autism

I like to figure things out and solve problems.
Temple Grandin

You have got to keep autistic children engaged with the world. You cannot let them tune out.
Temple Grandin

I can remember the frustration of not being able to talk. I knew what I wanted to say, but I could not get the words out, so I would just scream.
Temple Grandin

"For success in science and art a dash of autism is essential." Hans Asperger

“when taken into a room, he completely disregarded the people and instantly went for objects, preferably those that could be spun”
Kanner

One of my sensory problems was hearing sensitivity, where certain loud noises, such as a school bell, hurt my ears. It sounded like a dentist drill going through my ears.
Temple Grandin
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.
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

aging is associated with decline in a variety of cognitive and motor abilities including balance, memory, ‘cognitive flexibility’, sensory processing speed, spatial navigation, and several forms of attention (provided that the attentional task is made difficult enough)

aging is associated with reduced brain volume resulting from reduced volume of white matter

the set-shift task reveals that aged humans and animals are impaired in extra-dimensional shifts in a way that mimics impairments resulting from damage to the medial prefrontal cortex
autism characteristics -

i. impairments in reciprocal social interactions

ii. abnormal development and use of language

iii. repetitive and ritualized behaviors and a narrow range of interests

iv. i-iii frequently co-occur with mental retardation and/or epilepsy

autism theories -

i. impaired frontal cortex function (e.g., inability to shift attention appropriately)

ii. impaired amygdala function (e.g., poor social interaction and failure to respond to emotion-filled faces)

iii. altered structure of cortical mini-columns

iv. hyper-connectivity (intense world syndrome)

v. imbalanced local vs. global cortical processing
altered brain development appearing at around 1-2 years of age – frontal and temporal cortices and the amygdala, in particular, show rapid growth.
the amygdala hypothesis:

Kluver-Bucy syndrome – loss of amygdala = diminished affect

Amygdala activity in autistics predicts whether or not they will gaze at a face and whether or not the fusiform face area responds

Amygdala lesion in monkey neonates results in subsequent development of repetitive behaviors

Amygdala mediates fear conditioning in animals

Bauman et al., Behav. Neuro., 2008
frontal cortex –

prevalence of large-diameter axons is reduced in autism

when actually attending to a face, autistic brains appear to respond similarly (at least as far as fMRI reflects brain activity)

but...medial regions of the prefrontal cortex exhibiting greater fMRI BOLD responses to familiar faces are not activated

other studies report decreased synchronization of frontal cortex with other regions of cortex
the search for alterations in fine structure of the cortex – mini-columns!

mini-columns were proposed by Mountcastle to compose functional units of the cortex

mini-columns grow in size in early development – in adulthood, they are twice as wide in frontal cortex as in visual cortex

frontal and temporal cortices of autism patients are associated with reduced mini-column sizes
the search for alterations in fine structure of the cortex – hyper-connectivity, hyper-plasticity, and the ‘intense world’ hypothesis

valproate, a drug used to treat epilepsy, drastically increases the incidence rate of autism when taken during a specific point in pregnancy

a rat model of autism has been created based on this phenomena – such rats have reduced social interactions, increased repetitive behaviors, are more anxious, and have long-lasting fear memories

cortical neurons in such animals are ‘hyper-connected’ and exhibit enhanced synaptic plasticity

this is proposed to lead to hyper-excitability of neurons
the search for alterations in fine structure of the cortex – local vs. global connections
evidence for connectivity changes in the resting EEG

- each dot marks the position of a recording electrode

– each line connects to recording sites where autistics show reduced EEG coherence relative to controls for the 8-10 Hz frequency band

– red lines correspond to relatively close electrodes (<10 cm apart) while blue and grey lines correspond to more distant connections (>10 cm apart)

- in the 8-10 Hz band, autistics show weaker coherence overall and coherence within prefrontal cortex is especially poor

-as in the figure above, this figure depicts differences in coherence between autistics and controls

-- here, however, each line connects points whose associated EEG signals show greater coherence in autistics in not the 8-10 Hz band, but the 3-6 Hz frequency band

-- in this 3-6 Hz band, stronger than normal EEG coherence occurs between frontal recording sites and distant electrodes

-- autistics also show high localized coherence among nearby electrodes of the temporal and parietal cortex