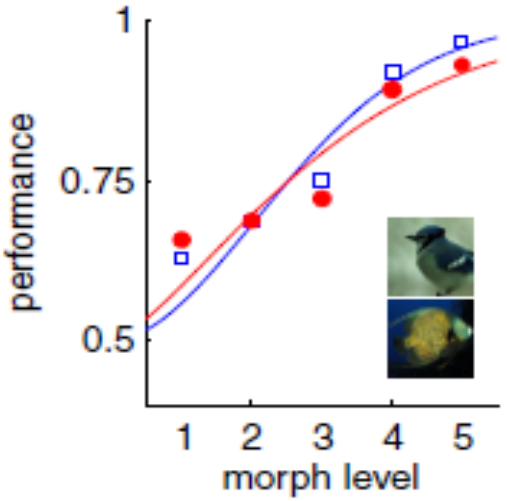
monkey is taught to fixate…then one picture is shown (the sample stimulus)…a delay is followed by presentation of the two non-morphed versions of the picture and the monkey must decide (by saccade) which matches the sample



during the sample stimulus phase, IT neurons have preferential responding to one of the stimuli (red) and less response to the other (blue) when the images are most different (morph level 5)…the preference is reduced at morph 1



The extent to which the neuron exhibits firing rate differences to the two pictures matches its ability to tell which one it saw during the sample phase…that is, increased neural signal-to-noise = increased perceptual signal-to-noise



Liu and Jagadeesh, J. Neurophysiology, 2008

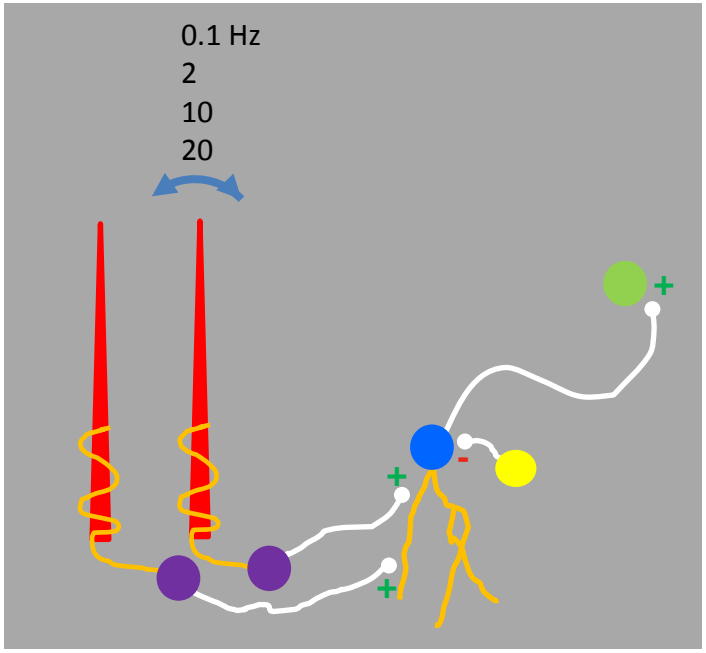
simplified outline of the whisker barrel sensory system in the rat
(to clarify data shown in the subsequent slides)

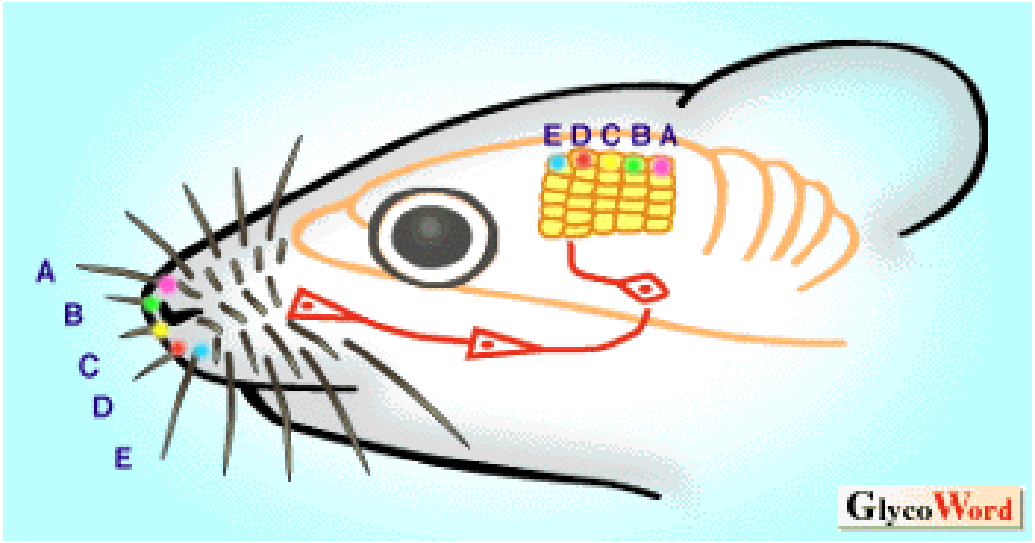
– trigeminal neurons (purple) of the brainstem wrap dendrites (orange) around whiskers (red) and send axons (white) to dendrites of neurons in the ventrobasal thalamus (blue) which sends axons to cortex (green)

– thalamic reticular neurons (yellow) send inhibitory input to the ventrobasal thalamic neurons

– the experimenter records the responses of ventrobasal thalamic neurons to vibration of different whiskers at different frequencies

– the experimenter repeats this protocol in the presence of high levels of either norepinephrine or acetylcholine -





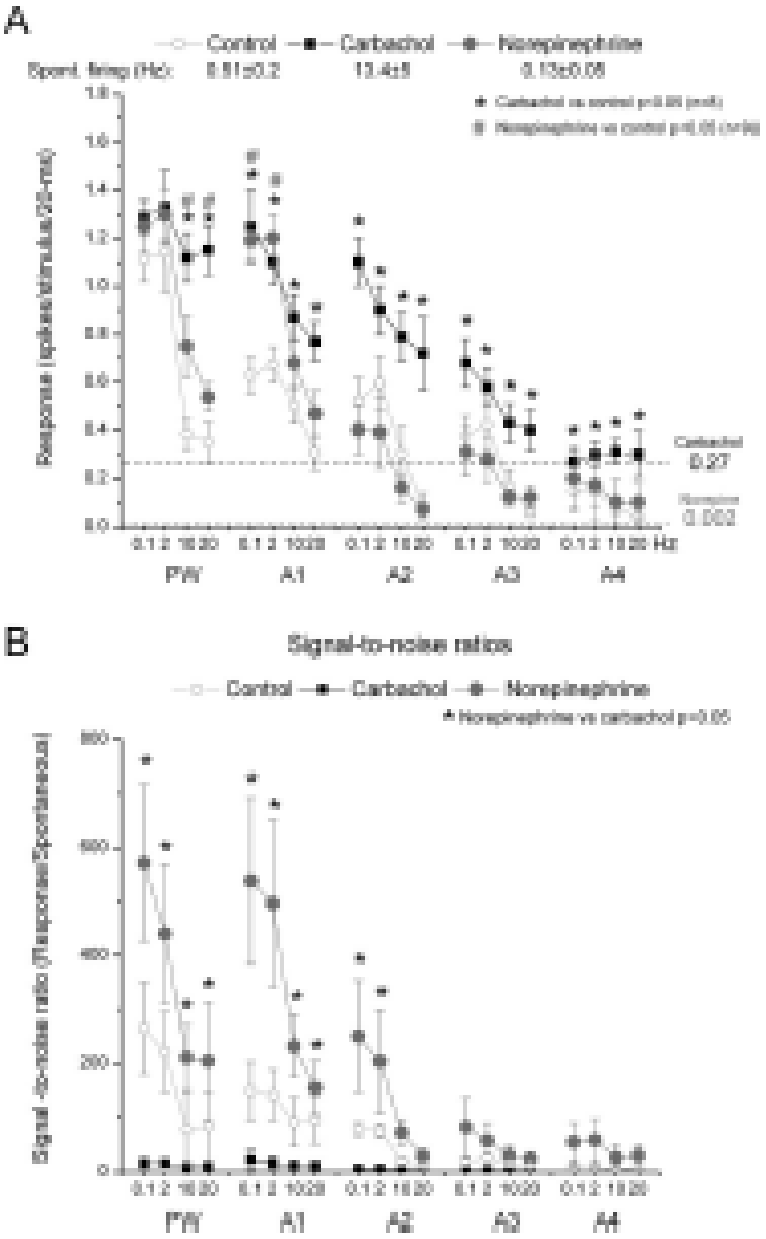
opposite effects of NE and ACh on signal-to-noise ratios

Top – application of carbachol (which mimics ACh) increases baseline firing rate of a ventrobasal thalamic neuron over control (13.4 Hz vs. 0.5 Hz) while application of NE reduces baseline rate (0.13 Hz)

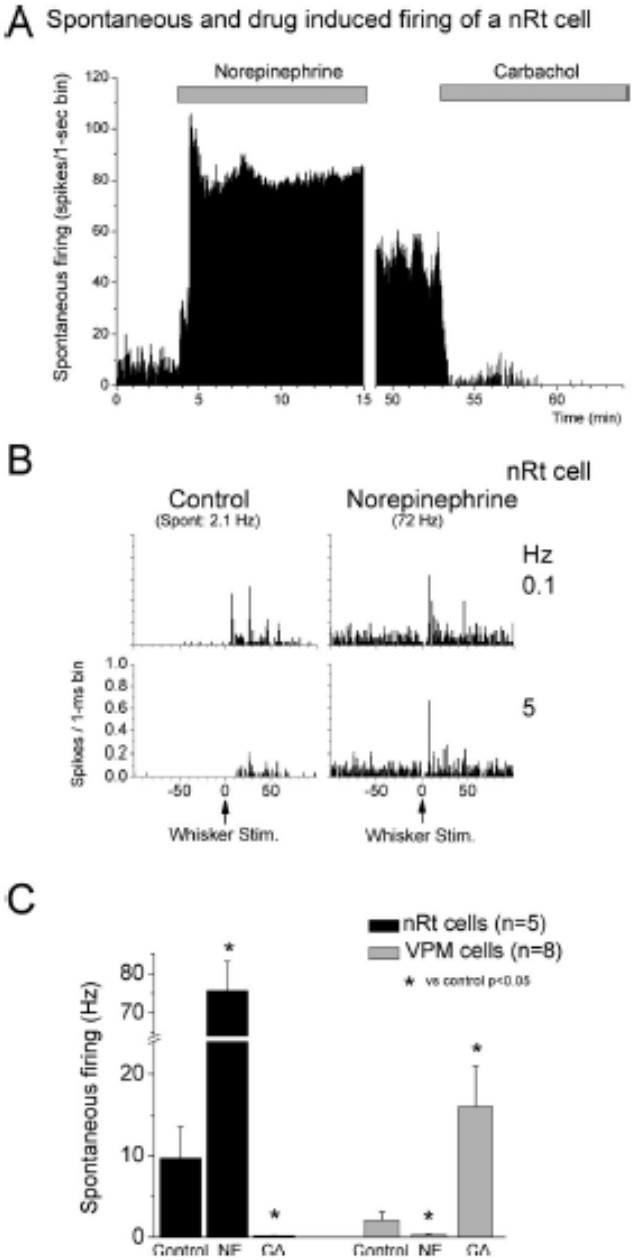
- Carbachol also increases the response of the same neuron to stimulation of the 'preferred whisker' (that yielding the biggest response - PW) as well as the response to adjacent whiskers (A1-A4)

- NE increases responses to the preferred whisker, but decreases responses to the adjacent whiskers

Bottom – by taking the ratio of the neuron's response under each condition to its baseline firing rate (i.e., response rate / baseline rate), the signal-to-noise ratio is calculated – it is clearly enhanced in the presence of NE and depressed in the presence of carbachol

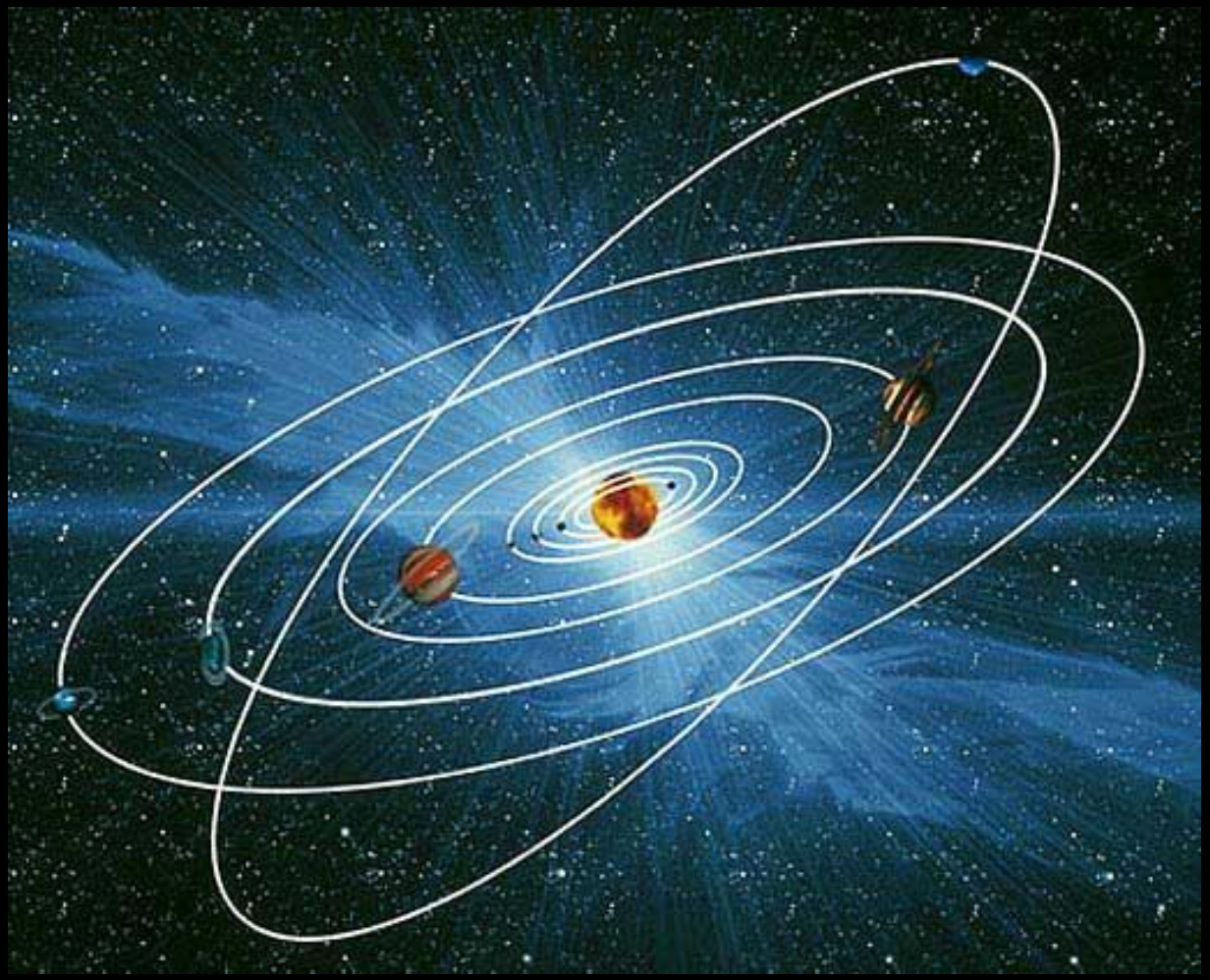


ACh and NE may exert their effects on the baseline firing rates of ventrobasal thalamic neurons partly through action on thalamic reticular (nRt) neurons (e.g., NE excitation of nRt neurons increases inhibition of ventrobasal neurons)



from sleep to attention – lecture 11 – May 2, 2012

neural mechanisms for attention II – temporal coherence of brain activity



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potential/likely questions for midterm 1:

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

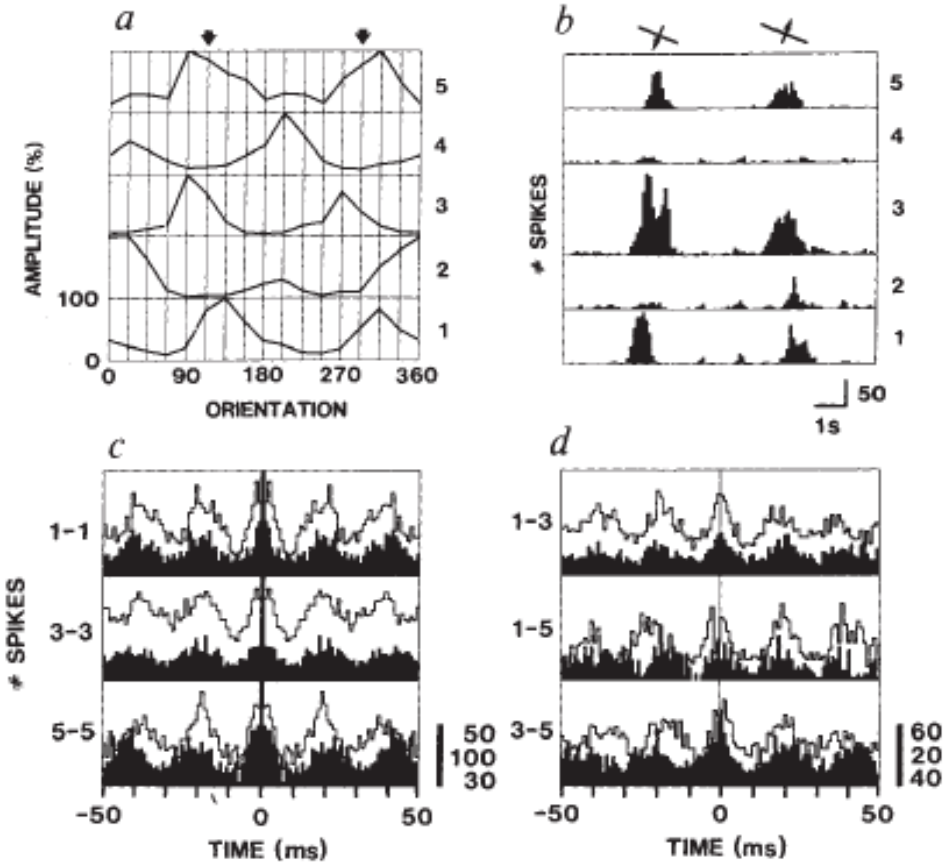
2. For 2 of the 4 potential functions of sleep discussed in class, describe how each is supported or not by work from the 3 scientific approaches of question #1.

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.

5. Perception appears to demand desynchronized (low-amplitude, irregular period) cortical EEG patterns. Describe the brainstem, thalamic, and hypothalamic neural mechanisms (in terms of brain nuclei, their anatomical connections and neural activity rates/patterns) that produce this state.

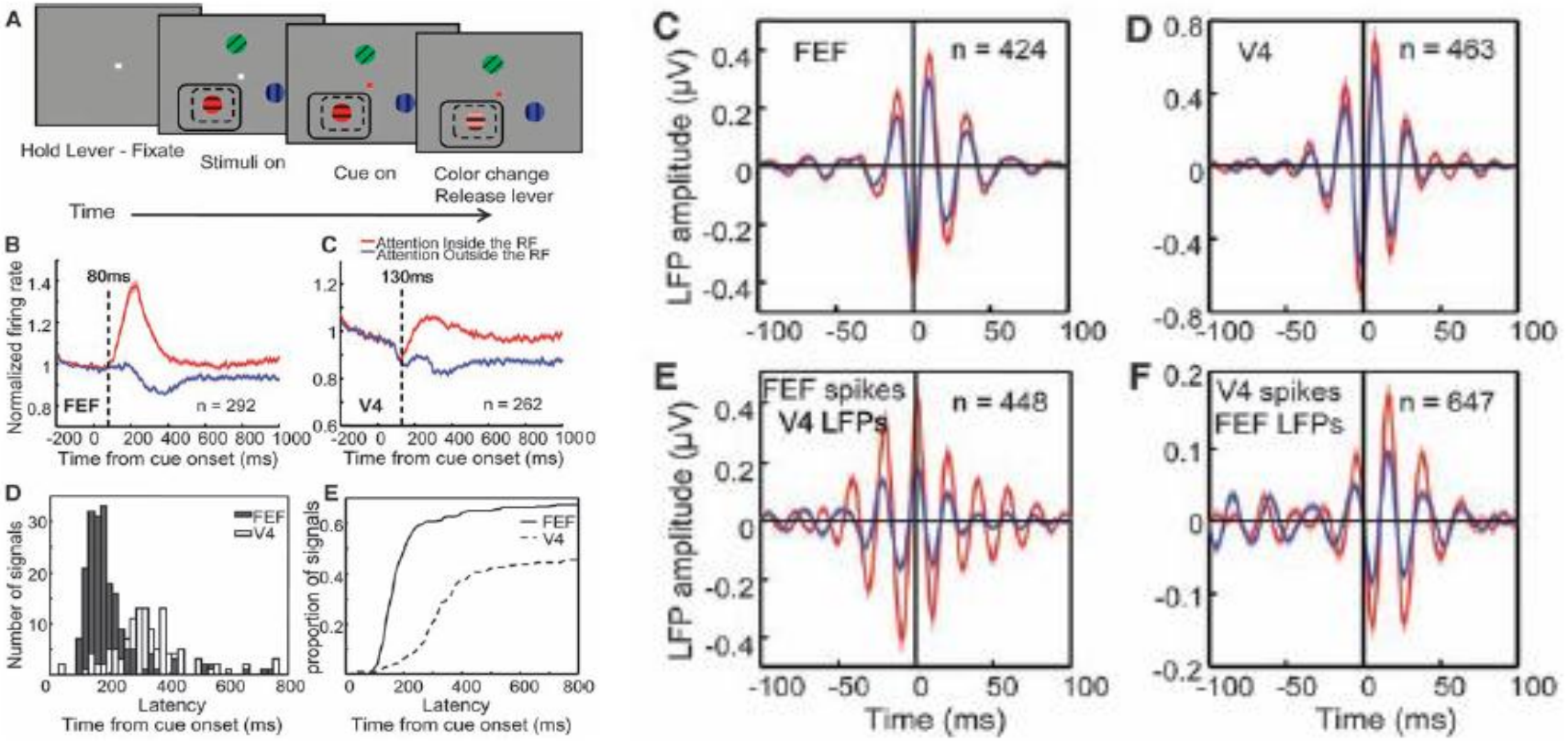
the initial demonstration of gamma-frequency rhythms – five neurons recorded 400 micrometers apart in the occipital/striate cortex exhibit similar (electrodes 1,3,5) or different sensitivities to orientation of visual stimulus bars – those with similar orientation preferences were found to exhibit coherent firing oscillations in the gamma-frequency range (~30-60 Hz) when their preferred stimulus was presented



Gray et al., Nature, 1989

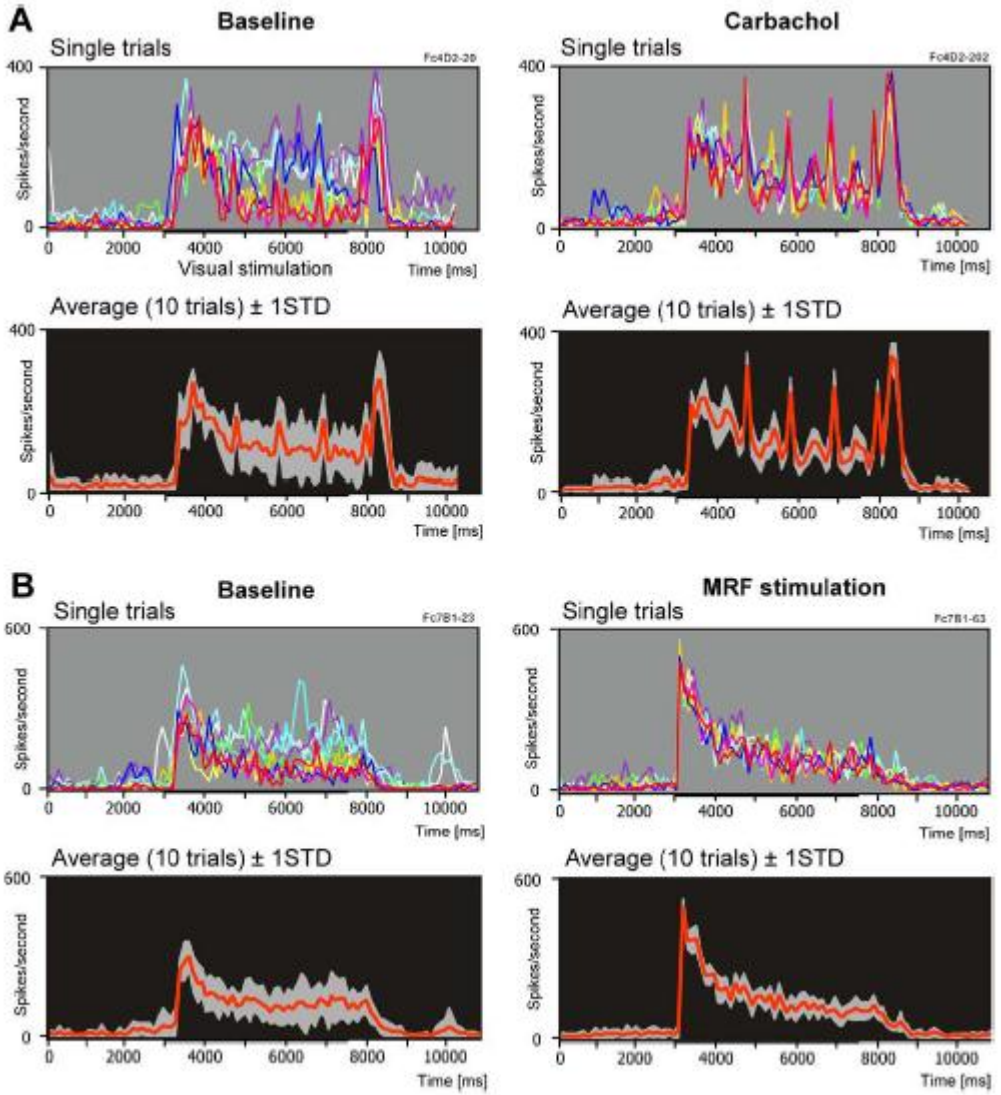
attention modulates activity rates in V4 and FEF (consistent with increased signal-to-noise ratio as a mediator of attention)

but…attention also modulates the degree of gamma-frequency firing rhythms in each region as well as gamma-frequency coherence between regions (consistent with increased gamma-locking as a mediator of attention)



Gegoriou et al., Science, 2009

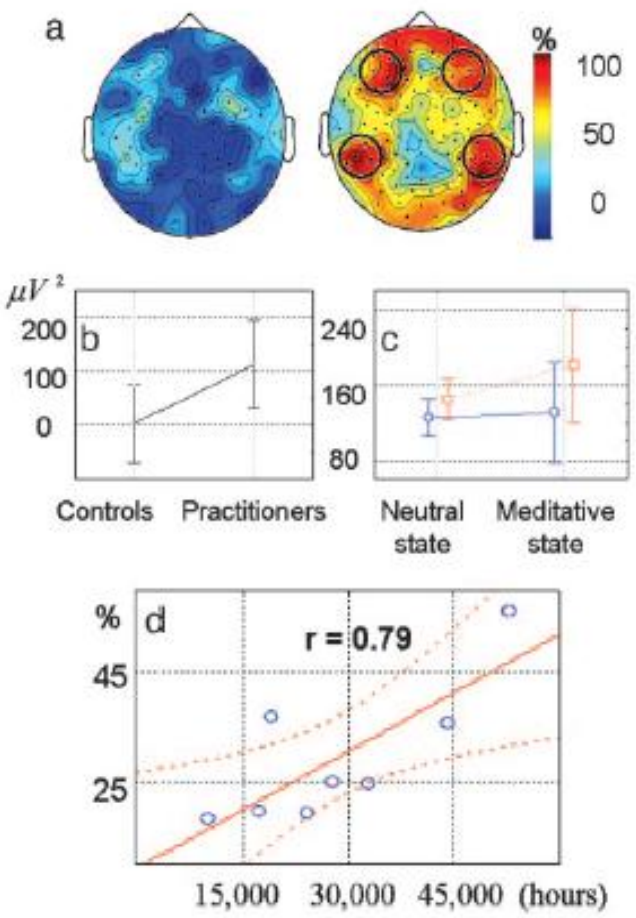
ACh and brainstem reticular formation stimulation enhance gamma-frequency oscillatory firing patterns

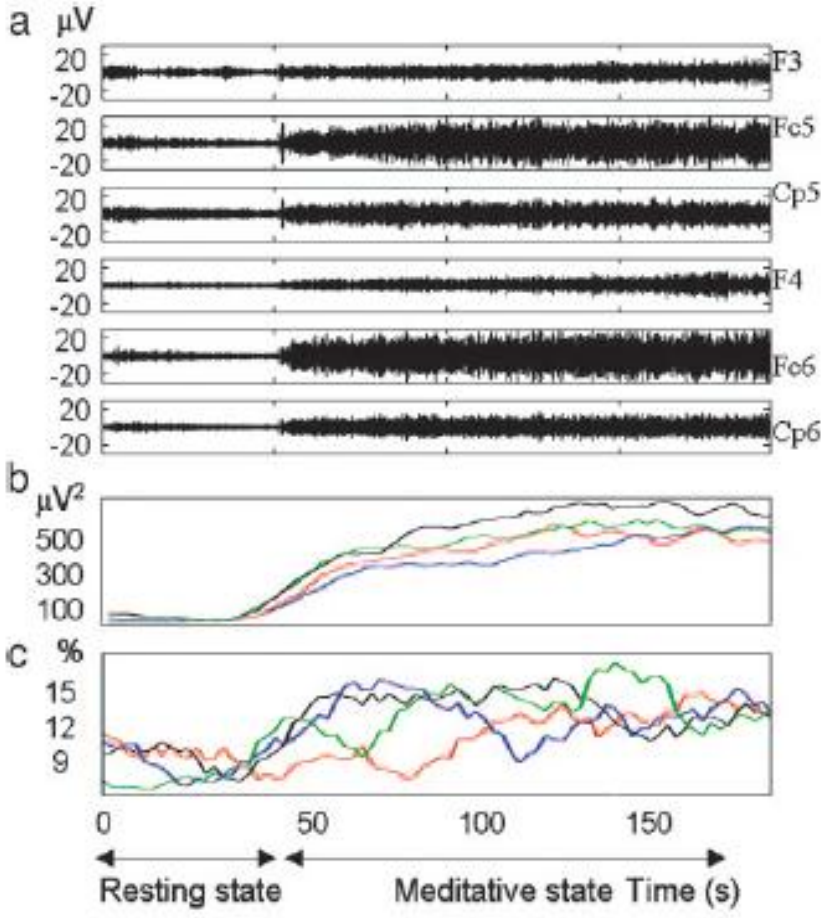


Rodriguez et al., Neuroscience, 2010

oooooommmmm…ooooooooommmmm…well, not exactly

expertise in mediation on compassion is correlated with massive increases in EEG gamma-frequency oscillations





Lutz et al., PNAS, 2004

from sleep to attention – lecture 12 – May 4, 2012

neural mechanisms for attention III – input selection / functional anatomy

themes I –

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themes II –

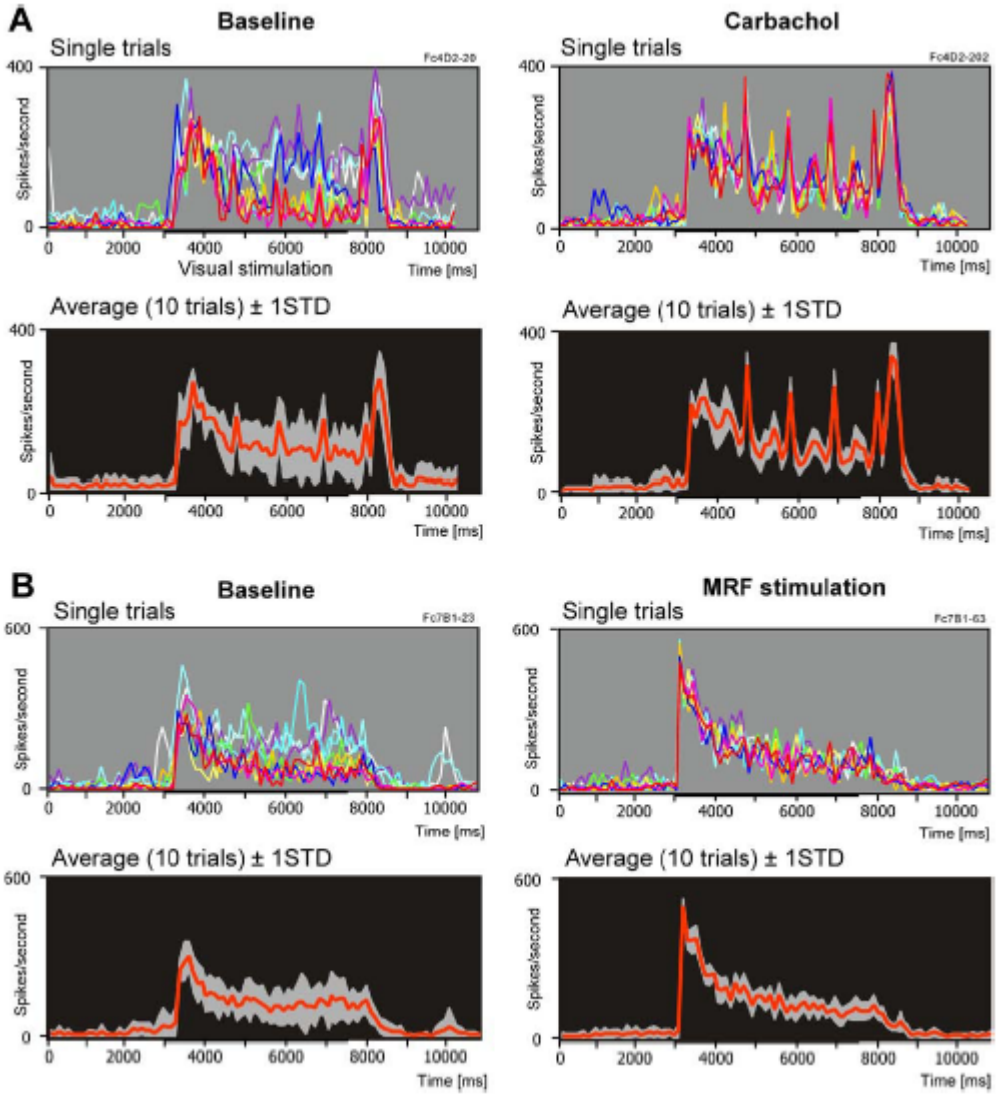
Neurally, attention is associated with either changes in the overall patterns of firing across a group of neurons (increased action potentials in response to the attended stimulus, and fewer to the unattended stimuli) and/or changes in the temporal firing patterns of neurons (neurons responding to attended 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?

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.

ACh and brainstem reticular formation stimulation enhance gamma-frequency oscillatory firing patterns



Rodriguez et al., Neuroscience, 2010

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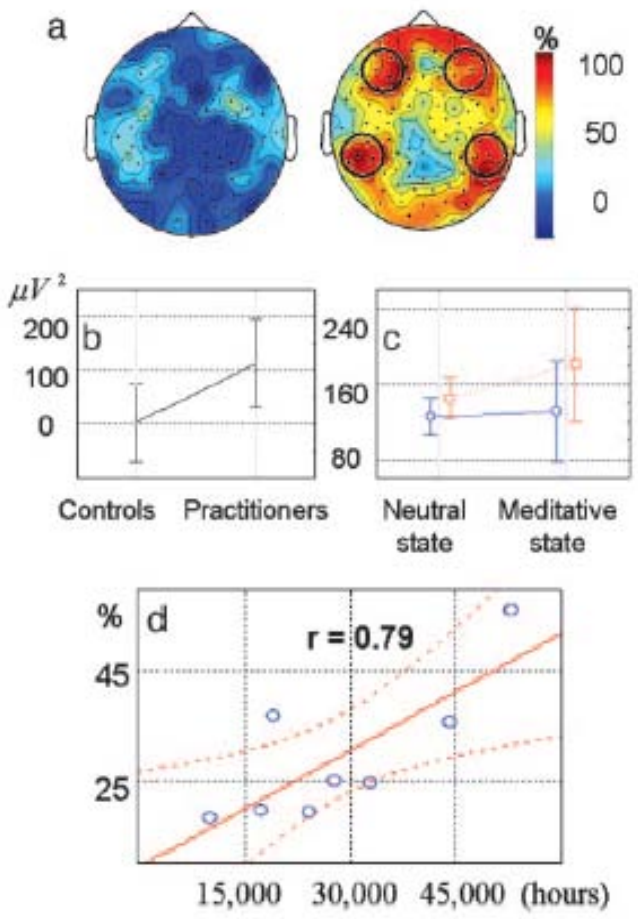
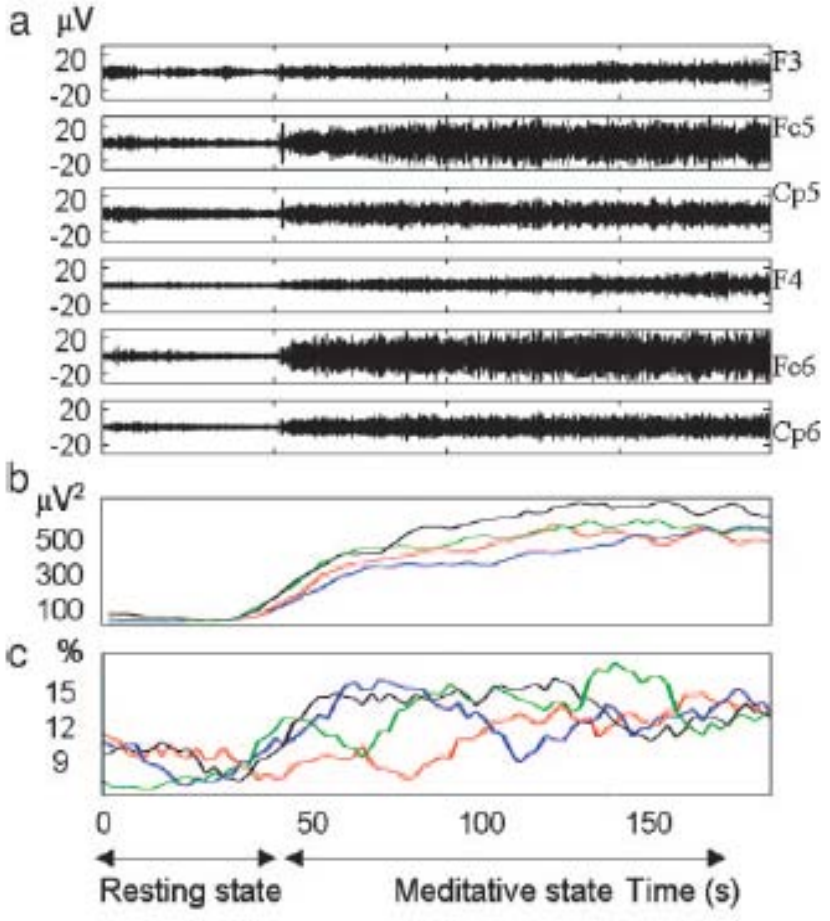


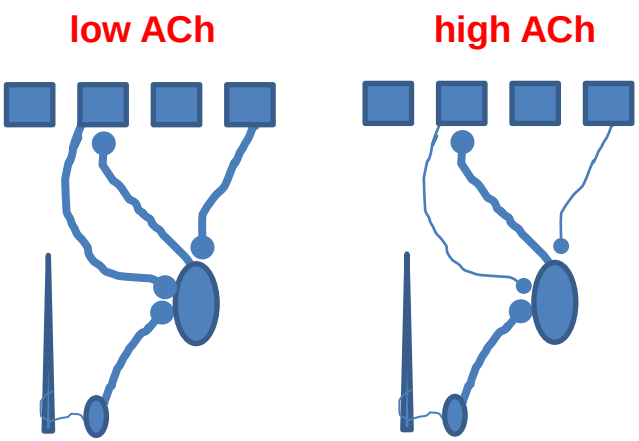


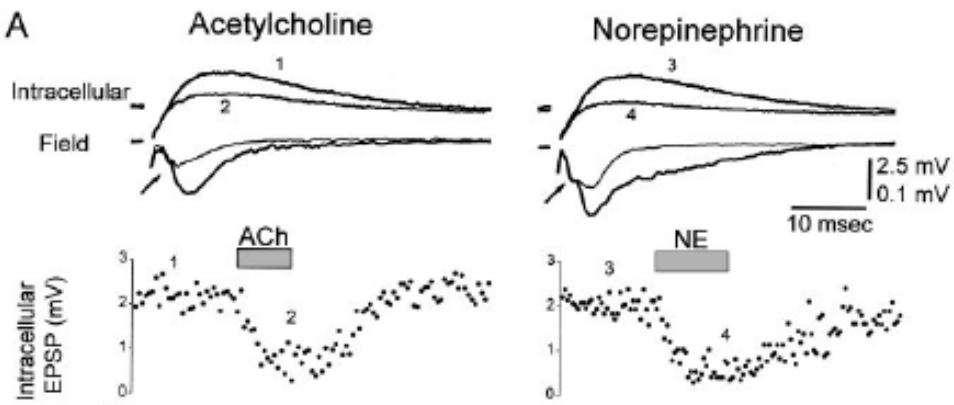
Lutz et al., PNAS, 2004

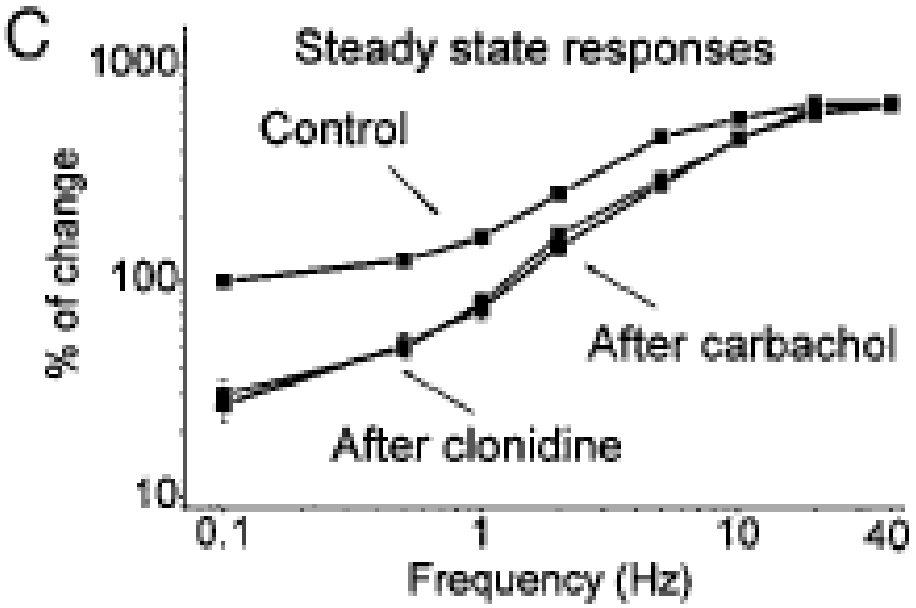
neuromodulation of sensory responses I

ACh and NE depress responses of ventrobasal thalamic neurons (which relay input from vibrissae) to the inputs they receive from the cortical area (barrel field) to which they project.

But…, this depression is specific to low-frequency inputs…responses to high frequency inputs are actually enhanced

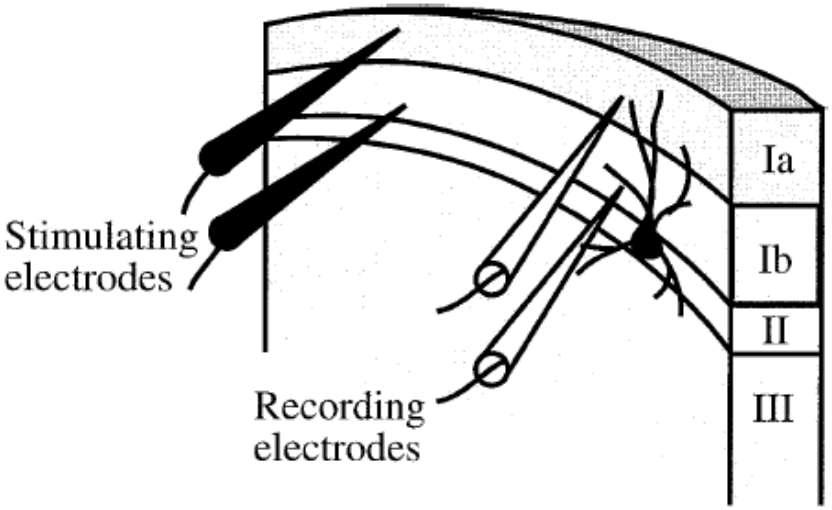


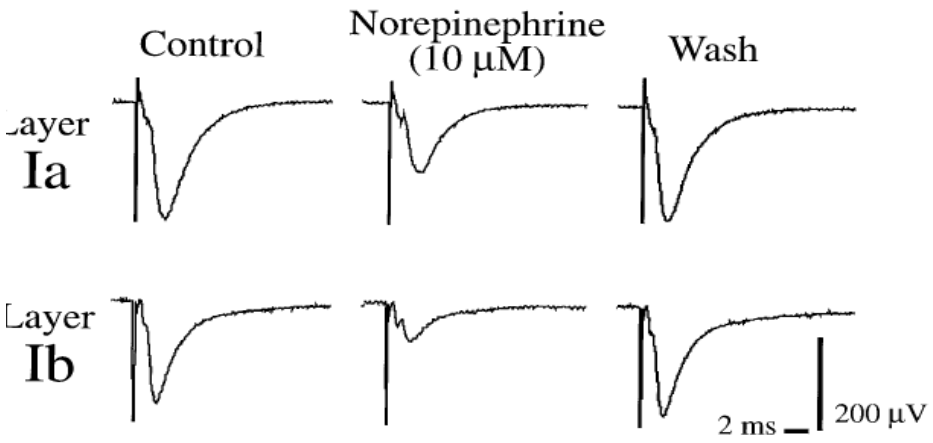




Castro-Alamancos and Calcagnotto. Neurophysiology, 2001

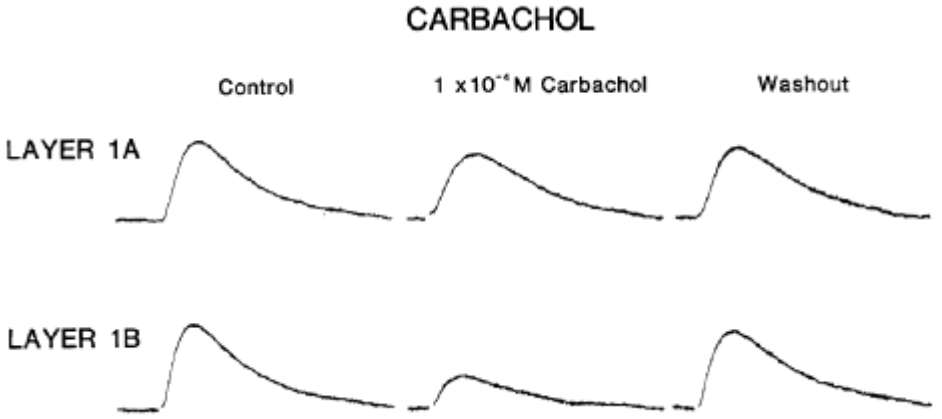
neuromodulation of sensory responses II





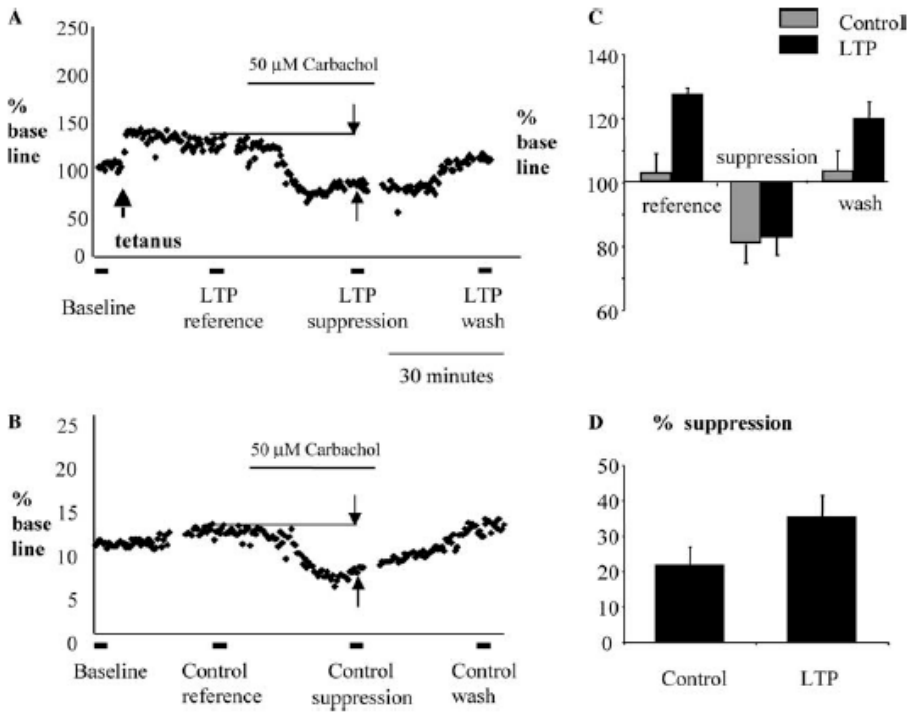
ACh and NE slightly depress responses of olfactory cortex neurons to inputs from the olfactory bulb (= direct sensory inputs = layer 1a inputs).

ACh and NE strongly depress responses of olfactory cortex neurons to inputs from other regions of cortex (=association inputs = layer 1b inputs)



Hasselmo et al., J. Neurophysiology, 1997

ACh can differentially modify strong versus weak synaptic inputs



Linster et al., Neurobiology of Learning and Memory, 2003

this may explain deficits in the following olfactory discrimination task

odor A versus odor B – choose A

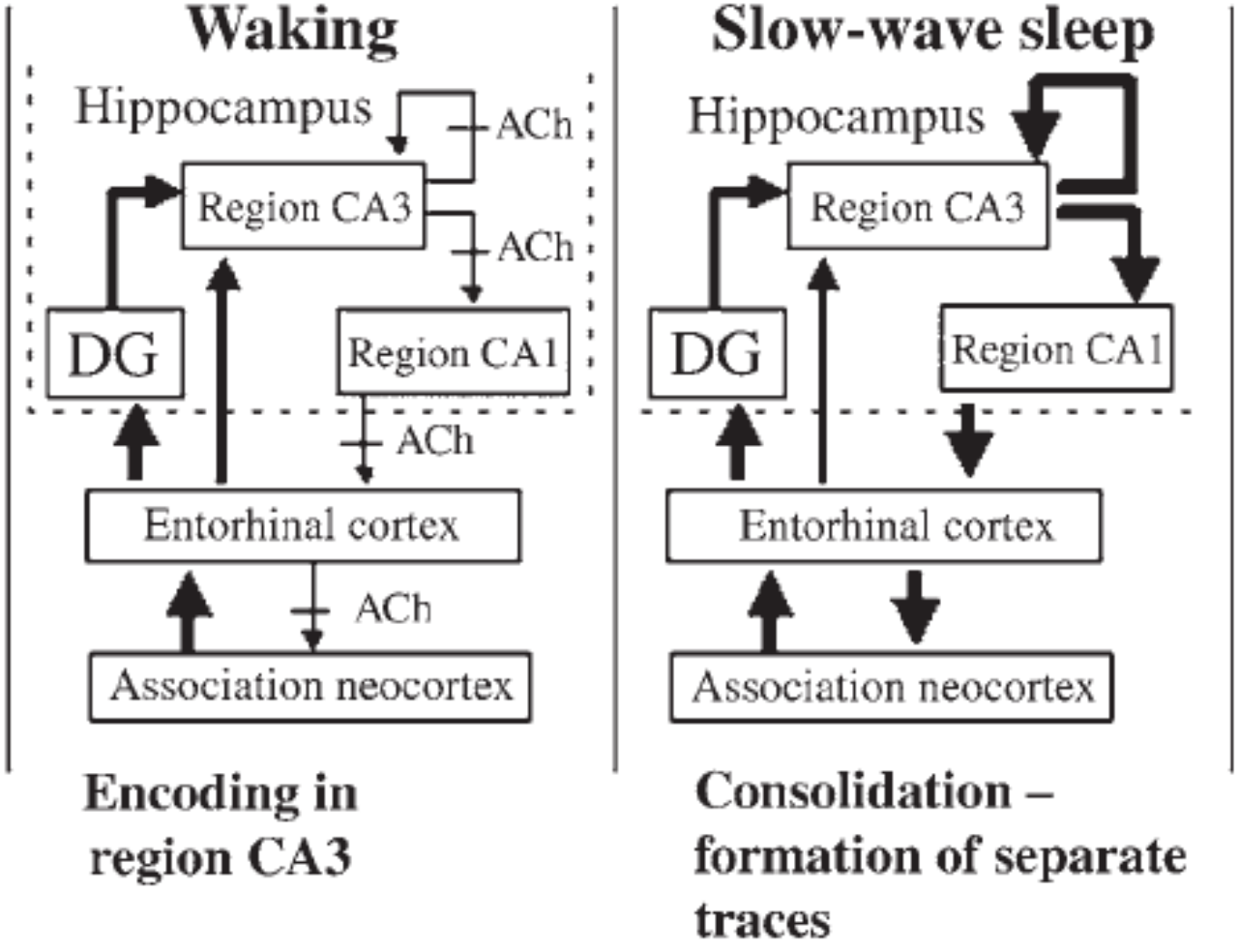
once learned:

odor A versus odor M – choose M

odor D versus odor E – choose D

Animals with ACh lesions have trouble with the A/M, but not D/E, pairing. ACh is thought to permit A/M learning by depressing, specifically, those inputs potentiated during learning of the A/B pairing

attention within sleep – ACh may modulate what CA3 and cortex respond to in sleep versus wake and thereby form a mechanism for memory transfer



Hasselmo and Giocomo J. Mol. Neuroscience, 2006