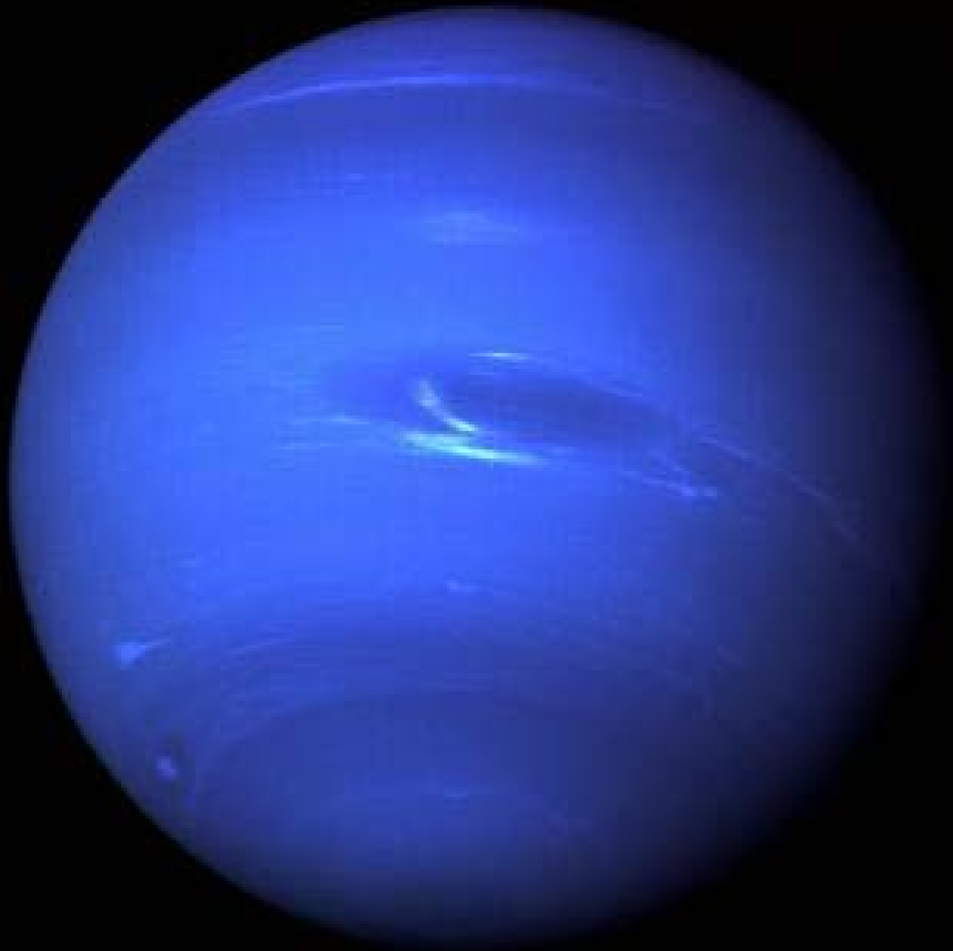
from sleep to attention – lecture 14 – May 14, 2012

the locus coeruleus (i.e., the blue spot)



either you repeat the same conventional doctrines everybody is saying, or else you say something true, and it will sound like it's from Neptune. -Noam Chomsky

themes I –

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).

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.

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.

‘from sleep to attention’ – UCSD COGS 176 – spring, 2012 – midterm2 questions

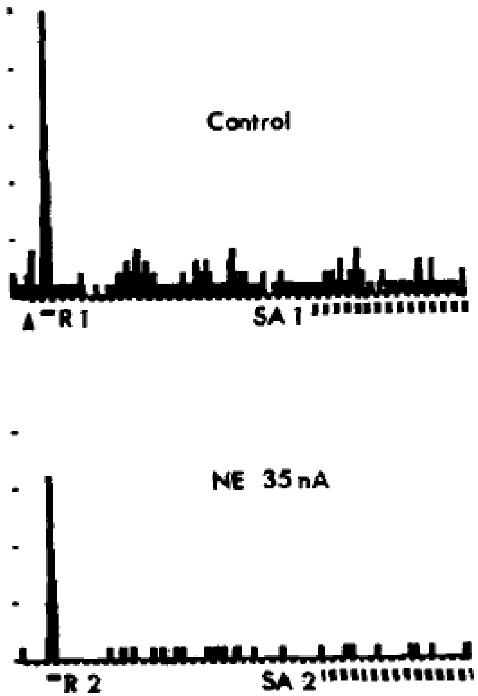
1. The cerebral cortex is required for the actual perception of sensory stimuli. Attention modulates which sensory stimuli, of all present, are perceived. Therefore, it has been useful to consider what changes in neurophysiology of cerebral cortex accompany attentive states. Three such changes to cortical activity were discussed extensively in class. List these, briefly detail how such changes are measured (e.g., comparisons of firing rates and which ones, consideration of relative timing of neural events, modification of synaptic efficacies, etc.). Be sure to include whether the changes described pertain to action potentials or synaptic potentials.

2. Nikos Logothetis undertook a series of studies concerning what structures in the visual system are responsible for the actual perception of visual objects. This was done by comparing the responses of neurons when a stimulus was presented but not perceived versus when a stimulus was presented and also perceived. List the four regions of the visual system of the cortex that were examined and name the types of visual stimuli that were used to study responses in each. Name the behavioral/stimulus paradigm used in these tests. Discuss which brain regions were simply stimulus responsive versus stimulus+perception responsive.

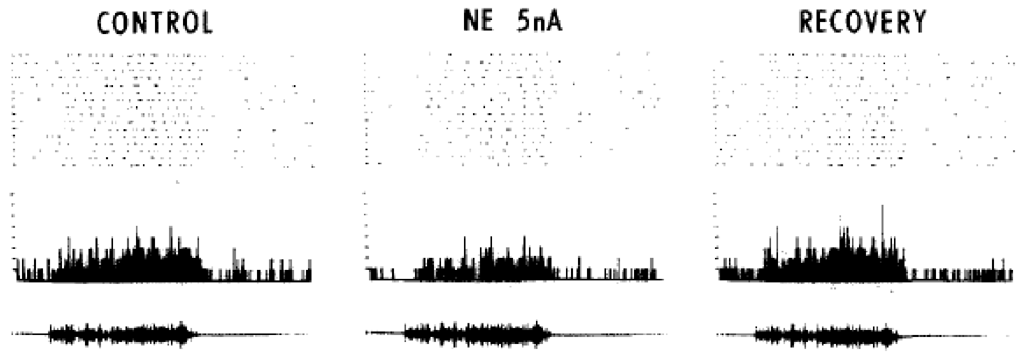
3. Locus coeruleus norepinephrine neurons appear to play an important role in producing the changes in cortical activity that accompany attention (as considered in question 1). The impact of NE on the cortex and thalamus is spatially global in one sense, but spatially local in another. Consider the anatomical and/or neurophysiological data that support this assessment. The responses of noepinephrine locus coeruleus neurons across time are also critical in dictating performance on attention tasks. In this respect, Aston-Jones refers to two forms of firing patterns among locus coeruleus neurons. What are these forms and how have they been recognized in recording experiments? Which form might underlie good performance on tasks requiring target-recognition and which on tasks requiring extra-dimensional shifts in attention?

4. The parietal cortex appears to play a major role in what feature of attentional bias? Its role in attention is perhaps best seen in hemi-neglect patients. List two experimental techniques that can be utilized to detect hemi-neglect. What simple maneuver might allow a hemi-neglect patient to perceive a touch to the left hand? What simple maneuver might allow a hemi-neglect patient to see a visual stimulus hitting the part of the retina associated with the left visual field? In such patients, what might further decrease the likelihood that a left-visual-field stimulus will be perceived? BONUS: Describe an experiment demonstrating that the brain of hemi-neglect patients does respond to left visual field items despite their not being perceived.

NE increases the signal-to-noise ratio of somatosensory cortex neurons and auditory cortex neurons

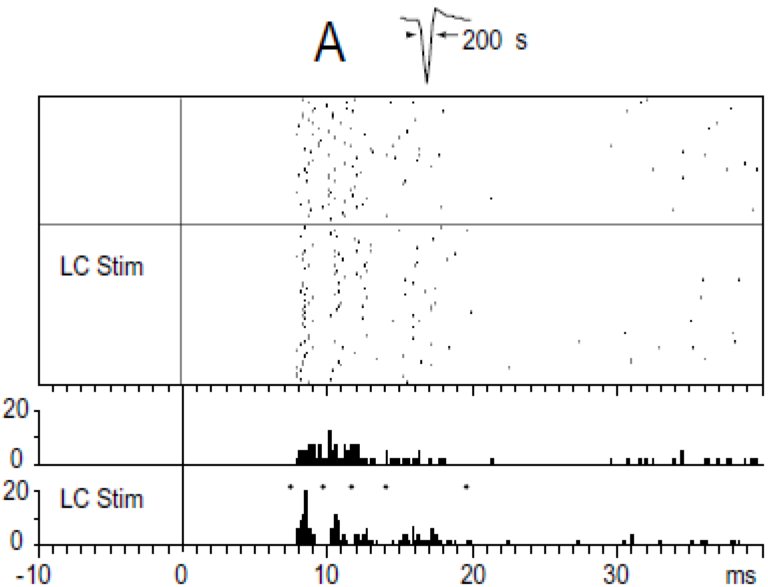


Waterhouse and Woodward,
Exp. Neur., 1980



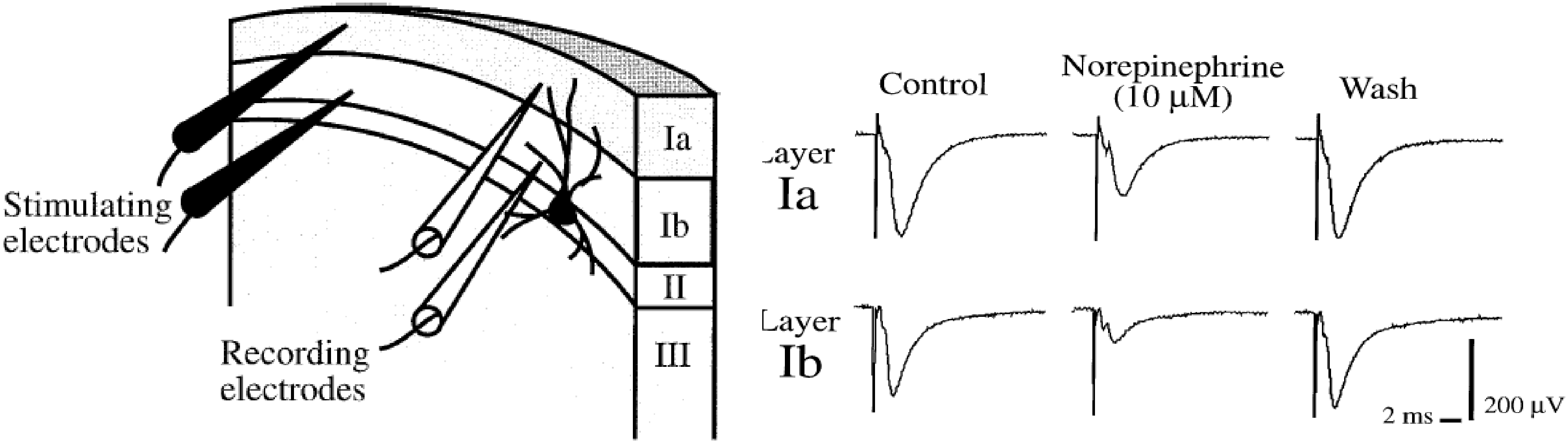
Foote et al., Brain Res., 1975

NE may alter the timing of responses of somatosensory cortex neurons

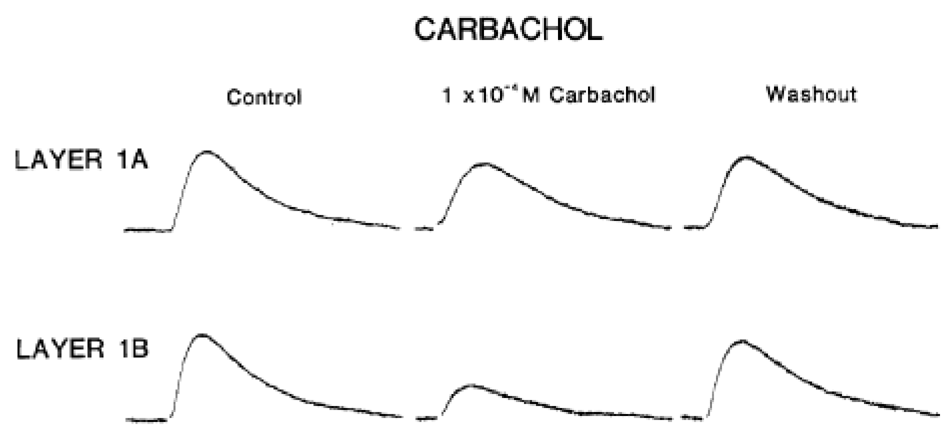


Lecas, Eur. J. Neuroscience, 2004

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).



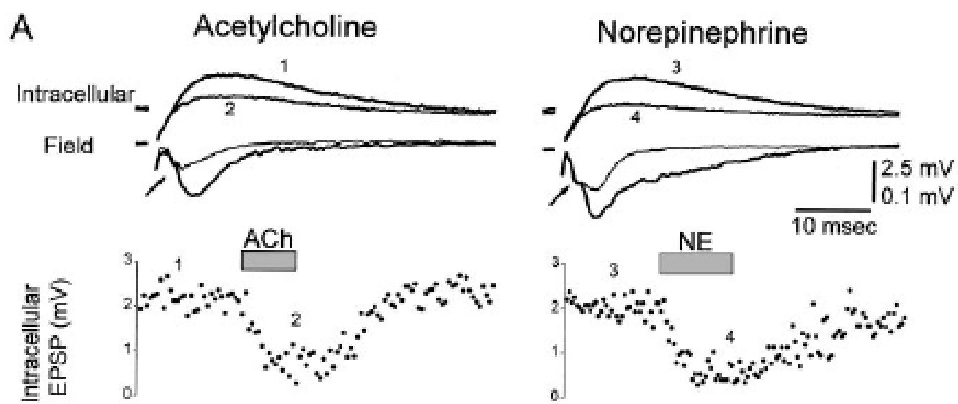
ACh and NE strongly depress responses of olfactory cortex neurons to inputs from other regions of cortex (=association inputs = layer 1b inputs)

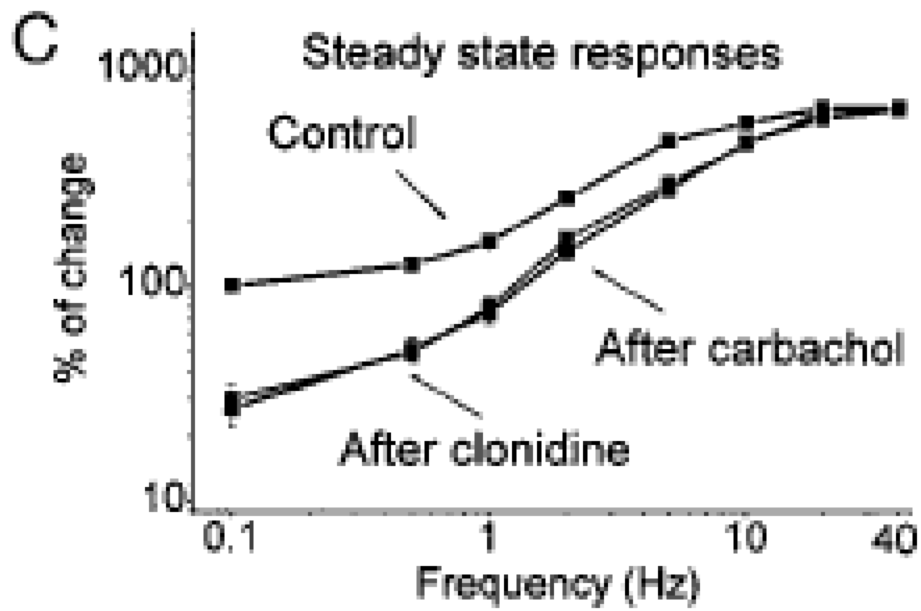
Hasselmo et al., J. Neurophysiology, 1997

NE can affect the functional anatomy of target neurons (i.e., the subset of synapses to which they are sensitive at any given time)

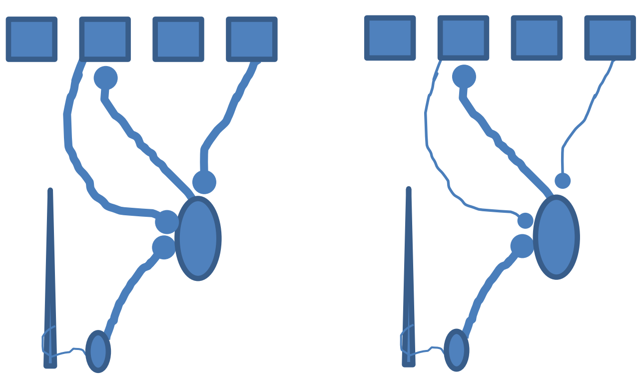
ACh and NE depress responses of ventrobasal thalamic neurons (which relay input from vibrissae) to the inputs they receive from the cortical area (barrel field) to which they project.

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





low ACh **high ACh**



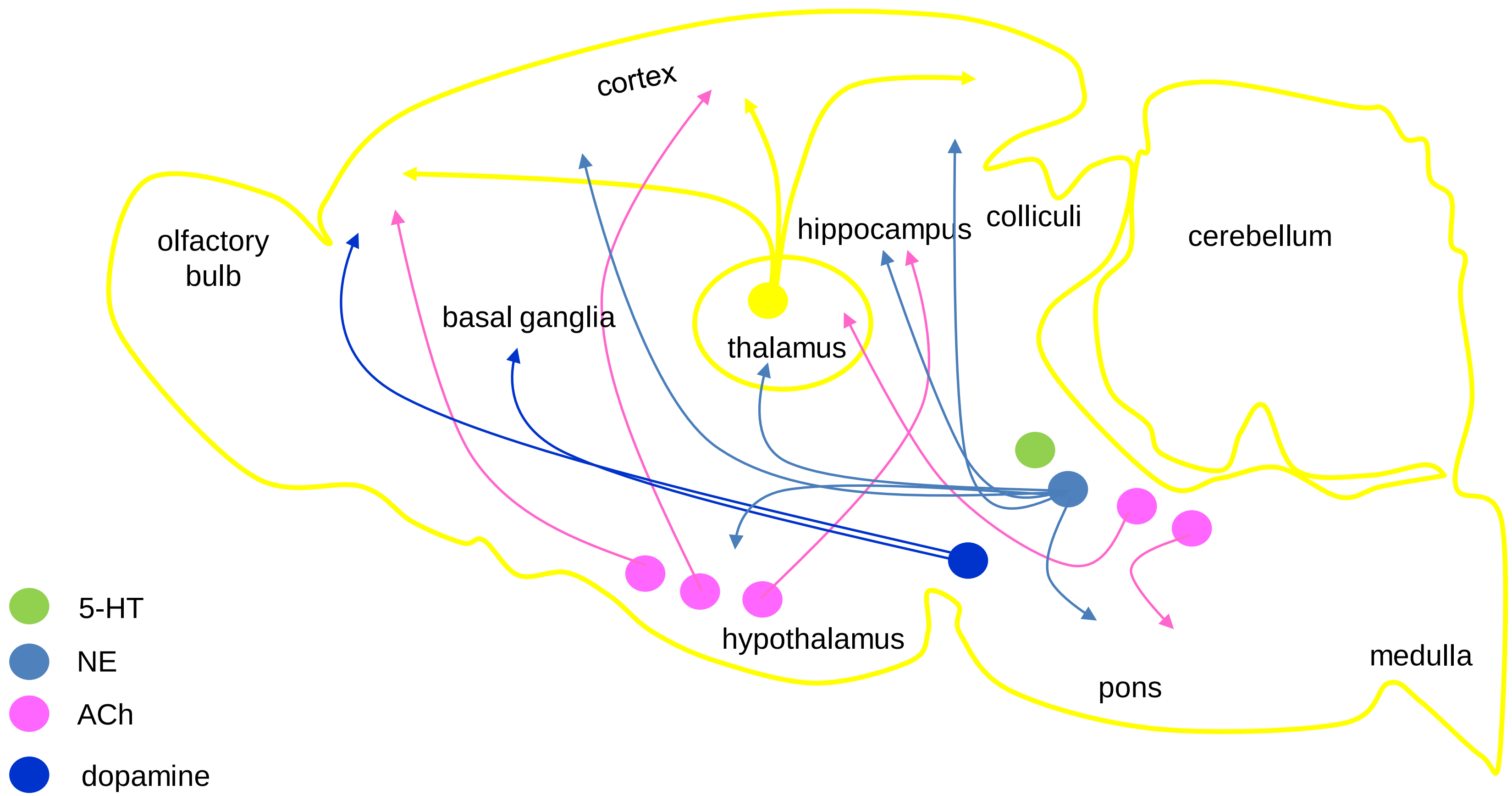
Castro-Alamancos and Calcagnotto. Neurophysiology, 2001

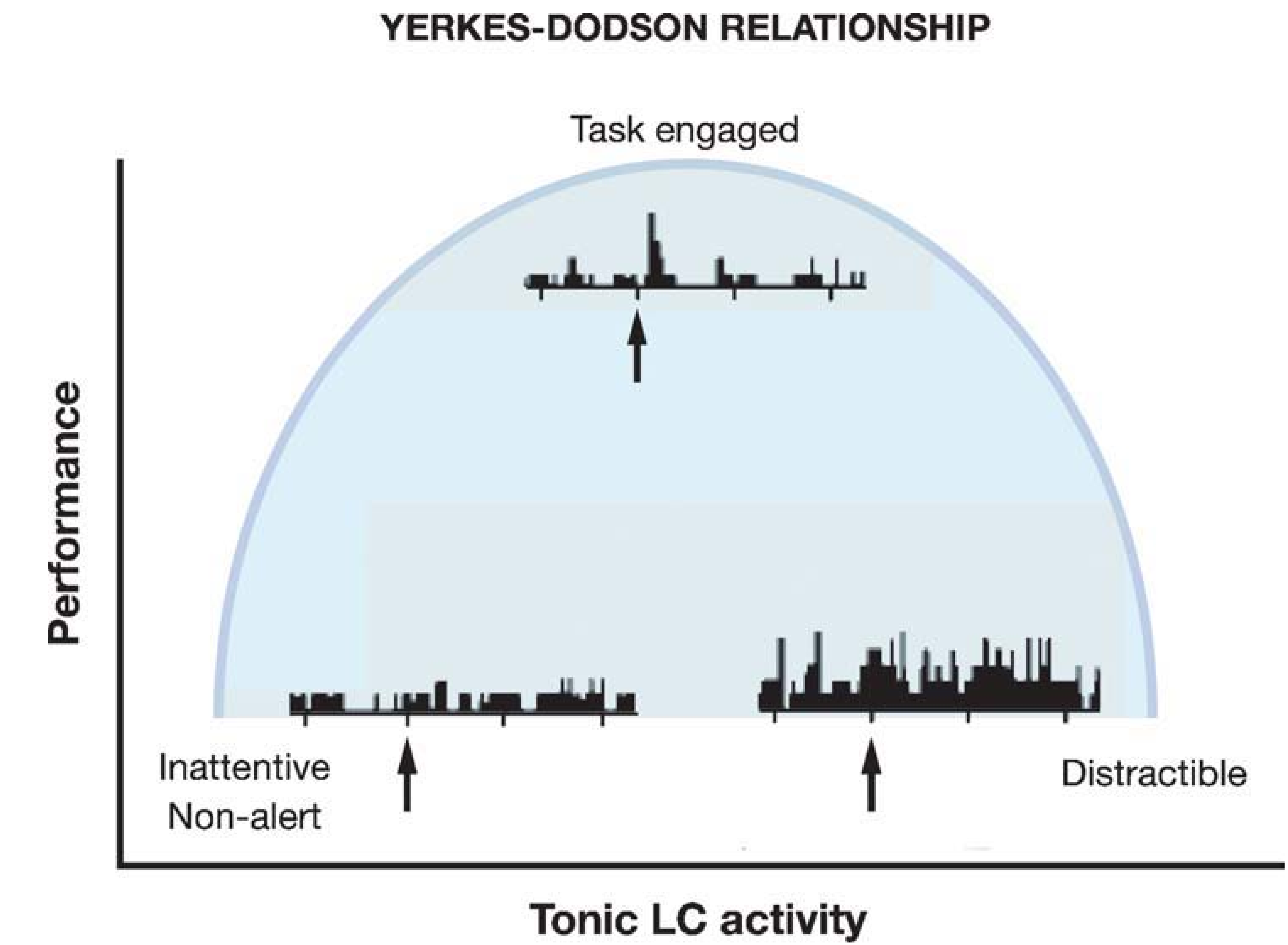
the divergent impact of the brain's neuromodulatory systems:

neuromodulators may often exert the <u>same</u> effect on the neurons they target (e.g., increasing their signal-to-noise ratio in response to an appropriate stimulus)

nevertheless, they may exert <u>different</u> effects on the brain depending on differences in the areas of the brain that they innervate (compare, for example, DA and NE) and/or depending on whether individual neurons send axon terminals to a broad (e.g., NE) versus restricted (e.g., ACh) set of brain regions

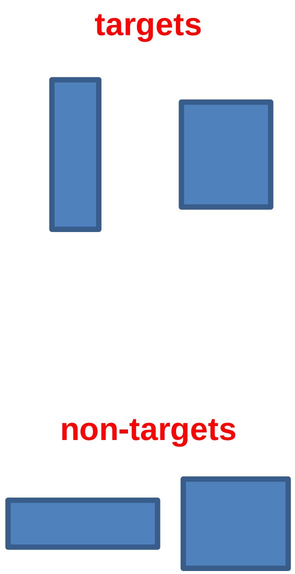
they may also exert <u>different</u> effects by being activated by different types of stimuli – for example, DA is strongly activated by stimuli that are related to reward, NE neurons are activated by novelty, and 5-HT neurons are activated whenever total amount of movement is high

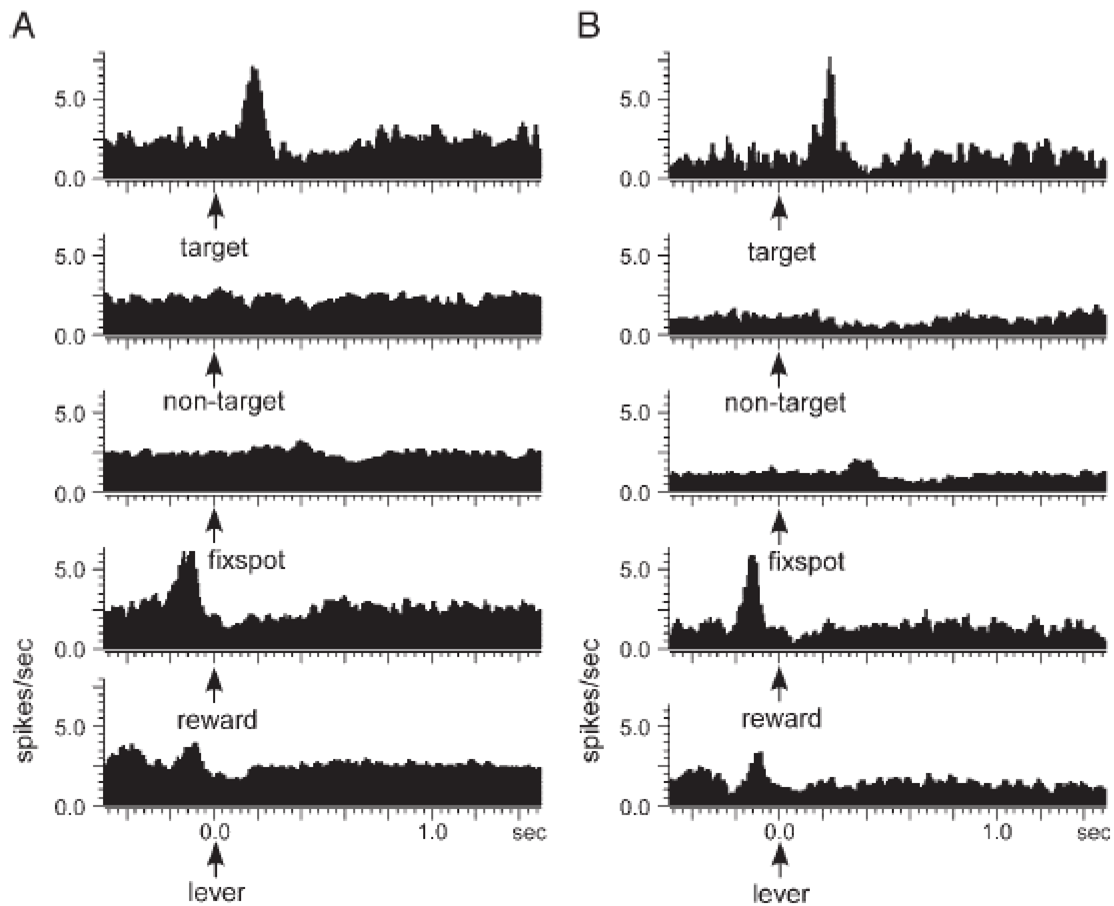




YERKES-DODSON RELATIONSHIP
Task engaged
Performance
Inattentive
Non-alert
Distractible
Tonic LC activity

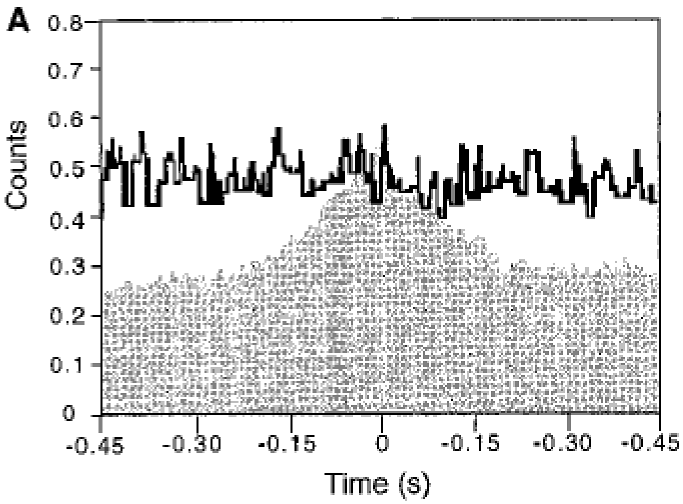
NE responses I: locus coeruleus neurons discharge in response to presentation of target stimuli – prior work has identified robust responses to surprise and/or novel stimuli and when stimuli are suddenly given importance (by virtue of association with reward)

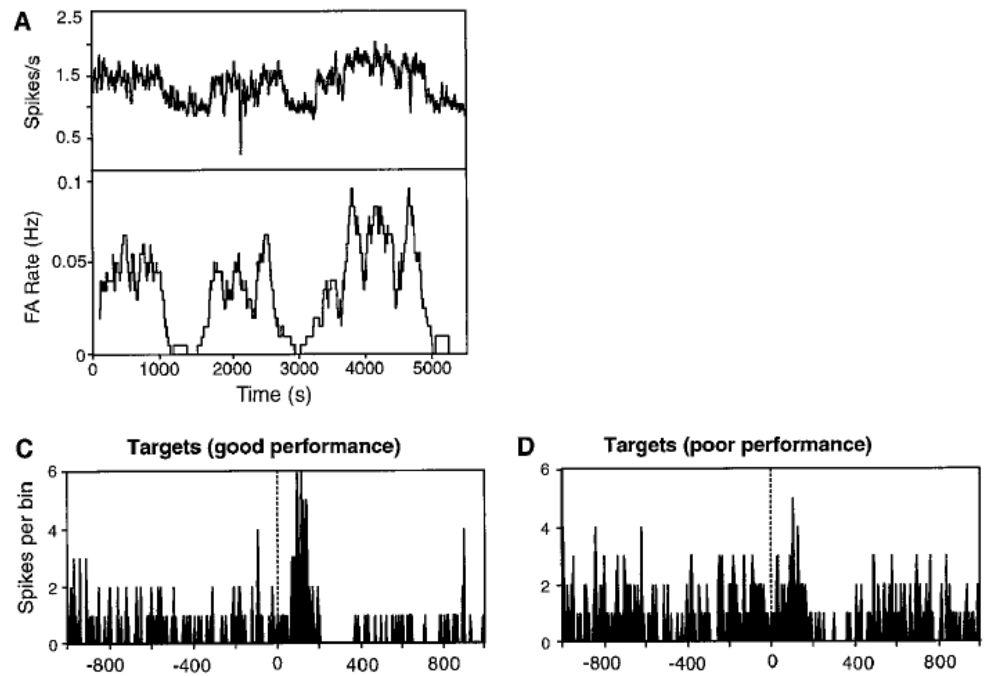




Rajkowski et al., J. Neurophys., 2004

the ‘type’ of NE activity may matter as well – high NE activity can increase the ‘false alarm’ rate and correlated firing among LC neurons is associated with stronger ‘hit’ versus ‘false alarm’ performance





Usher et al., Science, 1999

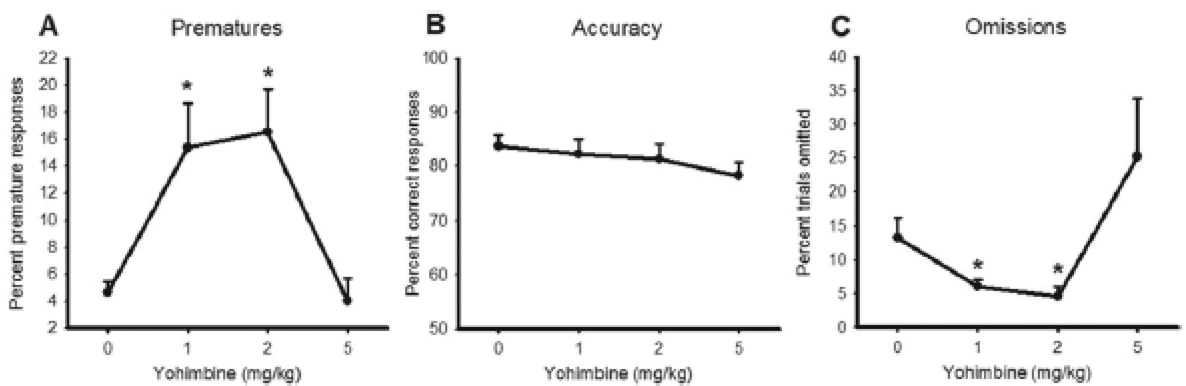
increasing the release of NE in orbitofrontal cortex through the drug yohimbine impairs performance on a simple five-choice serial reaction time test

the animal's task is to detect a brief flash of light and then to make a 'nosepoke' into the hole from which the light came

high NE release results in a greater incidence of 'premature' nosepokes (i.e., nosepokes prior to a light flash)

at the same time, accuracy (hole-choice) is unaffected, but the likelihood of missing a flash is increased

interpretation – high NE heightens the probability that sensory neurons will respond too strongly to irrelevant stimuli (resulting in premature responses / impulsivity) – because of this, relevant stimuli will be missed some portion of the time (yielding higher ommissions)

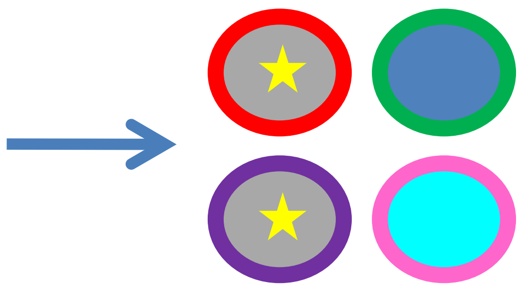


Sun et al., Biol. Psychiatry, 2010

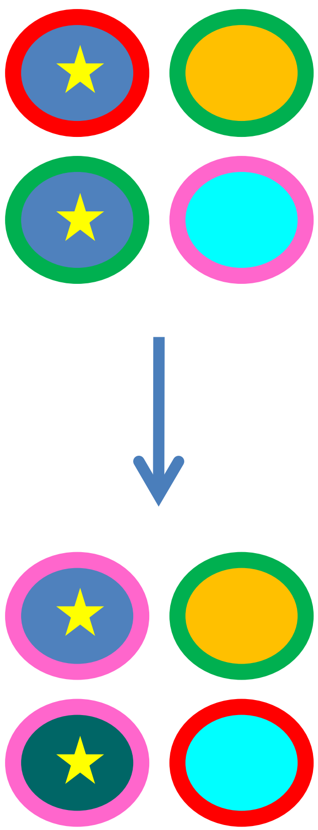
when high NE levels might be good – NE depletion in PFC impacts the ability of animals to make 'extra-dimensional' shifts of attention

circles = cups full of digging medium, some with reward at base   color of outer ring = digging medium (e.g., sand)

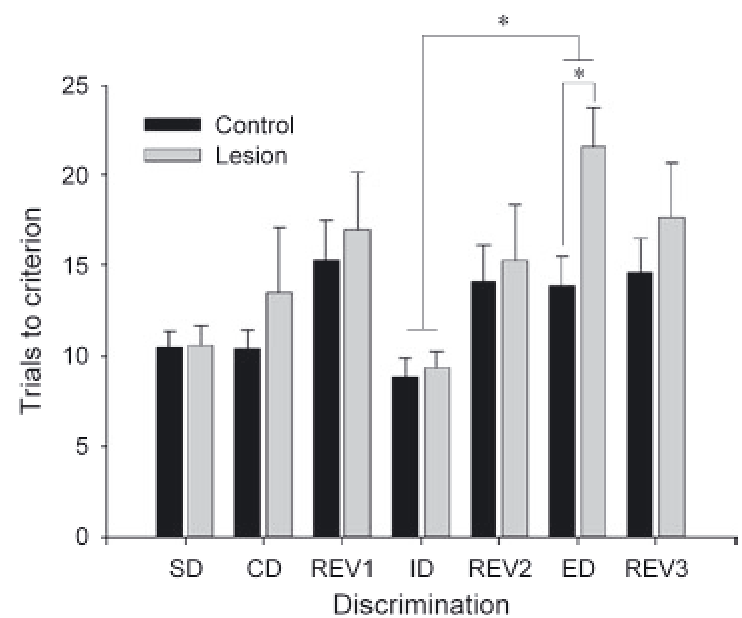
color of fill = odor (e.g., cinnamon)   star = correct choice (i.e., reward beneath digging medium)



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



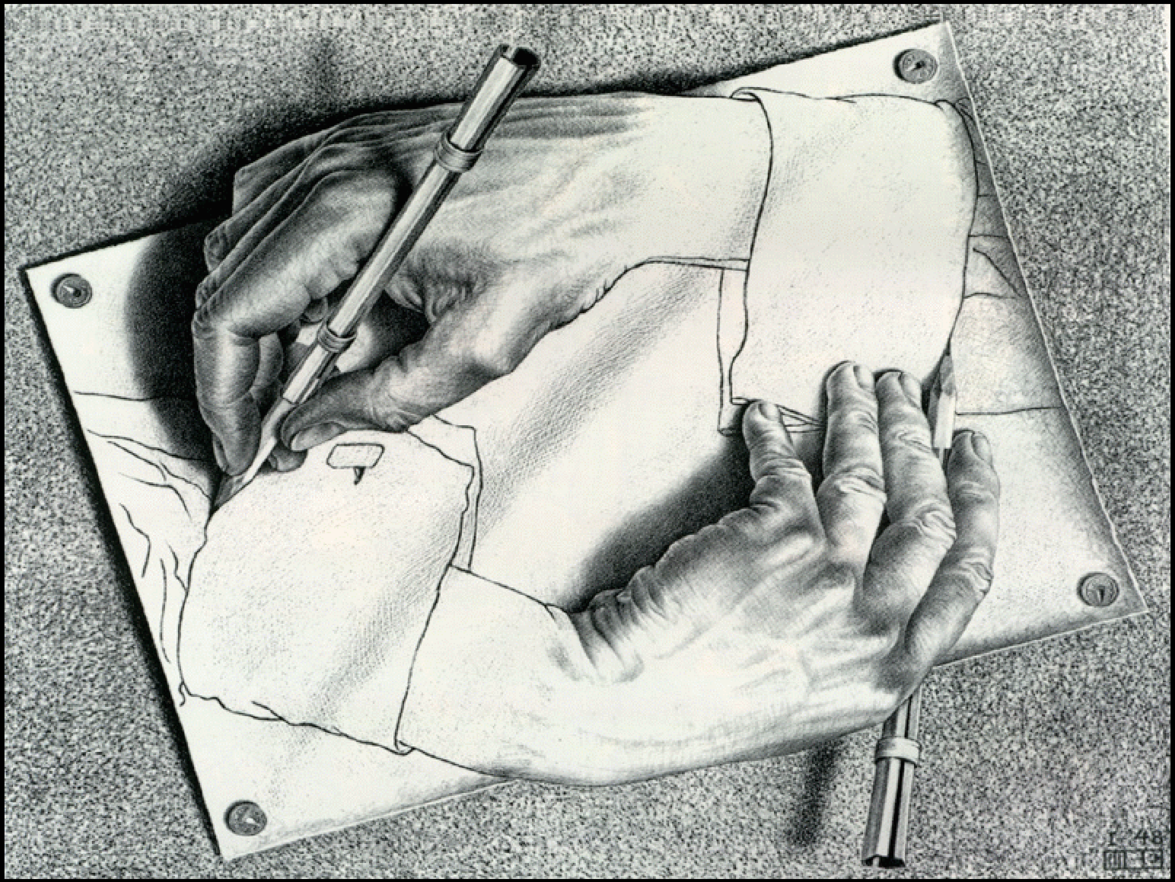
extra-dimensional shift
(i.e., digging medium matters)



Tait et al., Eur. J. Neurosci., 2007

from sleep to attention – lecture 15 – May 16, 2012

the basal forebrain



We adore chaos because we love to produce order. - M. C. Escher

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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.

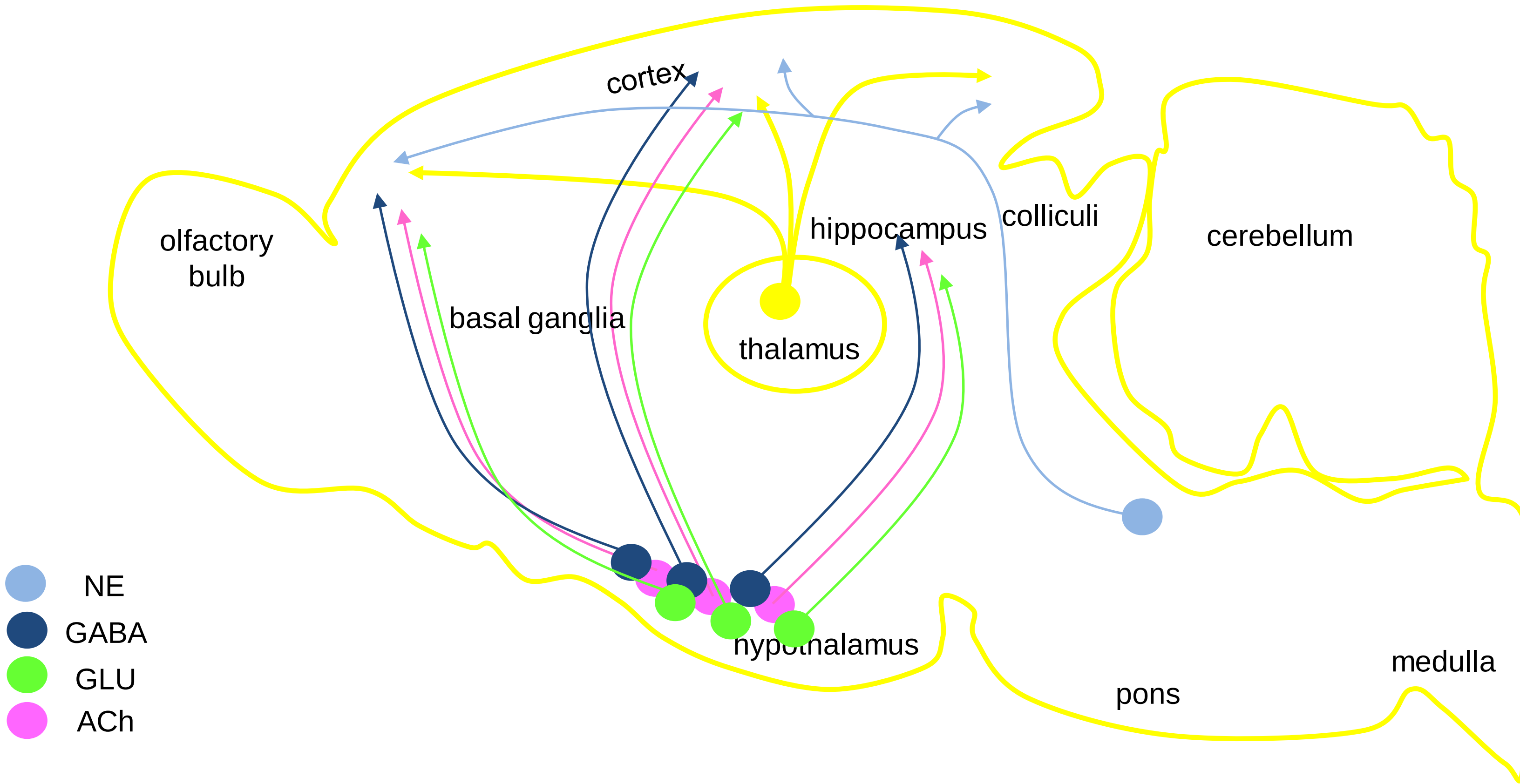
recall two pieces of evidence that suggest that hemineglect can occur not only for egocentric space, but also for object-centered space

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

in comparison to NE neurons of the locus coeruleus, the projections of the basal forebrain are anatomically more complex

whereas NE neurons projecting to cortex are tightly grouped within the locus coeruleus and may send axons to widely spaced regions of cortex, cortically-projecting basal forebrain neurons form several sub-groups which project to discrete regions of the cortex (e.g., only to prefrontal cortex).

furthermore, at least three types of cortically-projecting basal forebrain neurons exist – ACh-releasing, GABA-releasing, and glutamate-releasing



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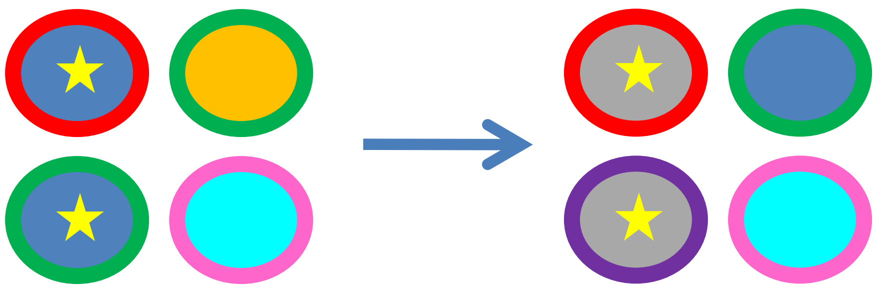

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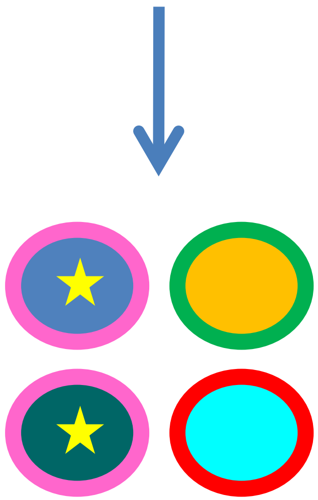

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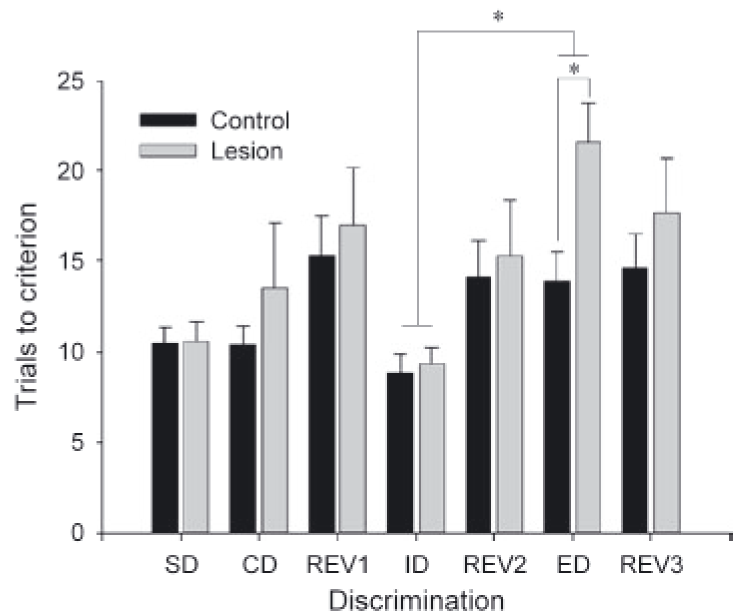
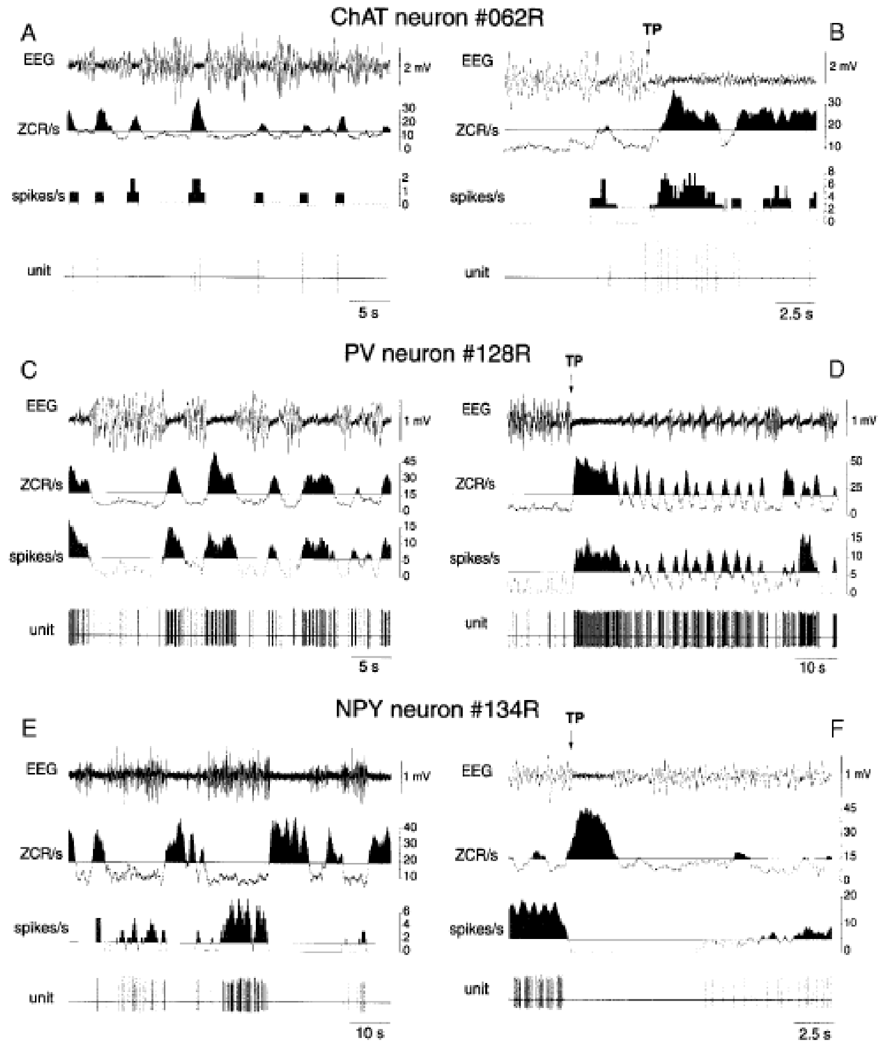


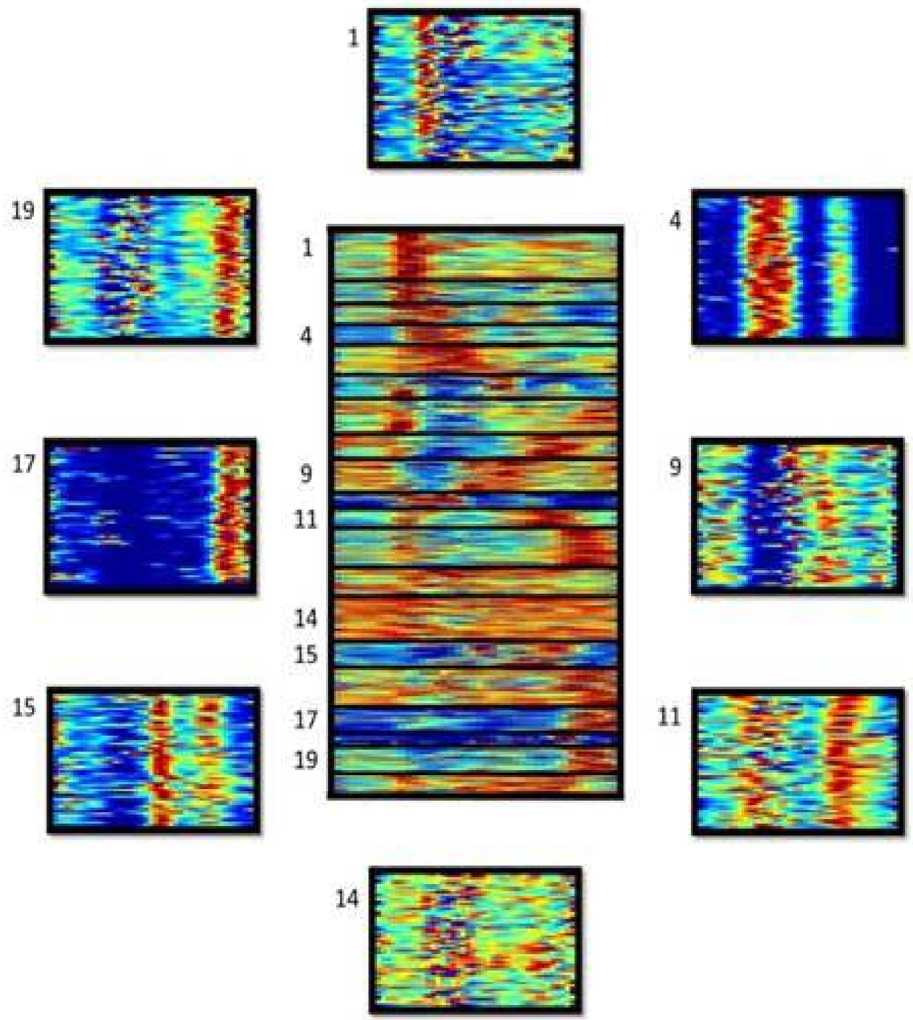
Tait et al., Eur. J. Neurosci., 2007

different types of basal forebrain neurons appear to have different relationships to cortical EEG patterns (note, PV and NPY neurons are different types of GABA neurons)



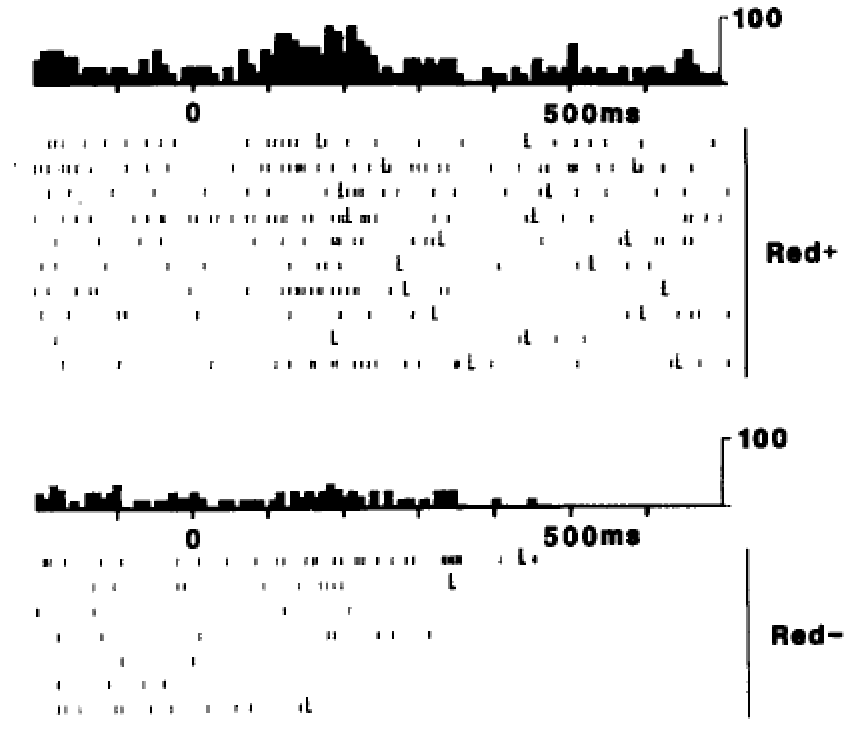
Duque et al., Eur. J. Neurophys., 2000

during performance on a selective attention task, basal forebrain neurons exhibit distinct 'categories' of activity pattern – this possibly serves to modulate cortical targets according to the changes in attentional demands that play out across different task phases



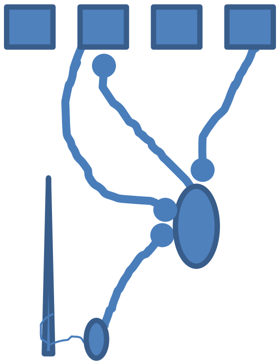
NE neurons 'learn' quickly as shown by quick changes in their responses to stimuli depending on whether they are novel , newly relevant, or newly irrelevant

similarly, basal forebrain neurons 'learn' quickly: in the figure below, a basal forebrain neuron regularly responds to the 'red' visual stimulus when it predicts reward (sucrose drop). later, when the 'red' stimulus now predicts a punishment (saline drop), the neuron ends its response after the first trial

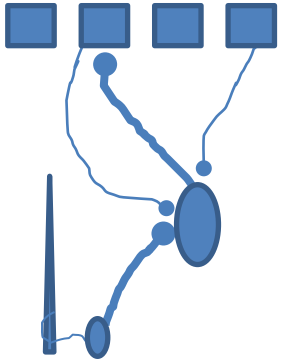


Wilson and Rolls, J. Neuroscience, 1990

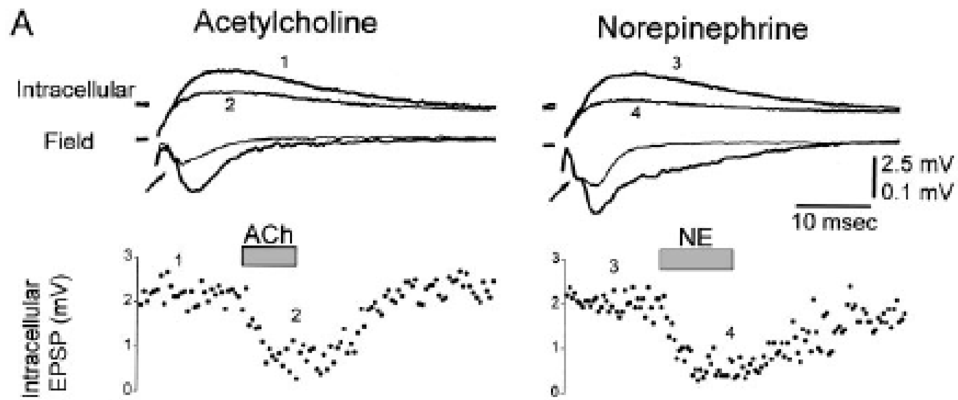
mainlining sensation? – ACh decrements the responses of both ventrobasal thalamic and barrel cortex neurons to inputs from barrel cortex itself – a similar response is observed for whisker barrel cortex (decrement in responses to inputs from other regions of cortex - in this way maximal response to only the whiskers themselves may be achieved



low ACh

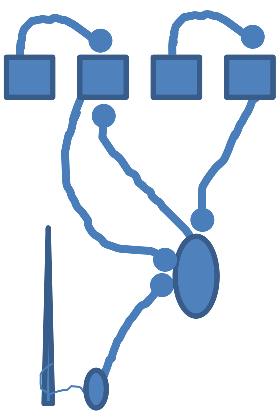


high ACh

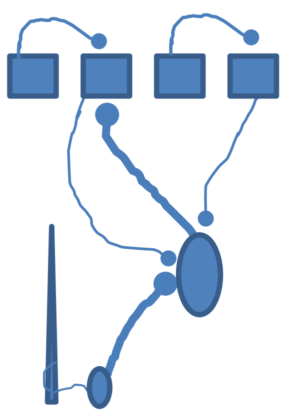


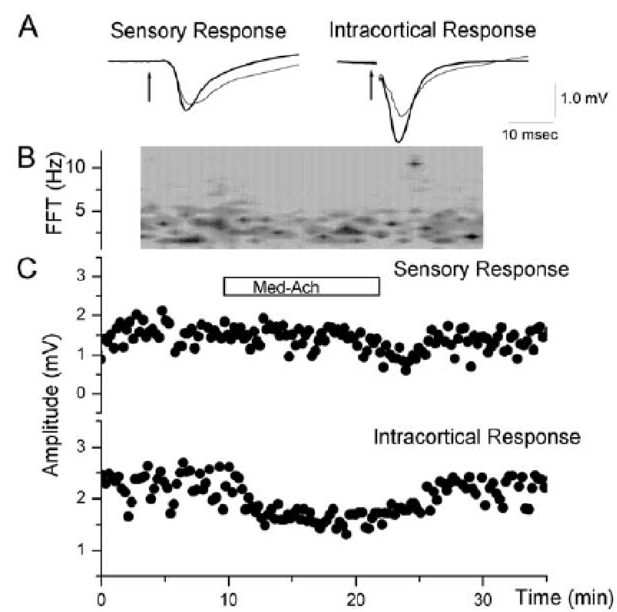
Castro-Alamancos and Calcagnotto. Neurophysiology, 2001

low ACh



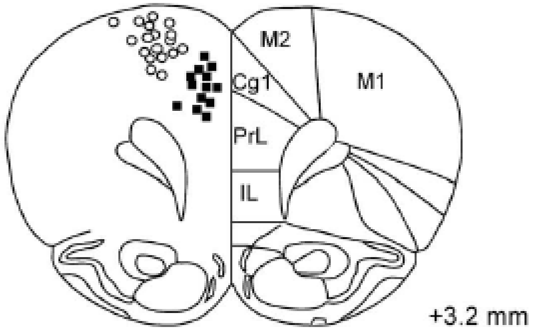
high ACh



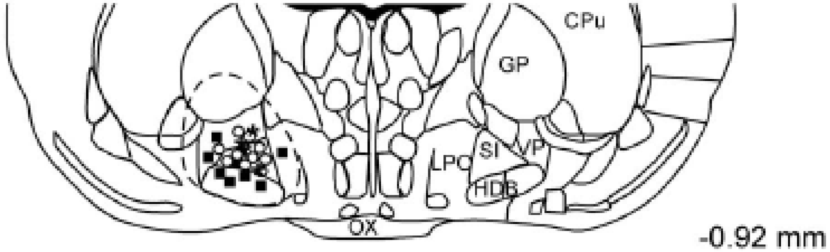


Oldford and Castro-Alamancos. Neuroscience 2003

electrophysiological evidence that the basal forebrain can independently modulate the responsiveness of somatosensory and visual cortex (via the prefrontal cortex) – Golmayo et al., Neuroscience, 2003 – part I

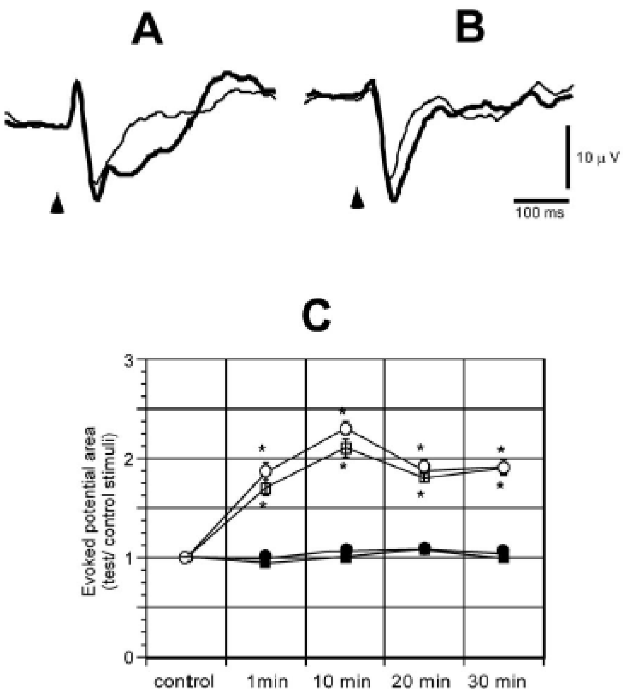


different regions of prefrontal cortex are activated by stimulation of visual cortex (black squares) versus somatosensory cortex (white circles)

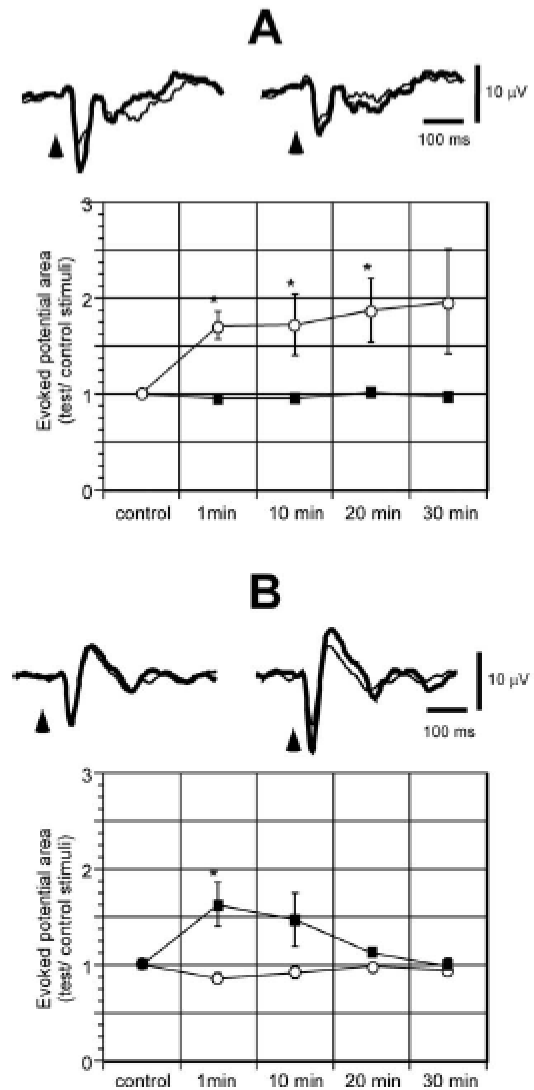


different neurons of the basal forebrain are activated by stimulation of these two different regions of the prefrontal cortex – however, they intermingle anatomically

electrophysiological evidence that the basal forebrain can independently modulate the responsiveness of somatosensory and visual cortex (via the prefrontal cortex) – Golmayo et al., Neuroscience, 2003 – part II



basal forebrain stimulation increases the amplitude and extends the response of both visual and somatosensory cortex to visual and touch stimuli – this effect is blocked by antagonists of acetylcholine

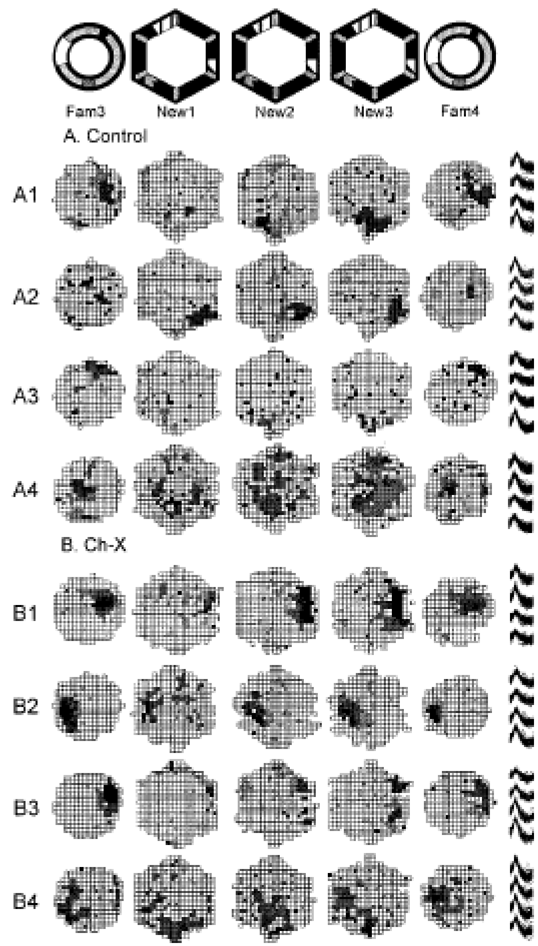


stimulation of the prefrontal region responsive to visual cortex enhances the response of visual cortex to visual input, but not the somatosensory cortex to touch stimuli

similary, stimulation of the prefrontal region responsive to somatosensory cortex enhances the response of somatosensory cortex to touch input, but not the visual cortex to visual input

both effects are reversed by antagonists of acetylcholine

ACh depletion in hippocampus decreases the degree of place-cell discrimination for two similar environments – one interpretation is that this arises from a decreased attention to external stimuli that differ between environments



Ikonen et al., Hippocmapus, 2002