Frontal Lobe Function and Dysfunction

Core deficits associated with PFC

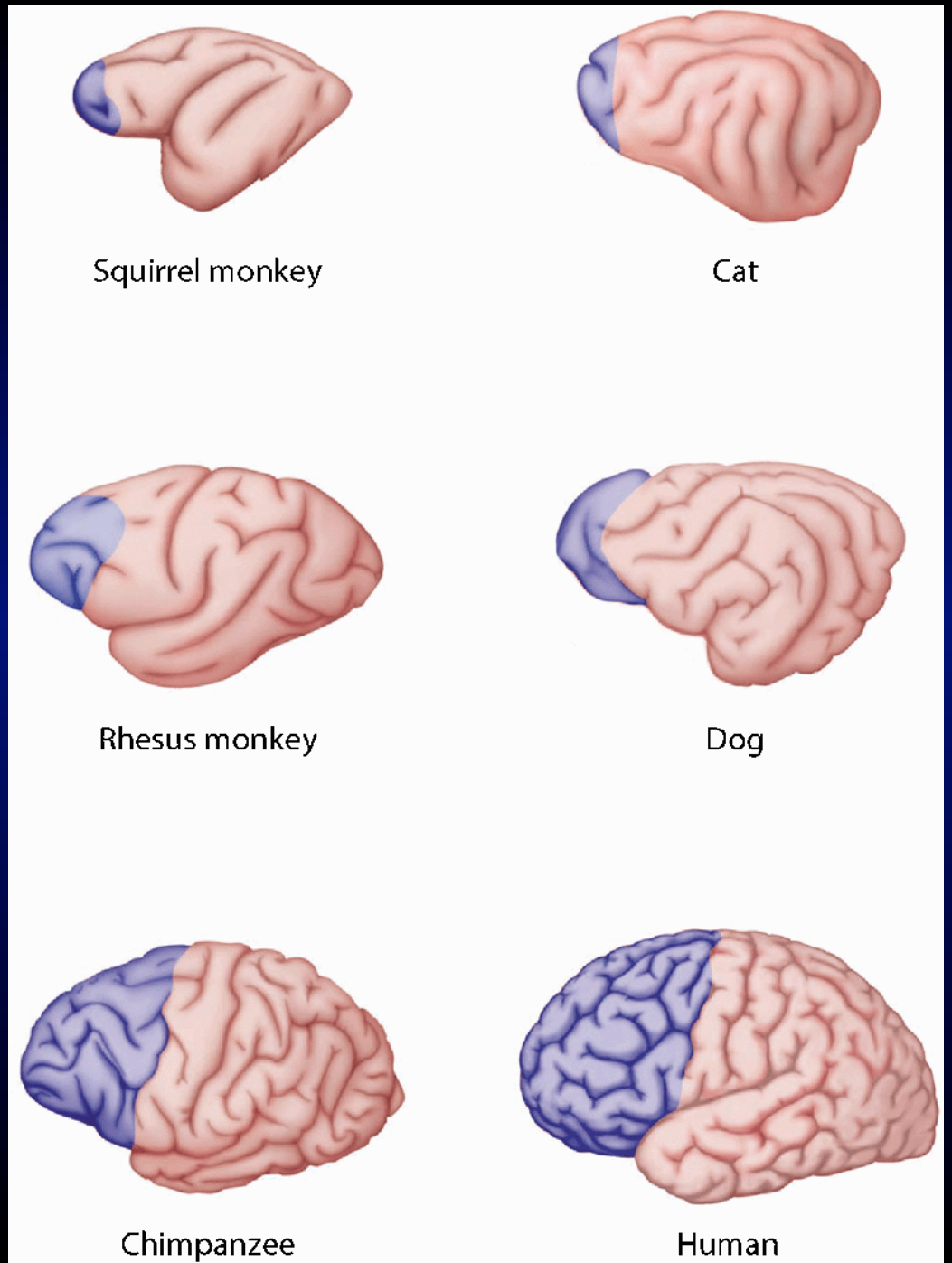
- Motor Planning, Gaze, Speech
- Loss of divergent thinking
- Impaired response inhibition and inflexible
- Inability to manage delay
- Impaired social behaviour
- Personality change

The Frontal Lobes

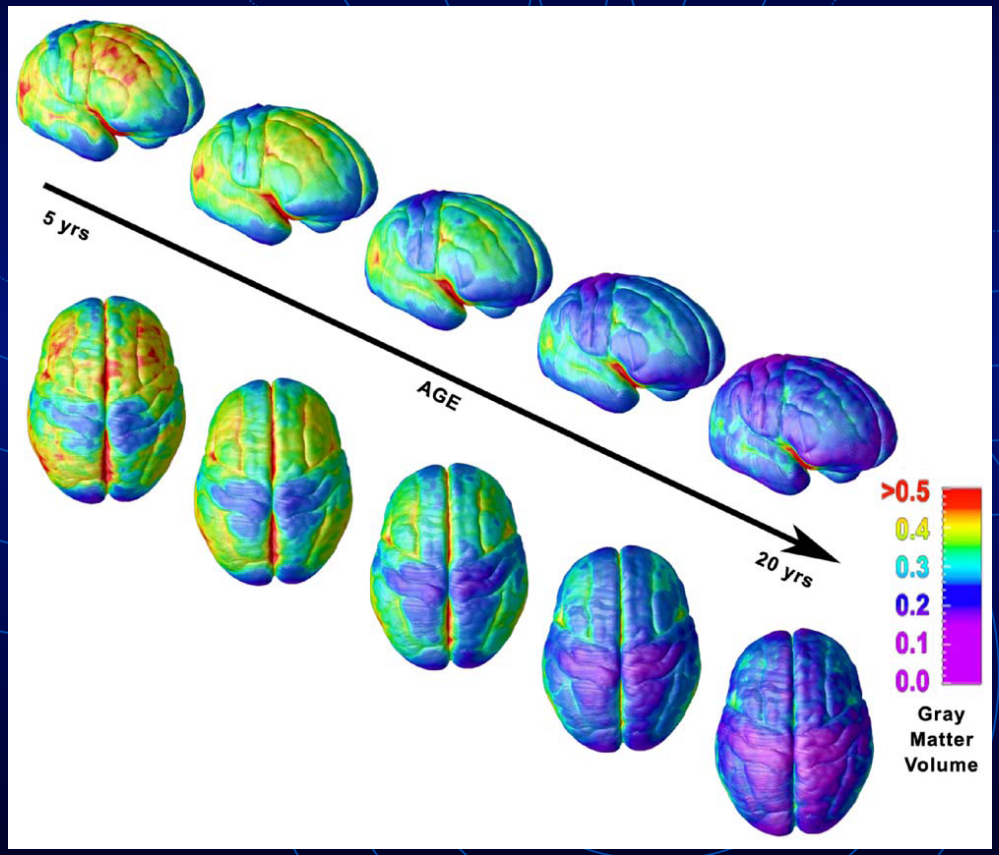
- Comprise about 1/3 of the cerebral cortex
- Present in all mammalian species
- Have undergone tremendous evolutionary expansion
- Associated with the expansion of cognitive abilities

Evolution of the Frontal Lobes

- Ratio of Frontal Lobe to Brain largest in humans
- This ratio considerably smaller in other species
- Associated with cognitive ability

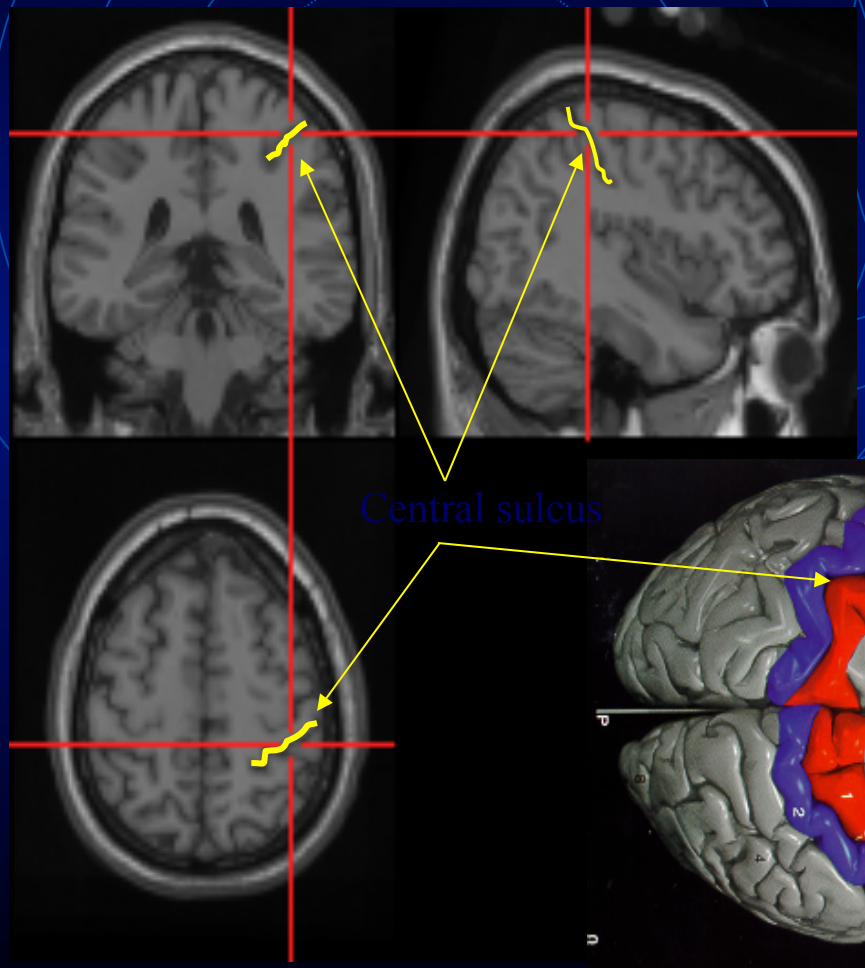


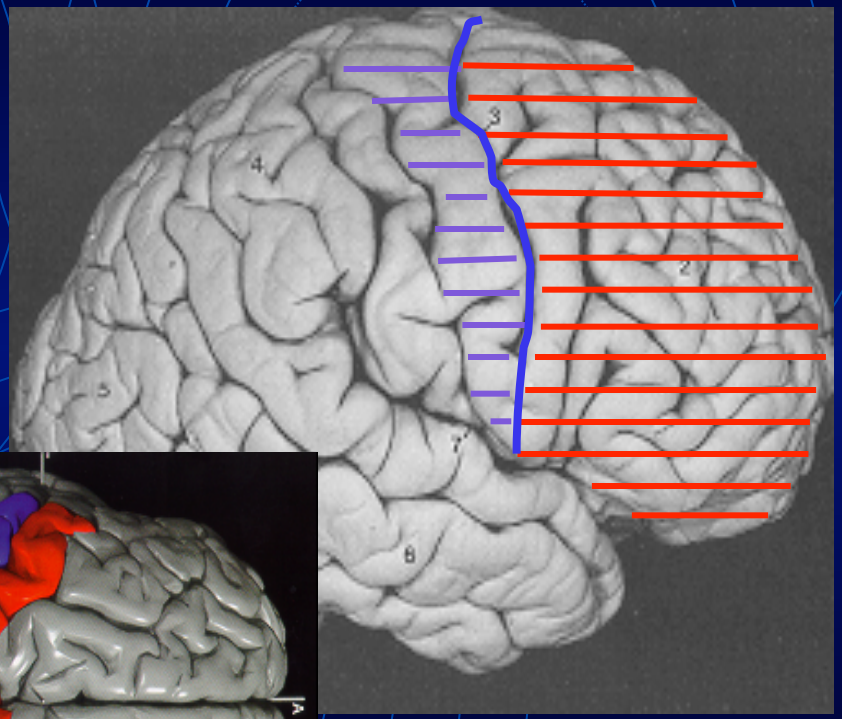
Maturation of the Frontal Lobes

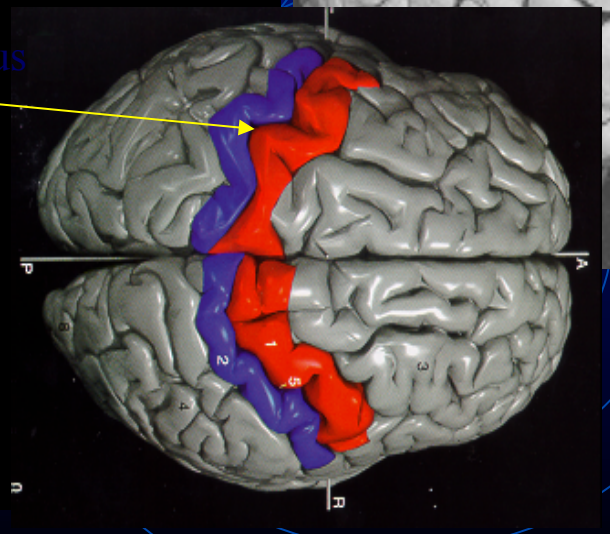


Lenroot and Giedd (2006) *Neuroscience and Biobehavioural Reviews*

The Frontal Lobes: Gross Anatomy

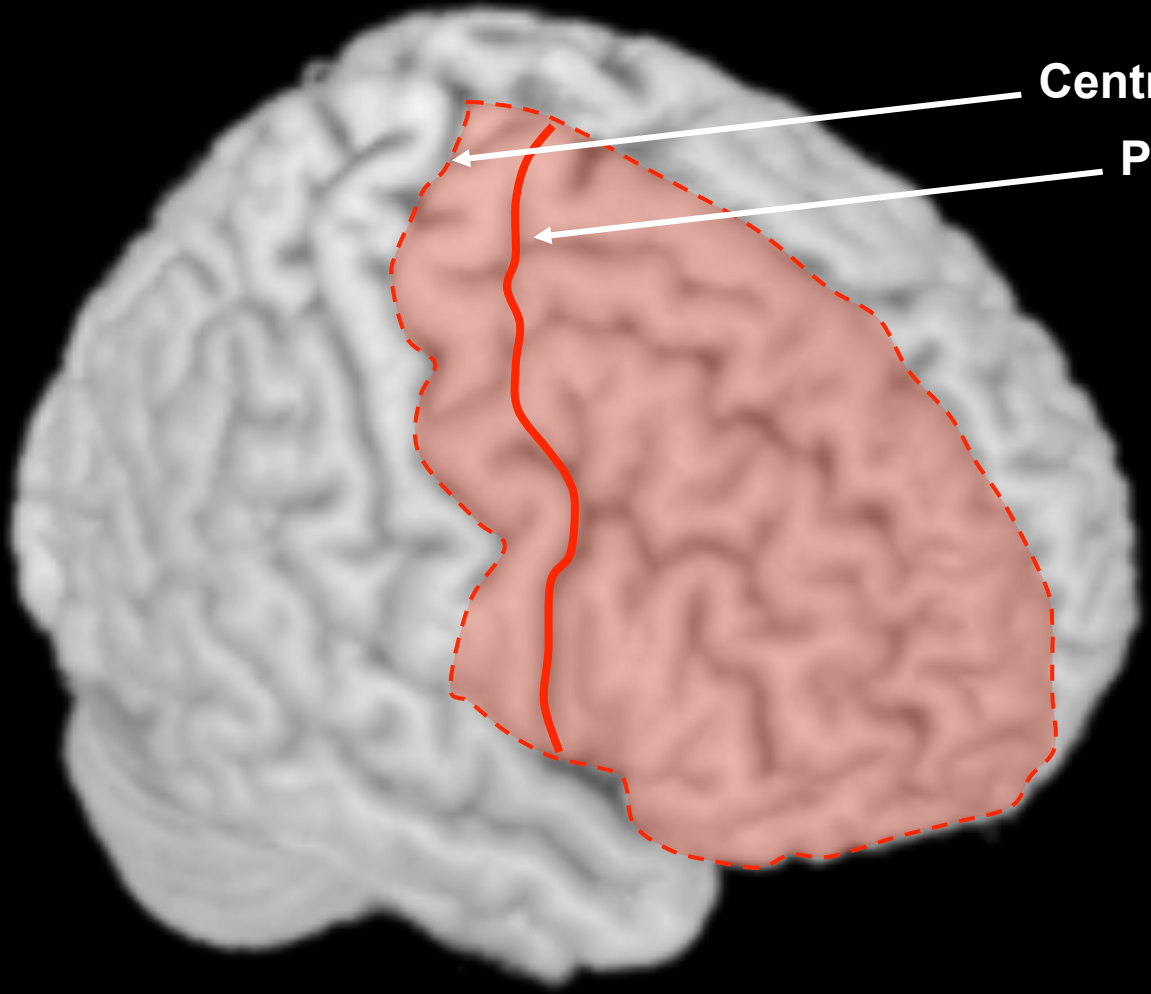






The Frontal Lobes: Gross Anatomy

The Frontal Lobes: Gross Anatomy

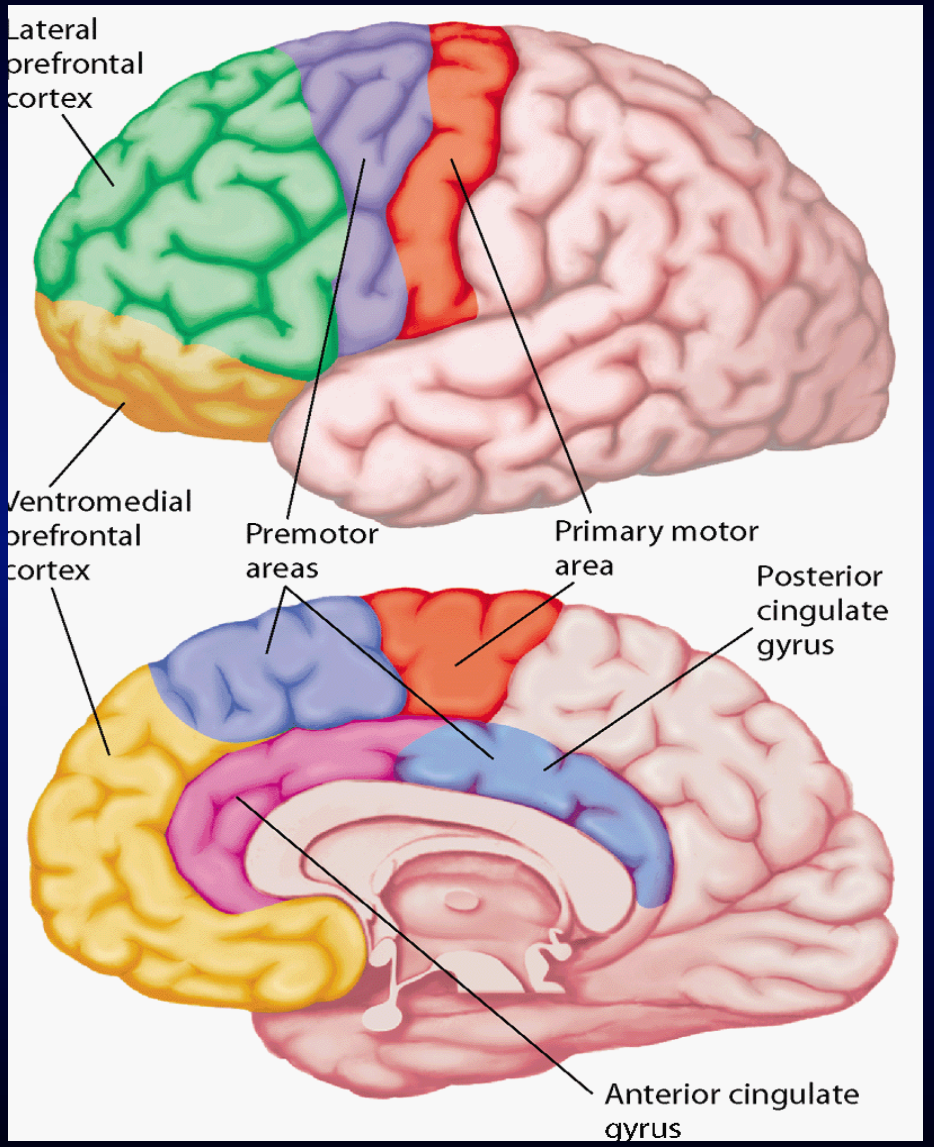


The central sulcus divides the frontal lobe from the parietal lobe.

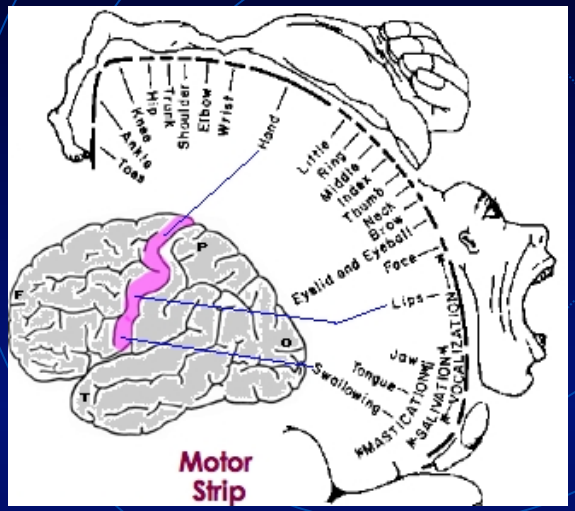
The precentral sulcus divides the rest of the frontal lobes from the ‘motor strip’.

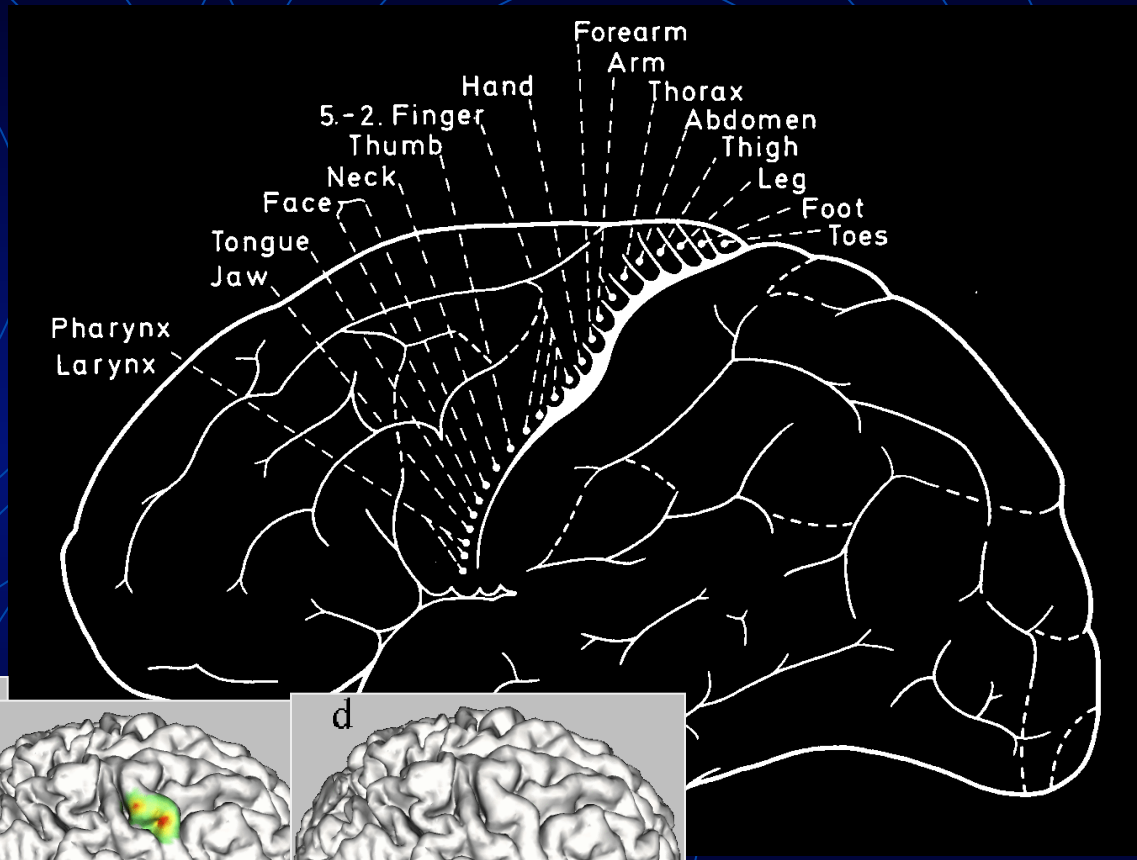
The Frontal Lobes

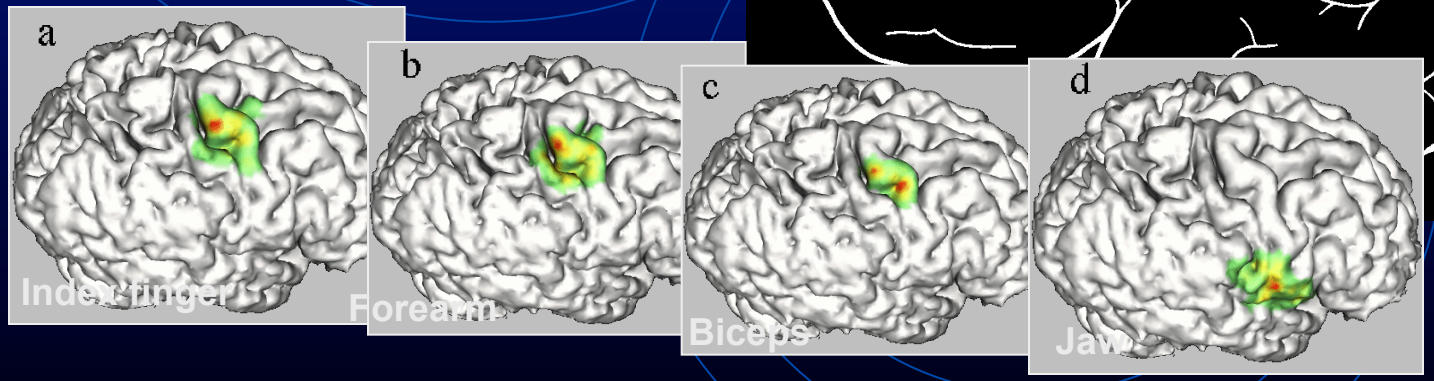
- Extends from the central sulcus anteriorly
- Ventrally along the medial and lateral surfaces



Primary Motor Cortex







TMS motor response amplitude maps for four muscles. Green indicates small response. Red corresponds to the largest response.

Cortical Motor System

Connections of the Motor Cortex

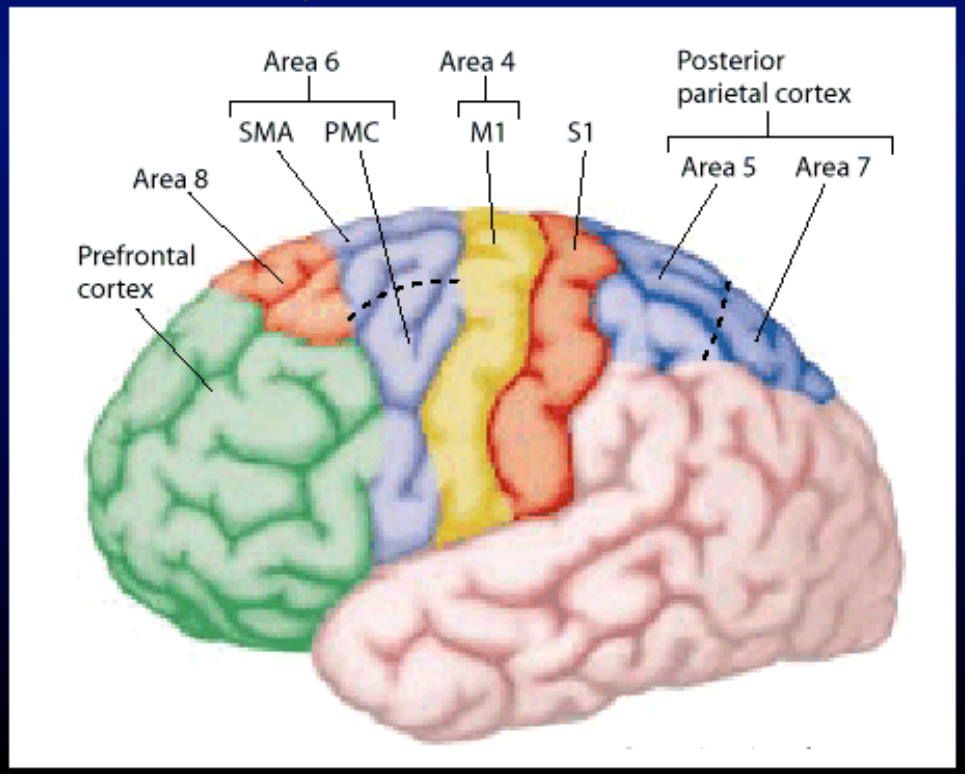
- Spinal motorneurons to control limb, hand, finger, trunk and facial movements
- Subcortical areas also concerned with motor movements-basal ganglia and cerebellum
- Receives input from prefrontal cortex and cingulate cortex

Cortical Motor System

Pre-motor cortex

Movement planning/sequencing

- Many projections to M1
- involved in the intention or preparation to move; neurons in this area discharge before, rather than during, a movement
- Stimulation => more complex mov't
- Two distinct somatotopically organized subregions
  - SMA (dorso-medial)
    - May be more involved in internally generated movement
  - Lateral pre-motor
    - May be more involved in externally guided movement



Disturbance of Motor Function

Primary Motor

pronounced weakness in affected body parts

Stimulation => simple movements

Premotor

lesions do not produce paralysis

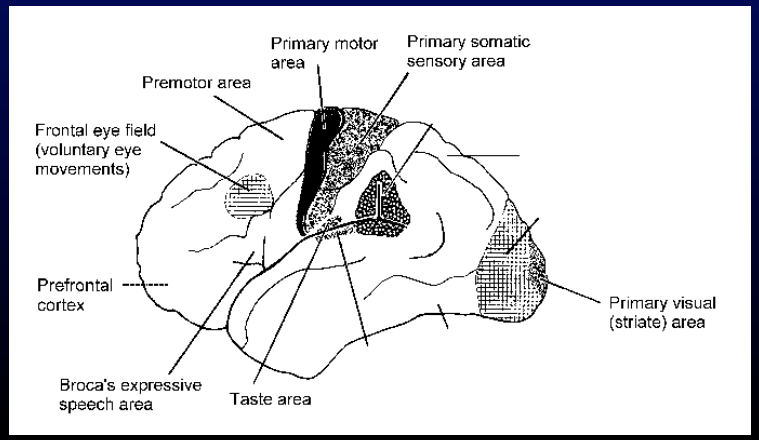
more complex motor deficits

Stimulation => complex movement

Cortical Motor System

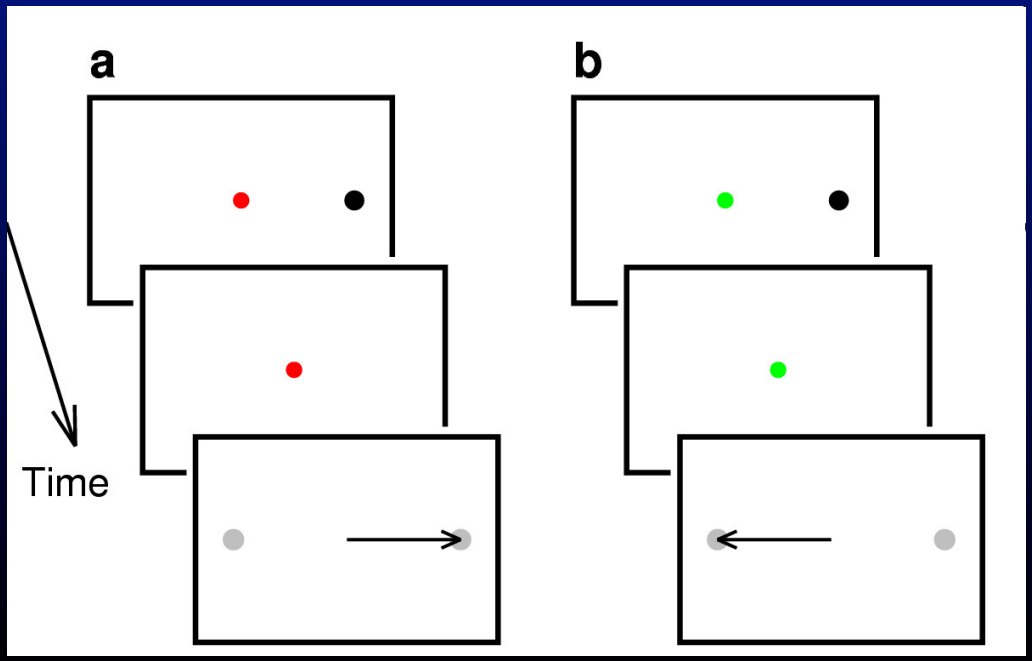
Connections of the Premotor Cortex

- Directly to motorneurons and also to motor cortex;
- Receives projections from posterior parietal areas 5 and 7
- Frontal eye fields (FEF: 8 and 8a) reciprocal projections



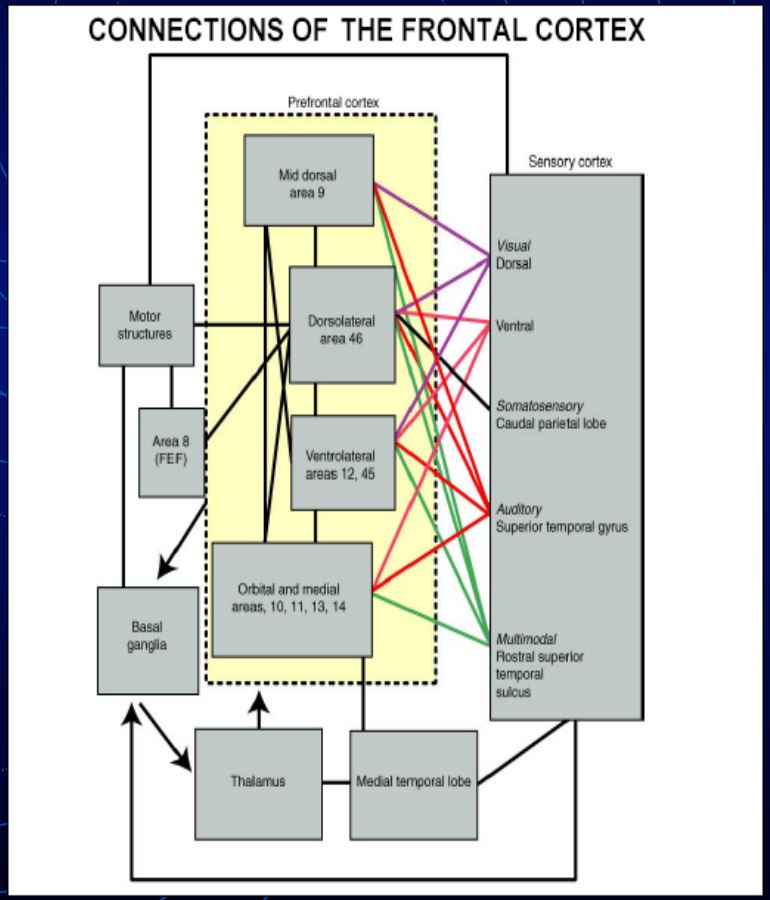
Cortical Motor System

- frontal eye fields and supplementary eye fields play an important role in initiating purposive eye movements and directing attention
- Damage results in disruption of purposeful eye movement



‘All neural roads eventually lead to the frontal lobes’ Kolb & Whishaw (2009)

- A massive network - prefrontal cortex is the most highly interconnected of all cortical regions
- Interconnects:
  - motor, perceptual, and limbic regions
  - parietal and temporal cortex
- Subcortical structures (e.g., brainstem, basal ganglia, cerebellum) project indirectly to PFC via thalamus
- In a perfect position to **coordinate**



Prefrontal cortex – the top of the hierarchy

- Executive function – flexible, goal-directed behaviour in response to internal and external cues
  - + Planning
  - + Managing Delay
  - + Contingencies and Rules
  - + Filtering
  - + Flexibility

Goal-oriented behaviour – formulate, monitor, adapt

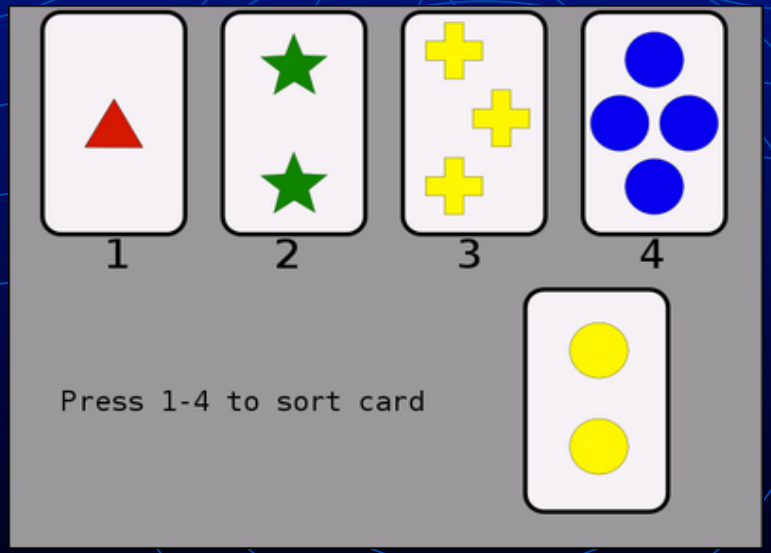
Assessment of Frontal Lobes

- Most complex aspect of neuropsychological assessment
- Surprisingly few sensitive tests available
- Isolated cognitive functions may be unimpaired
- How to measure self-regulation?
- Ecological validity ?
- Lack of insight

Neuropsychological Assessment

Convergent vs divergent thinking

Wisconsin Card Sorting Task = reactive flexibility
Alternate Uses, Fluency tests = spontaneous flexibility

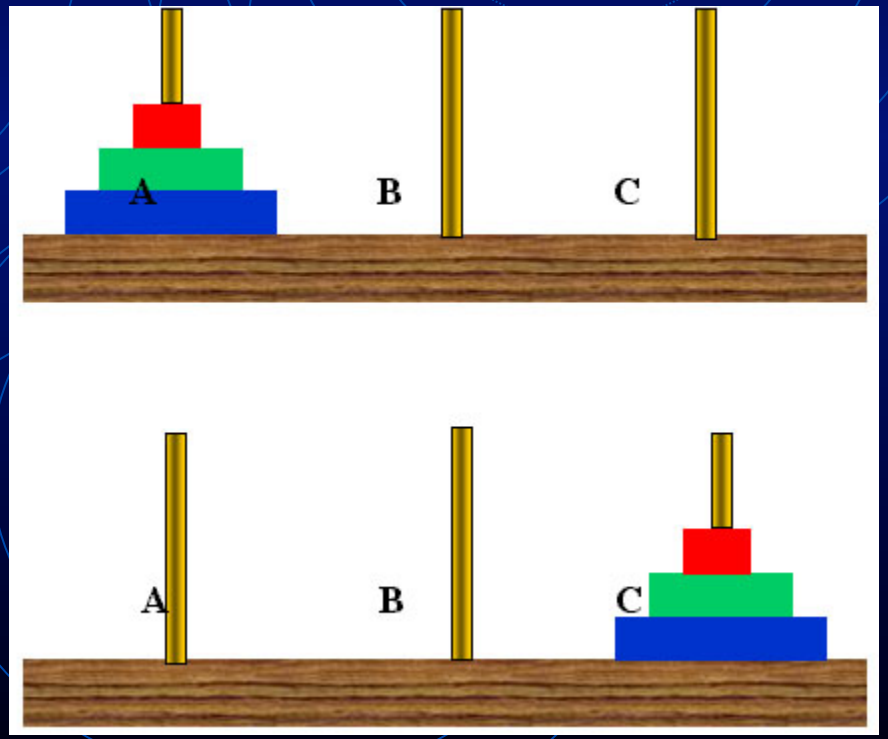


Work out the sorting category according to examiner's feedback

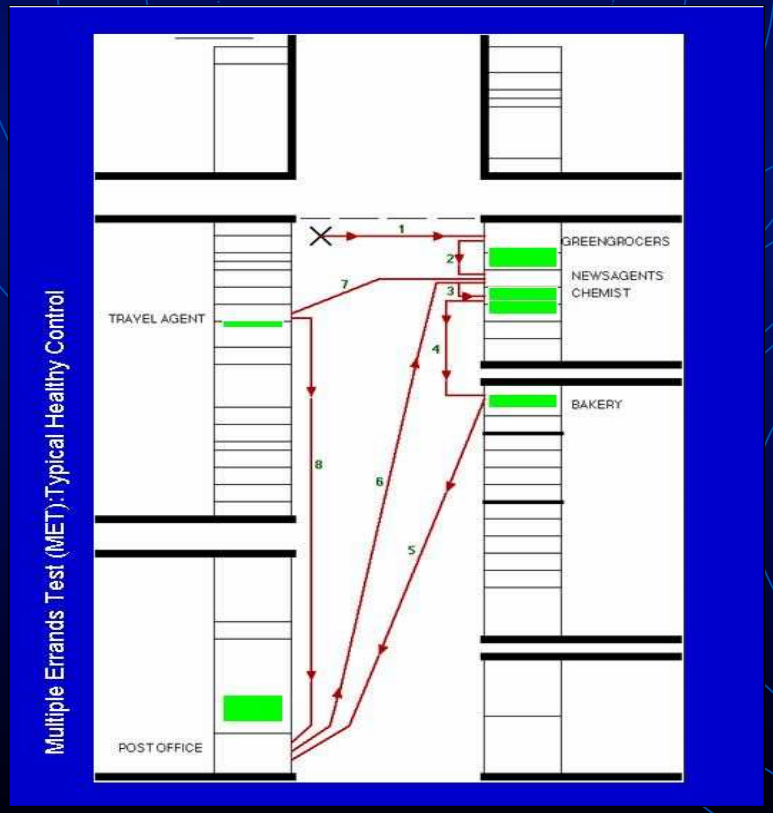
- Stroop task (response inhibition)

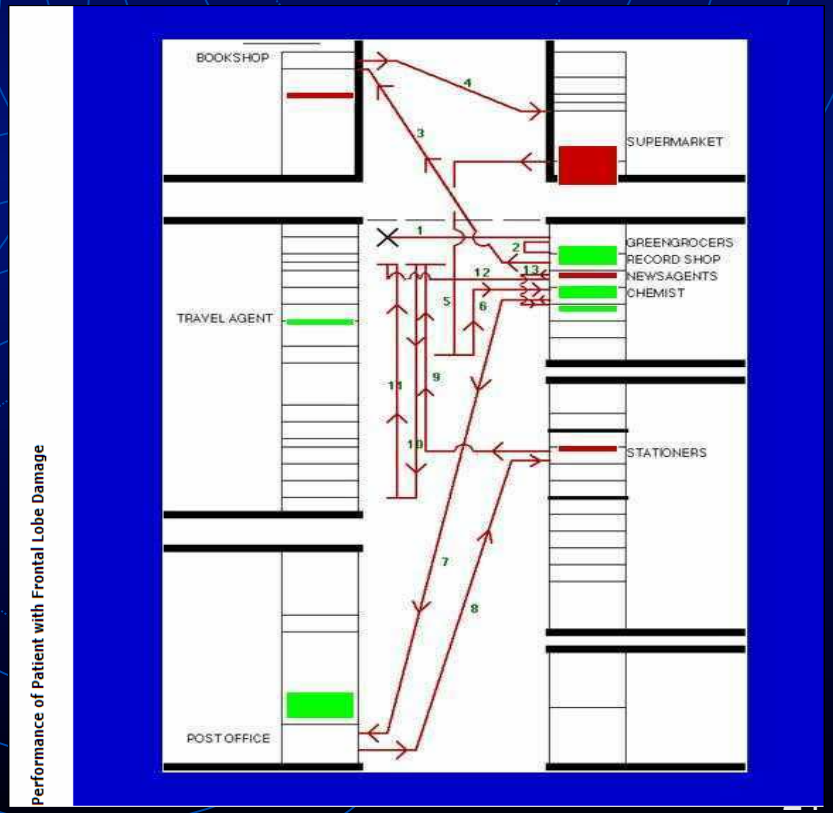
BLUE GREEN

- Tower tasks (planning)

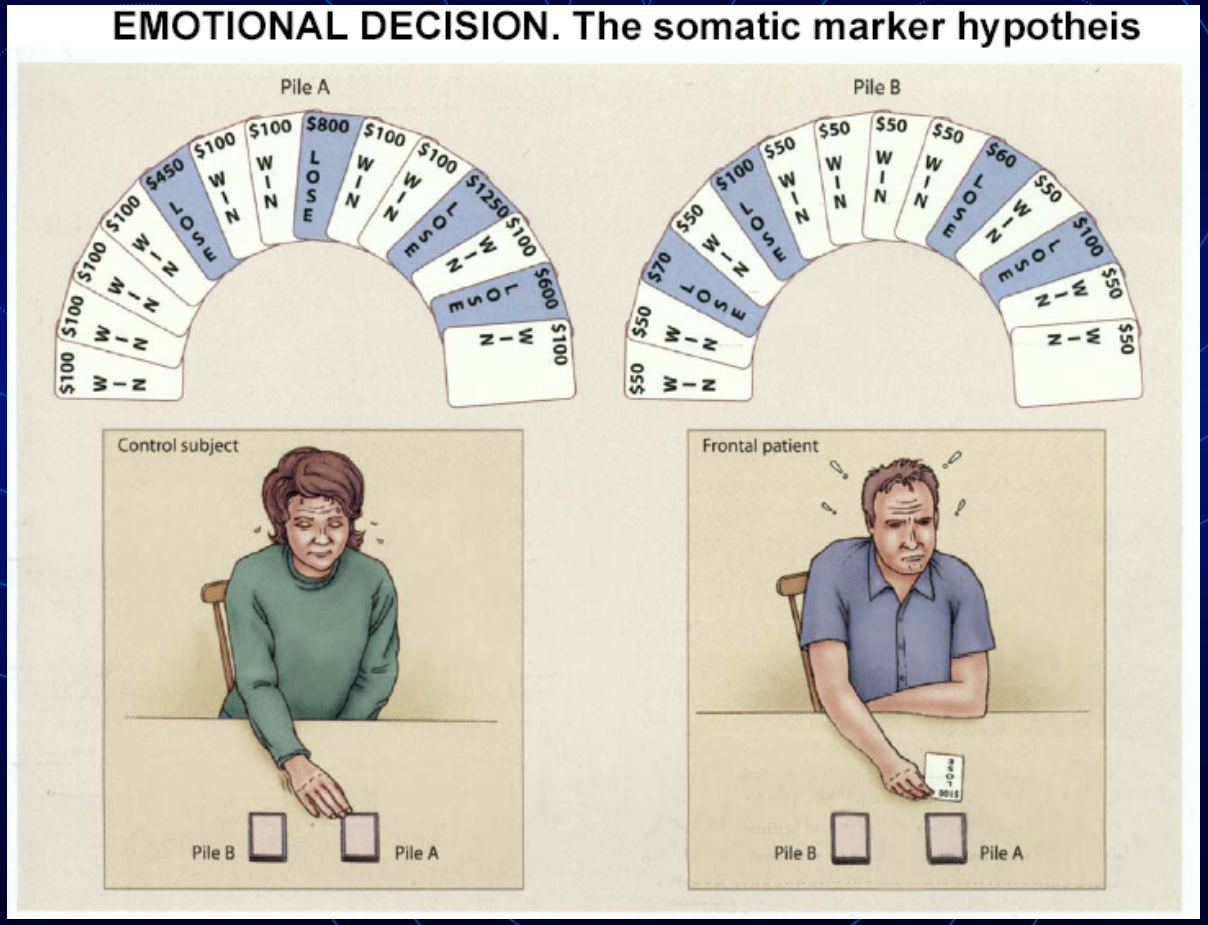


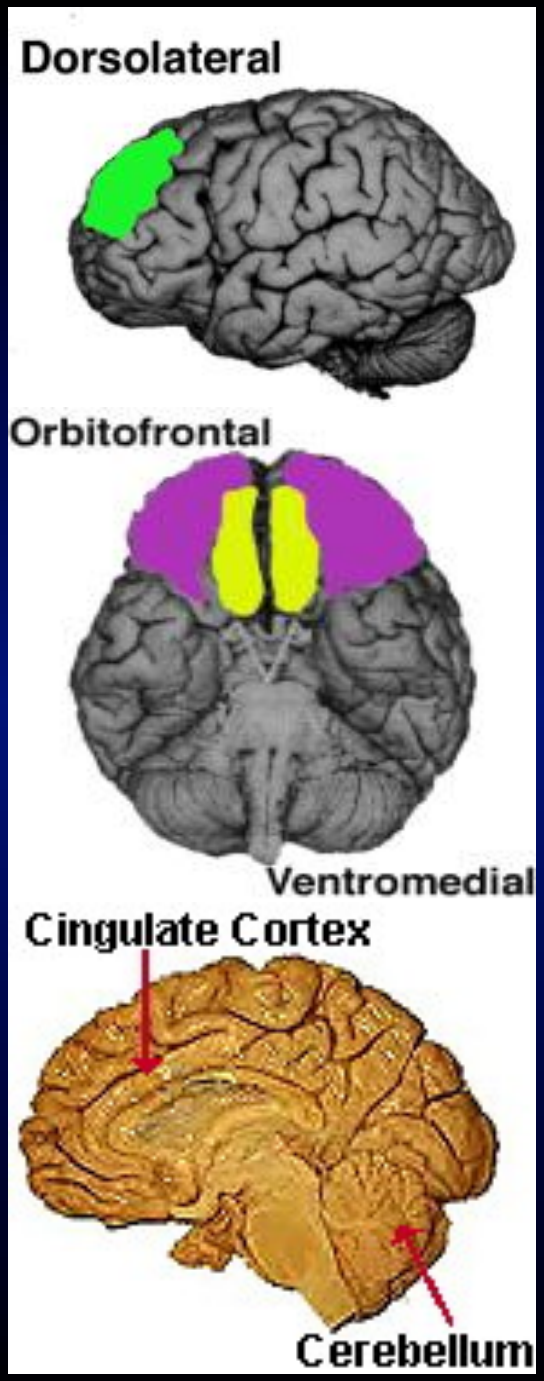
- Multiple Errands Tests (Shallice & Burgess, 1991):
  - **Strategy Formation**
  - **6 errands, prospective task, incidental information, rules**
  - **NB Novelty**





Damasio Gambling Task – Risk Taking





Dorsolateral Prefrontal cortex:

Working memory, filtering & interference control, sustained attention.

Ventromedial and orbitofrontal cortex:

Inhibitory control, planning, social guidance and decision making

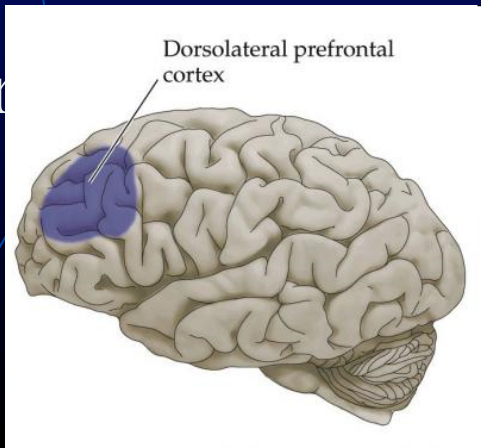
Anterior Cingulate:

An executive attention system that responds to task difficulty, novelty, error detection and correction and overcoming habitual responding.

Dorsolateral Prefrontal Cortex (DLPFC)

Broadman areas 9-12, 45-47

- Difficulty in shifts in attention and behavior;
- Rigidity or stereotypy of behaviour
- Impairment of temporal memory
- Inability to dissociate one's self from immediate surroundings
- Loss of foresight and planning
- Inability to sustain goal-directed behaviour absentmindedness
- Lack of drive



Dorsolateral Prefrontal Cortex

"some form of temporary storage of information is necessary for performing a wide range of cognitive skills including comprehension, learning and reasoning" (Baddeley)

A set of instruction such as:

"Align the screw hole on the metal plate with the corner hole on the baseplate and insert the 2 cm screw through the two holes, ensuring that the nut is on the underside of the baseplate"

Good example of a set of behavioural goals which must be kept active simultaneously in working memory

Most normal people find this very difficult to do

DLPFC seems critically important for working memory.

DLPFC and Working Memory

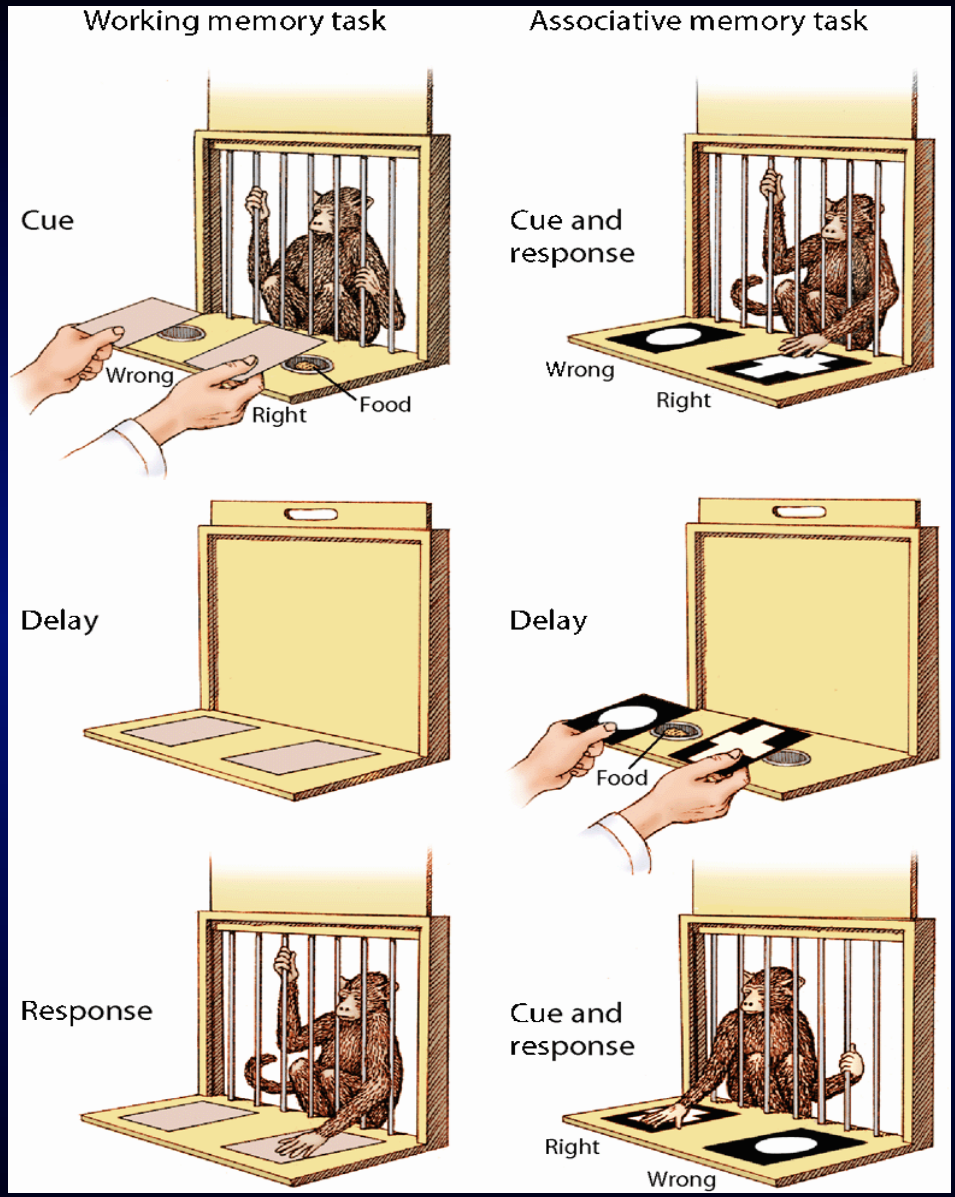
- A representational system that may be used to guide behavior
- Transient representations of task-relevant information
- Long-term memory representations may be activated in short-term memory to constrain and shape behavior in the present
- Integration of current perceptual information with stored knowledge
- Flexible vs stimulus-driven behaviour

'The blackboard of the mind' Goldman-Rakic

Working memory vs associative memory and the Delayed Response Task (Goldman-Rakic 1992)

Associative and recognition memory are not affected by DLPFC lesions

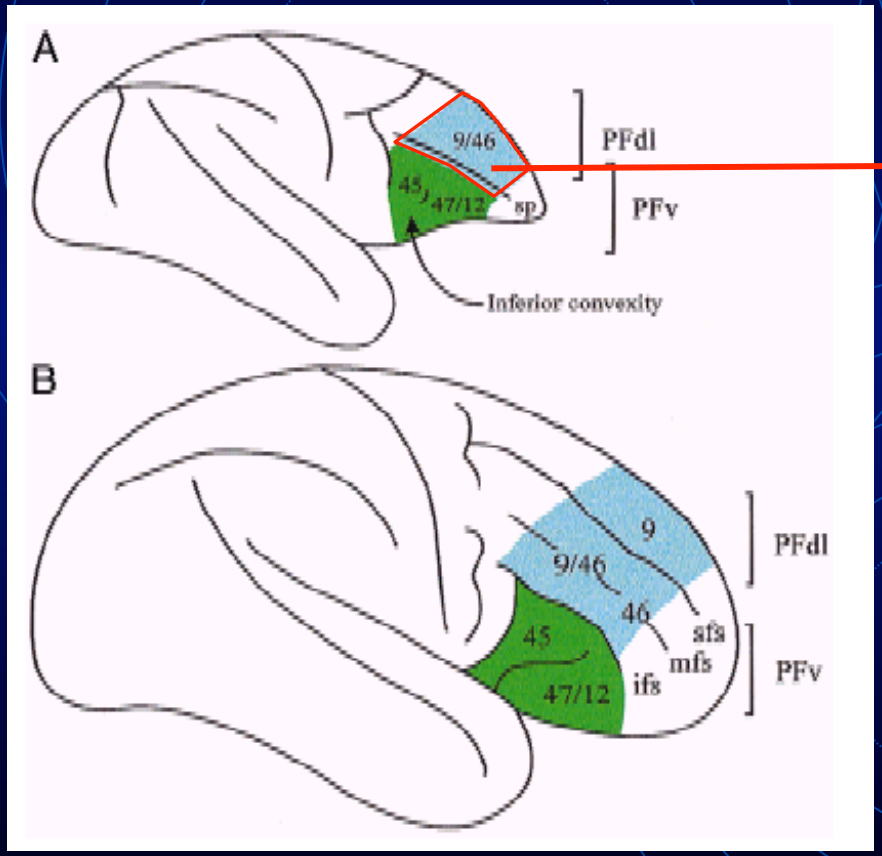
Human equivalent – perseveration on Wisconsin Card Sorting Task

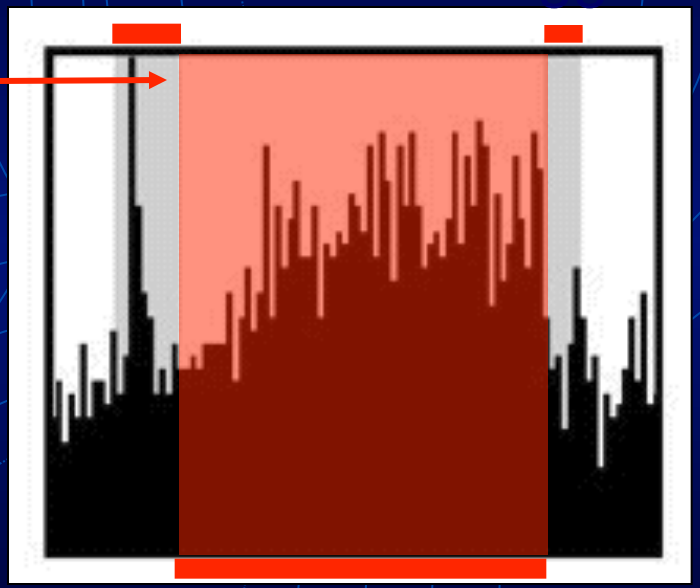


Working Memory

- Performance on WM Task suggests two functions of DLPFC
  - Access of stored information
  - Active maintenance of information
- Single cell recording in monkeys indicates its role in information maintenance

Working Memory





‘Working memory’ delay

(Constantinides, et. al. J. Neurosci. (2001), 21:3646-3655)

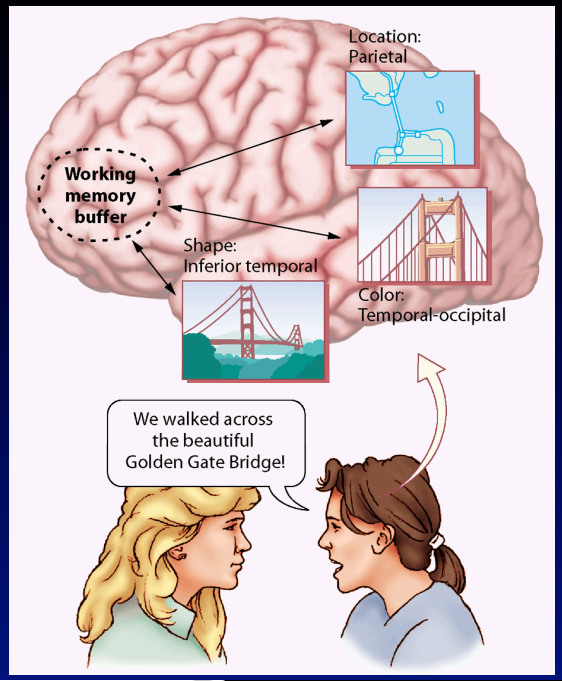
Delayed response tasks activate ‘memory fields’ in the prefrontal cortex.

Selectivity of Prefrontal Cells

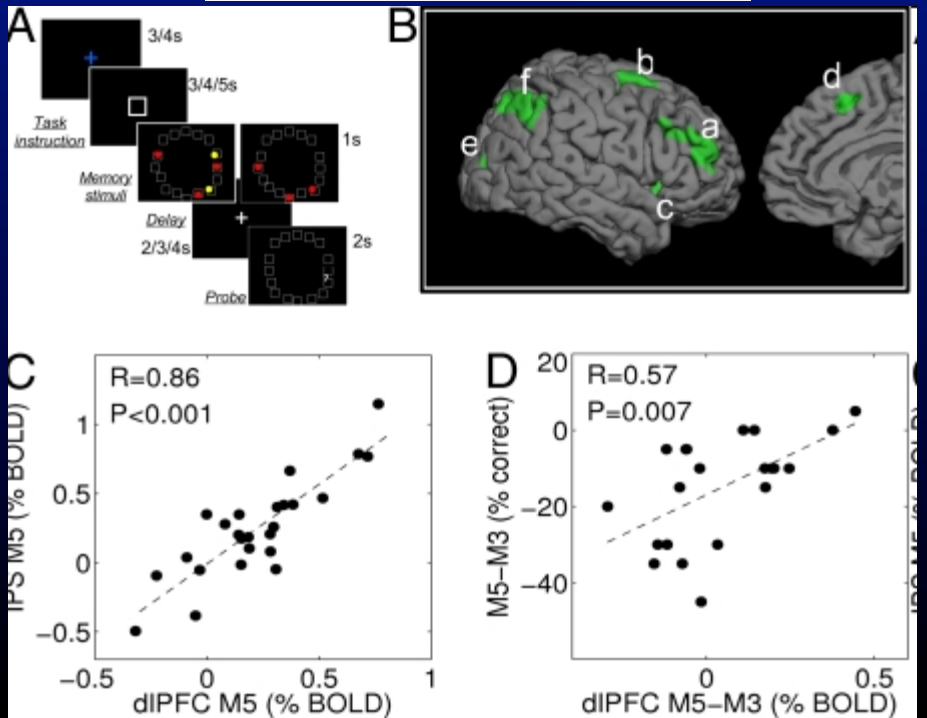
- What, where and what/where cells (Rao et al, 1997)
- Stimulus type (Fuster et al 2000)

Unlike in earlier visual areas, if task contingencies change, frontal cells change their firing patterns to a new set of stimuli

PFC's role in working memory may be as a buffer for activated long-term memories



Klingberg et al (2009)
DLPFC boosts spatial-working memory capacity in parietal regions



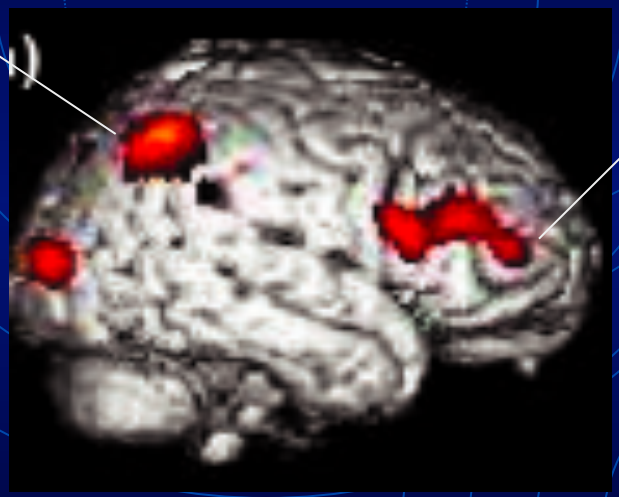
Other Frontal Memory Problems

- Recency memory
- Source memory

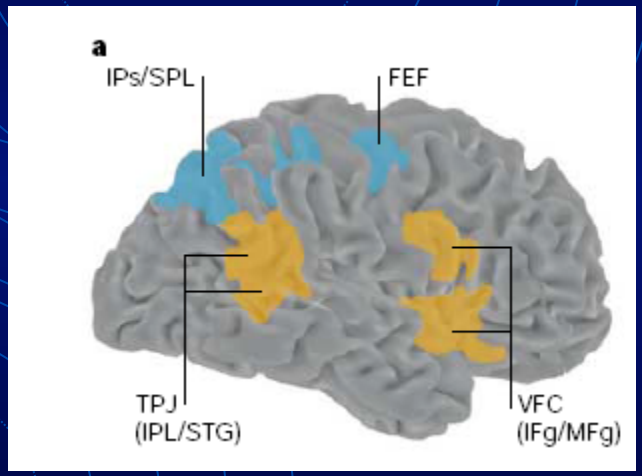
Common theme: temporal memory

DLPFC and Dynamic Filtering - Attention

Right parietal



DLPFC

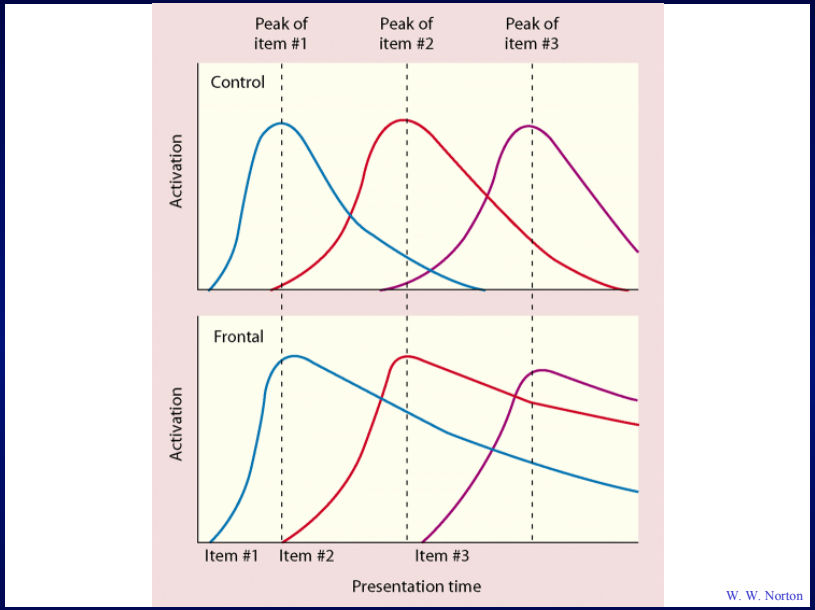


Manly, Robertson et al., 2003

Corbetta and Shulman, 2002

DLPFC and Dynamic Filtering - Inhibition

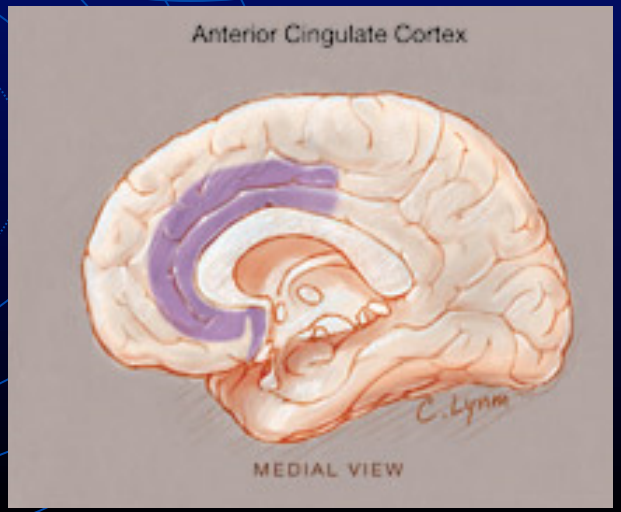
Series of items for a recency-memory task



- PFC may hasten decay processes by inhibiting activation of no-longer-relevant information

Clinical characteristics of Anterior Cingulate damage

- Decreased spontaneity; decreased productivity; decreased initiative
- Lack of ambition and drive;
- “pathological inertia”
- Lack of follow-through on plans



ACC and Attention/Executive Control

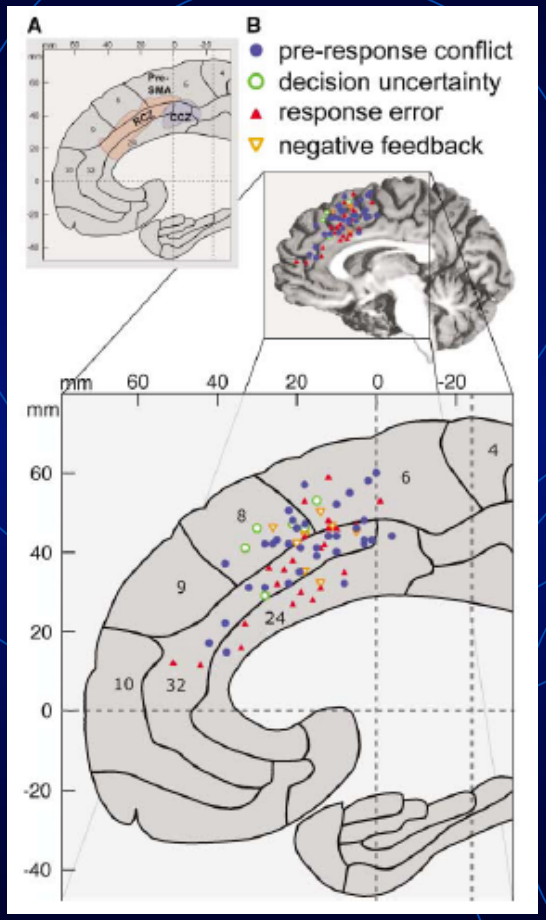
- Key role in coordinating activity across attention systems
- Numerous studies show activation of the anterior cingulate in tasks requiring the resolution of response conflict (e.g., Stroop tasks, divided attention).
- Modulates activity within networks subserving Working Memory
- Interaction with Lateral PFC to implement adjustments
- Key region for flexility

Required function of the SAS	Evidence indicating function related to anterior cingulate
Difficult situations	Blood flow increases during divided attention studies in comparison to focused attention studies
Novel situations	Blood flow increases during word generation task in comparison to word repeat task
Error correction	Evoked potential studies
Overcoming habitual responses	Blood flow increases during incongruent Stroop trial in comparison to congruent Stroop trials

Models of ACC function

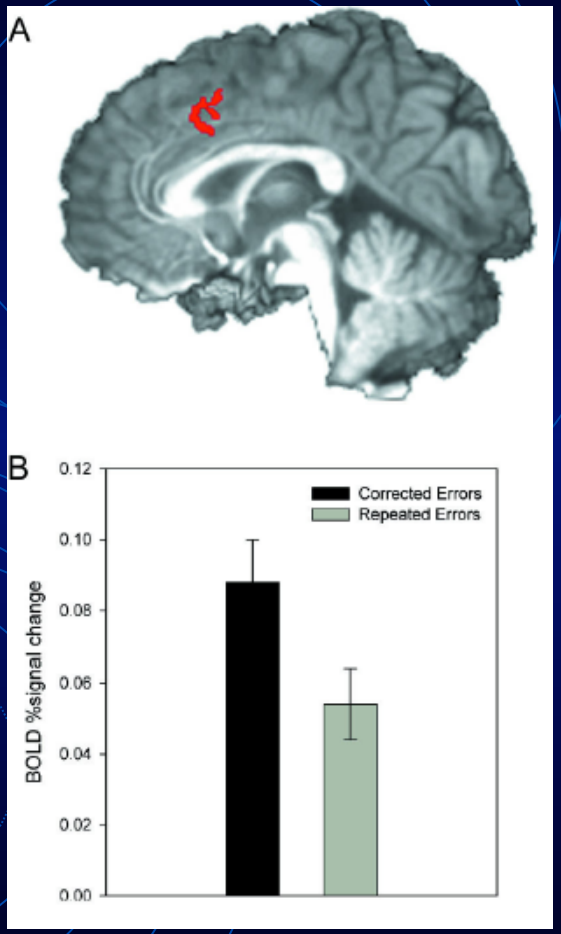
- Conflict Resolution (Cohen et al)
- Reward Anticipation (Ridderinkhof et al)

Models of ACC function



ACC task activations

Ridderinkhof et al (2004) *Science*



Learning from Errors

Hester et al (2009) *J Neurosci*

But...

doi:10.1093/brain/awh405 *Brain* (2005), **128,** 788–796

Is anterior cingulate cortex necessary for cognitive control?

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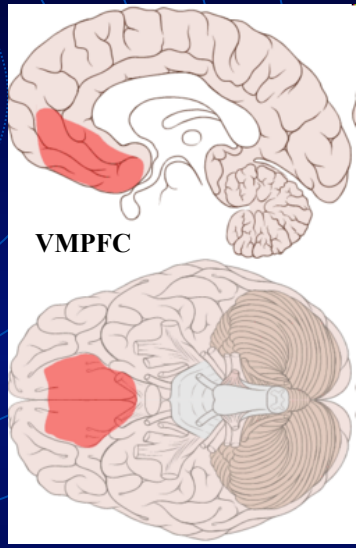
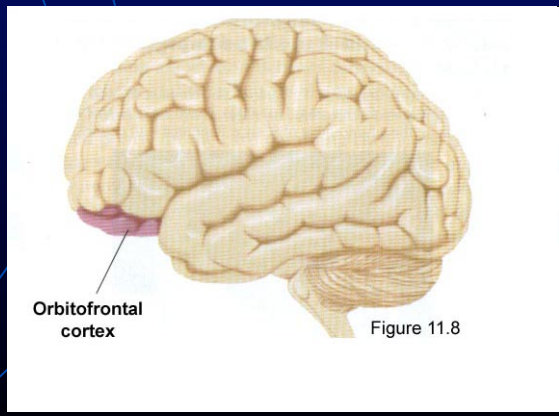
Summary

Functional neuroimaging studies in normal humans suggest that dorsal anterior cingulate cortex (dACC) plays an important role in cognitive control. This brain area is reliably activated when tasks require the ongoing adjustment of the allocation of attention. The dACC has come to occupy a central role in theories of attention and cognitive control, which hold that dACC either monitors response conflict, signalling the need for adjustments in cognitive processes, or directly mediates such adjustments. However, functional imaging results cannot establish that a brain area is necessary for a particular cognitive process. This requires evidence from loss-of-function studies. Here we assessed cognitive control in four human subjects with damage to dACC and 12 age- and education-matched control subjects using several measures drawn from the functional imaging literature. All four subjects with dACC damage showed normal adjustments in performance following manipulation of response conflict in both Stroop and go–no go tasks. Furthermore, damage to the dACC did not impair the phenomenon of post-error slowing, nor alter the ability to adjust performance in response to explicit speed or accuracy instructions. Thus, cognitive control, as assessed by four different measures in two different tasks, appears to be intact in these subjects, arguing against a necessary role for dACC in this process.

Clinical characteristics of Ventromedial/ Orbitofrontal damage

- Normal intellectual abilities, normal long-term memory and Working memory
  - Disinhibition, impulsivity;
  - Inability to hold back responses
  - Imitation and utilization behaviours
  - Lack of awareness of effect of own behaviour on others;
  - Lack of self-criticism with euphoria and self-satisfaction
  - Reduced emotional risk perception
  - Acquired sociopathy
  - Abnormal sexual behaviour



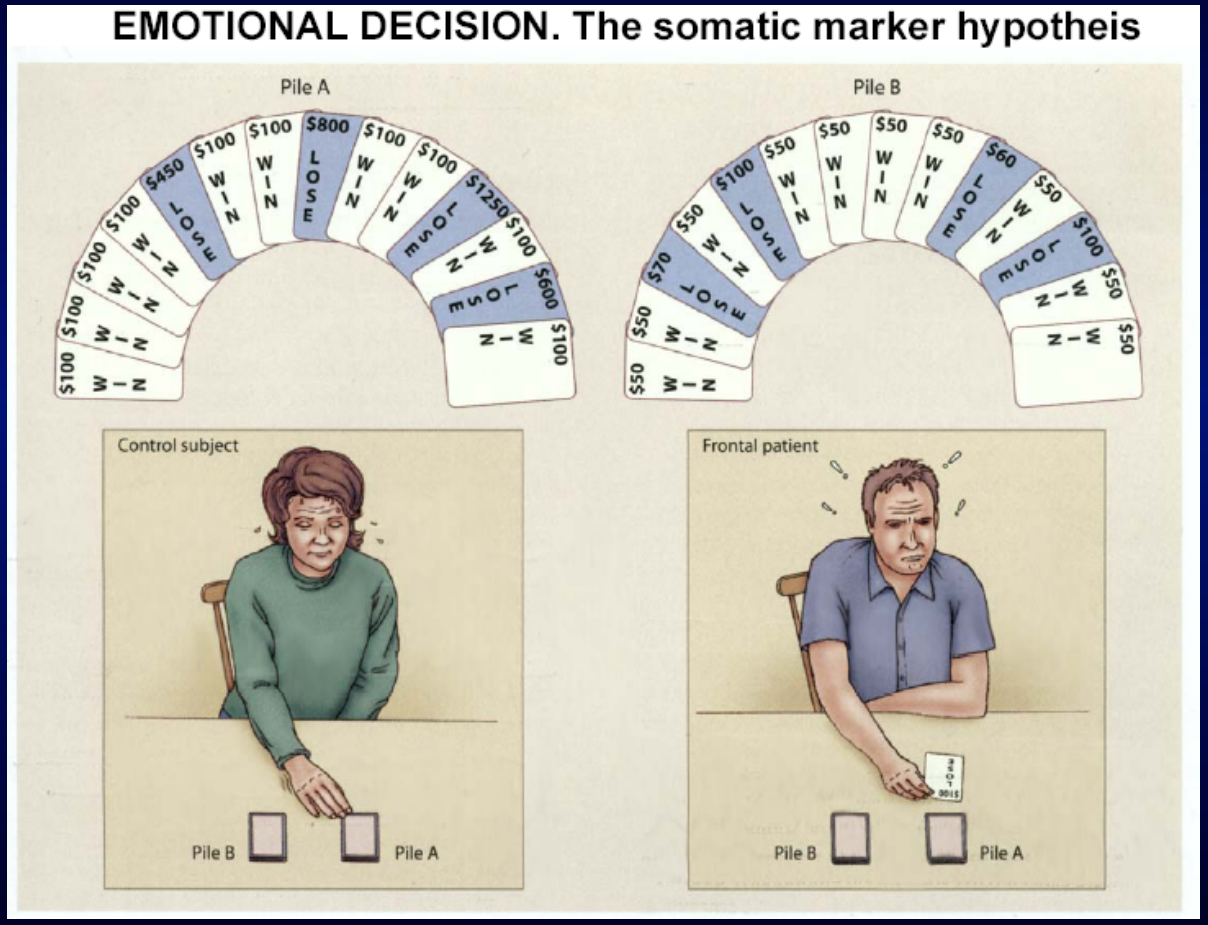


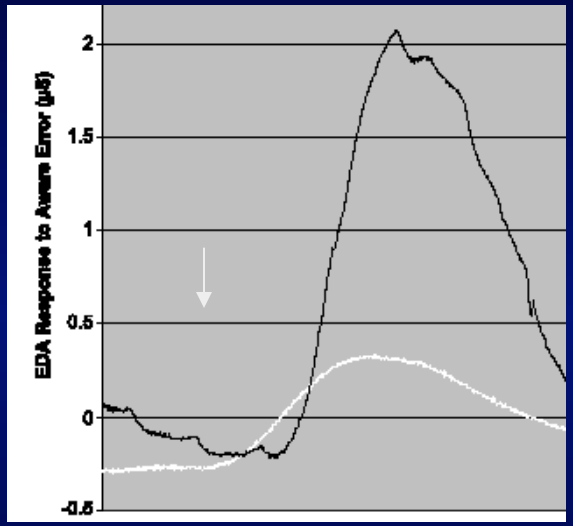
Social guidance and decision making

Distinction between decision making ‘in the abstract’ and decision making about personal and social involvement e.g. Elliot (Damasio, 1994)

- Includes the capacity to formulate goals
- To plan and organise goal-directed behaviour
- To carry out such behaviour fully and effectively
- To emotionally evaluate and correct behaviour
- Sensitivity to contextual cues

Damasio's Somatic Marker Hypothesis





O'Keeffe et al, 2004

Damasio's Somatic Marker Hypothesis

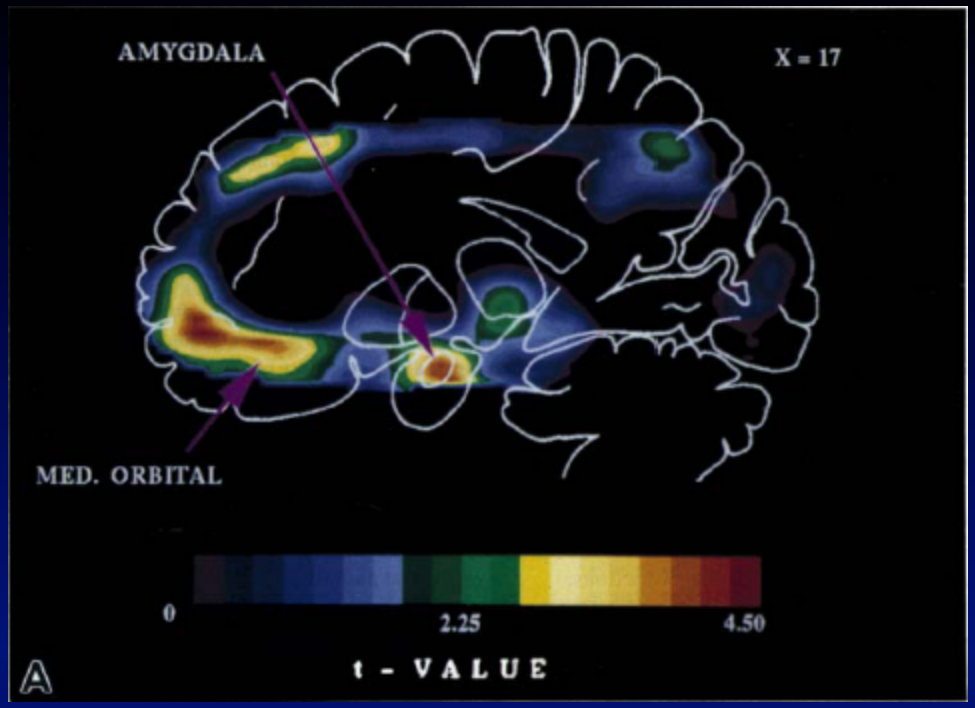
Mechanism to sort through options and assess their potential benefit quickly and efficiently

Somatic markers: bodily sensations that are linked to cognitive processes ("gut feeling") guide decision making

Chicken and Egg Problem

Alternative viewpoint: Rolls (1999) role of the OFC is to rapidly evaluate the reinforcement properties of a stimulus

e.g. poor reversal learning



Connections between the orbitofrontal areas and the limbic system (particular the amygdala) may be important in the formation of somatic markers.

When a representation is activated by a stimulus, connections between the amygdala and prefrontal cortex activate somatic markers to guide appropriate decisions.

Summary

Associate goals with perceptual info and long-term memory

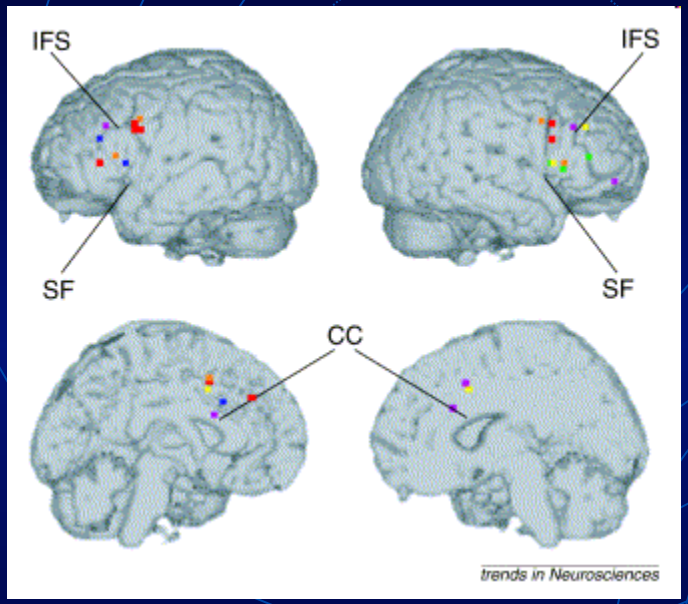
-DLPFC

Monitor performance, flexibility, adapt to changing contingencies

-ACC

Integration of personal desires; inhibit, evaluate and act on social and emotional information

- OFC/VMPFC



Regional specificity exists in the frontal lobes but…..

Functional imaging studies indicate that certain prefrontal regions are simultaneously activated by an extremely diverse range of cognitive problems (Duncan and Owen (2000)

Reading

- Gazzaniga et al, Chapters 11-13
- Kolb and Whishaw, Chapter 16
- Halligan et al, Handbook of Clinical Neuropsychology: Chapter 17: Assessment of Executive Function
- Ridderinkhof KR, Ullsperger M, Crone EA, Nieuwenhuis S (2004) The role of the medial frontal cortex in cognitive control. Science 306:443-447.
- Duncan J & Owen AM (2000). Common origins of the human frontal lobe recruited by diverse cognitive demands. Trends in Neuroscience 23:475-483

http://www.neuroscience.cam.ac.uk/directory/profile.php?johnduncan