

Functional Neurocircuitry of Cognition and Cognitive Syndromes

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Critical cognitive operations that must be carried out by the nervous system

- Process information about external environment (sensory-perceptual representations)
- Prepare and execute actions (motor planning and output)
- Communicate with other humans (language)
- Encode, store, and access information (memory/learning)
- Rapidly determine the most salient and/or potentially dangerous aspect of the current environment (attention)
- Select, control, and monitor these complex operations (executive control functions)

Methods for identifying and characterizing networks and their functions

- **Non-Human Animal Investigations**

- Experimental neuroanatomy (neuronal tracer studies in animals)
- Recordings of neuronal activity in awake behaving monkeys
- Placement of focal lesions

- **Human Investigations**

- Depth electrode studies
- Task-related fMRI (or PET) studies that carefully manipulate relevant variables
- Surface event-related potential investigations during task performance
- Resting state functional connectivity mapping
- Structural MRI--regional tissue loss/cortical thinning in neurodegenerative disease; diffusion tensor imaging (WM tracking)
- Impact of focal lesions—clinical symptoms and syndromes

Case

- 75 yo retired man with h/o HTN and hyperlipidemia presents with 3 years progressive visual difficulties
- Problems accurately reaching for objects and distinguishing objects from background
 - Could not find his cat who was on his couch
 - Sat on a table instead of the adjacent chair
- No difficulty reading text or recognizing faces

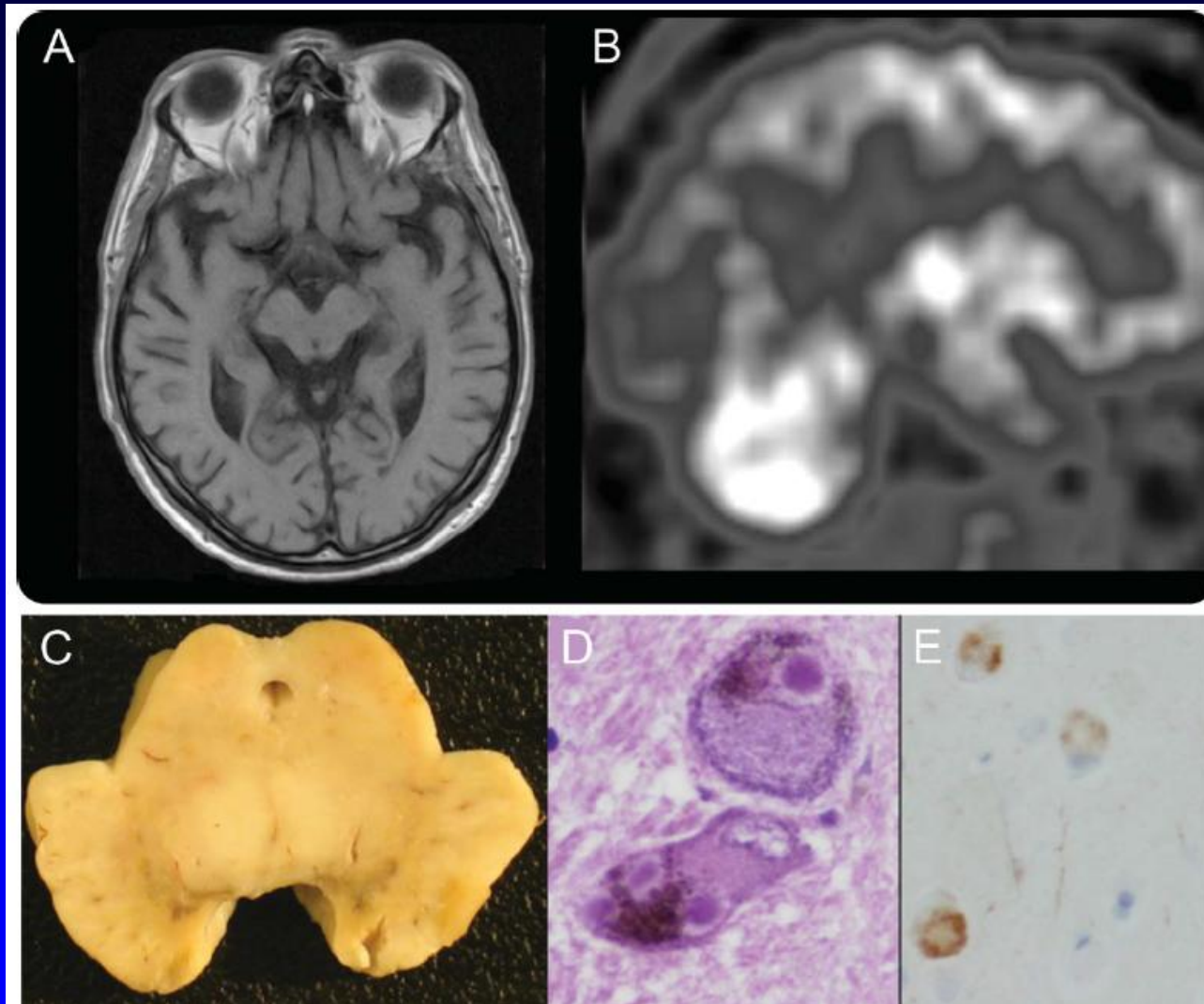
Case: initial exam

- Normal memory, language, motor fxs, gait
- Mild impairment of attention & calculations
- Probs drawing a clock and intersecting pentagons
- Unable to interpret Ishihara color plates despite discriminating individual colors
- Normal visual acuity, fields, and ocular ductions
- Unable to initiate horizontal saccades to visual targets or reach accurately on finger-nose-finger testing

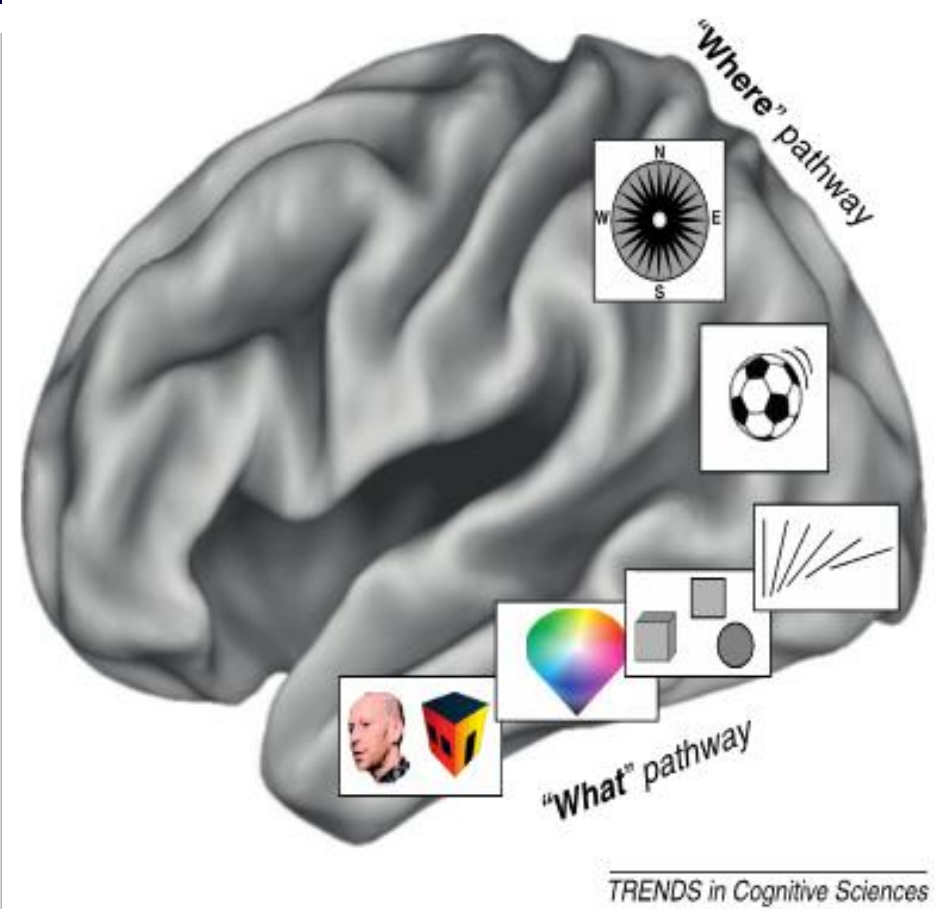
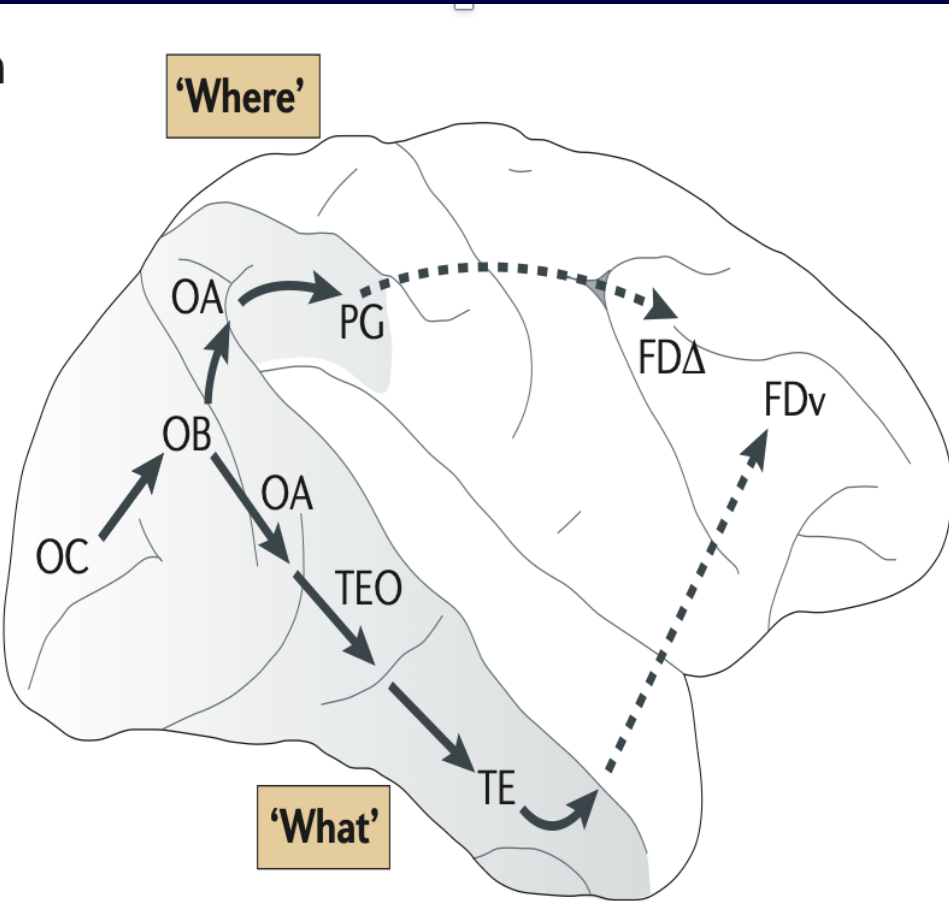
Case

- **Balint Syndrome**
 - Ocular apraxia
 - Optic ataxia
 - Simultanagnosia
- **Suggests bilateral disruption of parieto-occipital regions**
- **Pace of illness c/w neurodegenerative process**
- **Posterior Cortical Atrophy**
 - AD pathology most common
 - Dif dx includes Lewy body disease, tau pathology, and prion disease

Neuroimaging and Neuropathology: PCA-LBD



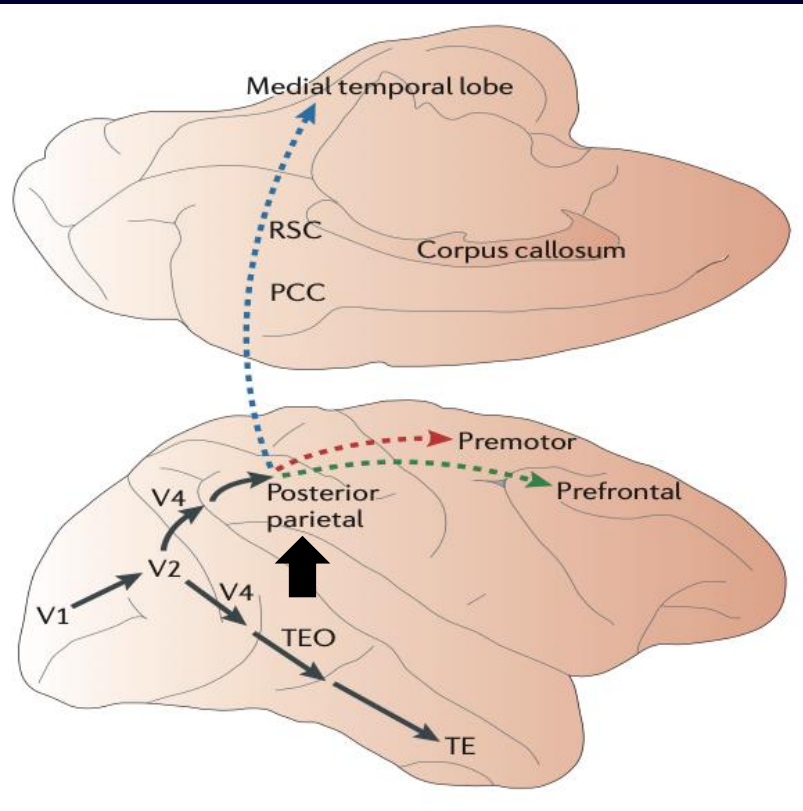
Ventral (What) & Dorsal (Where/How) Pathways



Kravitz et al., 2011

de Haan and Cowey, 2011

3 Dorsal Pathways from Posterior Parietal Cortex

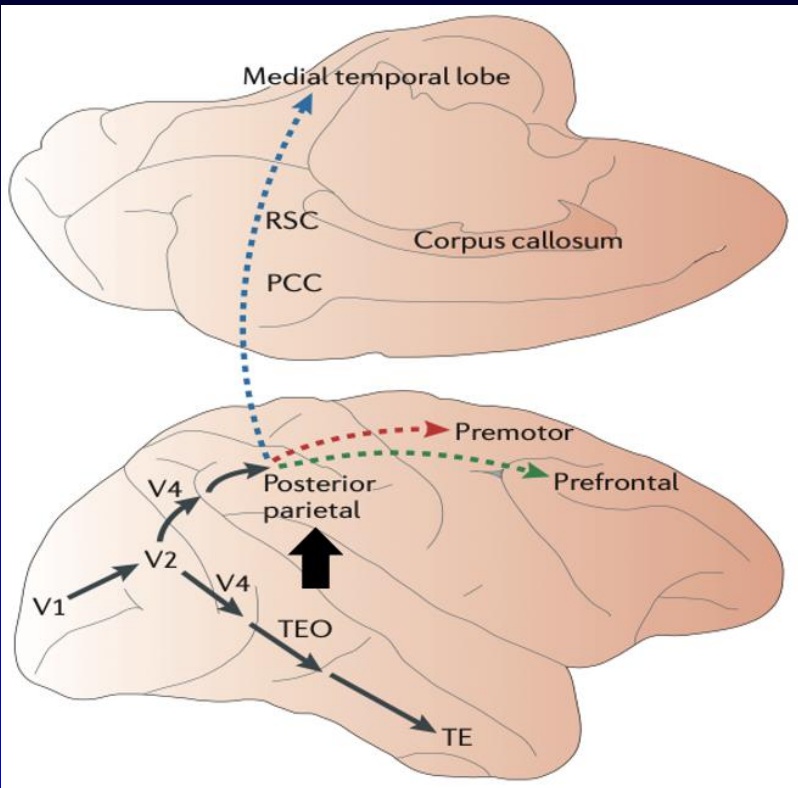


Posterior Parietal Cortex:

- represents space from an egocentric frame of reference
- Integrates information from central and peripheral visual fields



3 Dorsal Pathways from Posterior Parietal Cortex



Parieto-medial temporal pathway

--complex spatial processing
required for navigating through
the environment

Parieto-premotor pathway:

--coordinated maps of space and
body position
--visually guided action in
peripersonal space (e.g.,
reaching and grasping)

Parieto-prefrontal pathway:

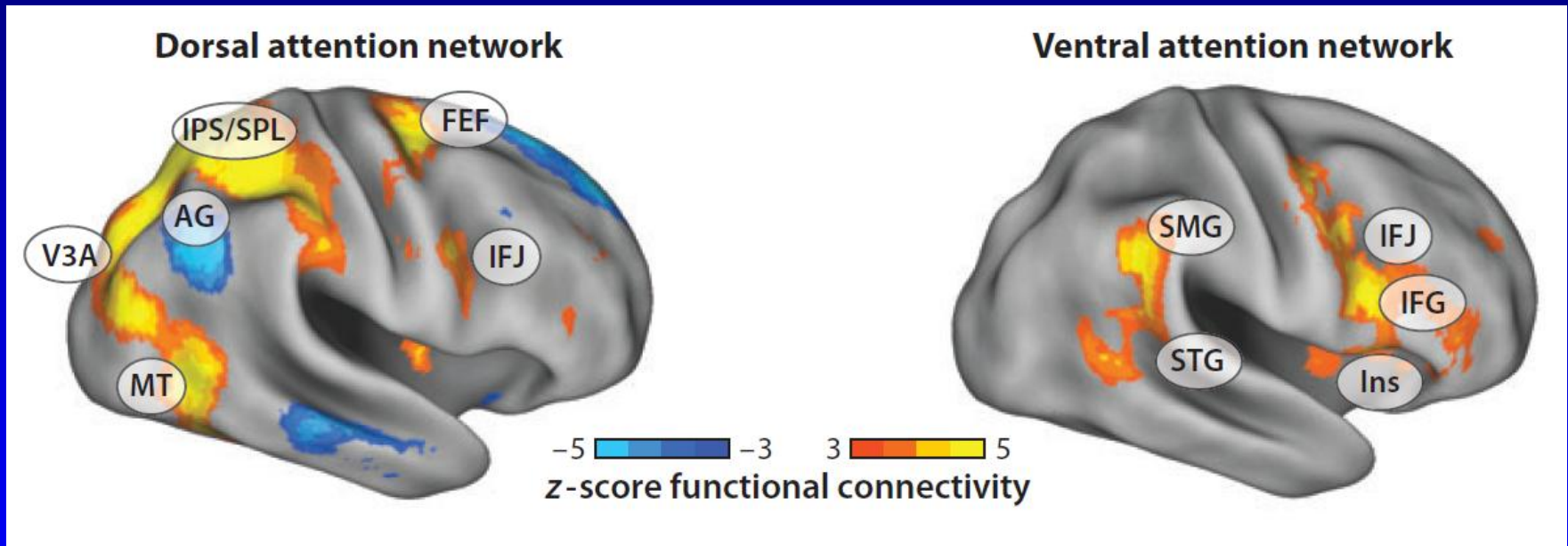
--Spatial WM
--Top-down control of
eye movements

Posterior Parietal Cortex:

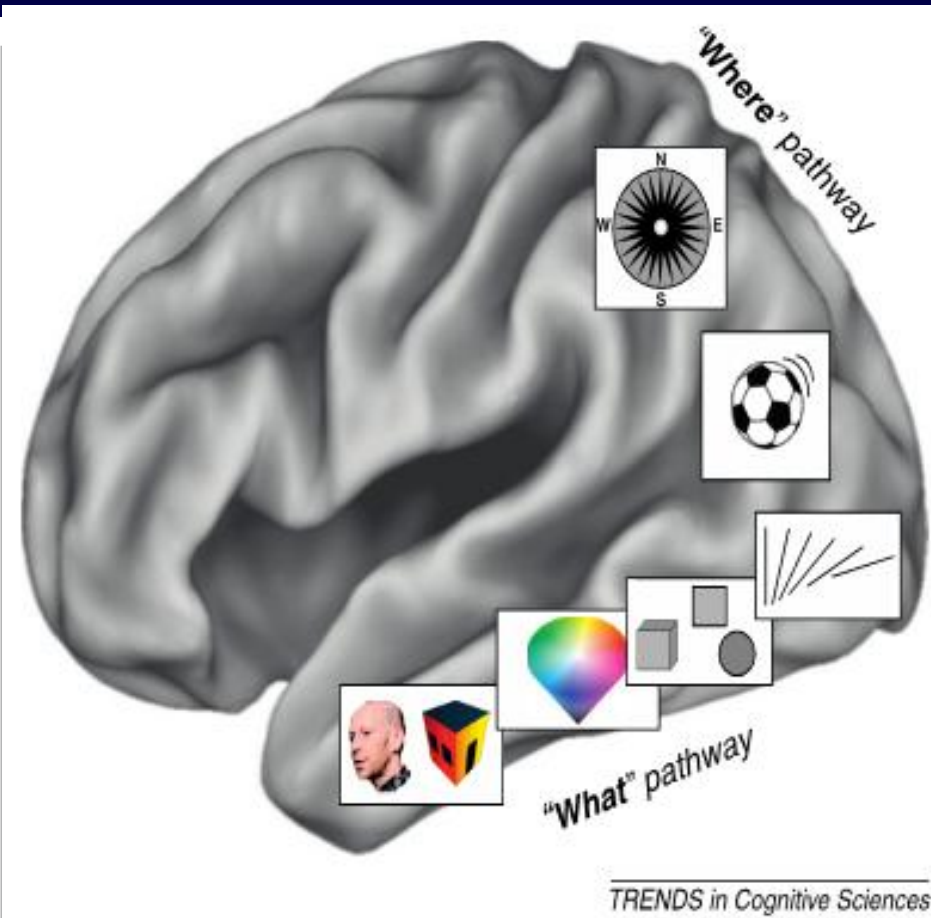
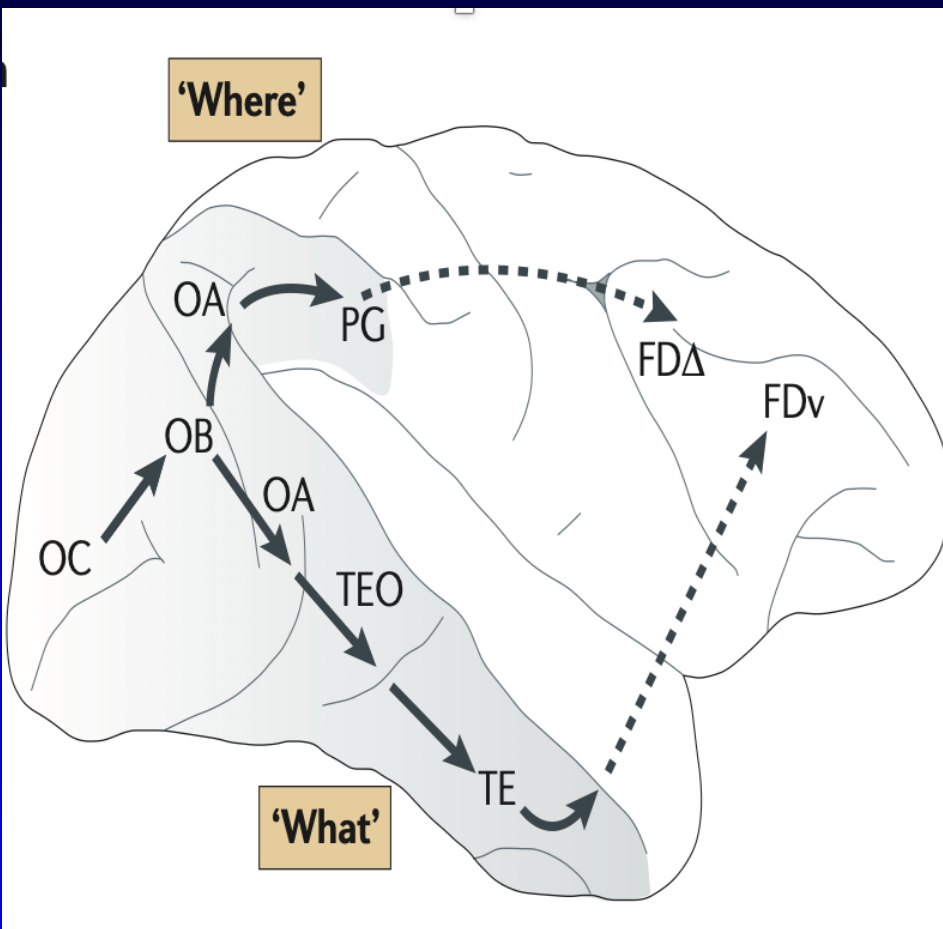
--represents space from an
egocentric frame of reference
--Integrates information from
central and peripheral visual
fields

**The “Where” Pathway is often labelled
the “How” Pathway**

Dorsal and Ventral Attention Networks



Ventral (What) & Dorsal (Where/How) Pathways



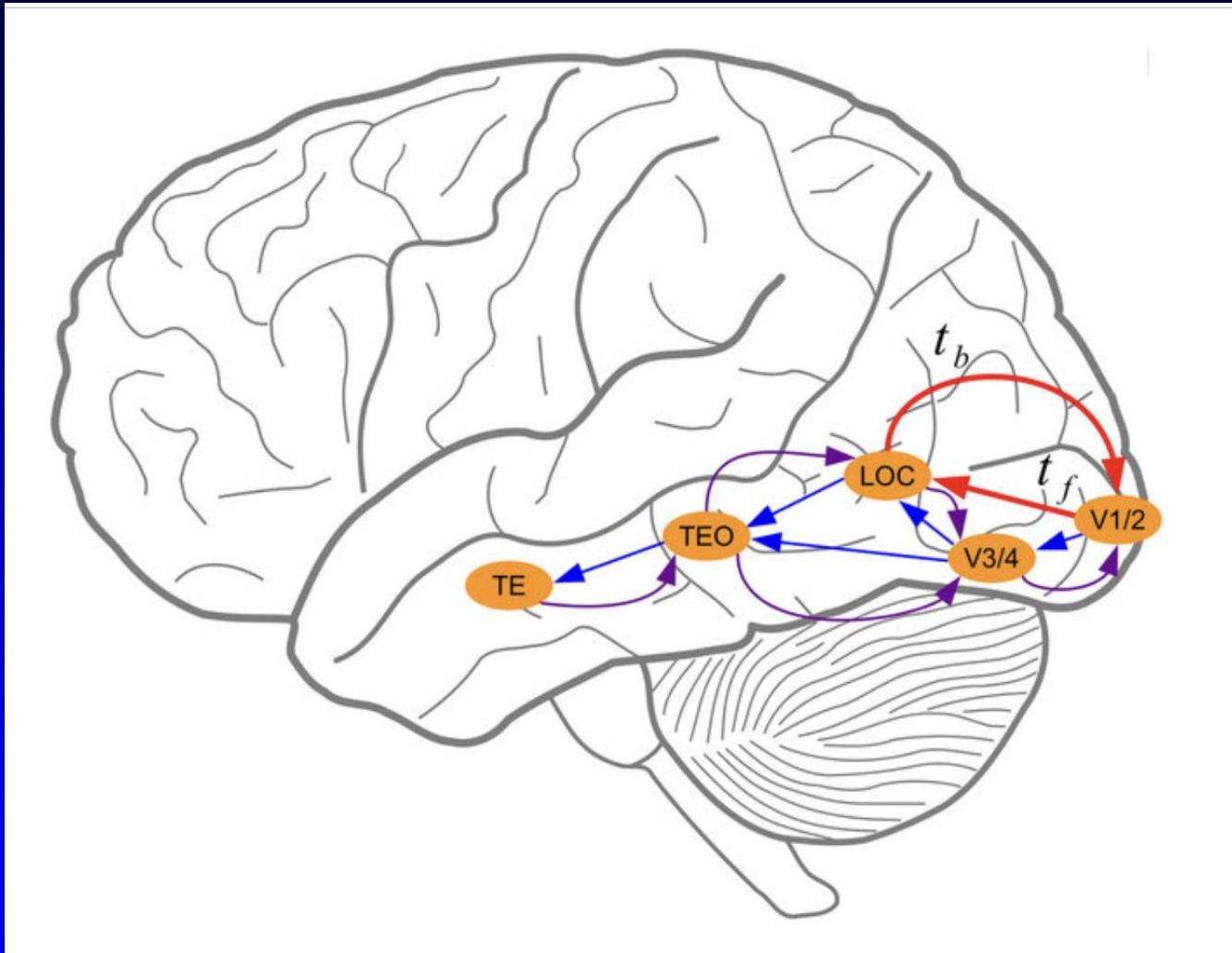
Kravitz et al., 2011

de Haan and Cowey, 2011

Ventral (What) & Dorsal (Where/How Pathways

- The serial, hierarchical processing model of visual processing represents a beautiful and coherent theory
 - Perceptions are built step-by step-from the bottom up
- Unfortunately, the model is not accurate

Feedforward and Feedback Processing



Feedforward = bottom-up processing

Feedback = top-down processing

The Brain's Predictive Activity

- The brain actively generates and updates predictive models about sensory input, internal physiologic and affective states and the potential reward value of objects and actions
- Some investigators suggest the process of prediction, data input, interpretation and updating occurs across all stages of cortical information processing
 - from earlier ones that encode basic sensory information to later ones that mediate perception, identification, and meaning
- Predictions (expectations) are conveyed from higher areas in the processing hierarchy to lower areas (via feedback projections) prior to, for example, the arrival of sensory signals via the thalamus--Predictions are compared with incoming sensory input

The Brain's Predictive Activity

- If there is a mismatch between expectation and sensory-perceptual input, a prediction error message is generated and the back-and-forth “dialogue” between synaptic levels continues until a compromise or best fit is reached
- Ideally, this interactive process can result in a more accurate, adaptive models to account for incoming data and update expectations about the probability of future events
- A potential downside to this system is a decrease in fidelity due to excessive influence of top-down processing

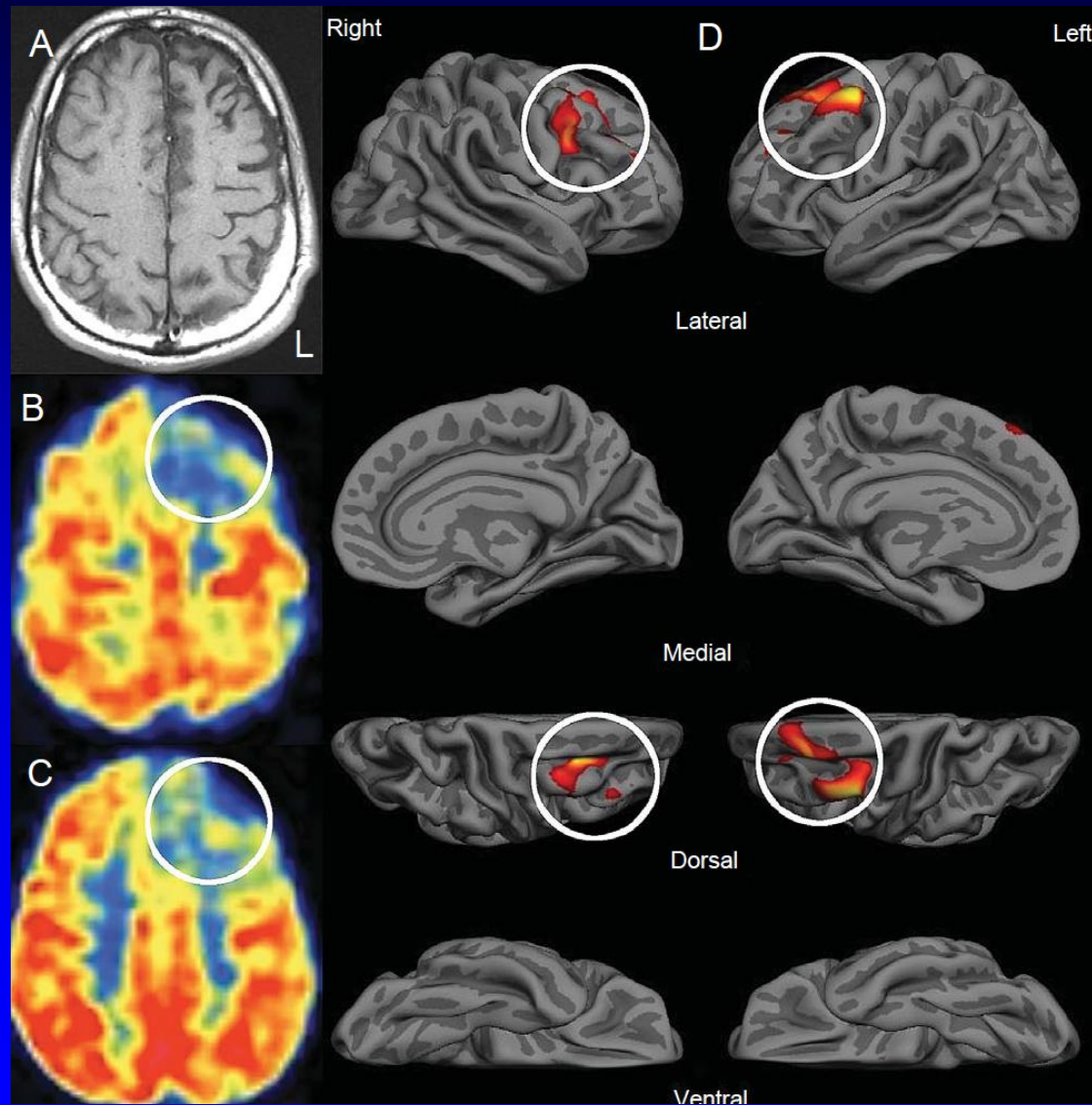
Visual processing relies on predictive activity

- Emotional, motivational, and social factors likely can influence visual perception (early in the visual processing stream)
- Advantage: increases the ability to make rapid decisions about whether to approach or avoid an object
- Risk: Perceptual distortions that can inappropriately “color” the world we see
 - **Motivational factors** regarding the desirability of an object may **influence** perception of size, brightness, distance, steepness, and salience of visual stimuli
 - **Social category cues** modulate early visual processing of faces (e.g., larger early electrophysiologic response to in-group vs out-group faces)
- To be adaptive, the relative influence of top-down and bottom-up processing needs to be flexible and sensitive to context
 - **Imbalance** between top-down predictions and bottom-up input can be a source of neuropsychiatric symptoms

Case

- 58 yo r-handed retired engineer with 2 yrs progressive ↓ verbal output
- No changes in memory, personality, iADLs
- No FH neurodegenerative disease
- Normal EOMs. No Parkinsonism. Paucity of spontaneous speech; ↓ ability to produce cohesive narratives
- Naming, repetition, comprehension, writing normal
- Marked ↓ of generative speech.
 - Letter fluency (FAS)-1st %tile; Category fluency-25th %tile; Design fluency 12-25%tile

Neuroimaging



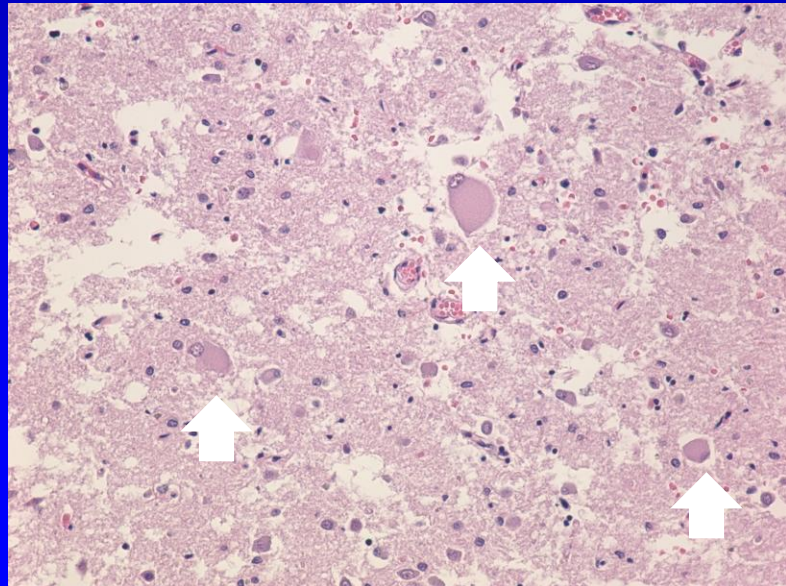
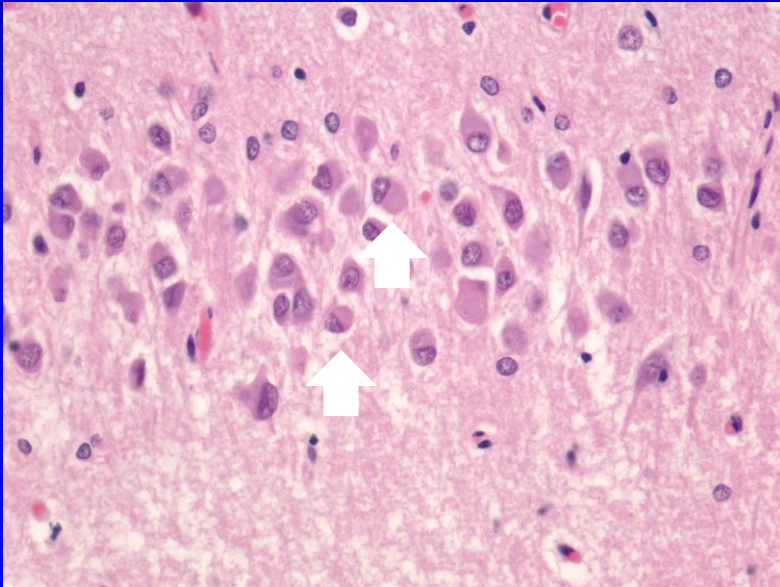
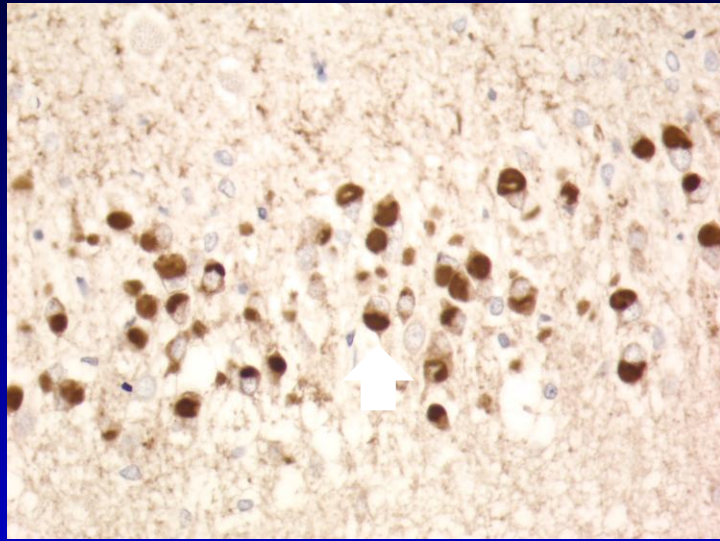
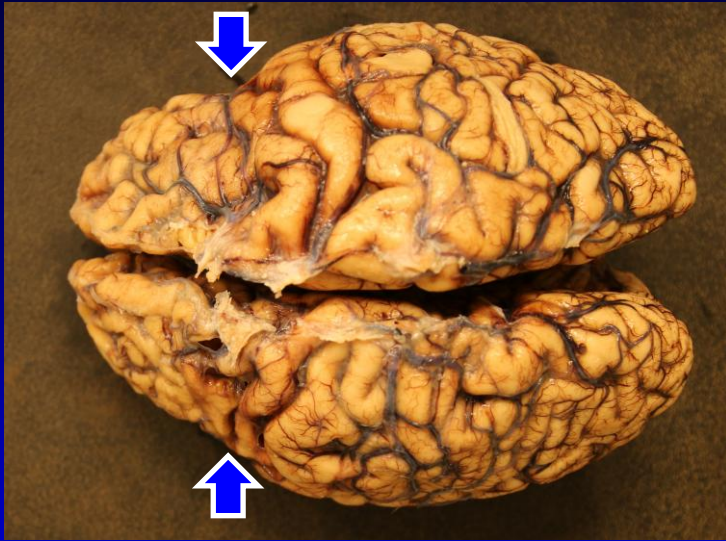
Case

- Dx: Progressive Dynamic Aphasia (transcortical motor aphasia)
 - Reduced activation/initiation of speech
 - Impaired lexical search strategy and verbal planning
 - Disrupted executive aspects of language output
 - Intact repetition and comprehension
- Left Prefrontal cortex (PFC) critical for verbal action-retrieval functions

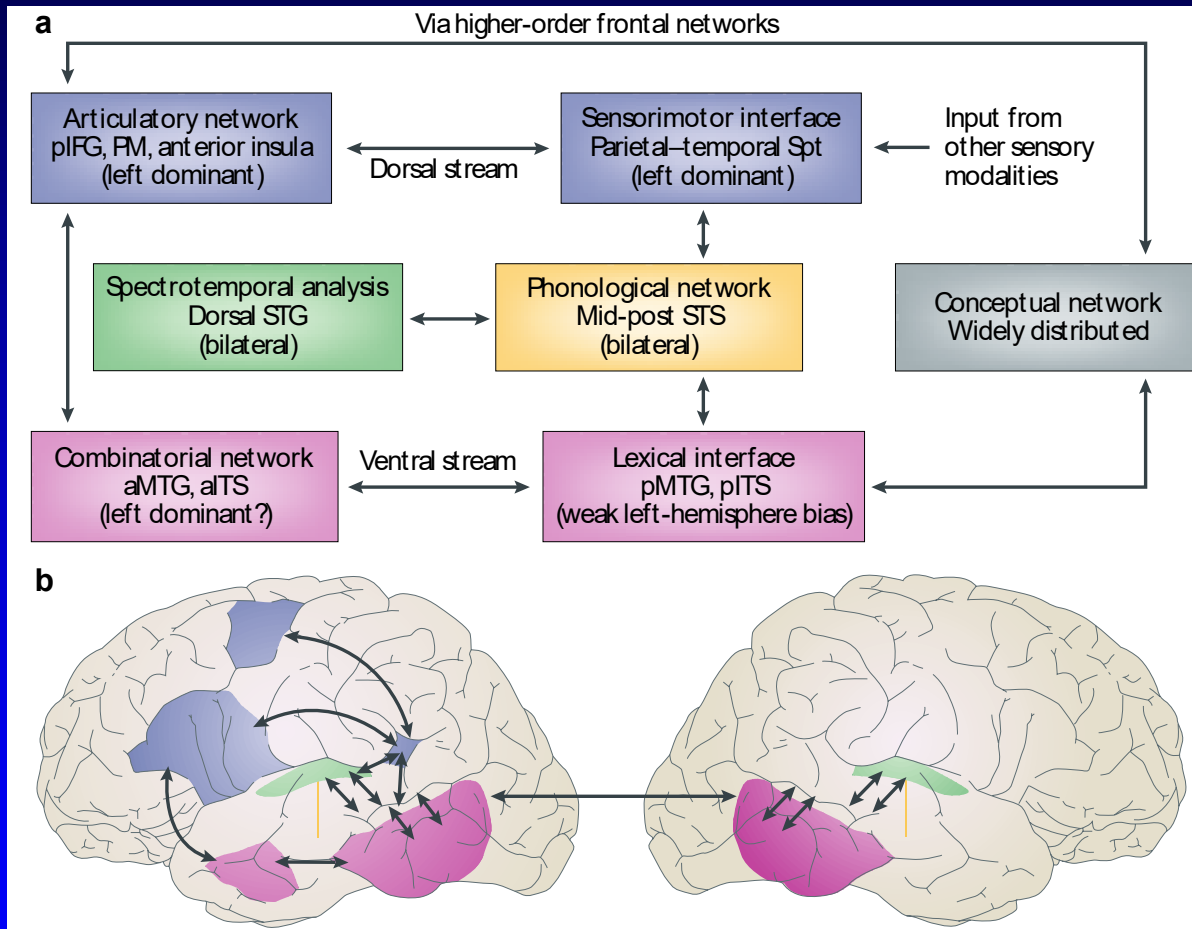
Slow Symptom Progression over the next decade

- Over next ~5 years, pattern morphed into **non-fluent, agrammatic PPA** (↑d atrophy on MRI-- spread inferiorly, posteriorly, and bilaterally)
 - Spontaneous speech ↑ effortful, non-fluent, halting, with inconsistent speech sound errors
 - ↑ grammatical errors in writing, then speech
 - ↓ comprehension of syntactically complex material, ↓ ability with naming and sentence repetition
- ~10 years into the illness, the patient was mute, incontinent, completely dependent
- Covid-19--immediate cause of death

Case, Neuropathology—Pick's Disease



Dual-stream model of the functional anatomy of speech

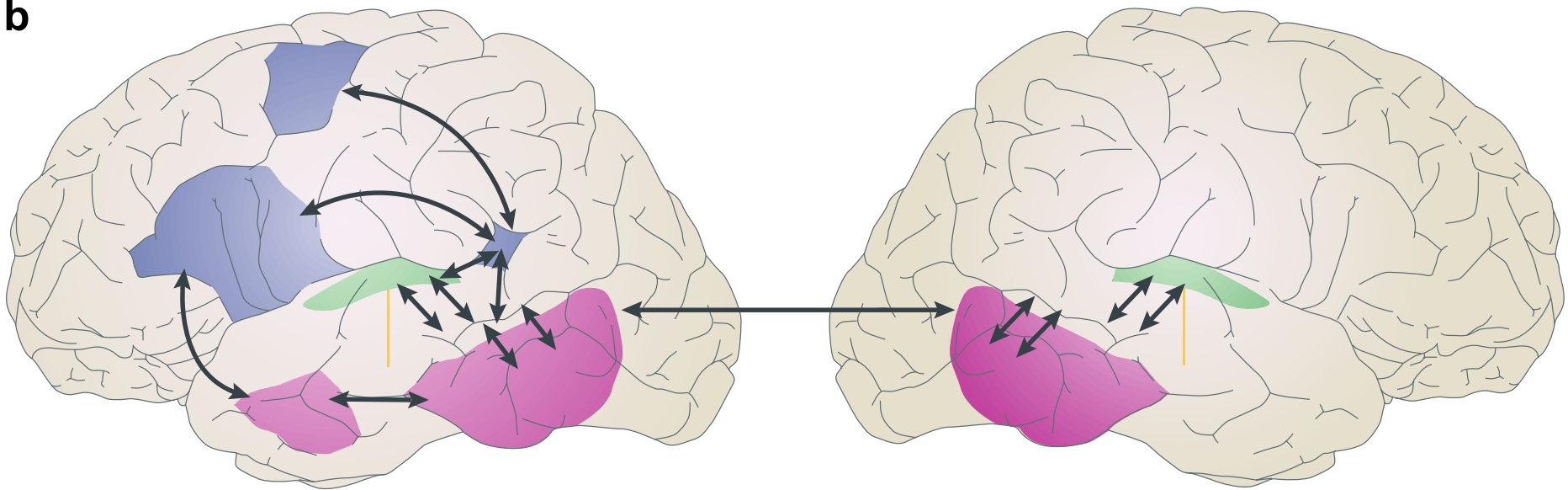
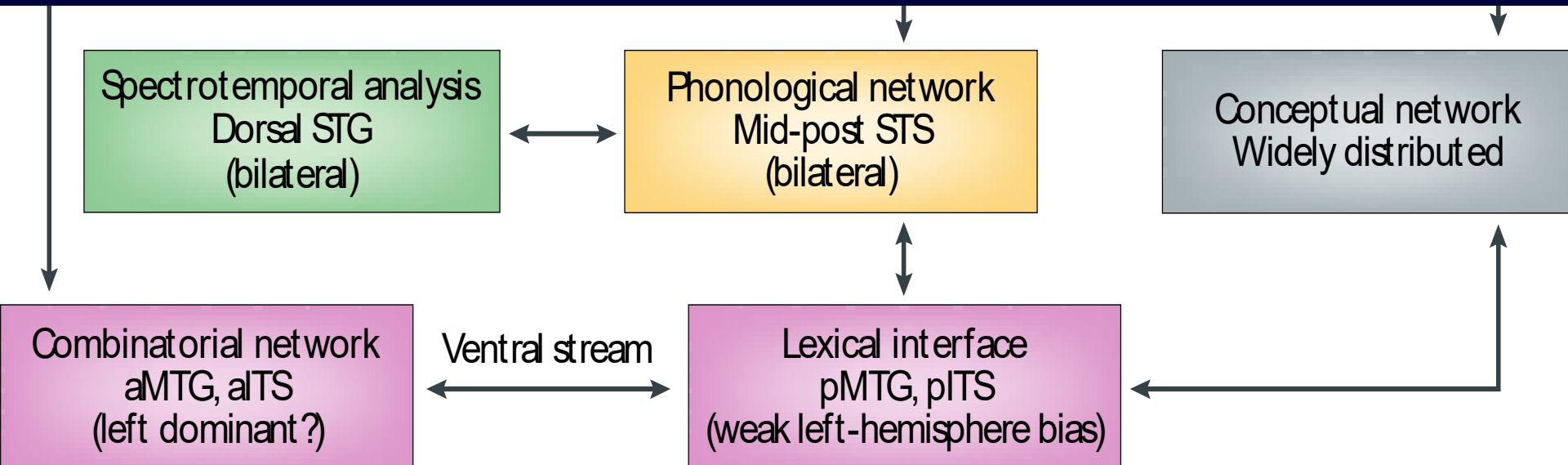


- **Dorsal Stream:** “sound to action/articulation” pathway (directs acoustic speech signals to frontal articulatory networks)

- **Ventral stream:** “sound to meaning” pathway (processing speech signals for language comprehension)

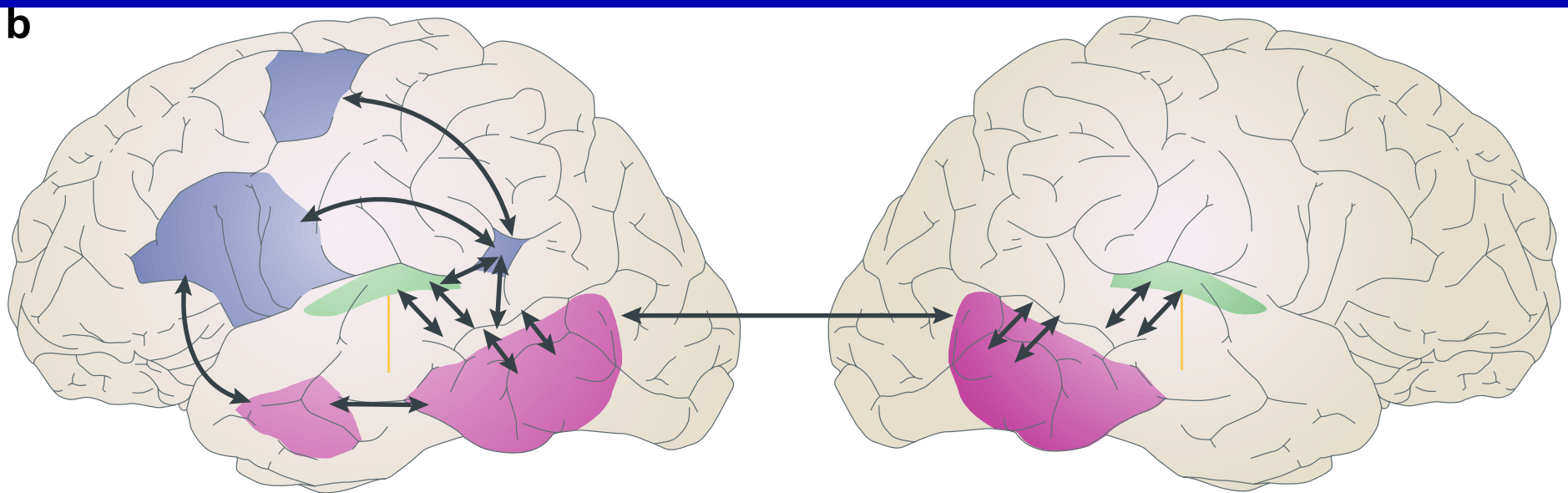
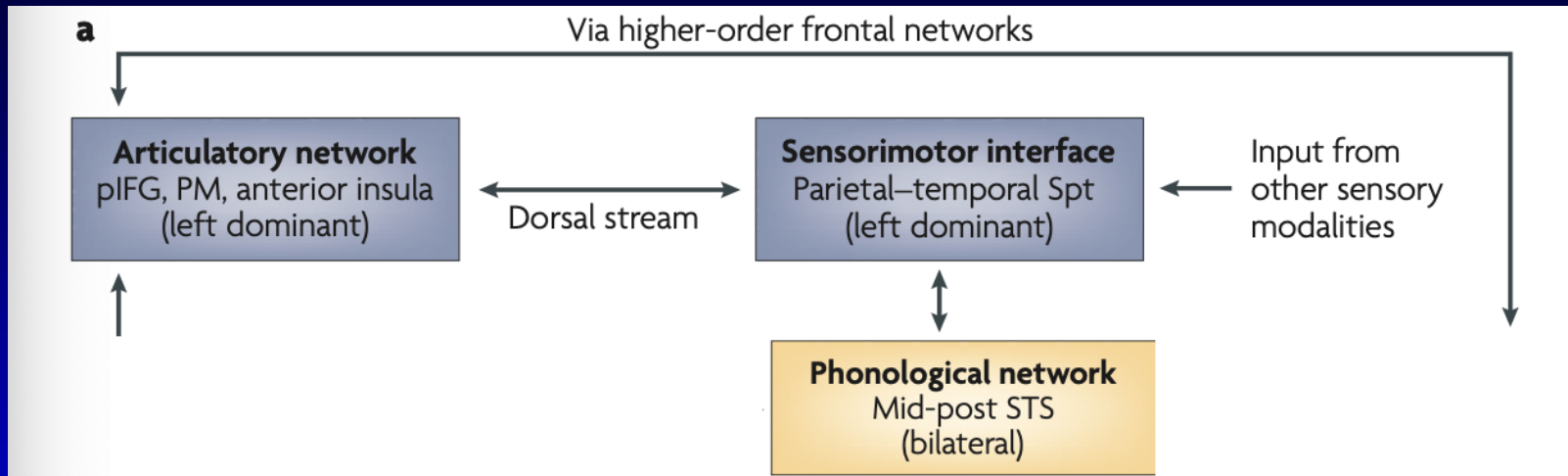
Dual-stream model of the functional anatomy of speech

Ventral Stream

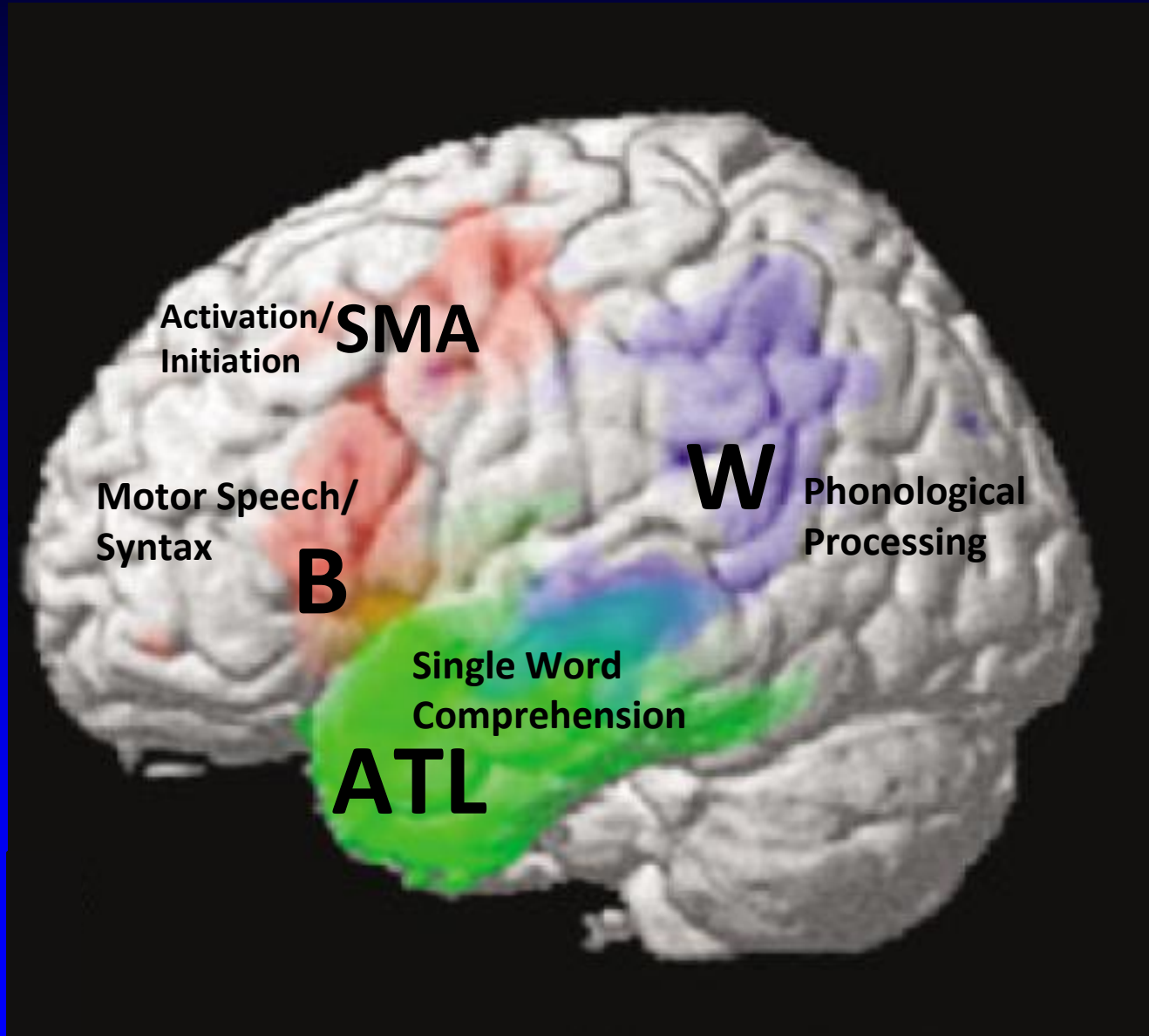


Dual-stream model of the functional anatomy of speech

Dorsal Stream



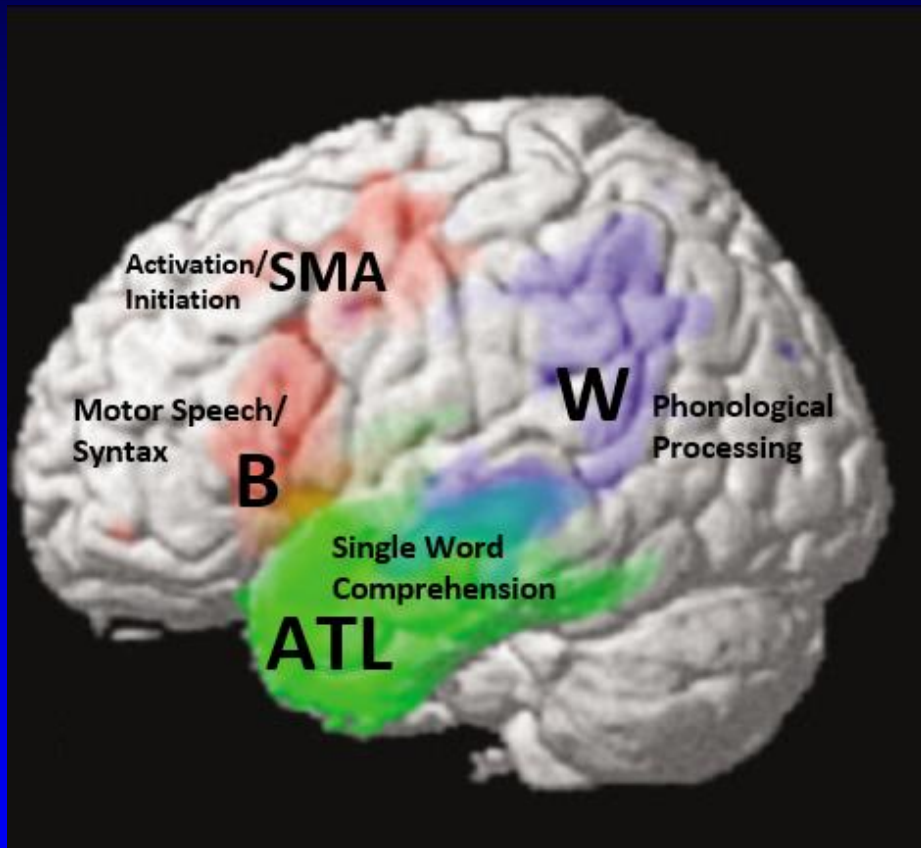
The Language Network



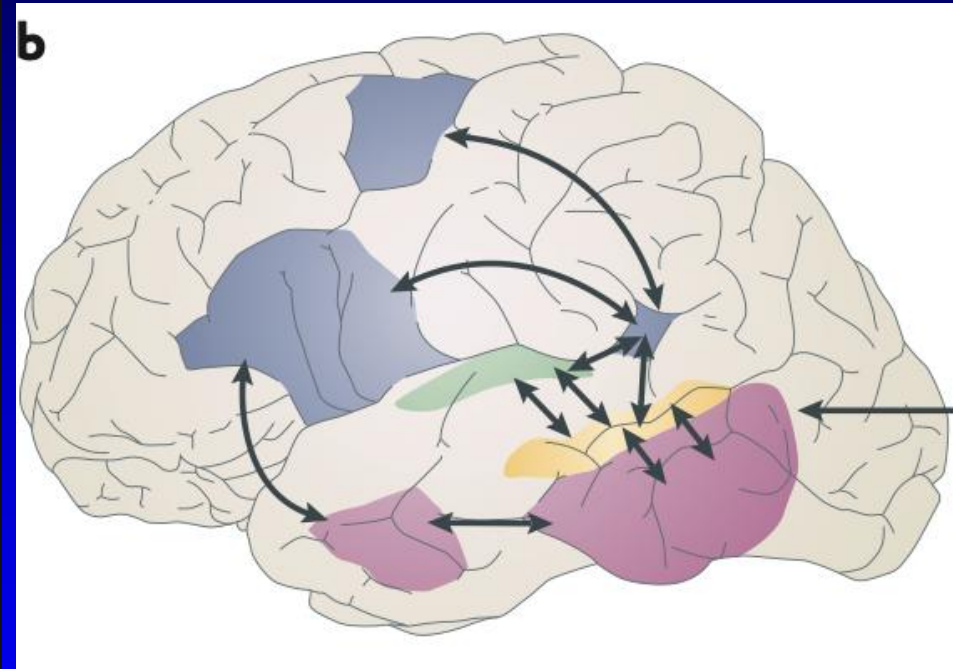
Language comprehension is a predictive process

- The language comprehension system does not simply work in a bottom-up fashion (passively waiting for the next word to be presented)
- By making predictions, our brains have a “head start,” allowing language comprehension to be faster and more efficient
- Evidence includes
 - Anticipatory neural activity occurs before the appearance of strongly predicted words
 - Altered neural activity in response to words not matching semantic predictions, mediated by left temporal (and frontal) regions
- Left anterior temporal lobe may use contextually-relevant prior knowledge to carry out top-down operations to guide word representations from generic to increasingly specific word forms

The Language Network—Wernicke's Area



Modified from Gorno-Tempini et al., 2004



Hickok and Poeppel, 2007

Classical Aphasiology Syndromes

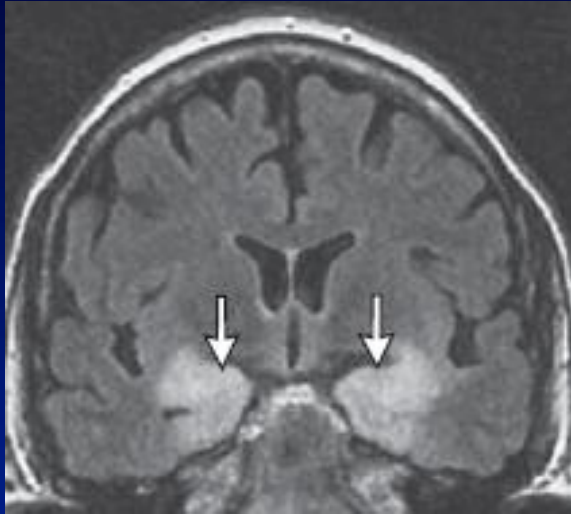
For Future Reference

Aphasia Label	Comprehension	Repetition	Fluency
Normal	+	+	+
Wernicke	–	–	+
Transcortical sensory	–	+	+
Broca	+	–	–
Transcortical motor	+	+	–
Conduction	+	–	+
Global	–	–	–

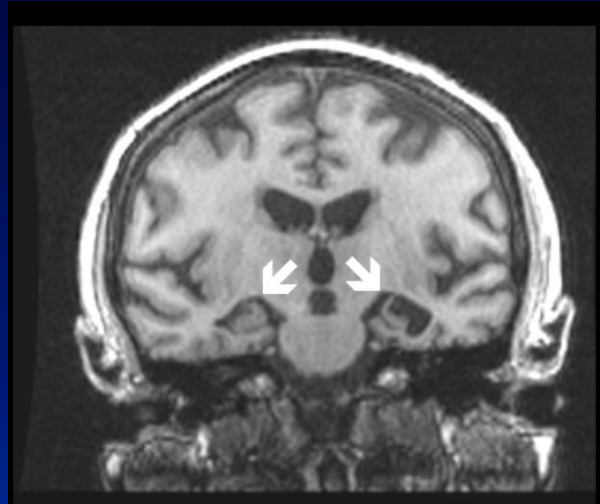
Case

- 65 yo right-handed man admitted for memory loss and confusion.
- Onset 4 w before admission. c/o “living in a fog.” Recently lost driving to sister’s home.
- On exam in the ED, alert, oriented to his name and the season, but not day, month, year. Could recite months of year backwards. No language impairment. 0/3 words at 3 minutes. No recall of day’s events.
- Neuropsychological testing:
 - profound, circumscribed memory deficit. Anterograde amnesia. Limited encoding, severely impaired consolidation of information
 - Intact attention, executive functions, language, semantic knowledge

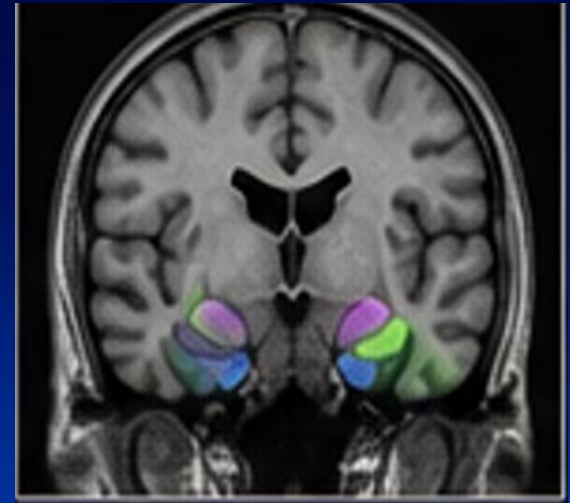
Where is the damage? Functional Neuroanatomy Matters



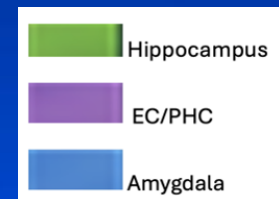
This patient
Paraneoplastic limbic encephalitis



Alzheimer disease
medial temporal atrophy



Medial temporal /
limbic anatomy

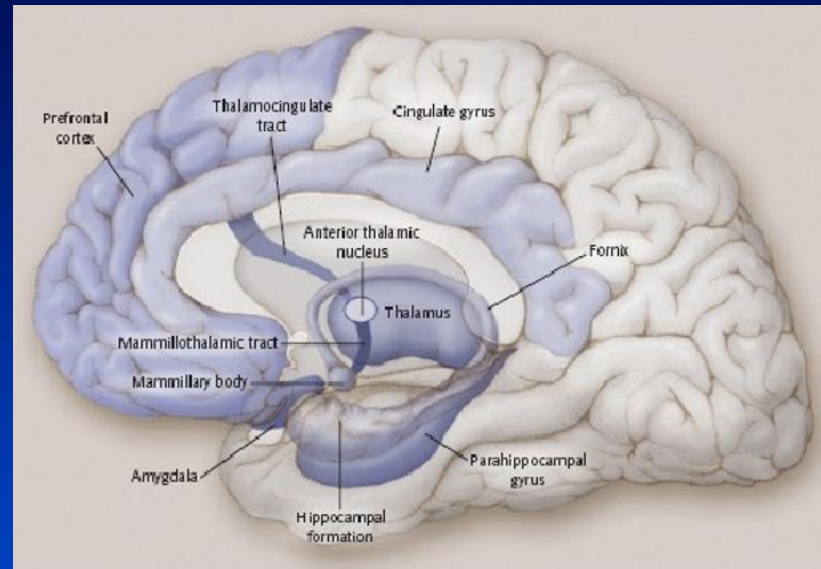


Different disease processes can disrupt overlapping medial temporal memory circuitry and produce a similar amnesic syndrome.

Amnestic Syndrome

- Relatively well-preserved attention
- Anterograde memory loss
- Retrograde memory loss — events closest to onset are recalled least well (Ribot's law)

This pattern of deficits implicates dysfunction of the limbic system, especially hippocampus and its connections



Budson & Price, 2005

Papez Circuit: Hippocampal formation to the mammillary bodies of the hypothalamus (via the fornix); to the anterior thalamic nucleus (via the mammillothalamic tract); to the cingulate cortex; to the parahippocampus; and back to the hippocampus.

Major Memory Systems

EXPLICIT / DECLARATIVE MEMORY

Conscious recollection

- Episodic
Events / experiences — what, where, when
- Semantic
Facts, concepts, meanings

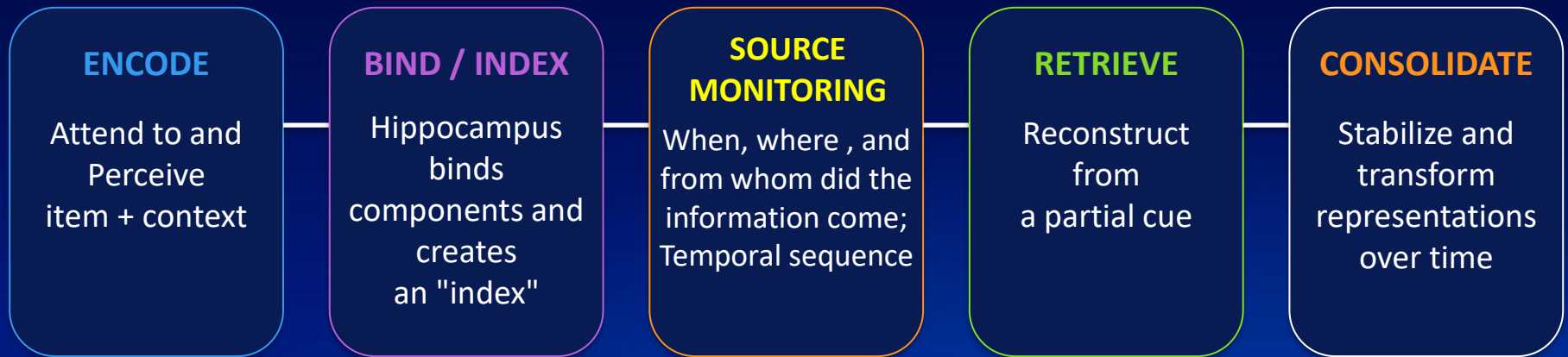
IMPLICIT / NONDECLARATIVE MEMORY

Unconscious influence on behavior

- Skills / habits (procedural)
- Classical conditioning
- Priming

The remainder of this section focuses on episodic memory

Episodic Memory Processing: Overview



Episodic memory is constructive, distributed, and dynamic

Memories Are Not Stored Like Photographs

The episode



Episodes Are Represented by Distributed Neural Activity

The episode



SOUNDS & LANGUAGE

Superior temporal gyrus
auditory / language
networks

EMOTIONAL / SOCIAL / SEMANTIC

Anterior temporal lobe /
temporal pole

PLACES & SPATIAL CONTEXT

Dorsal visual pathway
posterior parietal /
retrosplenial

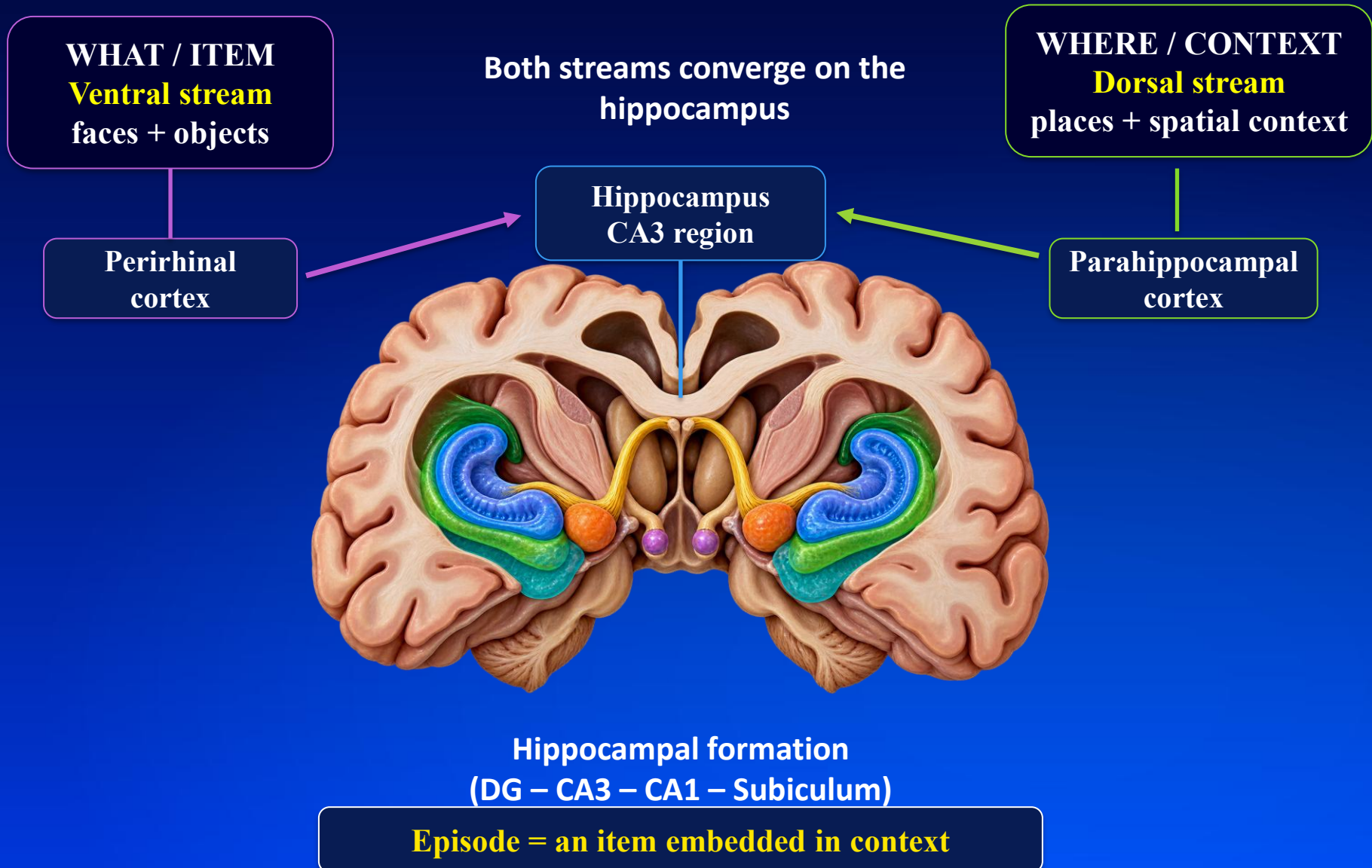
FACES & OBJECTS

Ventral visual pathway
OFA / FFA; ventral
occipitotemporal cortex



The hippocampus does not store these elements. It binds them and provides an index to the distributed neural activity representing the episode

What + Where Converge to Form an Episode



Hippocampal Operations: Separate • Bind/Index

SEPARATE (pattern separation in DG/CA3)

Overlapping experiences



More distinct representations



BIND / INDEX – FORMATION

Item
(distributed
cortical
representation)

+

Context
(distributed
cortical
representation)



Hippocampal index
(relationship among
distributed neural activity)



INDEX USE – REINSTATEMENT

Partial cue
activates index,
which reinstates
cortical activity



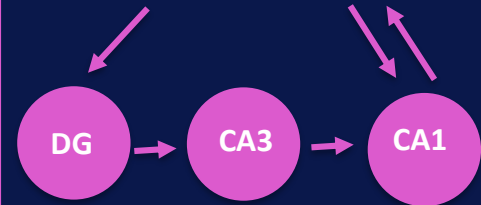
Item

Context



Simplified hippocampal circuit

Entorhinal cortex

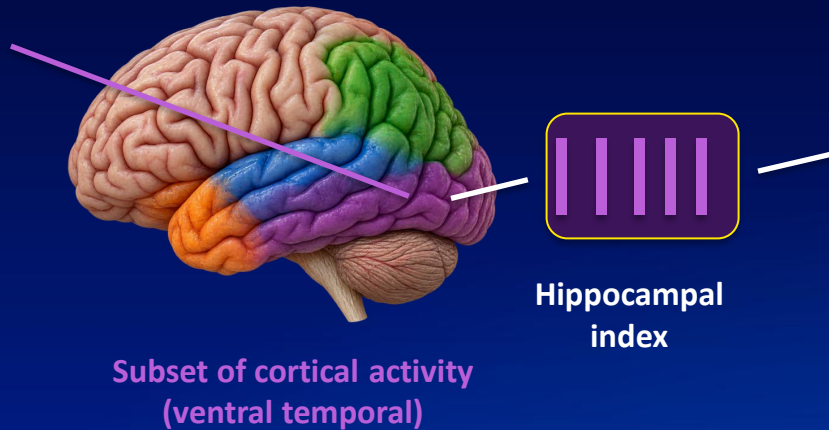


Retrieval from a Partial Cue: Reconstruction, Not Replay



Bottom-up
Partial sensory cue
(e.g., her face)

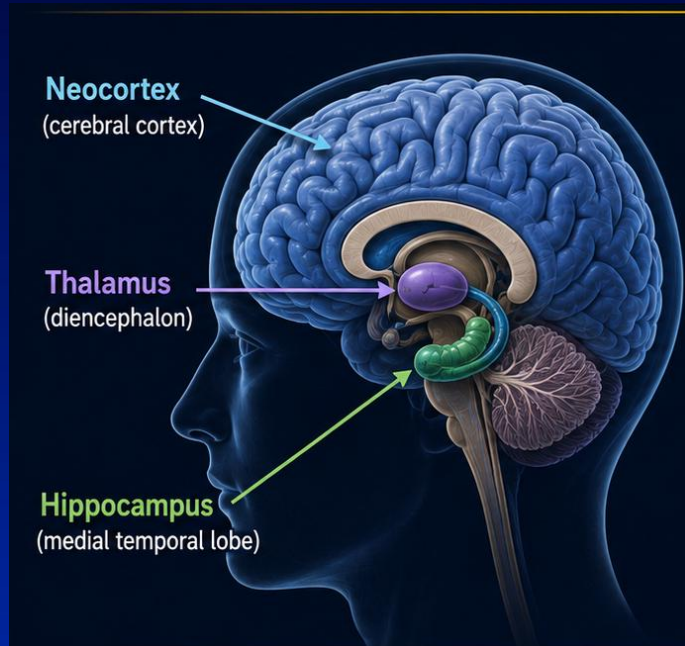
or
Top down
(e.g., thinking about
the date at the
cafe)



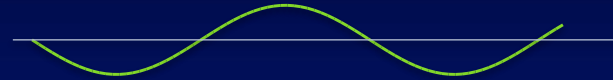
Reinstate distributed neural activity
associated with the episode

A partial cue activates part of the cortical pattern;
the hippocampal index helps reinstate the remaining distributed neural activity.

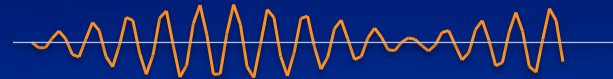
Sleep Supports Consolidation (NREM)



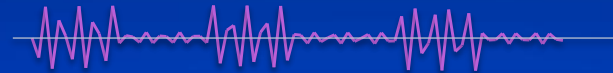
Slow
oscillation
(~0.5–1 Hz)



Sleep spindle
(12–15 Hz)



Sharp-wave
ripple
(~80–150 Hz)



- 1 Slow oscillations provide timing windows
- 2 Spindles gate cortical communication
- 3 Sharp-wave ripples replay recent experience
- 4 Repeated cycles strengthen and transform memory

REM sleep may contribute to emotional/affective processing, but its precise role is less settled

Memory Involves Coordination Across Networks



Prefrontal cortex

Focusing attention; strategic encoding and retrieval; source of information; temporal sequencing

Parietal cortex

Buffering retrieved information; directing attention to memory representations

Medial temporal lobe

Binding items and context; index formation; pattern separation

Anterior temporal lobe

Semantic knowledge; social & emotional meaning; affective value

Episodic memory emerges from coordination among distributed cortical systems and the hippocampus.

Neuromodulators Shape Memory Processing

Neuromodulator	Role in Memory Processing	Clinical / Teaching Point
Acetylcholine (ACh)	Attention and encoding of new information; helps bias hippocampal circuits toward encoding vs retrieval	Cholinesterase inhibitors increase cholinergic signaling; anticholinergic drugs can impair new learning
Norepinephrine (NE)	Arousal, attention and salience; strengthens memory for behaviorally important events	Memory is state-dependent; excessive stress/arousal can impair or distort memory
Dopamine (DA)	Novelty, reward and prediction error; promotes plasticity and persistence of salient memories	Novel or motivationally important events are preferentially retained

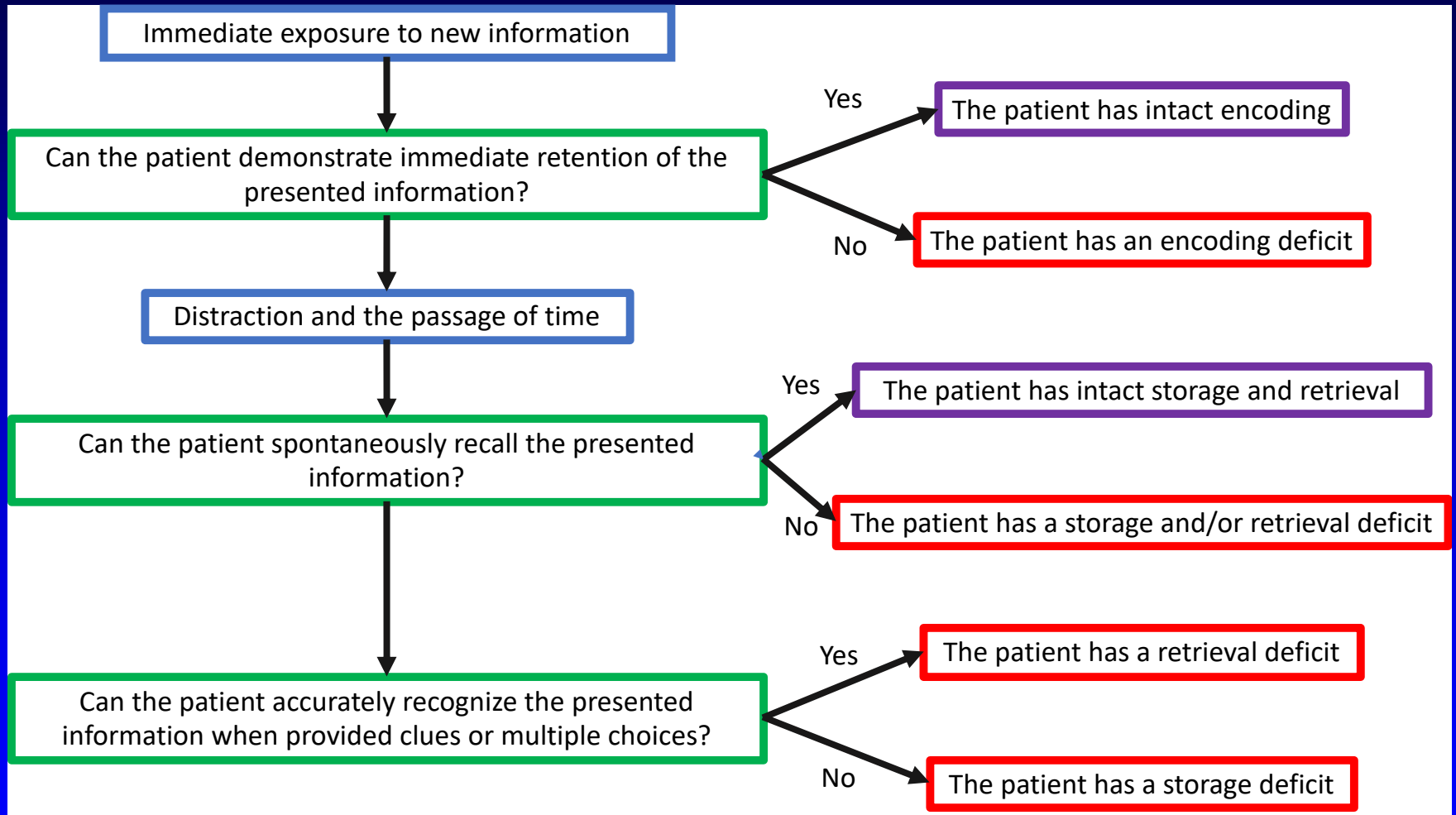
Memory depends not only on intact circuits, but also on the neurochemical state in which those circuits operate

Don't Forget

- Numerous causes of amnestic syndromes
 - Degenerative Dementia (Alzheimer's disease)
 - Wernicke-Korsokoff Syndrome
 - Traumatic brain Injury
 - Hypoxia/Ischemia injury
 - Posterior Cerebral Artery Stroke(s)/Ischemia
 - Anterior Cerebral Artery Aneurysm Rupture
 - Limbic Encephalitis
 - Infectious
 - Paraneoplastic Limbic Encephalitis
- Memories are actively reconstructed
 - Vulnerable to distortions, source misattributions, false recollections
- Critical link between present state and personal history

Schema for testing episodic memory

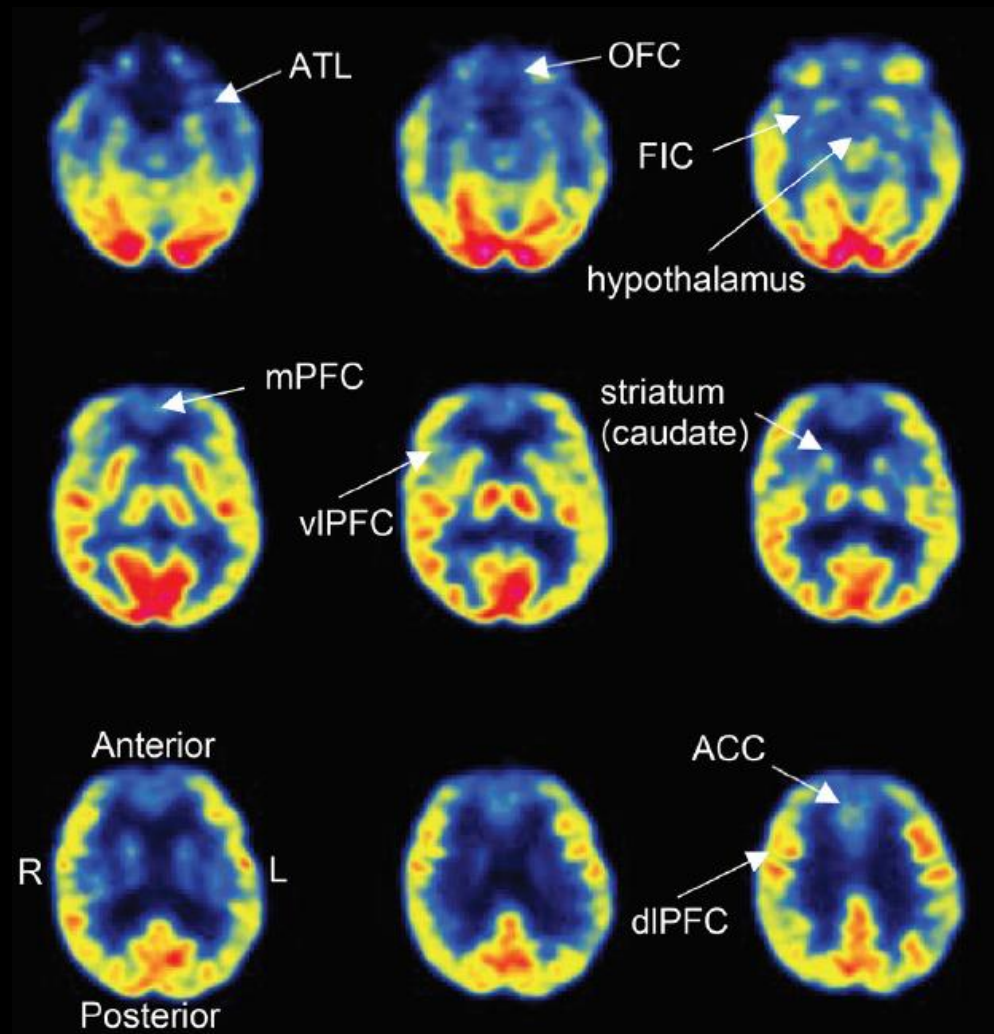
For Future Reference



Case

- 39-yo hard-working woman with progressive changes in personality and behavior
- Jobless; sleeping in the street
- Arrested for stealing ex-husband's van
- Numerous examples of very poor judgment
- 30/30 on MMSE; Digit span 7F, 5B, 14 S words/minute; well-constructed clock
- Behaviorally, very inappropriate, labile affect
- No insight into her predicament
- Mother: h/o progressive neuropsychiatric disorder; died in early 50s

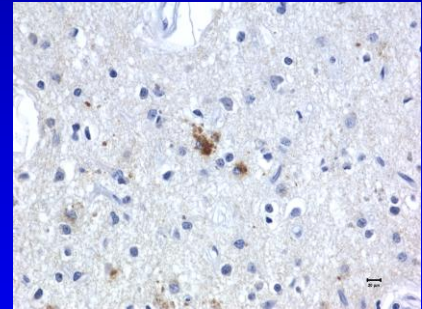
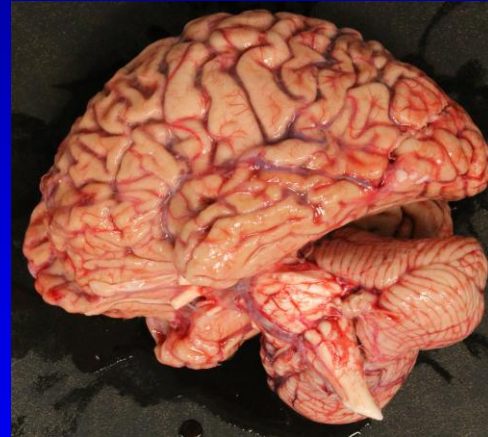
FDG-PET Imaging



Marked bilateral hypometabolic activity within the orbitofrontal cortex, extending to the cingulate gyrus and caudate bilaterally

Case, Neuropathology—FTLD, tauopathy

- FDG-PET Imaging
 - Marked bilateral hypometabolic activity within the orbitofrontal cortex, extending to the cingulate gyrus and caudate bilaterally
- Genetic Testing
 - Mutation of the MAPT gene on Chromosome 17
- Brain Pathology (death age 49)
 - FTLD due to tauopathy
- Diagnosis: Behavioral Variant Frontotemporal Dementia (bvFTD)



Conditions Associated with Frontal Network Dysfunction

- bvFTD
- Alzheimer's Disease
- Vascular Dementia
- Lewy Body Disease (e.g., PDD)
- Tauopathies (e.g., PSP)
- Traumatic Brain Injury
- White matter disease (e.g., MS)
- Tumor/NPH
- CNS infections (e.g., HIV, Syphilis)
- Developmental disorders (e.g., ADHD)
- ?Normal cognitive aging

Executive Control Functions

Complex set of cerebral processes that operate to exert top-down, volitional control over sensory input, cognition, social-emotion processing, and motor output, allowing individuals to carry out goal-directed behaviors.

Frontal Anatomy

Dorsolateral PFC (DLPFC)

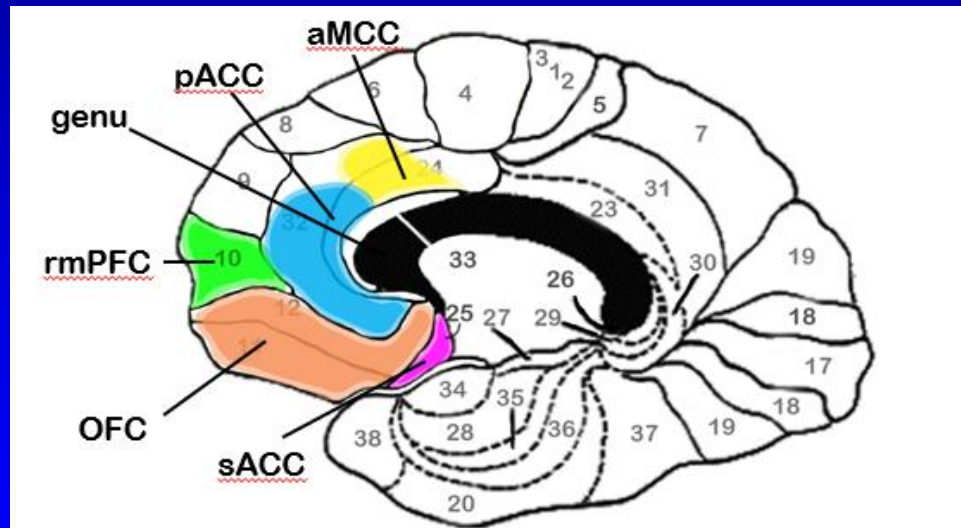
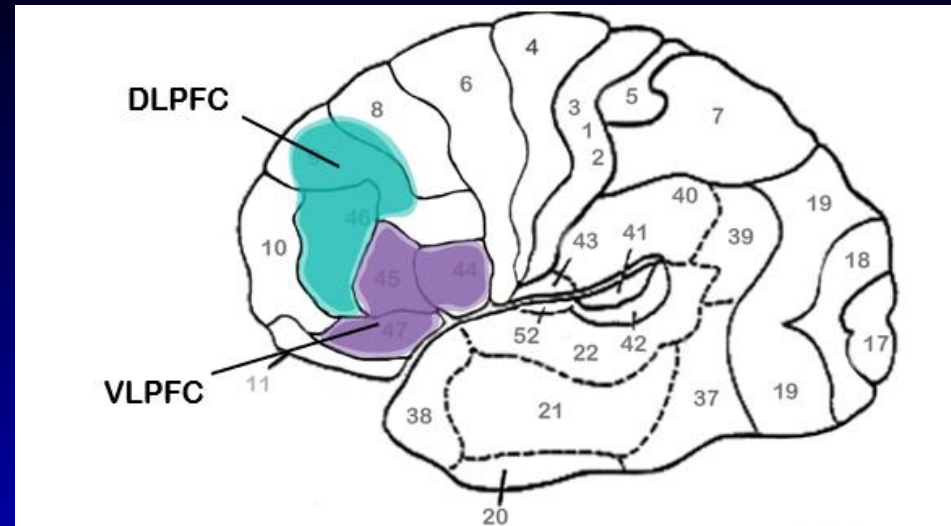
Ventrolateral PFC (VLPFC)

Ant Cing Cortex/aMCC (aka dACC)

Orbitofrontal Cortex (OFC)

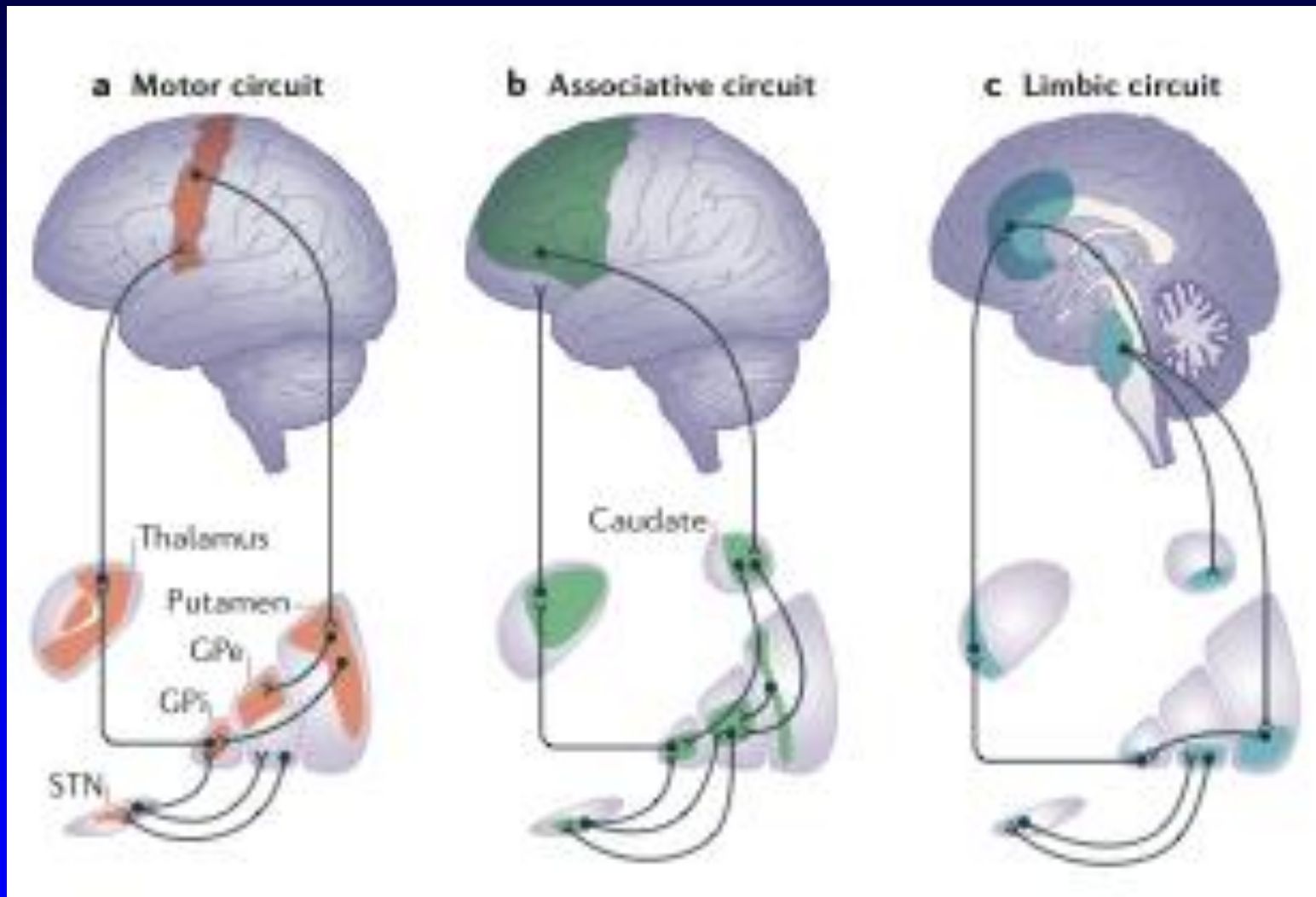
Rostromedial PFC (rmPFC)

Frontoinsular Cortex (FI)



ACC = anterior cingulate cortex; aMCC= anterior mid cingulate cortex
dACC = dorsal anterior cingulate cortex

Frontal-Subcortical Networks



Executive Control Functions

WM/ Goals-on-Line

Initiating/ Sustaining

Anticipation/ Monitoring

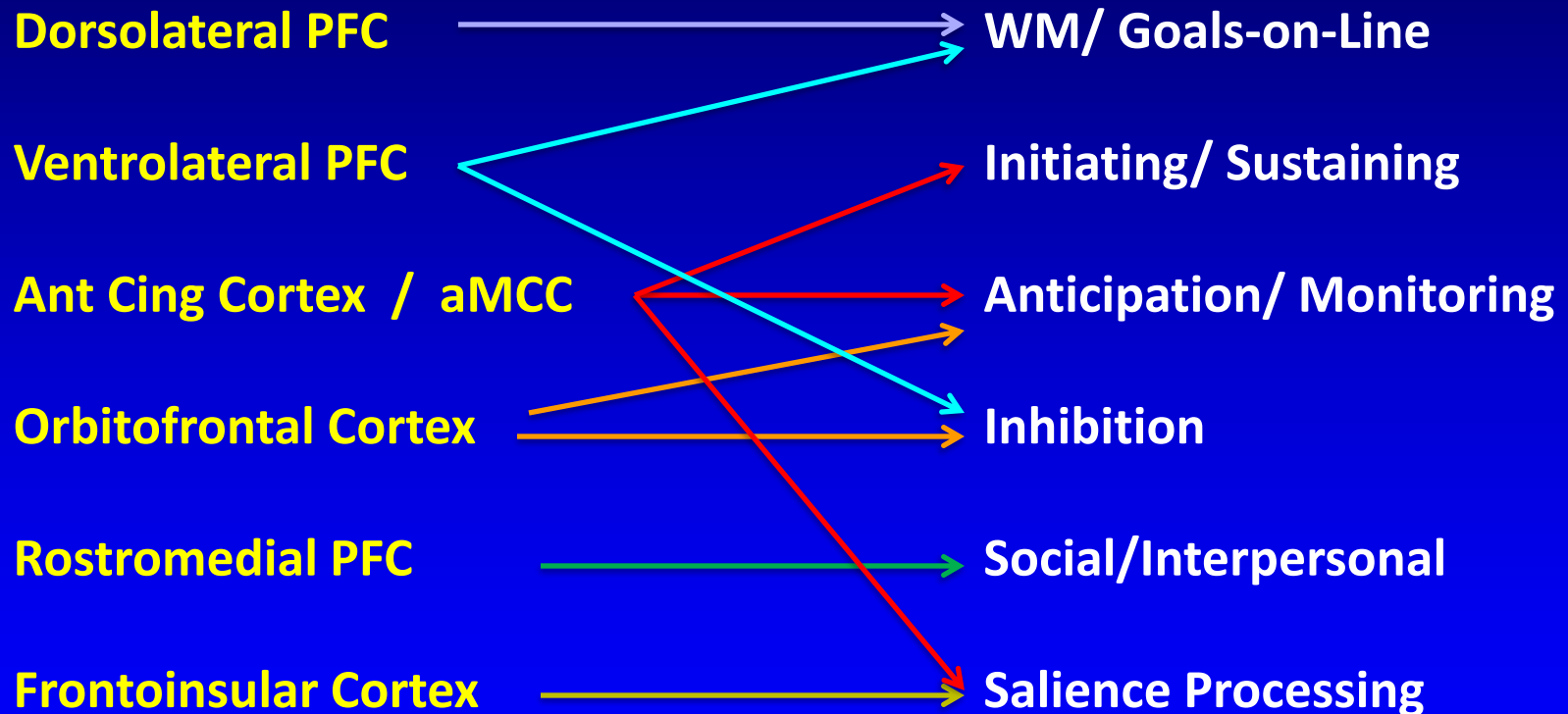
Inhibition

Social/Interpersonal

Salience Processing

Frontal Anatomy

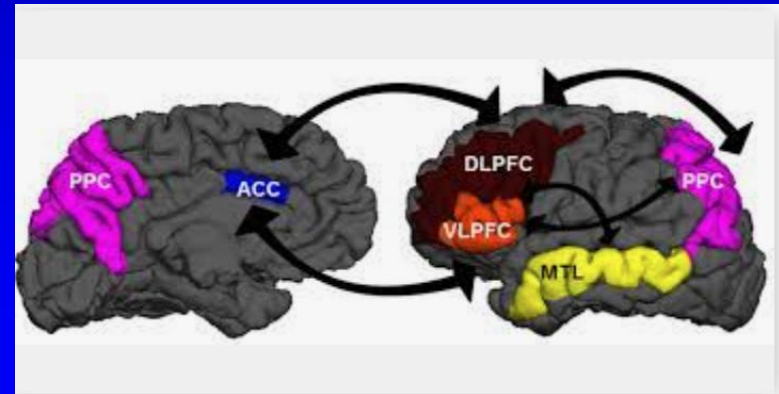
Control Function



Working Memory

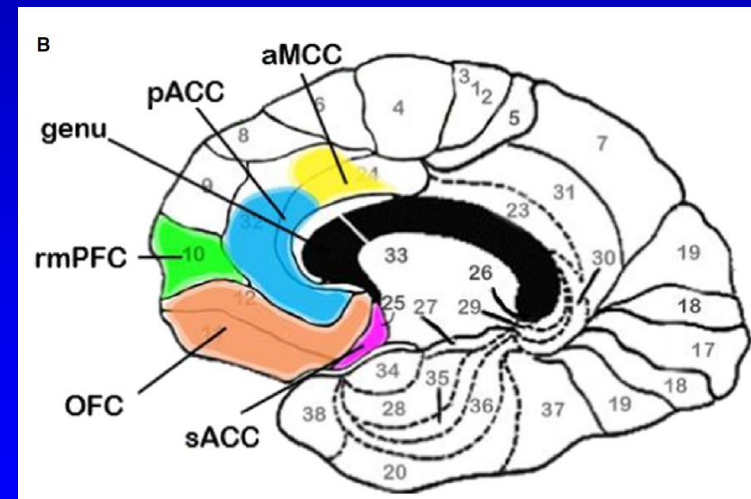
Keeping Task-Relevant Goals On-Line

- Critical function of Working Memory
 - Holding on-line and manipulating internalized representations to guide future behavior
- Executive Control Network
 - Dorsolateral PFC
 - Posterior Parietal Cortex (PPC)



Initiating and Sustaining Activity

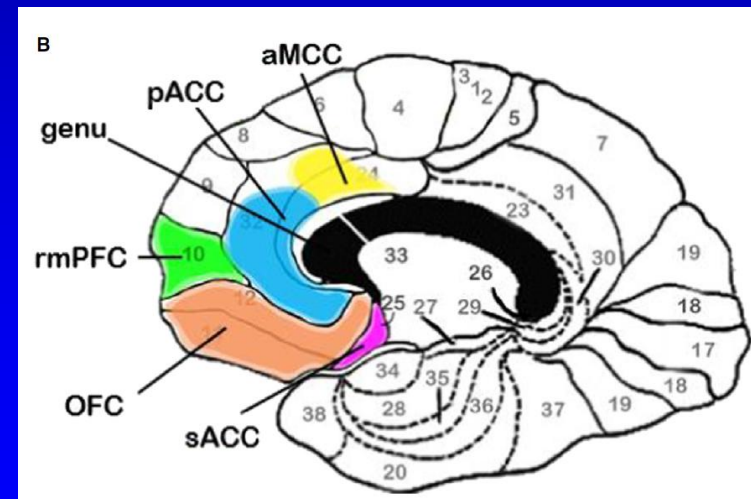
- Purposeful, self-generated commencement and maintenance of an overt act or mental activity
- Anticipating the potential reward value of actions serves as the basis of motivating/energizing behavior
- **Medial Prefrontal Cortex**



Initiating and Sustaining Activity

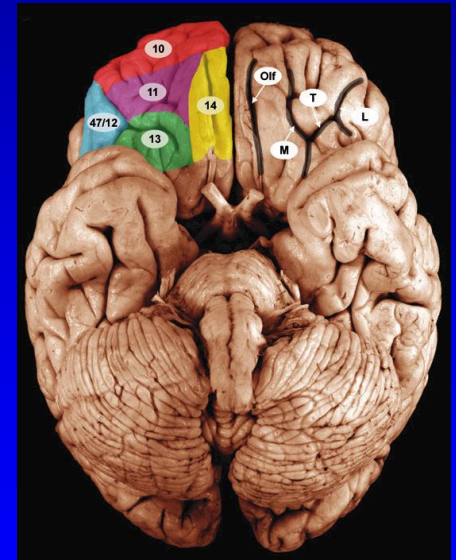
- **Medial Prefrontal Cortex**

- pgACC mediates affective appraisal of viscerosensory signals (internal/interoceptive sensations)
- sgACC serves as a visceromotor control center, regulating autonomic, endocrine, and other physiologic responses required to manage current (and likely upcoming) situations
- aMCC (= dACC) discussed shortly, functions at the intersection between initiating actions (by anticipating potential reward value) and monitoring their outcomes



Anticipating and Monitoring Outcomes/Rewards

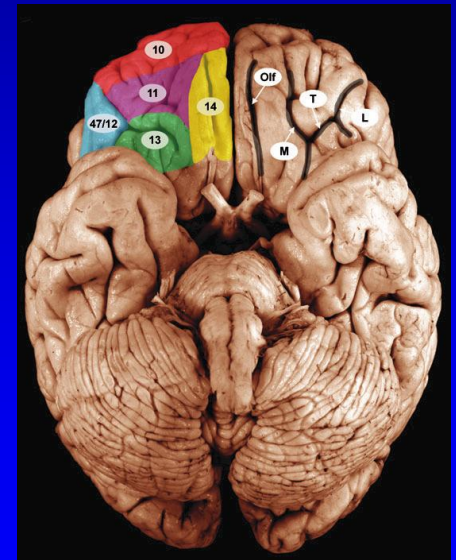
- Decoding/anticipating the reward value of sensory signals, objects, and choices
- **Orbital Frontal Cortex**



Anticipating and Monitoring Outcomes/Rewards

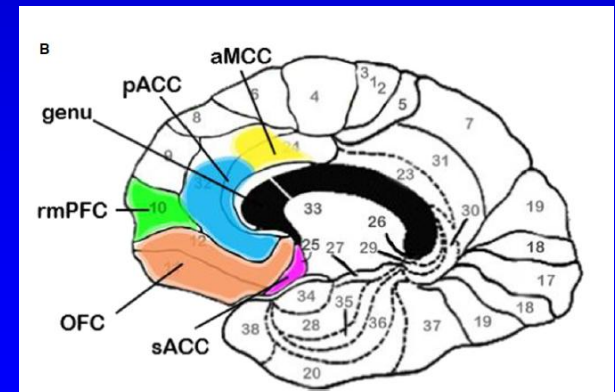
- **Orbital Frontal Cortex**

- Lateral OFC—assesses the goal-relevance of externally-generated events (sensory information/objects)
- Medial OFC
 - May appraise internally generated events—episodic memories and imagined future events



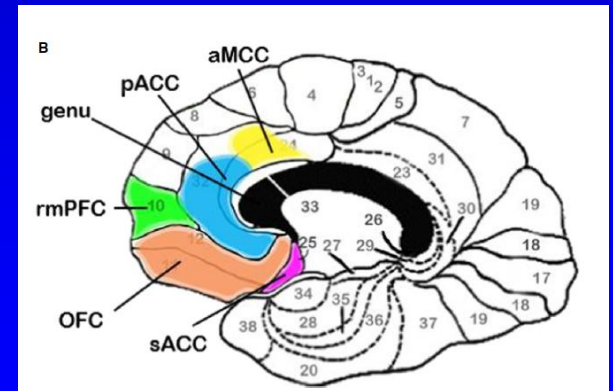
Anticipating and Monitoring Outcomes/Rewards

- Anterior MCC/ Dorsal ACC
 - Uses predicted outcomes, positive and negative, to evaluate actions and adjust behaviors based on the current context and anticipated outcomes.
 - Predicts not only the value of a reward but also the cost of the effort required to obtain it.
 - Disruption of aMCC function often results in the development of apathy.



Anticipating and Monitoring Outcomes/Rewards

- **Anterior MCC/ Dorsal ACC**
 - Plays central role in monitoring the impact of actions to determine if they match predictions
 - Outcomes that deviate from expectation can elicit an error signal from aMCC
 - Positive prediction errors elicits release of DA in the reward system facilitating learning
 - The aMCC can keep track of a designated set of external or internal stimuli. Discrepancies from expectation are registered and can trigger additional processing and response.





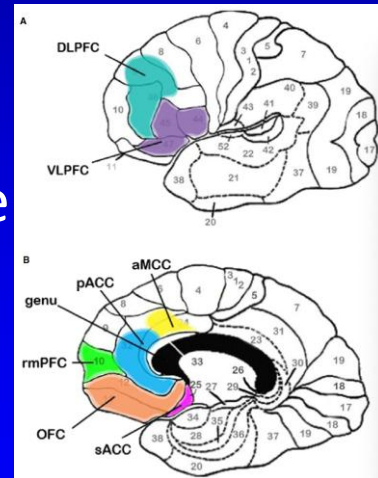
Stroop Effect: Color/Word Tests

Instructions: print on card stock and cut each page into horizontal strips. See the Science Buddies project [What Conflicting Mental Tasks Reveal About Thinking: The Stroop Effect](#) for complete information.

green	purple	blue	brown	brown	green	green	purple	red	green
purple	red	brown	brown	red	blue	blue	blue	purple	red
brown	blue	red	purple	purple	brown	green	blue	red	green
blue	green	brown	red	green	purple	red	blue	purple	brown
brown	green	brown	brown	red	purple	brown	purple	purple	green
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brown	purple	green	green	blue	blue	green	brown	brown	green
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blue	brown	brown	red	brown	brown	green	blue	red	green

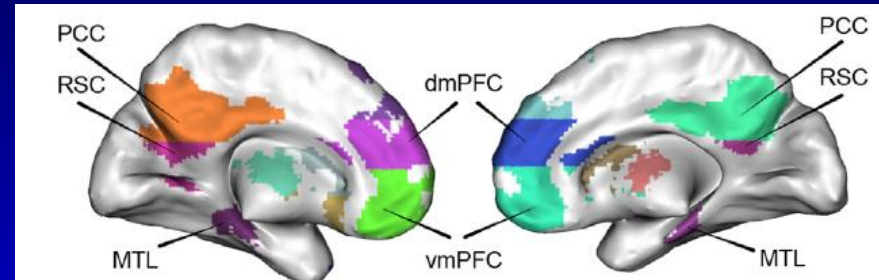
Inhibiting (Stopping) Activity

- Suppression of a specific behavioral output, mental activity, or emotional response (usually an automatic, prepotent, or overlearned)
- **Lateral Prefrontal Cortex**
 - Set shifting/ Stop signal/ No go tasks
 - Emotional regulation via reappraisal, redirecting attention, selection of long- term over immediate rewards
- **Orbitofrontal Cortex**—behavioral inhibition



Constructing a coherent internal narrative: mPFC and the Default Mode Network (DMN)

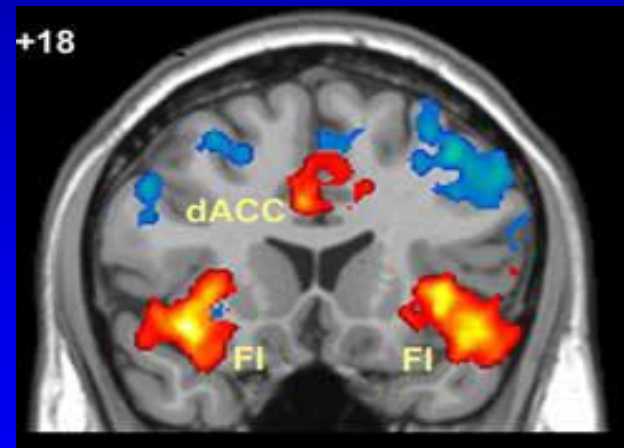
- **mPFC** is a core hub of the **DMN**
(subserves processing that allows individuals to reflect on the past and imagine the future)



- DMN helps to integrate memory, language, and semantic representations to construct an ongoing internal narrative for:
 - creating a coherent sense of self
 - monitoring of one's emotional states
 - understanding the intentions and mental states of others
 - navigating complex social environments
- **mPFC** is particularly engaged by the evaluation and elaboration of self-directed mental activity

Evaluating and responding to changes in salience

- Identifying the most homeostatically relevant stimuli and tasks through the rapid integration of sensory, visceral, autonomic, and hedonic signals
- **Frontoinsular Cortex**



Seeley et al., 2007

Summary of Frontal-Executive Functions

For Future Reference

- The **Dorsolateral Prefrontal Cortex** plays a major role in working memory and keeping information processing priorities (task-relevant goals) on-line.
- The **Ventrolateral Prefrontal Cortex** contributes to working memory and helps to mediate the inhibition of specified behavioral responses or mental activity.
- Components of the **Anterior Cingulate Cortex** are central to the evaluation of viscerosensory signals and the control over visceromotor activity in the service of allostasis and homeostasis.
- The **Anterior Mid-Cingulate Cortex** subserves the anticipation of the potential reward value of actions, which is critical for initiating and sustaining cognitive and behavioral activity. It monitors outcomes, especially ones that violate expectations, and adjusts behaviors accordingly.
- The **Orbitofrontal Cortex** helps to determine the goal-relevance and potential reward value of externally generated events (e.g., sensory information) and internally generated phenomena (e.g., episodic memories). It also subserves behavioral inhibition and the regulation of emotions.
- The **Rostromedial Prefrontal Cortex** contributes to the processing of social and interpersonal information. It processes and updates representations of the self and the mental states and intentions of others.
- The **Frontoinsular Cortex** serves as the afferent limb of the salience network, helping to determine the most homeostatically relevant stimuli or behavioral activity based on current context.
- **Many common neurologic conditions can disrupt frontal-executive functioning and result in profound changes in cognition, emotion, and behavior.**

The Brain's Predictive Activity and Frontal Networks

- At earlier stages of information processing, the interactive process between feed forward and feed backward neural exchanges tend to takes place outside of our conscious awareness
- In contrast, frontal lobes and their connections participate in the generation and updating of conscious representations involving large-scale models of the self and the environment
- Potential mismatches between incoming information and expectations based on our frameworks of meaning can result in
 - Altering/updating the models about the world and oneself to account for the new information (accommodation)
 - Fitting/integrating the new information into current models (assimilation)
 - Taking actions to change the environment or the way sensory systems sample it to fit our internal models
- A suboptimal balance between assimilation and accommodation likely contributes to the development of cognitive and neuropsychiatric symptoms
 - Predictive Models held with excessive certainty (“precision”), impervious to updating in response to new information (e.g., poor insight, delusions, hallucinations, functional neurologic disorders)
 - Bottom-up information processing not modulated or constrained by top-down models and control (e.g., inattention, impulsivity, stimulus-bound behaviors)

Frontal Lobe's Role in Processing Uncertainty, Surprise and Novelty

- Hypothesized purpose of our brains' predictive coding process is to MINIMIZE UNCERTAINTY and SURPRISE
- Countervailing force, mediated by frontal lobes and their connections, is to seek novelty and uncertainty
- Novel stimuli strongly activate prefrontal areas; the magnitude of prefrontal activation predicts the amount of time that the stimulus will attract attention
- **Frontal Networks** help orchestrate novel solutions to challenging situations
 - Elicit mental imagery to explore unconventional interpretations of events and develop counterfactual scenarios
 - Hold alternative possibilities online and sustain internal dialogue
 - Facilitate innovative, creative, and potentially risky (uncertain) solutions

Overall Summary

- Neural networks allow us to carry out essential cognitive functions
- Examples reviewed this morning
 - Visuospatial processing
 - Language
 - Memory
 - Executive Control
- No rigid boundary between emotional and cognitive processing
 - e.g., emotions influence what we remember, attend to, and perceive
- Dorsal and ventral streams often mediate different kinds of information processing (e.g., for language, visual functions, attention)

Overall Summary

- The brain generates and updates predictive models of experience
- Dynamic interactions between top-down and bottom-up cerebral processing
- Active construction and re-creation of perceptions and memories can lead to distortions and mis-recollections
- Marked clinical consequences can result from
 - Injury to the visual processing, language, memory, and executive control neural networks
 - Suboptimal balance between top-down and bottom-up processing

With Gratitude

- Michael Erkkinen, MD
- Seth Gale, MD
- Deepti Putcha, PhD
- Meghan Searl, PhD
- Kim Willment, PhD

from whom I have learned so much while working on relevant chapters and reviews, and sharing challenging patients