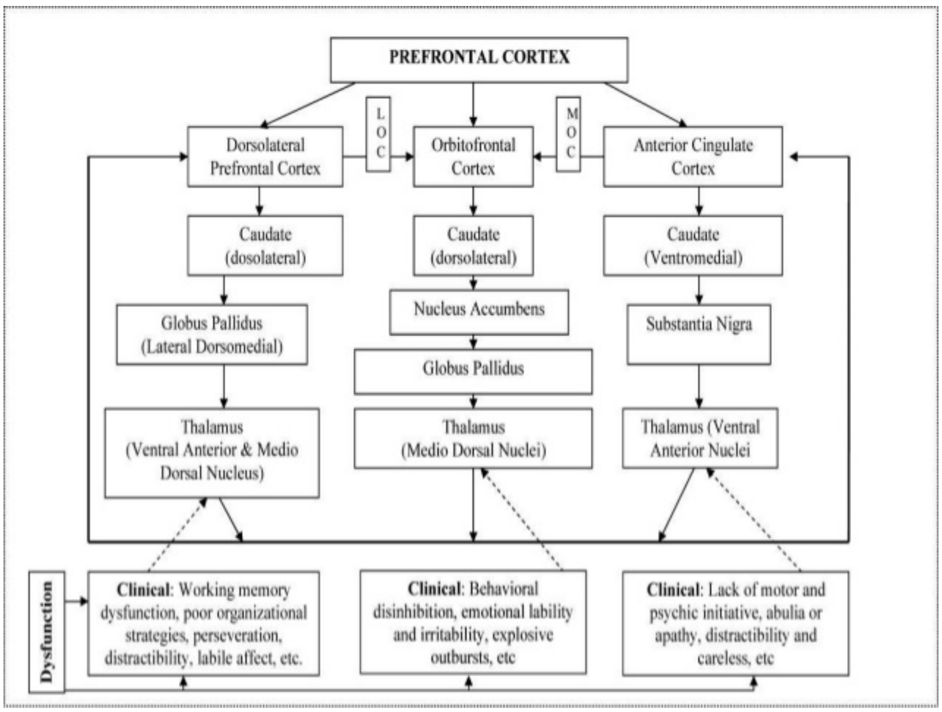
Lecture 37. Prefrontal Cortex and Cognition

Prof. Melissa Warden

Pre-Lecture Preparation

Watch Video 37-1: Prefrontal circuits
Understand this figure:



Required Reading

Be able to explain the following figures from Bear et al.: p.624-5, Box 18.2; p.831, Fig. 24.6; p.832, Fig. 24.7; p.833, Fig. 24.8; p.834, Fig. 24.9; p.835, Fig. 24.10

Optional Reading

Insensitivity to future consequences following damage to human prefrontal cortex. Bechara A, Damasio AR, Damasio H, Anderson SW.

Learning Objectives

1. To learn the behavioral outcomes produced by damage to different regions of the prefrontal cortex.
2. To learn how neural activity in the prefrontal cortex represents information relevant for working memory, cognition, and behavioral organization.
3. To learn how prefrontal cortical function is altered in psychiatric disease.

Lecture Outline

1. Anatomy (and comparative anatomy) of the prefrontal cortex
    a. Frontal region of the brain. Relative size is largest in primates (~30% of cortex).
    b. Defined as the area of cortex that receives projections from the mediodorsal nucleus of the thalamus.
    c. Subdivisions of the prefrontal cortex and their functions (dorsolateral, medial, orbitofrontal).

2. Prefrontal cortex damage and changes in behavior
    a. Ventromedial prefrontal cortex
        i. Phineas Gage
        ii. "Elliot" (Antonio Damasio's patient)
        iii. Deficits in personal decision making
        iv. Deficits in Iowa Gambling Task.
    b. Dorsolateral prefrontal cortex
        i. Deficits in working memory.
        ii. Inflexible behavior – inability to learn new rules.
        iii. Wisconsin Card Sorting task – attentional set shifting
        iv. Tower of Hanoi - planning and temporal organization of thought
    c. Inability to inhibit inappropriate behaviors, impulsivity. Stroop effect.

3. Neural activity in the prefrontal cortex
    a. Persistent activity during working memory for objects and locations
    b. Selective representation of behaviorally-relevant information.
    c. Representation of categories and rules

4. Dysfunction of the prefrontal cortex in psychiatric disease
    a. Mood and anxiety disorders: imaging and deep brain stimulation.
    b. Schizophrenia: structural and functional changes

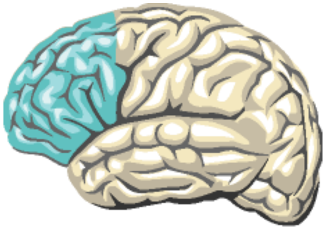
Study Questions

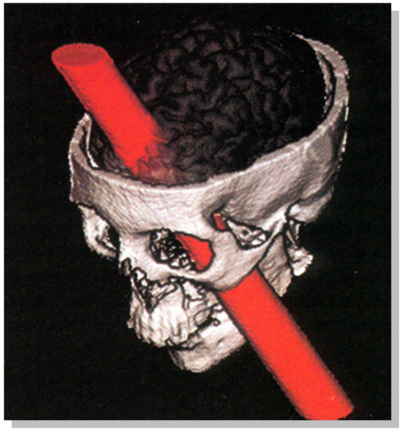
1. Phineas Gage suffered massive bilateral damage to the prefrontal cortex. Later analysis of the skull by Damasio et al. (1994) concluded that the damage included the orbitofrontal and ventromedial prefrontal, while sparing the dorsolateral prefrontal cortex. Describe some of the changes in Phineas Gage that provide clues to the function of ventromedial prefrontal cortex (vmPFC).

NEUROBIOLOGY AND BEHAVIOR II: INTRODUCTION TO NEUROSCIENCE

BioNB 2220

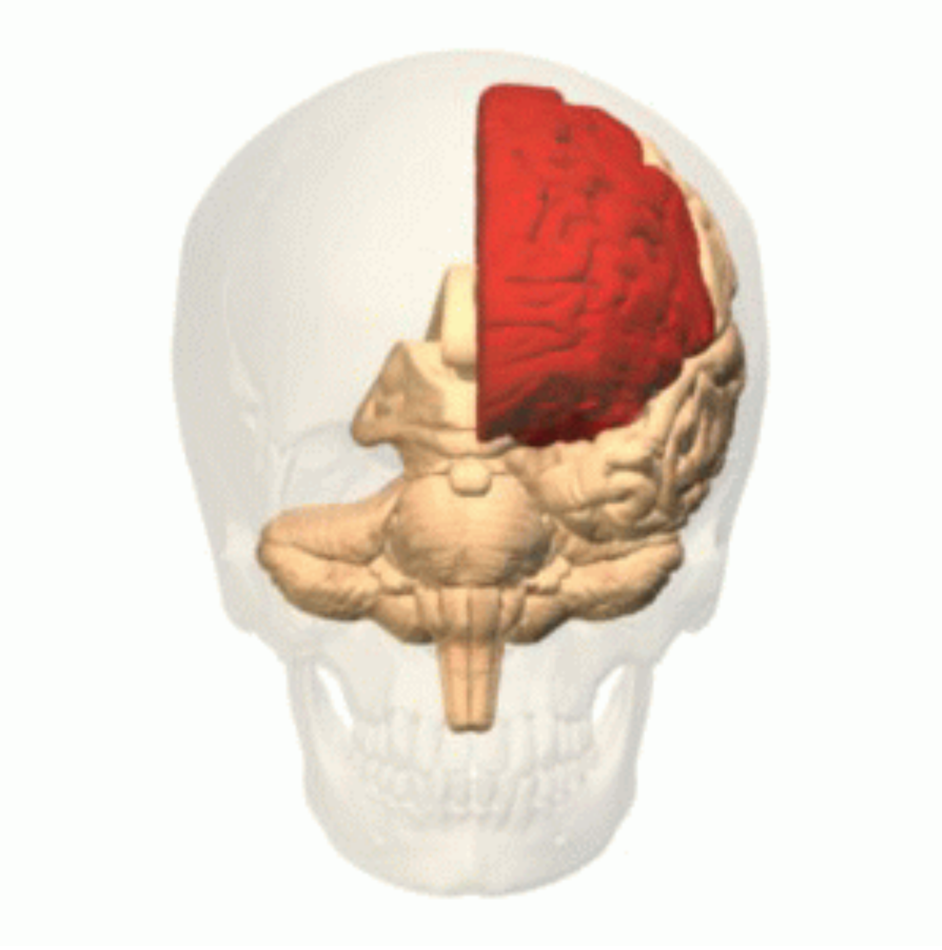
Lecture 37: Prefrontal Cortex
April 26, 2019





Melissa Warden, PhD

The frontal lobe and the prefrontal cortex

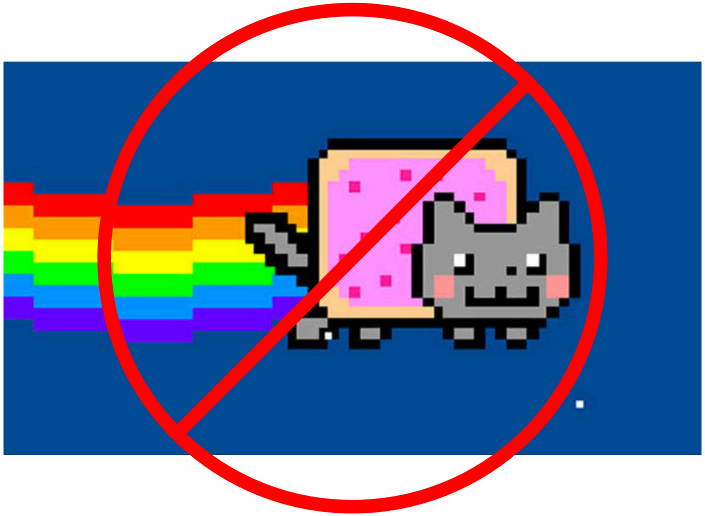


The prefrontal cortex

“The great intermediate net” between sensory input and motor output. (Walle Nauta).

What is the purpose of all of this neural tissue?

“To structure the present in order to serve the future” (Joaquin Fuster)



Functions of the prefrontal cortex

Promotes willful, coordinated actions directed toward achieving **long-term goals**

Suppresses behavioral reactions to environmental stimuli or to internal emotional states

Suppresses use of outdated rules to guide behavior

Flexible, context-appropriate behavior

Functions of the prefrontal cortex

How do you pursue long-term goals – like a college degree – without getting distracted along the way?

How do you change your behavior when the “rules of the game” change?

- you can learn to sort a deck of cards by suit
- you can suppress this rule to instead sort by number

How do you act appropriately and flexibly in different situations?

Why do you not always make a phone call when you see a phone?

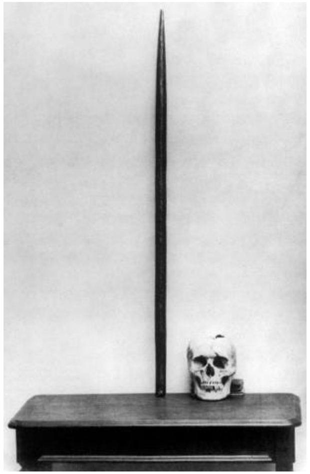
- talking on your phone is ok if you are outside
- and is ok if you are in your room by yourself
- but is not ok if you are in your room, it is 2 AM, and your roommate is sleeping
- is ok in the lecture hall when class is not in session
- but is not ok in the lecture hall when class is in session

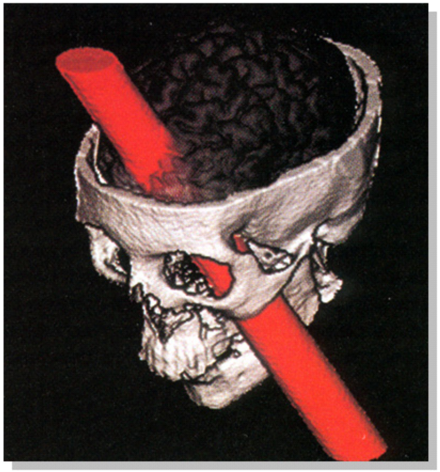
The Marshmallow Test

Small, immediate reward or large, delayed reward?

Auditory Go No-Go Task

Prefrontal damage and Phineas Gage



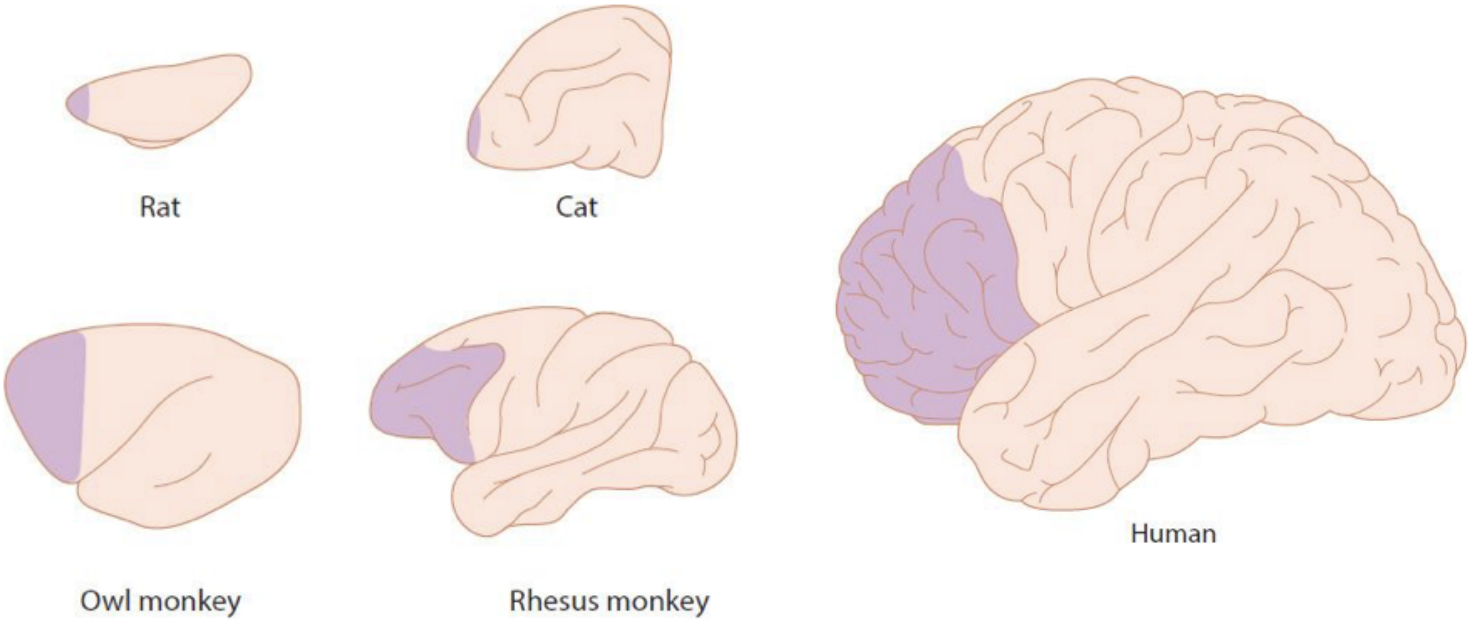


Phineas Gage (1823-1860) was a railroad construction foreman, known for being hardworking, responsible, and reliable.

Accident caused damage localized to ventromedial and orbitofrontal sub-regions of the prefrontal cortex

- Became impulsive, profane, impatient.
- Deficits in long-term planning.

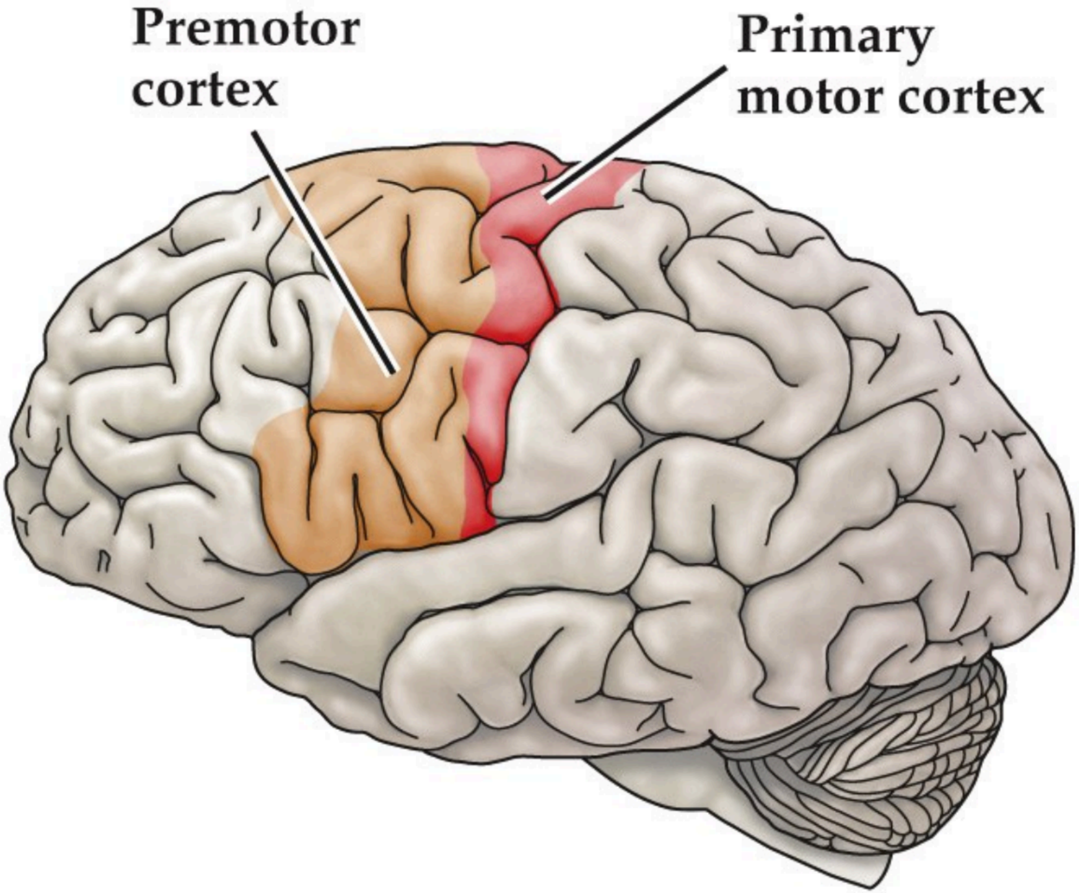
The prefrontal cortex has expanded greatly over mammalian and primate evolution



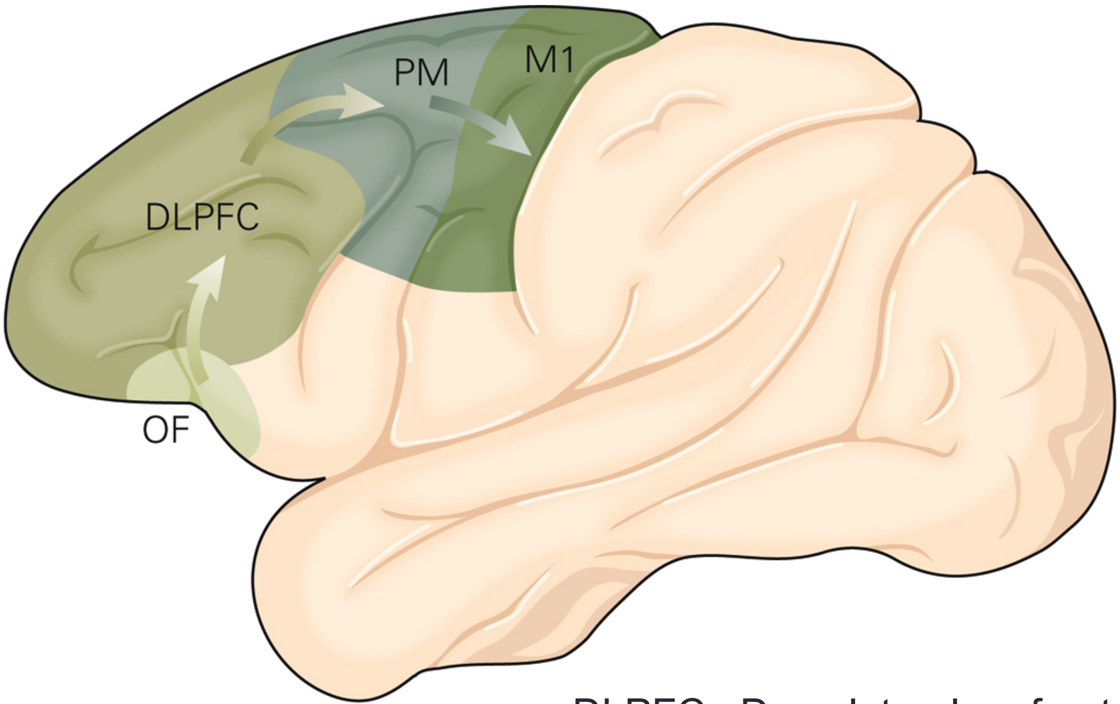
The size of the PFC varies enormously across species. The PFC is 3.5% of total cortex in the cat and 29% in the human

Kinematic neurons – Goals

Kinetic neurons – Muscles

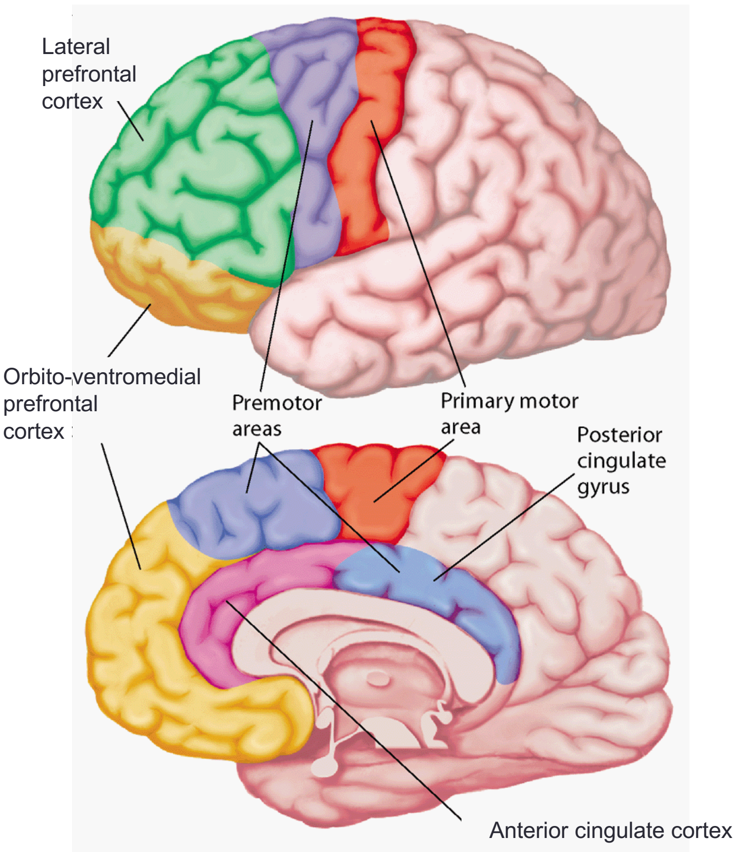


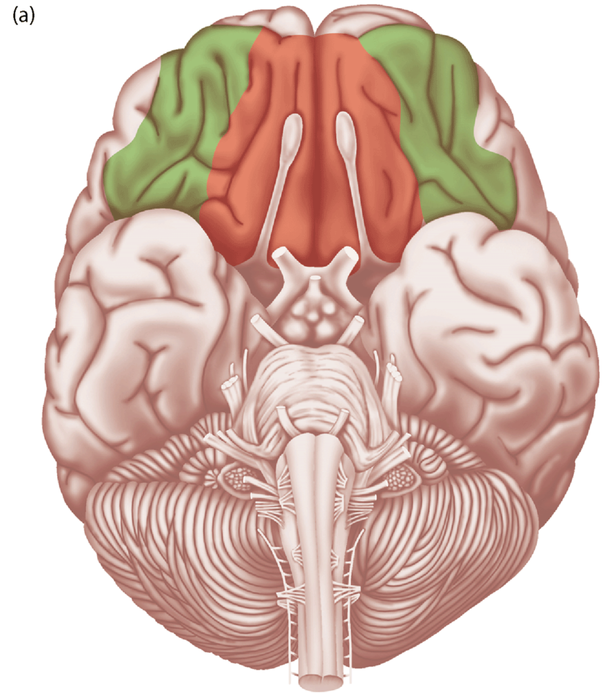
Prefrontal cortex can be thought of as high-order motor cortex



DLPFC: Dorsolateral prefrontal cortex
OF: Orbitofrontal cortex
PM: Premotor cortex
M1: Primary motor cortex

Prefrontal subregions in the human brain





The orbito-ventromedial cortex is divided into **ventromedial** (reddish in the above view) and the **orbitofrontal** cortex (green)

Dorsolateral prefrontal connections

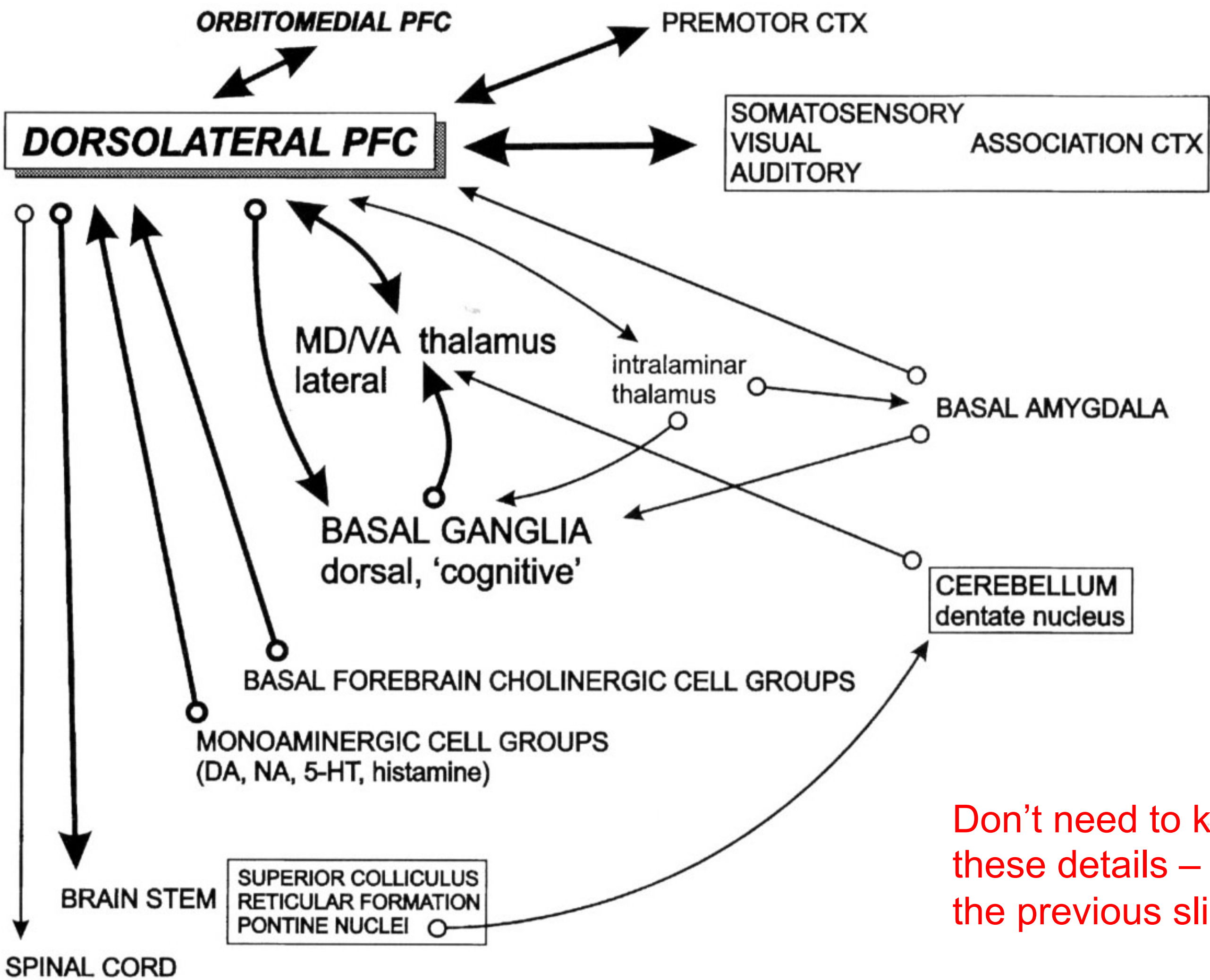
Bidirectional communication with secondary sensory and association cortex

- Visual
- Auditory
- Somatosensory

Projects to:

- Premotor areas, not primary motor cortex
- Dorsal basal ganglia (striatum) – cognitive and motor functions

Highly connected with other prefrontal areas



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Orbito-ventromedial prefrontal connections

Bidirectional communication with secondary sensory and association cortex

- Visual, Auditory, Somatosensory
- Chemosensation – olfactory and gustatory
- Visceral

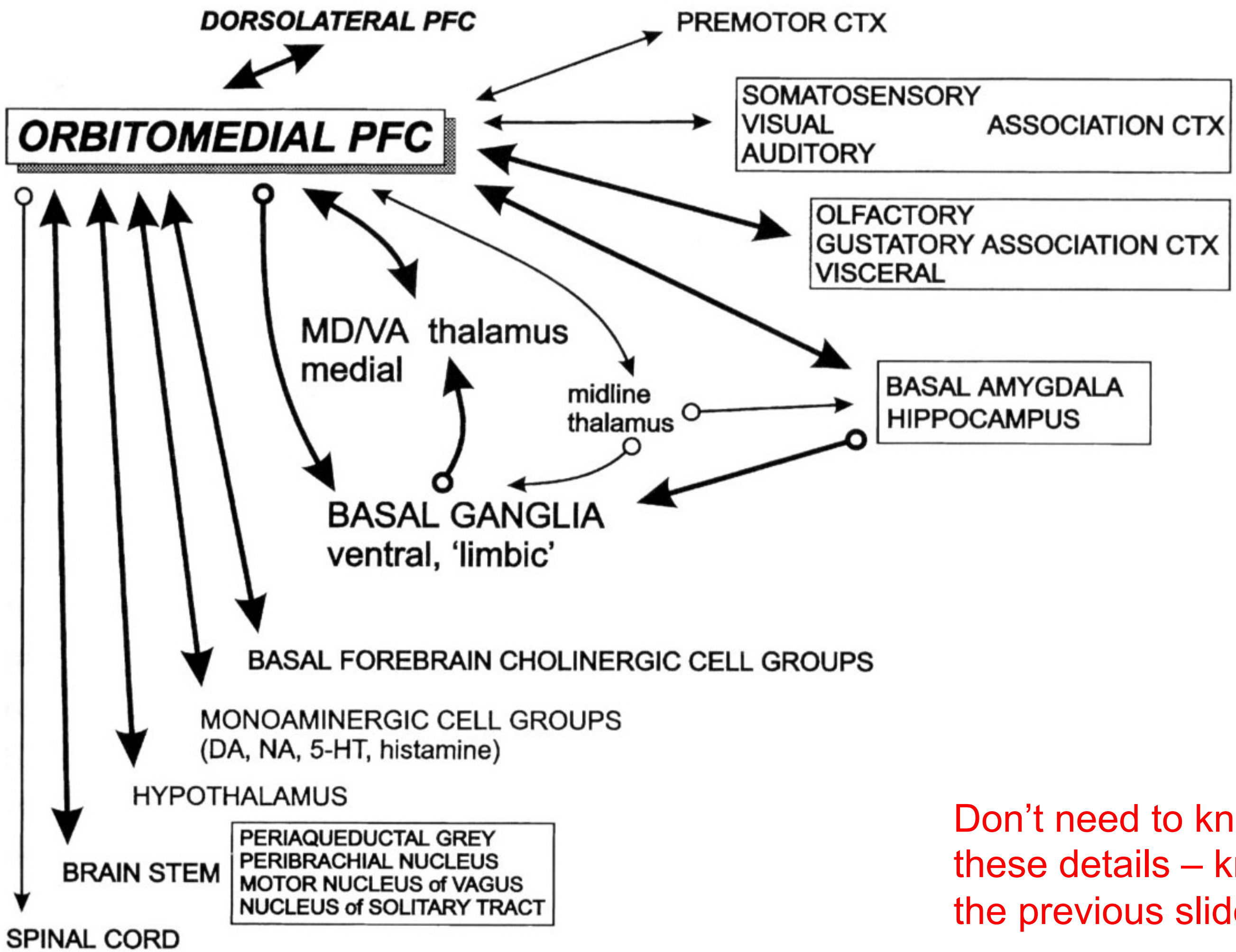
Bidirectional communication with limbic and brainstem structures

- Hypothalamus (limbic)
- Amygdala (limbic)
- Periaqueductal gray, parabrachial nucleus (brainstem)

Projects to:

- Dorsolateral prefrontal cortex
- Ventral basal ganglia (striatum) – limbic and emotional functions

Highly connected with other prefrontal areas



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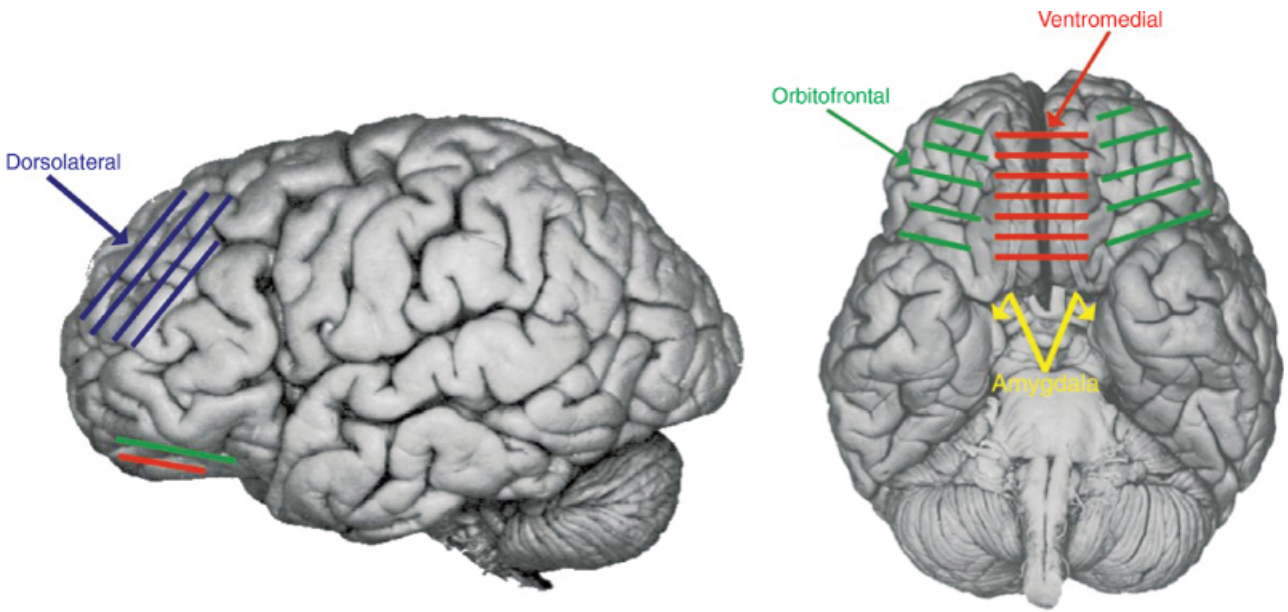
Hallmarks of prefrontal dysfunction

Disinhibition and lack of behavioral control
Stimulus-bound
Lack of goal-directedness
Impulsive
Quick to anger
Prone to making rude remarks
Emotionally shallow and indifferent to their condition
Apathetic
Unable to organize behavior

Caution: damage often extends to other nearby areas (cingulate, premotor)

Frontal lobe syndromes



Source: Davidson and Irwin, 1999.

Damage to different parts of the frontal lobes produces clinically distinct syndromes. The most common are dorsolateral and orbito-ventromedial syndromes.

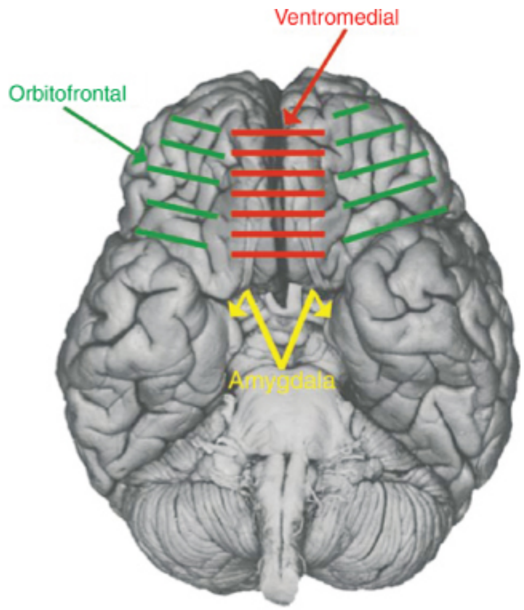
Frontal lobe syndromes – orbito-ventromedial

Most common symptoms of orbitofrontal syndrome are disinhibition and utilization behavior.

Disinhibition: Patients are behaviorally and emotionally disinhibited. Their affect is rarely neutral, constantly oscillating between euphoria and rage, with impulse control ranging from poor to non-existent.

Utilization behavior: A patient will drink from an empty cup, put on a jacket belonging to someone else, or scribble with a pencil on the table surface, merely because the cup, jacket, and pencil are there, even though these actions make no sense.

Deficits in real life decision making, value based decision making

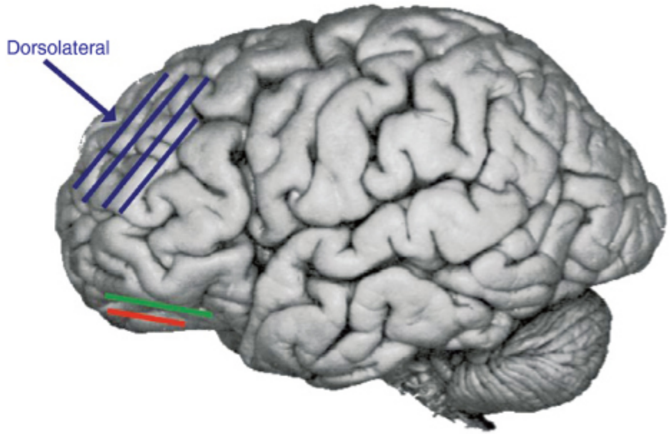


Frontal lobe syndromes - dorsolateral

Most common symptoms of dorsolateral syndrome are perseverative behavior, cognitive impairment, and mental rigidity.

Perseverative behavior: a patient will have an inability to initiate behaviors. Once behaviors are initiated, the patient is equally unable to terminate or change the behavior.

Mental rigidity is a frequent symptom of frontal lobe injury. Mental flexibility is a critical aspect of frontal lobe processing. These patients will show an inability to update the rules of the game.



Source: Davidson and Irwin, 1999.

Prefrontal subregions in the human brain

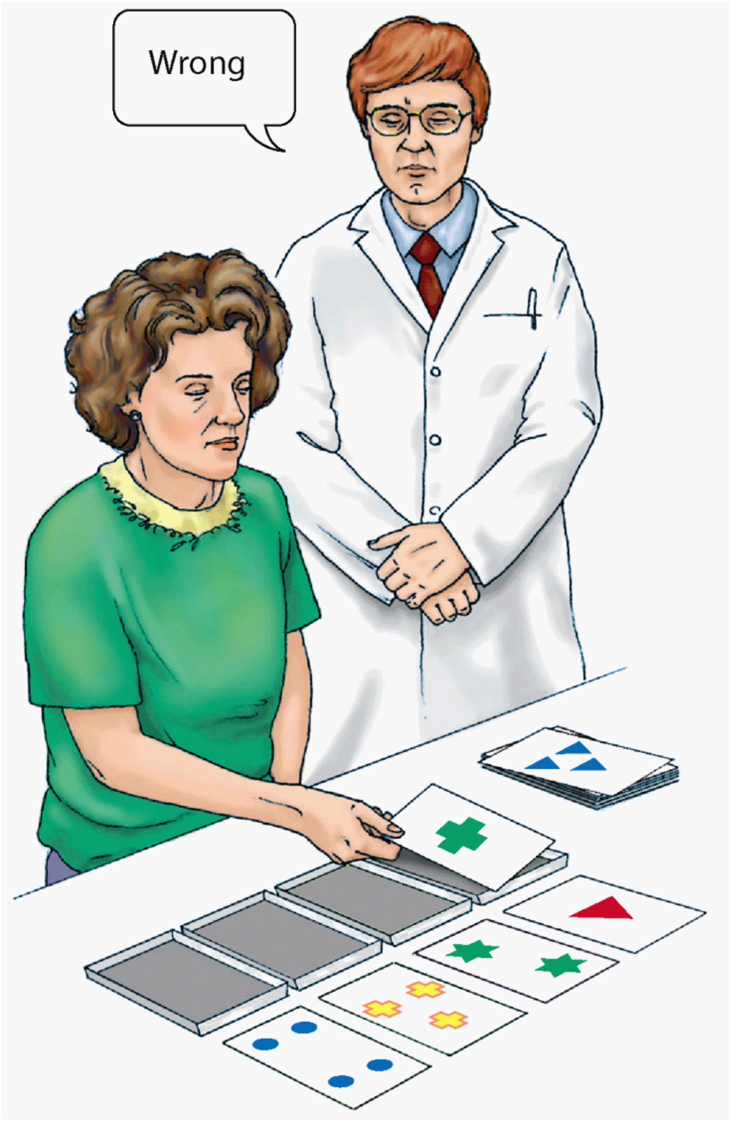
Dorsolateral prefrontal cortex

- Executive functions: working memory, cognitive flexibility, planning, abstract thinking, directing attention
- Underactive in schizophrenia and depression
- Lesions impair working memory in delayed response tasks, Wisconsin Card Sorting Task, Tower of Hanoi task (discussed later)

Orbito-ventromedial prefrontal cortex

- Value based decision making: personal decision-making, patience for large future rewards, dealing with uncertainty, ability to learn from punishment
- Lesioned in Phineas Gage
- Lesions impair performance in Iowa Gambling task (discussed later)

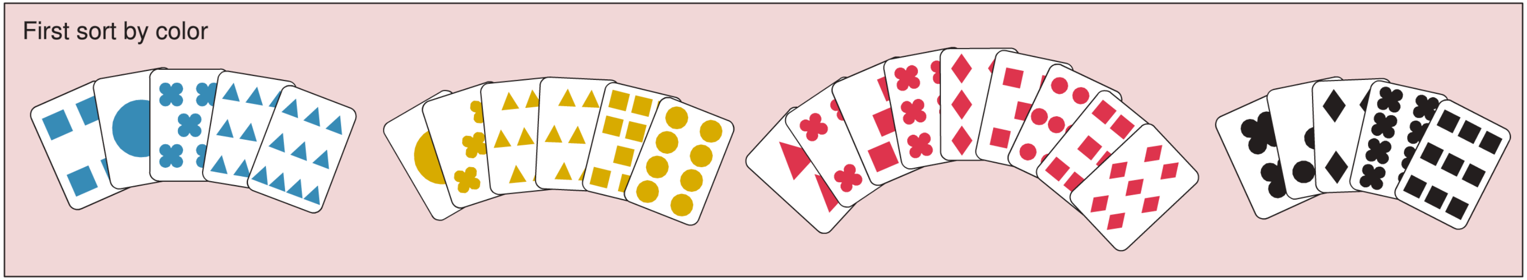
Dorsolateral prefrontal cortex: dysfunction and behavior



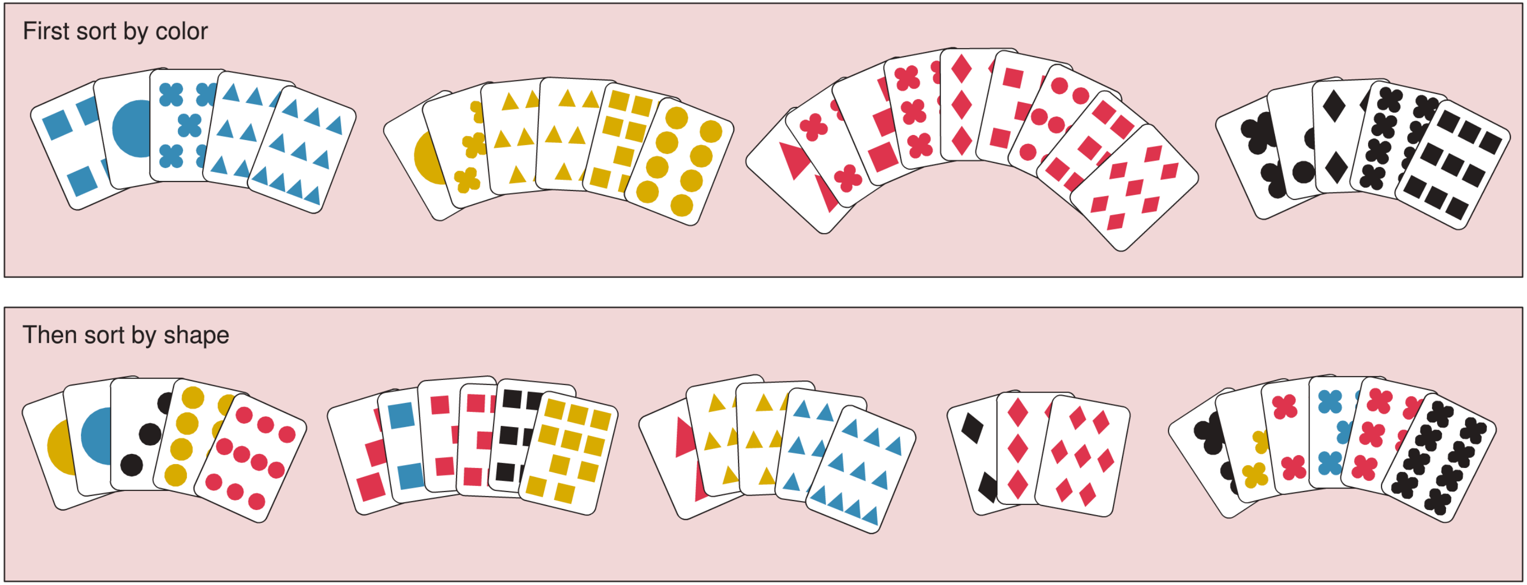
Wisconsin Card Sorting Task: SET SHIFT

Patients with damage in the lateral prefrontal cortex has difficulty on the WCST. On each trial, the subjects place the top card on the deck under one of the four target cards. The experimenter indicates whether the response is correct or incorrect, allowing the subject to learn the sorting rule by trial and error. The sorting rule changes whenever the subject makes ten consecutive correct responses (Gazzaniga, 2002).

Wisconsin Card Sorting Test



Wisconsin Card Sorting Test



Dorsolateral prefrontal damage leads to inability to inhibit prepotent rules

Wisconsin Card Sorting Test

Stroop effect

Flexible behavior requires the ability to update the rules of the game

Orbito-ventromedial prefrontal cortex: dysfunction and behavior

Orbito-ventromedial dysfunction

Orbito-ventromedial cortex patients perform poorly on tasks where:

- Situations are real-world and complex
- There is too much information to hold in mind
- There is uncertainty because of incomplete information
- **Must rely on ‘gut’ or intuition, not calculation**

Antonio Damasio on emotions and decisions

Patient Elliot (Antonio Damasio)

Orbitofrontal and ventromedial prefrontal cortex damage

- General intellect and problem solving capabilities remain intact (Wisconsin Card Sorting Test, self ordering, cognitive estimations, judgments of recency and frequency)
- Not perseverative
- Knowledge base and working memory are intact

- BUT has a severe impairment in **real life decision making.**
- Often decides against his best interests, and is unable to learn from his mistakes (like Phineas Gage)
- Takes hours to decide on a restaurant – inability to act for FUTURE emotional states

- How do we test for dysfunction in the lab?

Iowa Gambling Task

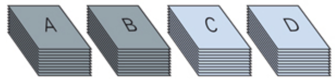
Developed by Bechara, Damasio, et al. 1994 at the University of Iowa

Attempted to simulate personal real-life decision making in the lab

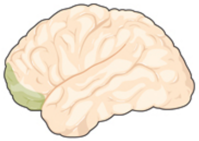
Involves **uncertainty** of premises, outcomes, reward, and punishment

Iowa Gambling Task

Gambling task

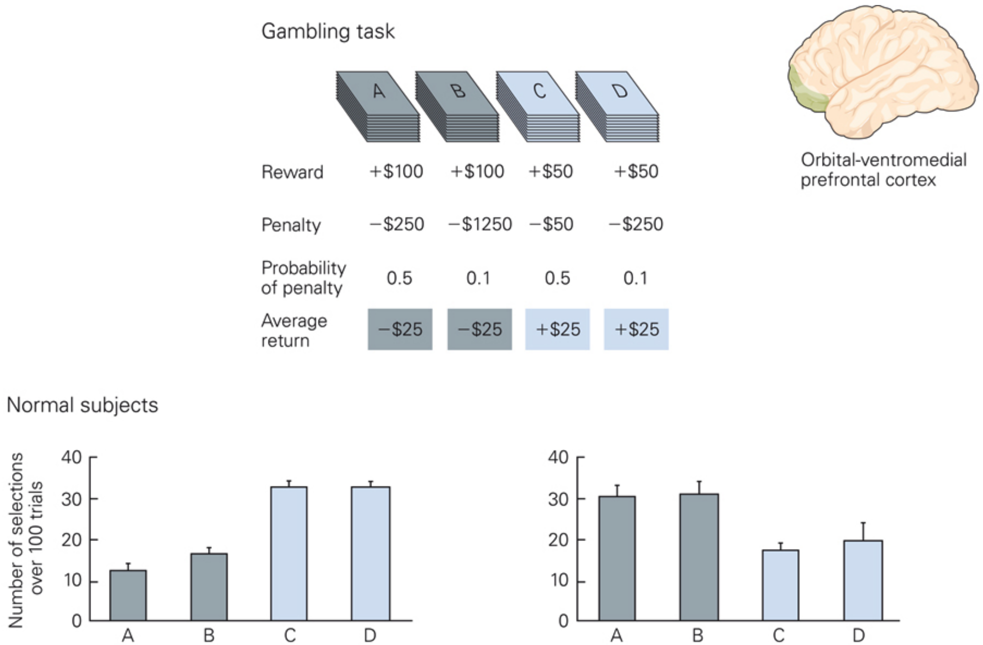


Reward	+$100	+$100	+$50	+$50
Penalty	−$250	−$1250	−$50	−$250
Probability of penalty	0.5	0.1	0.5	0.1
Average return	−$25	−$25	+$25	+$25



Orbital-ventromedial prefrontal cortex

Iowa Gambling Task



Normal

Prefrontal damage

Possible explanations for performance

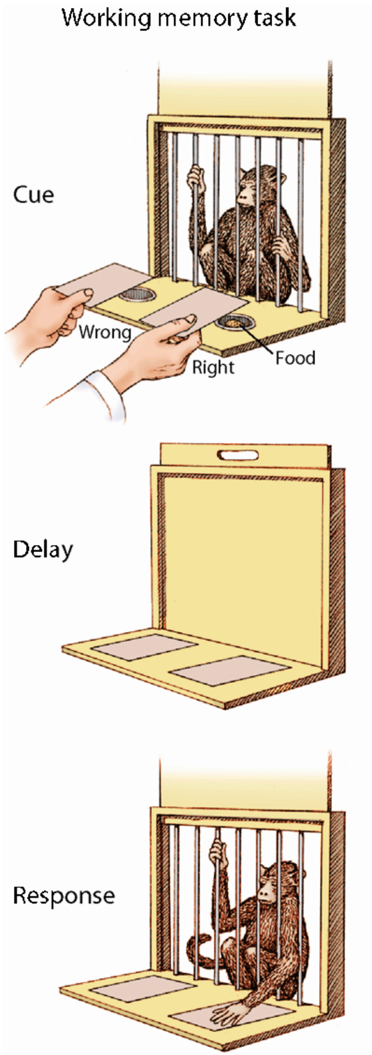
Can't integrate complex information over time to produce context-appropriate behavior.

Instead, react to immediate stimuli.

Subsequent work showed that while the control subjects exhibited an increased skin conductance response (autonomic) before they chose a risky deck, OFC patients did not.

Inability to represent potential future emotional states.

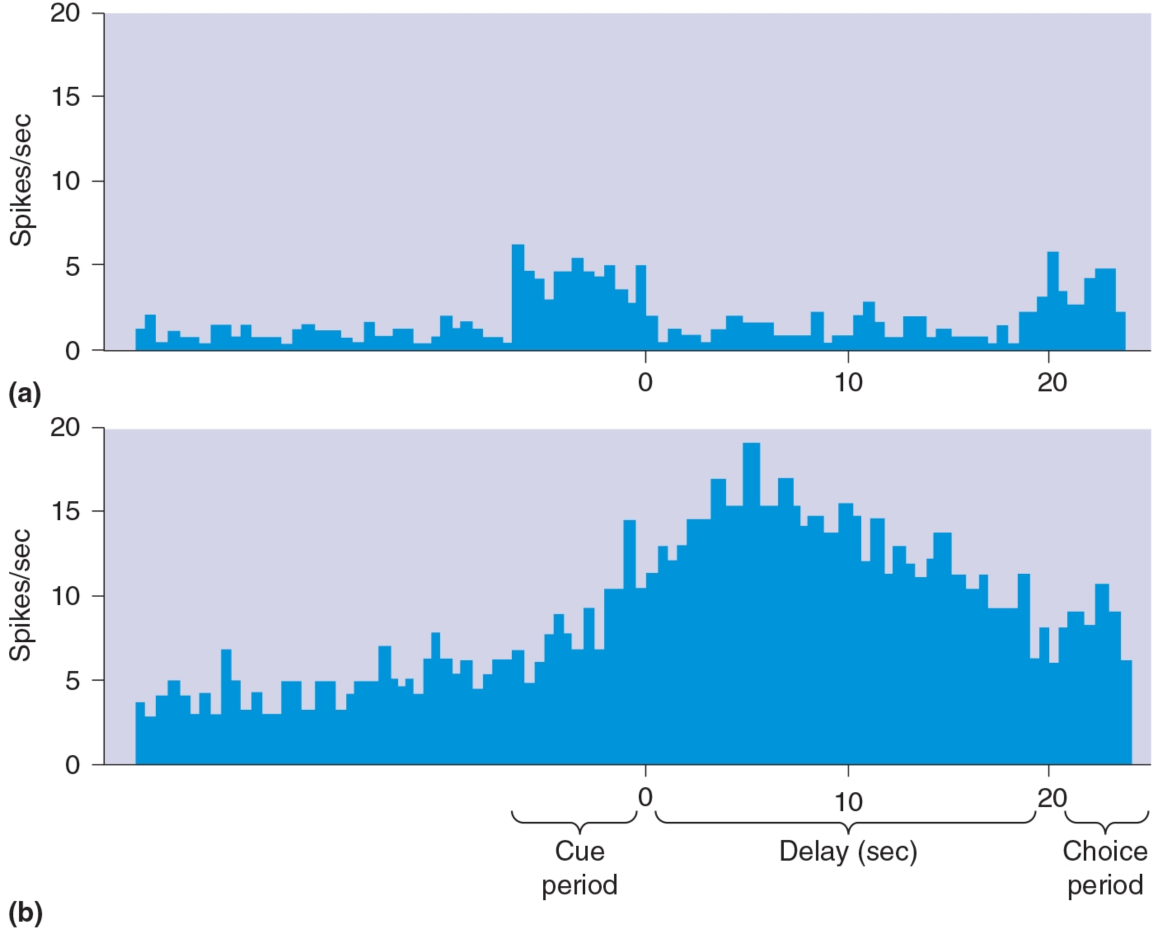
Dorsolateral prefrontal cortex: lesion studies and neurophysiology



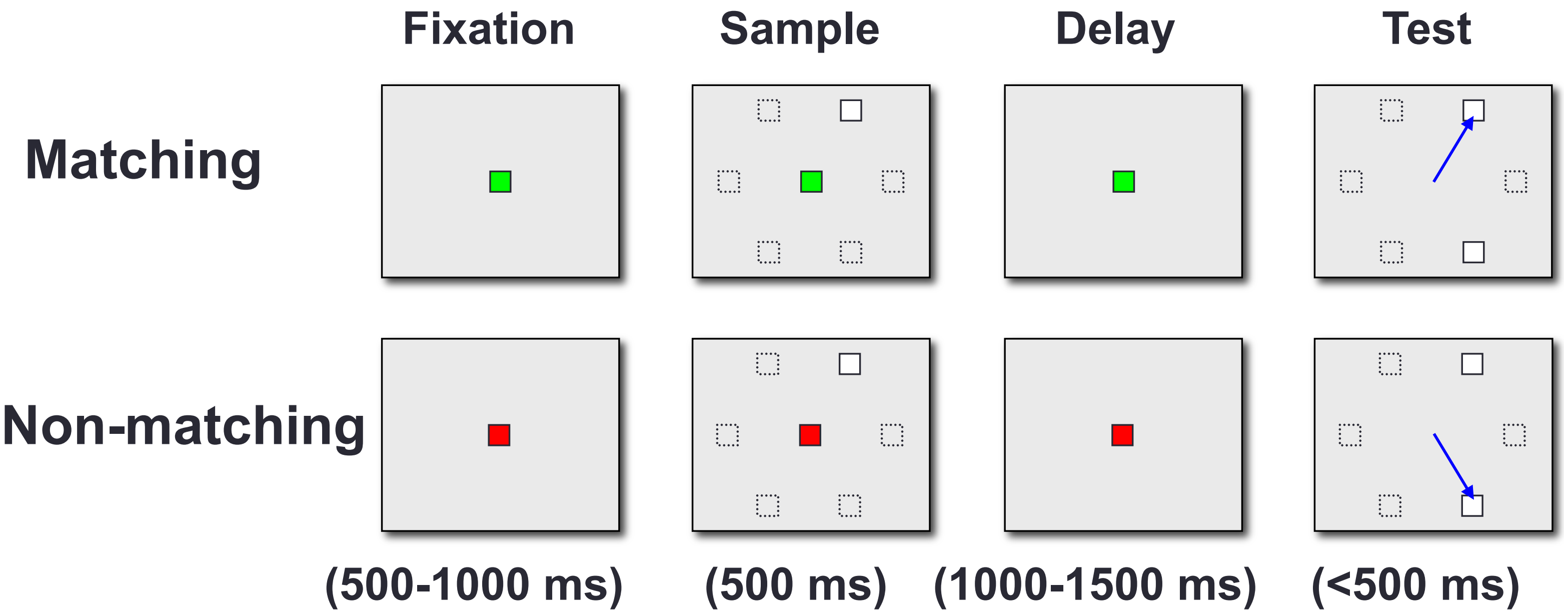
Monkeys are impaired on tests for working memory following dorsolateral prefrontal lesions.

Can’t remember where the food was after a delay of 10-30 seconds.

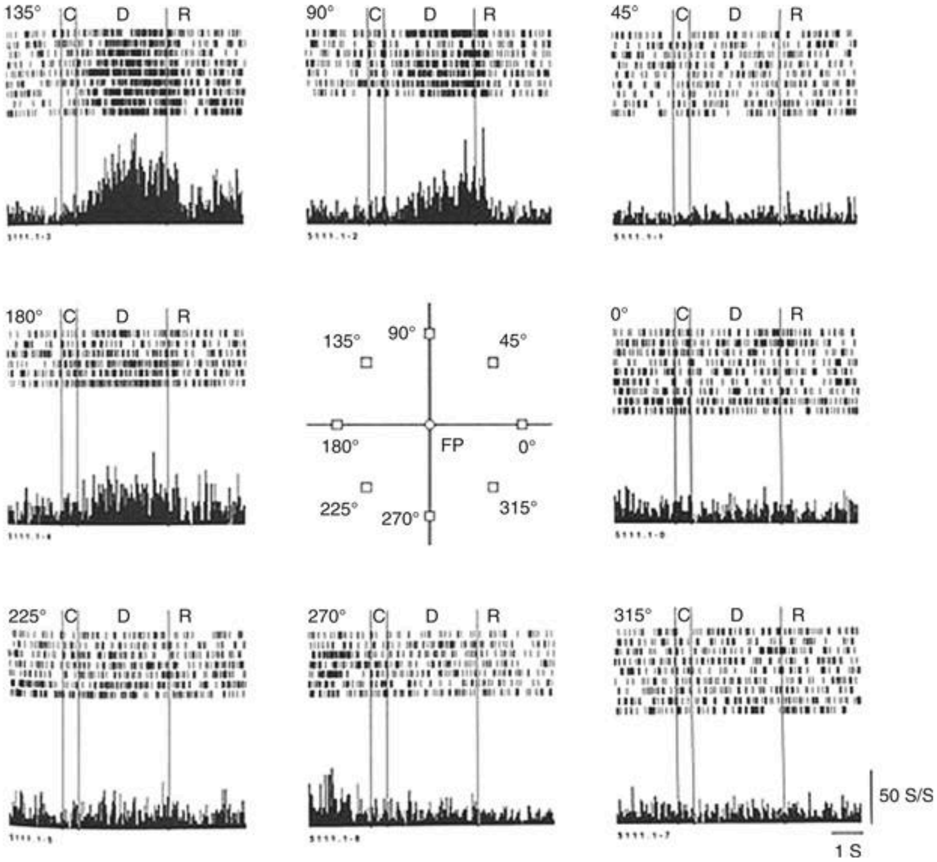
Dorsolateral prefrontal neuronal delay activity



Spatial delayed response tasks



Spatially tuned prefrontal delay activity

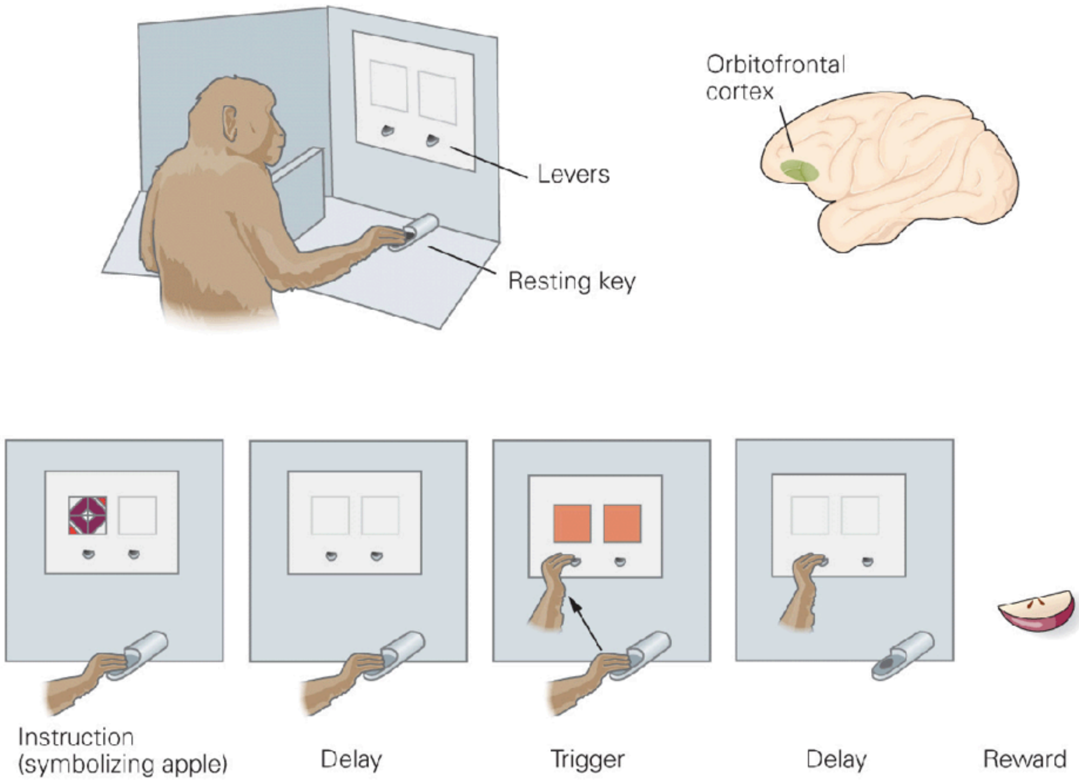


Patricia Goldman-Rakic

Funahashi et al. 1989

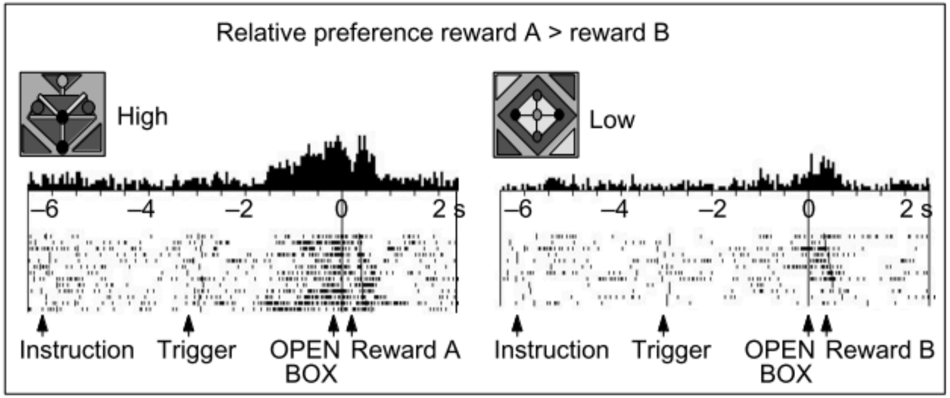
Orbito-ventromedial cortex: neurophysiology

Neurophysiology: Relative reward preference in primate orbito-ventromedial cortex

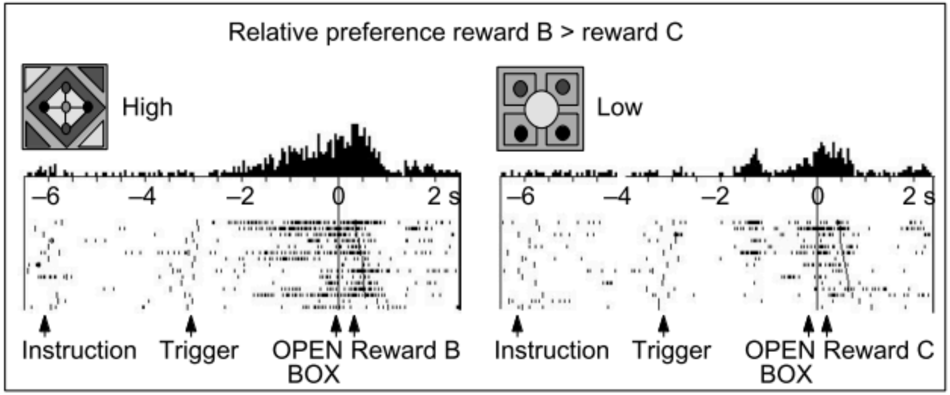


Tremblay 1999

Coding of relative reward preference



Reward A: raisin
Reward B: apple
Reward C: cabbage



Tremblay 1999