

THE PREFRONTAL CORTEX (PFC) AND COGNITION

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Bio Sci 38: Mind, Memory, and the Brain

OVERVIEW

- Basic anatomy of the prefrontal cortex (PFC)
- First insights into the role of the PFC in cognition
- The dorsolateral vs orbitofrontal prefrontal regions
- The “fragile” PFC
- The PFC and socially appropriate behavior

BASIC ANATOMY OF THE PFC

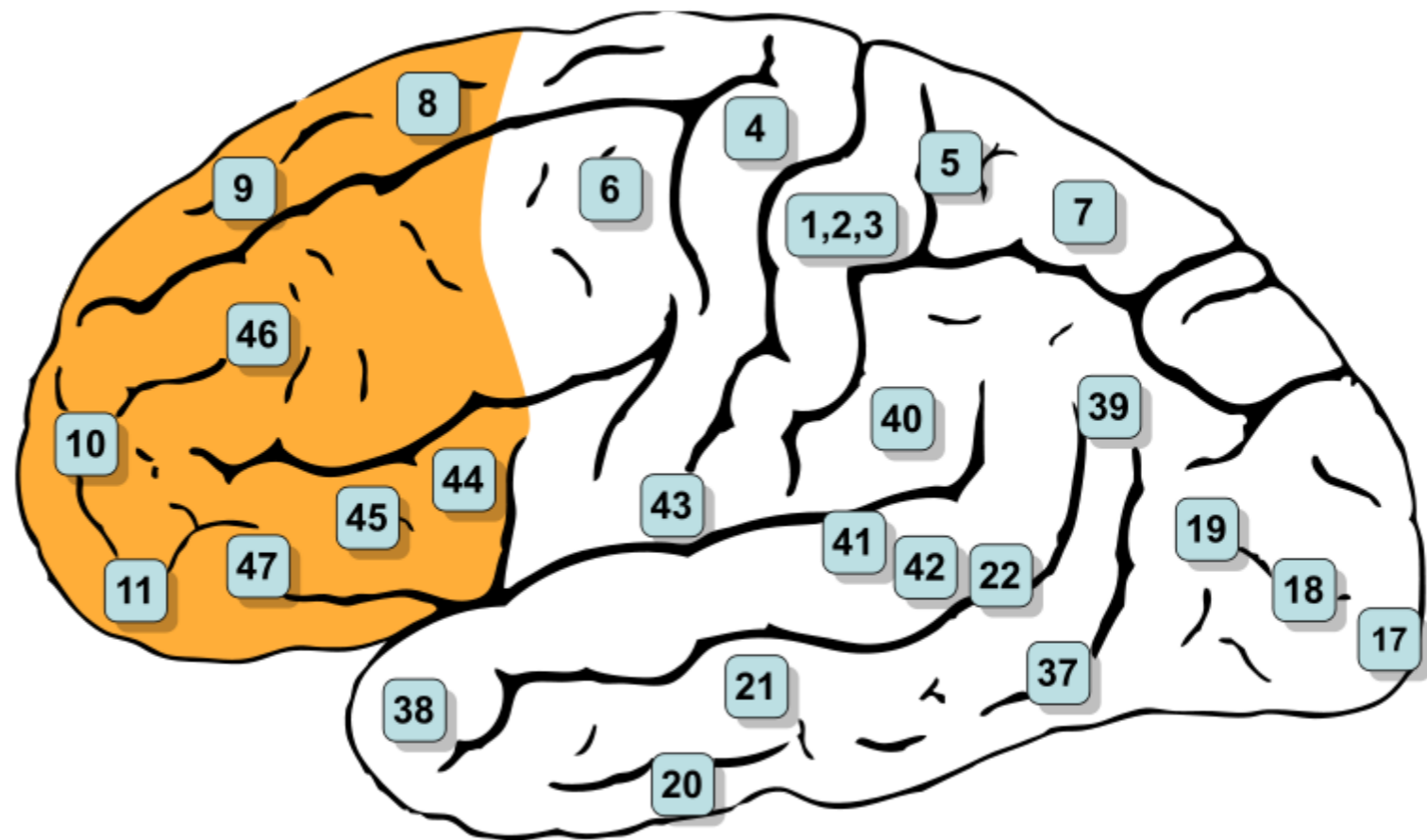
What is the PFC and where is it?



BASIC ANATOMY OF THE PFC

The PFC is actually a region composed of several distinct subdivisions, each with different connections profiles (within and outside the PFC)

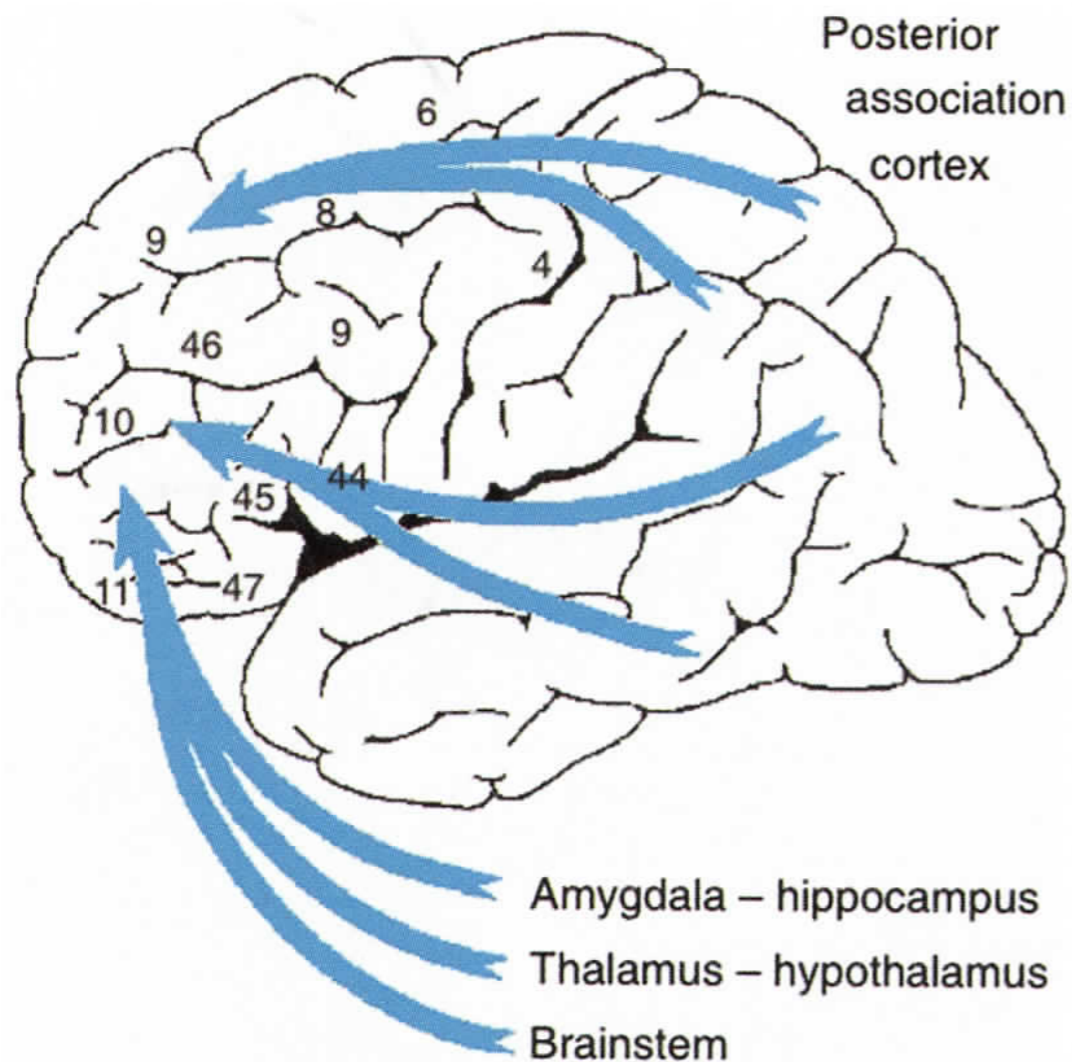
Prefrontal cortex
(PFC)



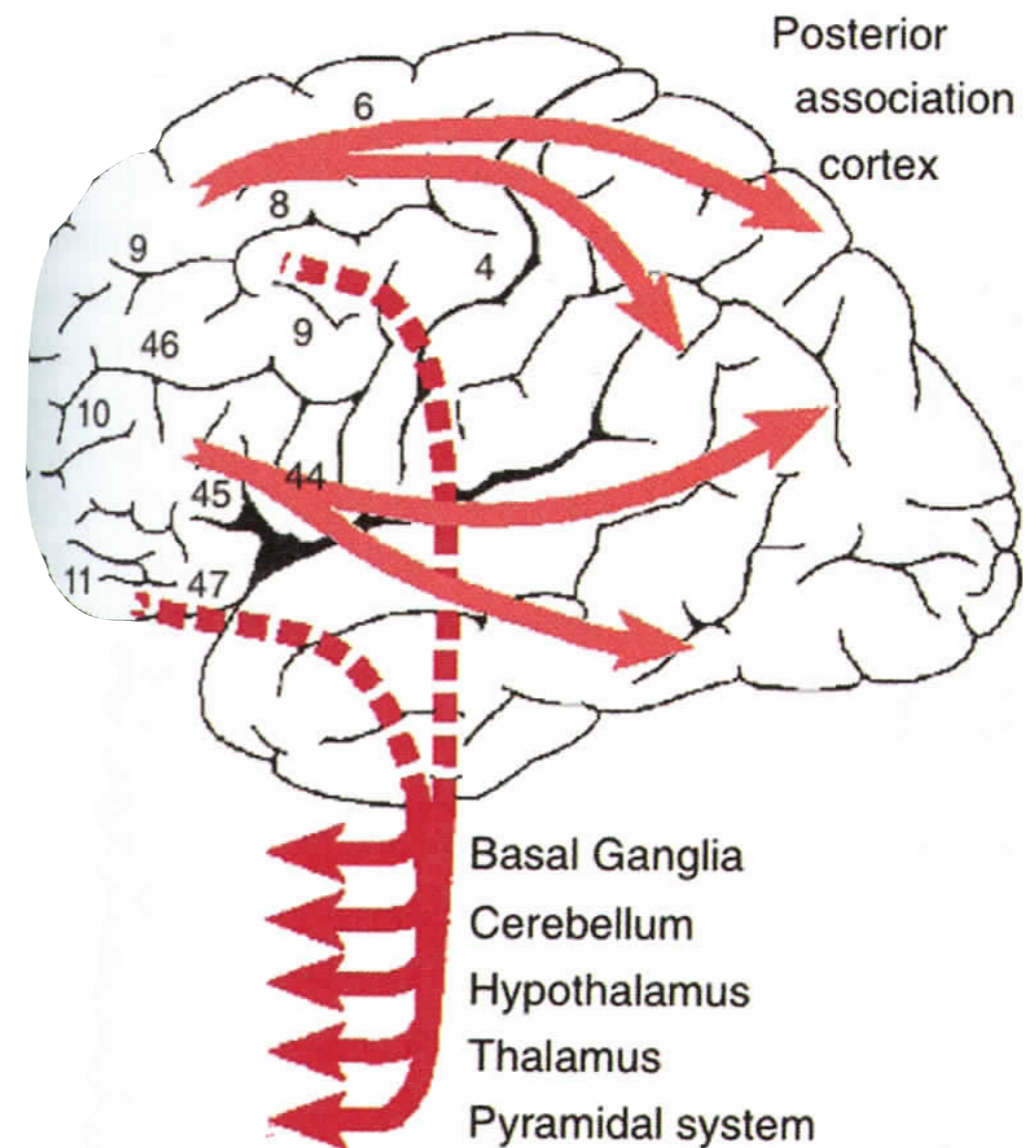
BASIC ANATOMY OF THE PFC

PFC is strongly connected with many other areas of the brain

Inputs to PFC

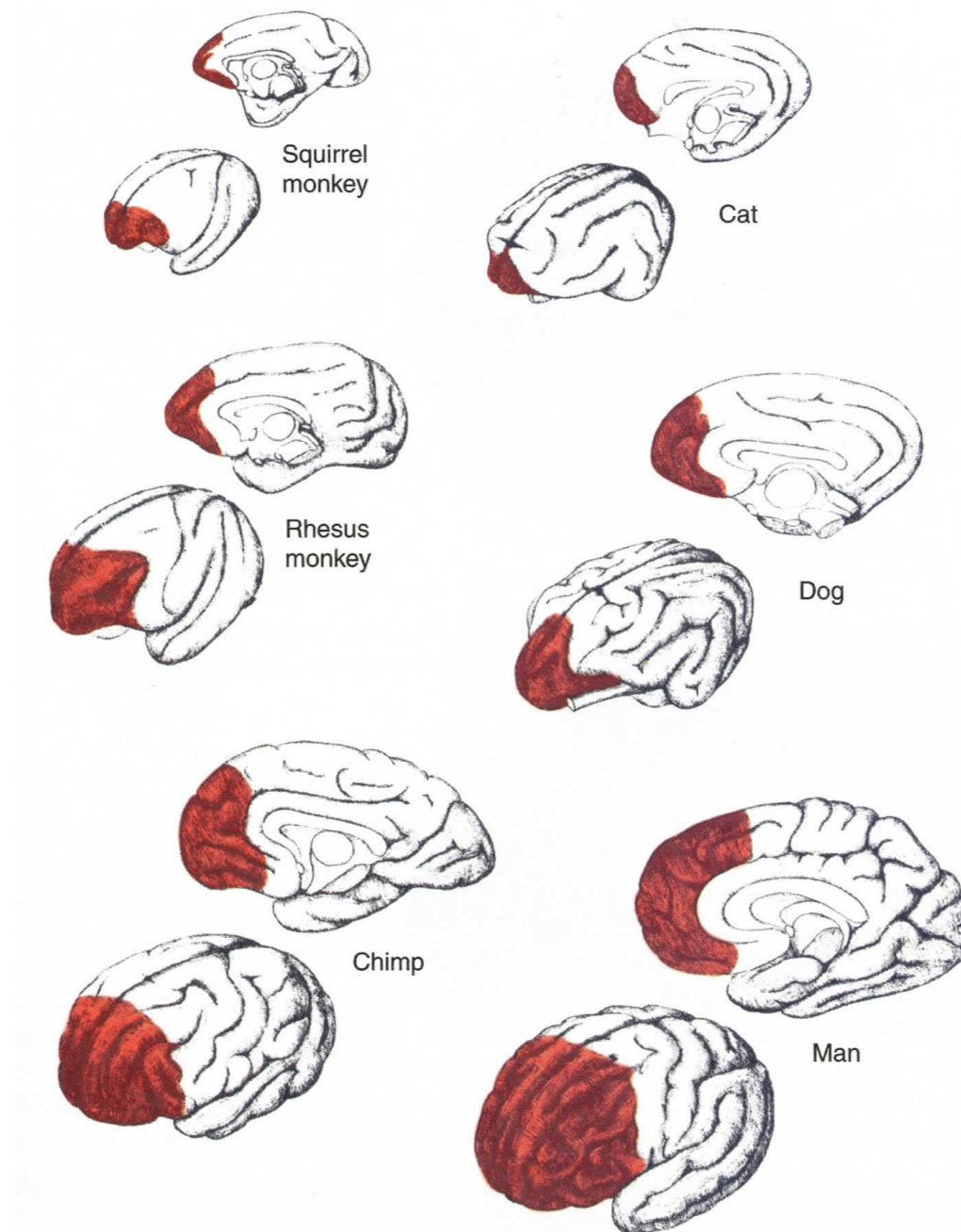


Outputs of PFC



BASIC ANATOMY OF THE PFC

Phenomenal expansion of PFC volume in primates, especially humans



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FIRST INSIGHTS INTO THE ROLE OF THE PFC

THE “SILENT LOBES”

Early on, prefrontal regions were called the “silent lobes” because scientists couldn’t figure out their function.

e.g., electrical stimulation did not lead to overt responses or thoughts in awake patients (Wilder Penfield at McGill University, ~1930s)

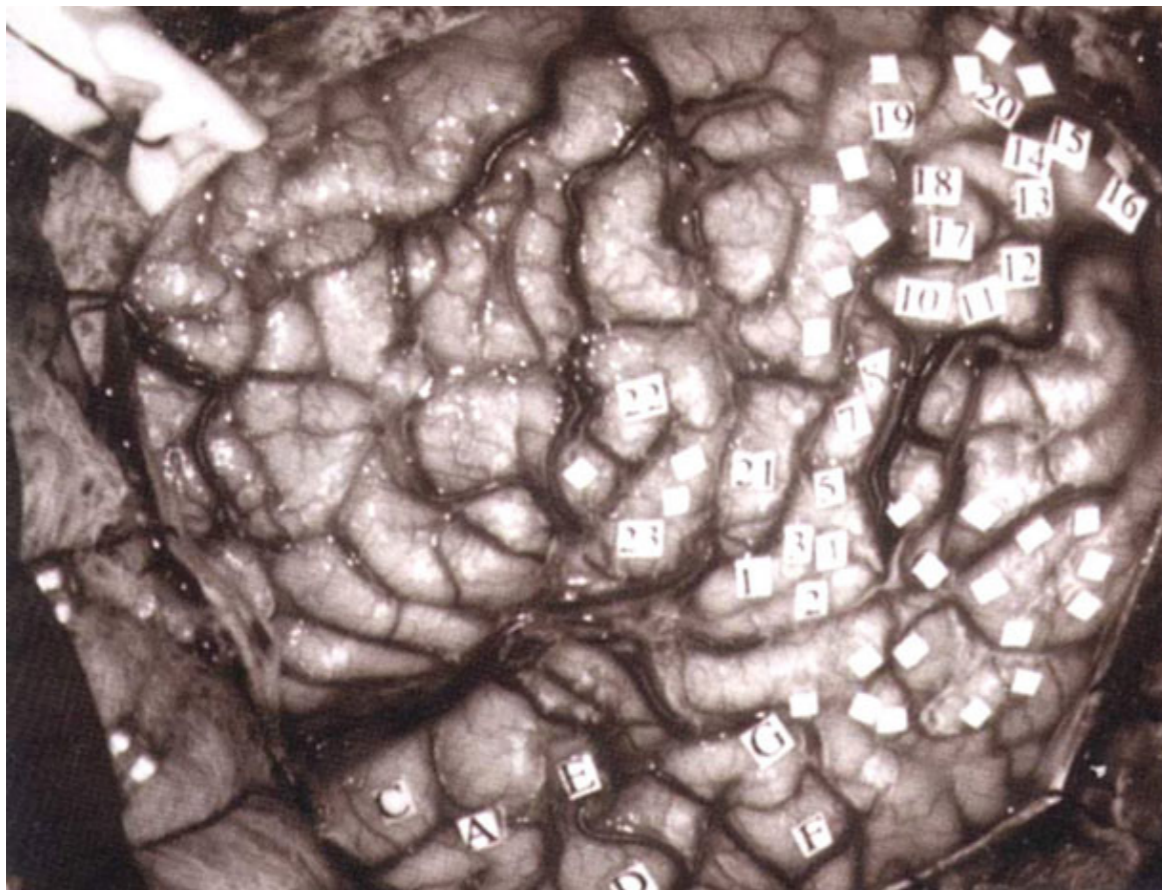
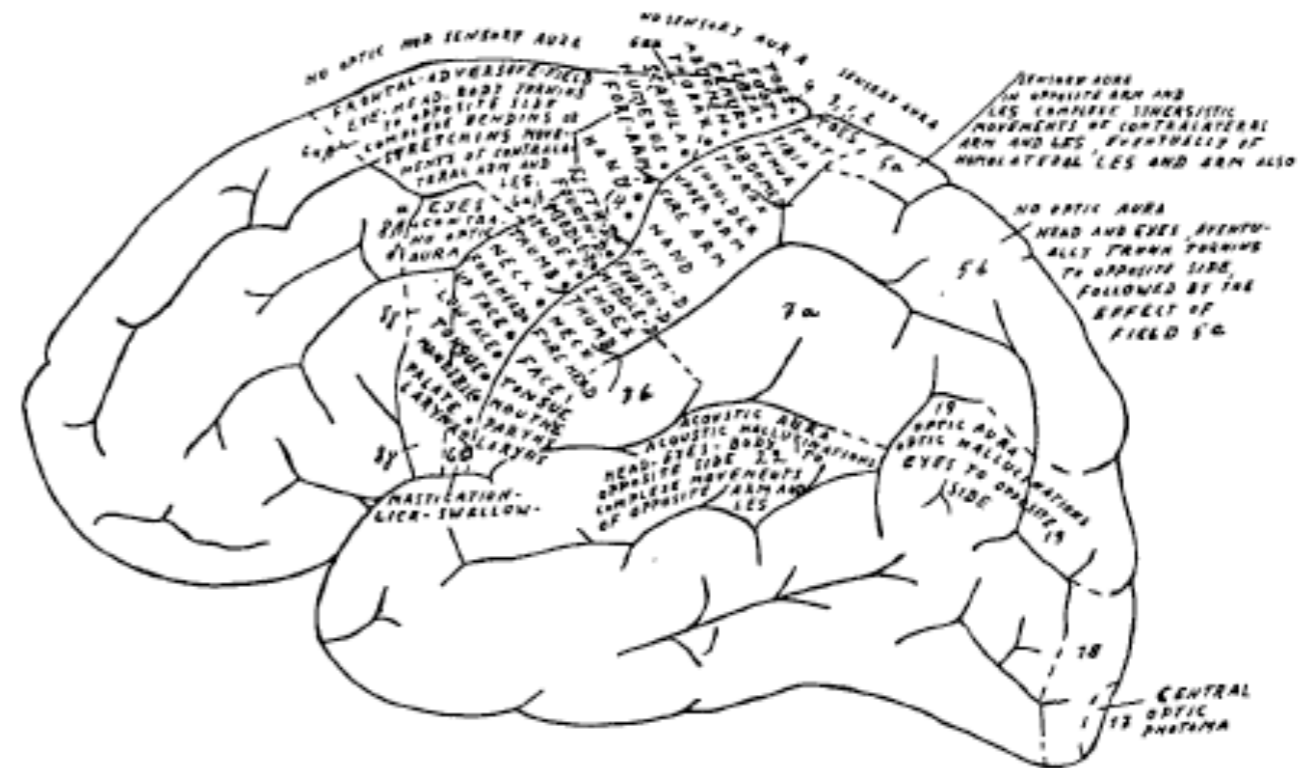


Figure 7. Human brain labeled as to cortical areas during neurosurgery. From Penfield.



Numbered tickets on the brain of a patient indicating the responses obtained by electrical stimulation of each point (Penfield & Boldrey, 1937).

FIRST INSIGHTS INTO THE ROLE OF THE PFC

PHINEAS GAGE: ONE OF THE FIRST DOCUMENTED CASE OF PFC DAMAGE

Railroad worker in charge of explosives, had a tampering rod go through his brain in 1848



<http://www.youtube.com/watch?v=yXiM-nDYzX0>

FIRST INSIGHTS INTO THE ROLE OF THE PFC

LOBOTOMIES: THE “LOGIC” BEHIND THEM

- ❖ Jacobsen and colleagues (1935) had shown that PFC damage had a “calming effect” in aggressive monkeys
- ❖ Brickner (1936) reported that removal of PFC in a patient (because of a tumor) did not appear to produce intellectual impairments
- ❖ Moniz (1935-1936), a well respected neurologist who developed cerebral angiography, concluded that:

António Egas Moniz



“if frontal-lobe removal [...] eliminates frustrational behavior, why would it not be feasible to relieve anxiety states in man by surgical means?”

(from Fulton, 1949, pp63-64)

*He won the **Nobel prize** in 1949 for developing the lobotomy technique*

FIRST INSIGHTS INTO THE ROLE OF THE PFC

LOBOTOMIES: A DESPERATE MEASURE GONE MAINSTREAM

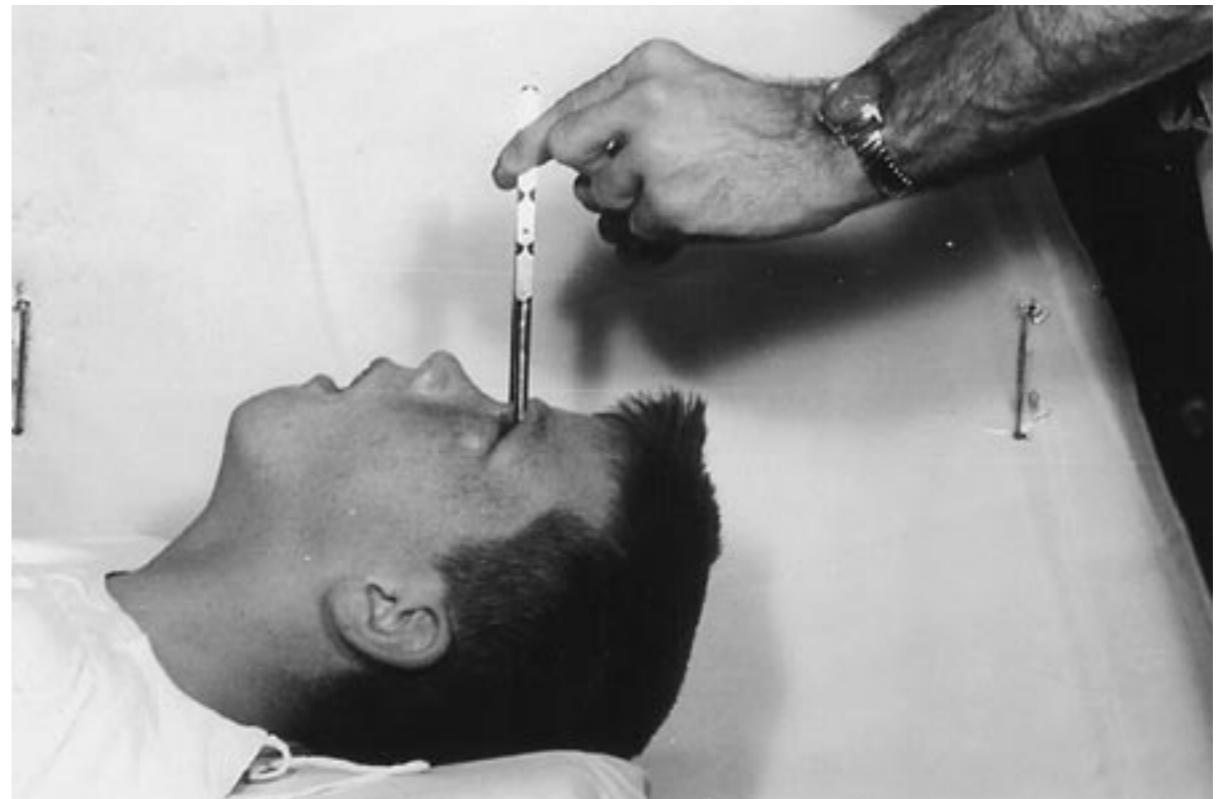
- ❖ Lobotomies are surgical disconnection of the white matter (axons) connecting the PFC with the rest of the brain
- ❖ Originally used to “treat” severe anxiety disorders, then depression, then schizophrenia, then pretty much anything...
- ❖ Tens of thousands were performed in the US before the introduction of neuroleptic medications in the 1960s

Walter Jackson Freeman II (right)



Popularized the lobotomy. A neurologist by training, he was working with a surgeon at first, but then developed the “ice pick” method.

The “ice pick” method



FIRST INSIGHTS INTO THE ROLE OF THE PFC

LOBOTOMIES: A DESPERATE MEASURE GONE MAINSTREAM

What was the outcome of the procedure?

- ❖ It did not solve the patients problems, often making them worse (e.g., Rosemary Kennedy at age 23 - JFK's sister).

Why do you think so many lobotomies were performed, and for so long?

- ❖ It made challenging patients easier to deal with and often they could be discharged to their families.
- ❖ Nowadays, medications are often used for the same purpose, but at least their effects are not permanent.

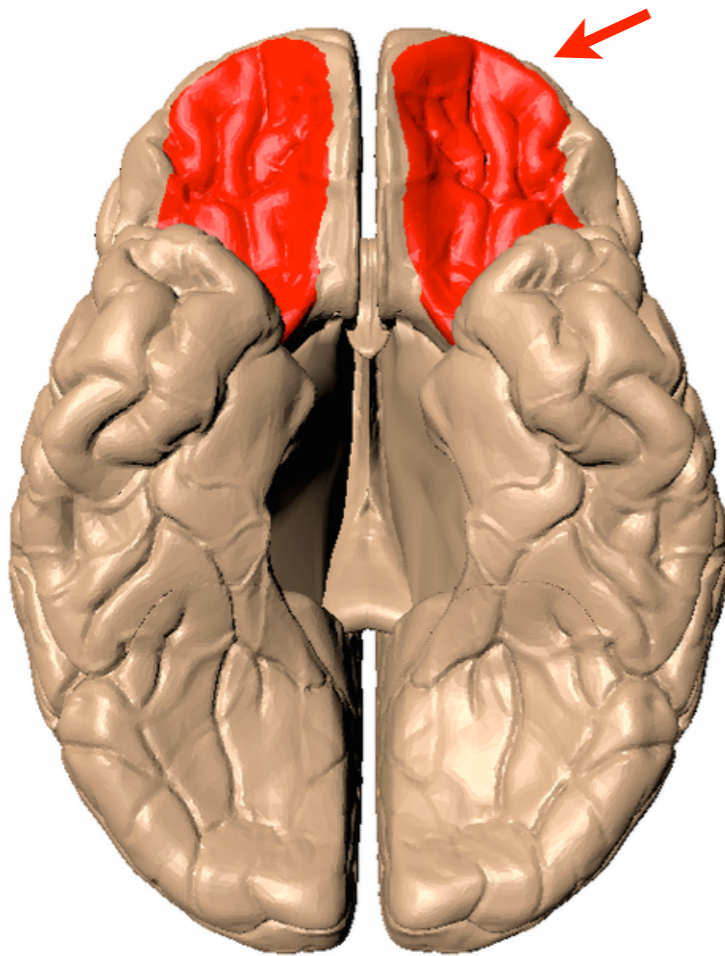
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DORSOLATERAL VS ORBITOFRONTAL PREFRONTAL REGIONS

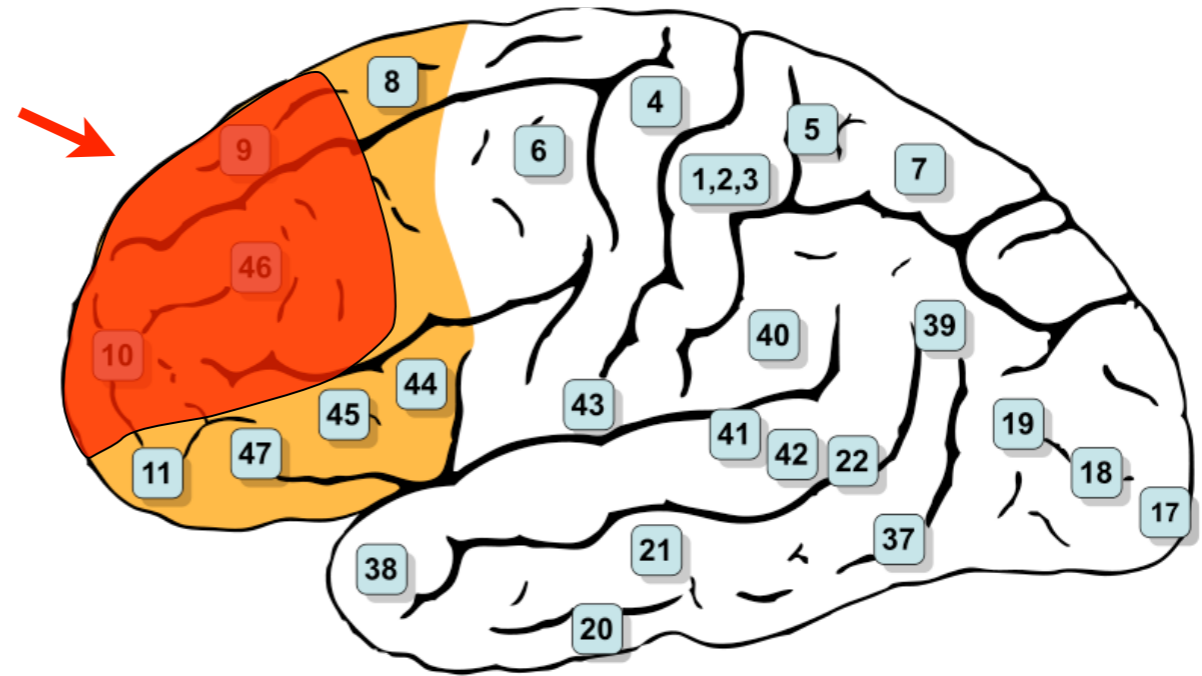
TWO DISTINCT PREFRONTAL SUBSYSTEMS

Orbitofrontal cortex



(view from below)

Dorsolateral PFC



(view from left side)

DORSOLATERAL VS ORBITOFRONTAL PREFRONTAL REGIONS

THE ORBITOFRONTAL CORTEX “SYNDROME”



*Phineas
Gage's injury*

Patients with orbitofrontal cortex damage:

- ❖ Show behavioral and emotional disinhibition
 - ❖ Rarely emotionally neutral (a lot of euphoria and rage)
 - ❖ Commonly selfish, boastful, childish, profane, sexually explicit
- ❖ Cannot inhibit urge for instant gratification
 - ❖ No foresight for the consequences of their actions
 - ❖ Antisocial, criminal behavior

DORSOLATERAL VS ORBITOFRONTAL PREFRONTAL REGIONS

THE DORSOLATERAL PFC “SYNDROME”

Patients with dorsolateral PFC damage usually show:

- ❖ Personality changes (e.g., flat affect, indifference)
- ❖ High susceptibility to incidental distractions
 - ❖ also a characteristic of ADHD
- ❖ Impaired ability to initiate, terminate, or change behavior
 - ❖ also a characteristic of schizophrenia
- ❖ **Impaired “executive functions”**
 - ❖ Thus, PFC is often called the “CEO of the brain”

DORSOLATERAL VS ORBITOFRONTAL PREFRONTAL REGIONS

THE DORSOLATERAL PFC: THE “CEO OF THE BRAIN”

What are “executive functions”?

- ❖ monitoring the world around us
- ❖ paying attention selectively to one item rather than another
- ❖ making plans and actions, and revising when needed

Too abstract?

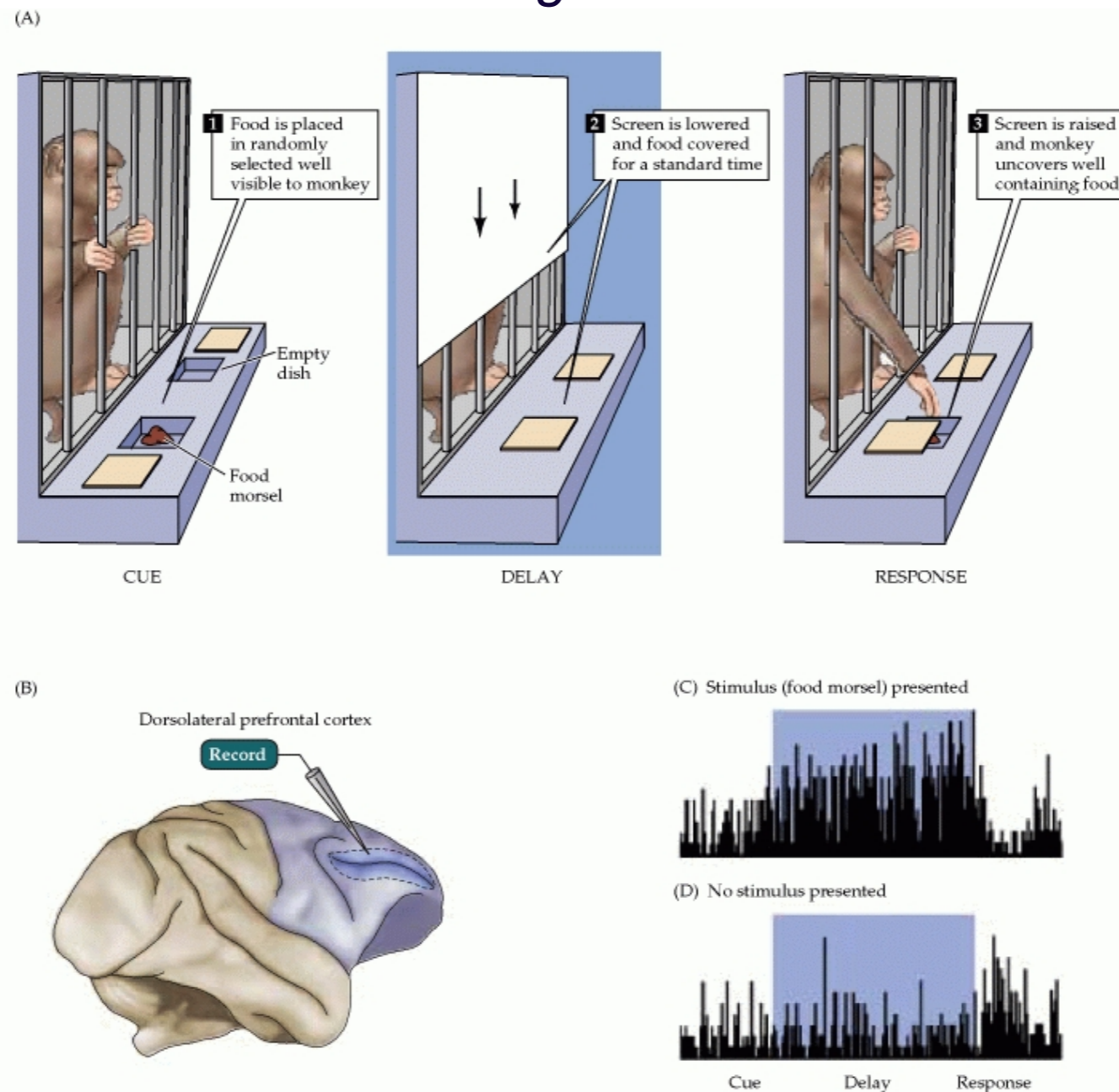
Let's talk about two concrete experimental examples...

DORSOLATERAL VS ORBITOFRONTAL PREFRONTAL REGIONS

THE DORSOLATERAL PFC: THE “CEO OF THE BRAIN”

- ❖ The dorsolateral PFC is important for **working memory**
 - ❖ capacity to hold info in mind, and perform mental operations on that info

PFC units holding stimuli in mind

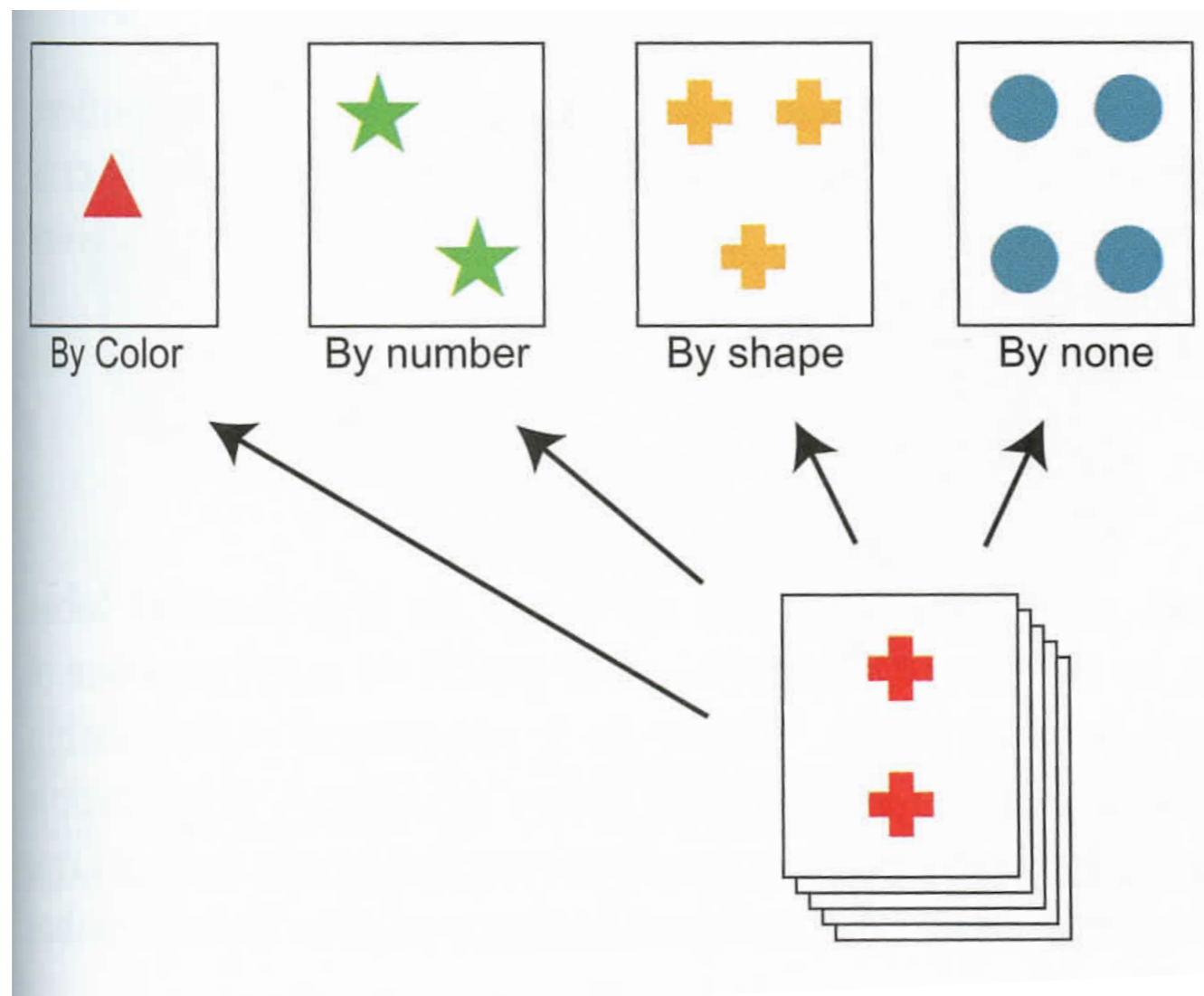


DORSOLATERAL VS ORBITOFRONTAL PREFRONTAL REGIONS

THE DORSOLATERAL PFC: THE “CEO OF THE BRAIN”

- ❖ The dorsolateral PFC is also crucial for **planning behavior**, **goal-directed behavior**, and **strategy-switching** to adapt to new contingencies in the world

Example of strategy-switching, impaired in patients with PFC damage



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THE “FRAGILE” PFC

THE PFC IS A “HUB” REGION OF THE BRAIN

- ❖ The PFC interconnects many distinct, functionally specialized regions of the brain (i.e., it is a “hub” region)
 - ❖ PFC dysfunction can affect information processing throughout the whole brain
 - ❖ Damage elsewhere in the brain is likely to interfere with PFC function as well
- ❖ This makes the PFC “fragile”
 - ❖ Low functional breakdown threshold
 - ❖ PFC dysfunction is the most common (and thus least specific) finding among neurological, psychiatric, and developmental conditions

THE “FRAGILE” PFC

PFC AND COGNITIVE DISORDERS

Many cognitive disorders are associated with PFC dysfunction (usually reductions in volume and/or connections)

- ❖ Schizophrenia
- ❖ Tourette’s syndrome
- ❖ ADHD
- ❖ Severe depression
- ❖ Bipolar disorder
- ❖ Antisocial behavior
- ❖ Addiction
- ❖ Autism (67% more neurons in PFC than controls)
- ❖ ...

The problem is that we don’t yet understand what goes wrong with the PFC in these disorders.

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THE PFC AND SOCIALLY APPROPRIATE BEHAVIOR

THE DEVELOPING PFC — SEE SARAH-JAYNE BLAKEMORE'S TED TALK

- ❖ The PFC is the brain region that takes the longest time to fully develop (~ age 25)
- ❖ Most of the development takes place in the late teens and early 20s, and involves the “myelination” of the PFC
- ❖ This evidence has led to the idea of “frontalization”.
 - ❖ Controlling one’s actions is not innate. It emerges gradually through development
 - ❖ PFC gradually becomes able to oversee and regulate behavioral responses initiated by the more “primitive” limbic structures

Does that help you understand the behavior of teenagers? Or why they are not prosecuted as adults? Should we take that into account?

THE PFC AND SOCIALLY APPROPRIATE BEHAVIOR

PFC DAMAGE AND ANTISOCIAL BEHAVIOR

The prevalence of head injury is:

- ❖ Much higher among criminals than in general population
- ❖ Much higher among violent than non-violent criminals

*Is this indicative of PFC damage? Should we take that into account?
What about athletes with CTE (Chronic Traumatic Encephalopathy)?*

Some drugs lead to long-lasting changes in PFC structure (e.g., shorter dendrites, fewer spines, fewer dopamine transporters)

- ❖ Methamphetamines
- ❖ Alcohol (in high doses)

Should we consider this in judging the criminal behavior of addicts?