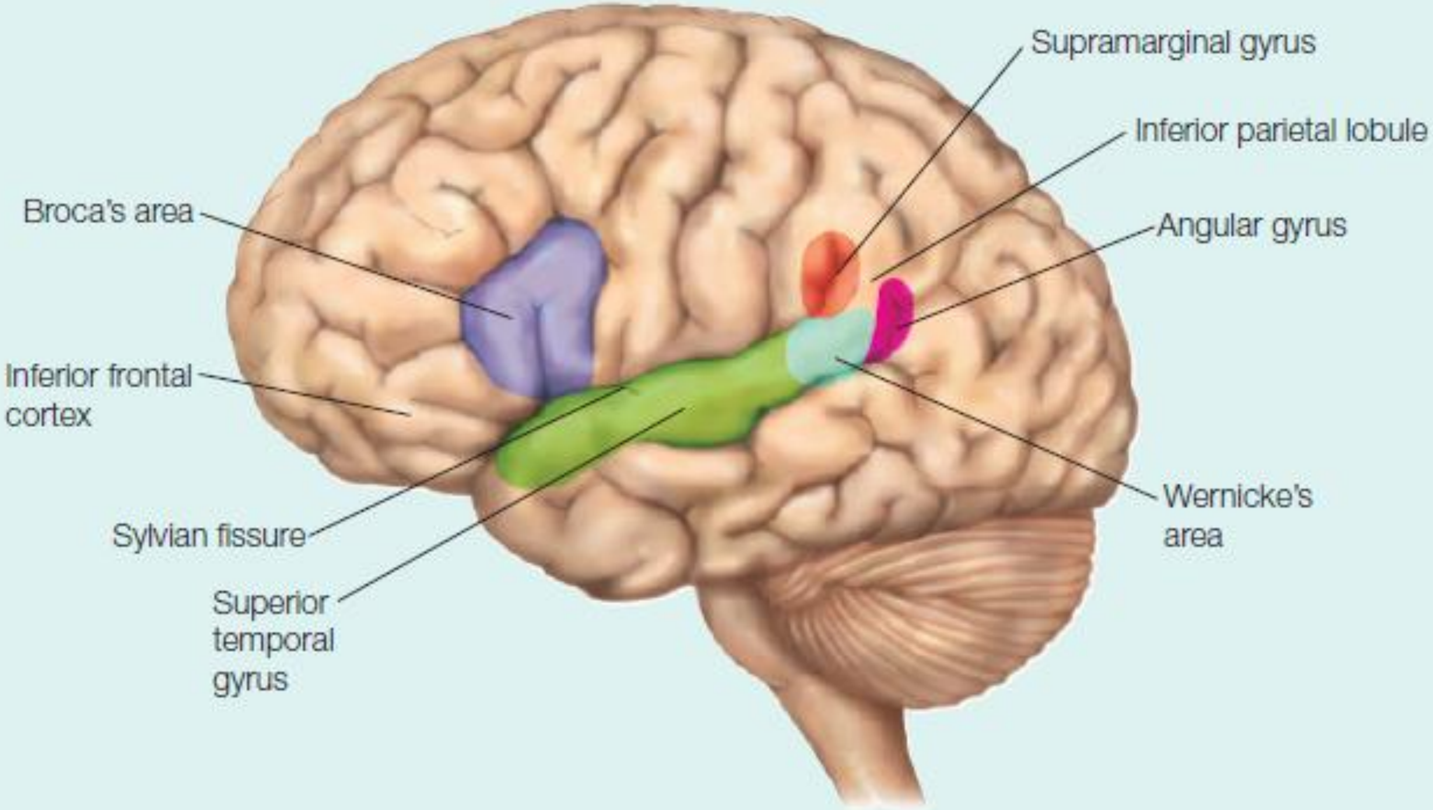
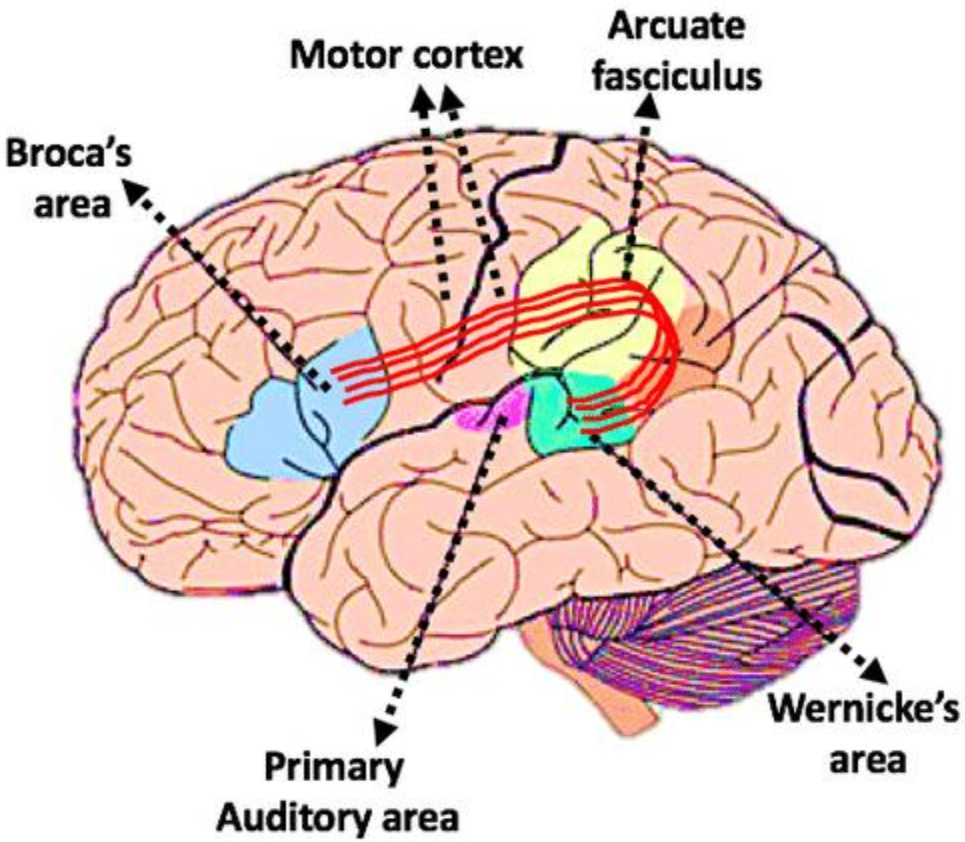
Language & communication

Anatomy of Language



Language is processed primarily in the left hemisphere. Many regions located on and around the Sylvian fissure form a language-processing network.

Left Inferior
Frontal Gyrus



Broca's area: involved in production of speech sound

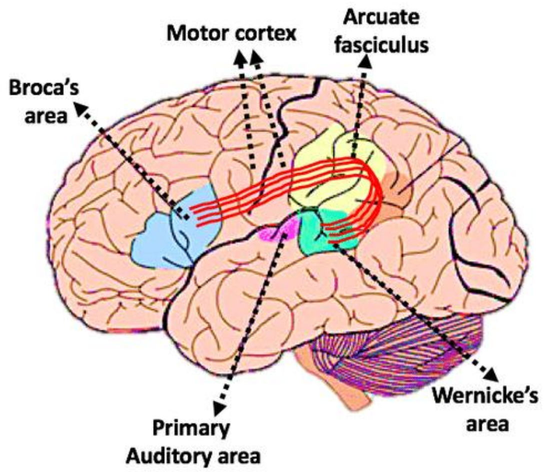
Wernicke's area: involved in Understanding of speech

Motor cortex: controls the Movements of muscles

Arcuate fasciculus: connects Wernicke's area to Broca's area.

<u>Parts of the Brain that controls Speech</u>

Age	Language Development
Birth	Sounds
0-3 months	Differentiating cries - baby uses a different cry for different situations
4-6 Months	Vocal Play - gurgling, babbling
7-12 Months	Speech like babbling including the use of consonants and vowels. First words - "mama", "doggie"
1-2 Years	Use of two word questions - "No doggie?", "Where ball?"
2-3 Years	Two/three word utterances. Use of attributes - "Big", "Furry"
3-4 Years	Combination of four or more words in sentence form
4-5 Years	Use of long and detailed sentences. Use of "adult-like" grammar



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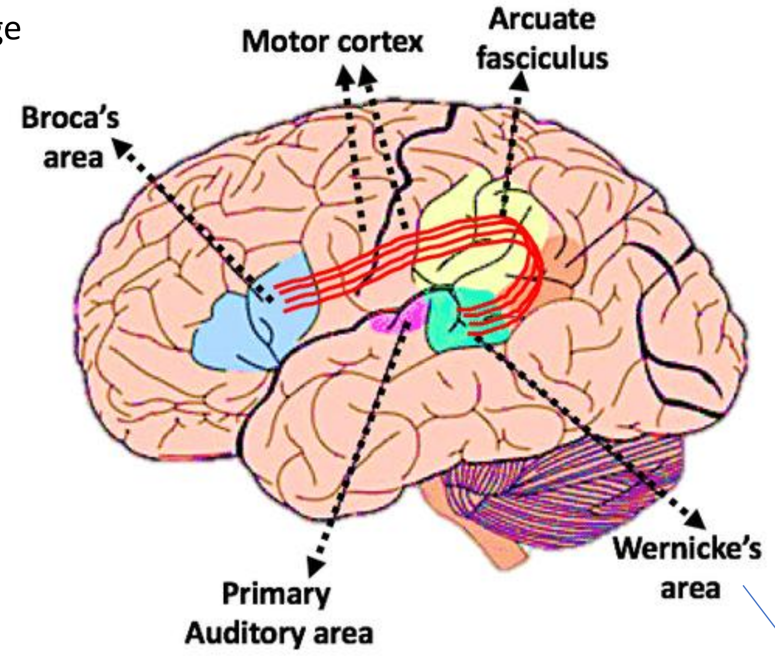
Parts of the Brain that controls Speech

Language disorders

Conduction Aphasia
inability to repeat words or phrases

Broca's or expressive aphasia
Impaired ability to produce language or articulate (spoken or written)



Parts of the Brain that controls Speech

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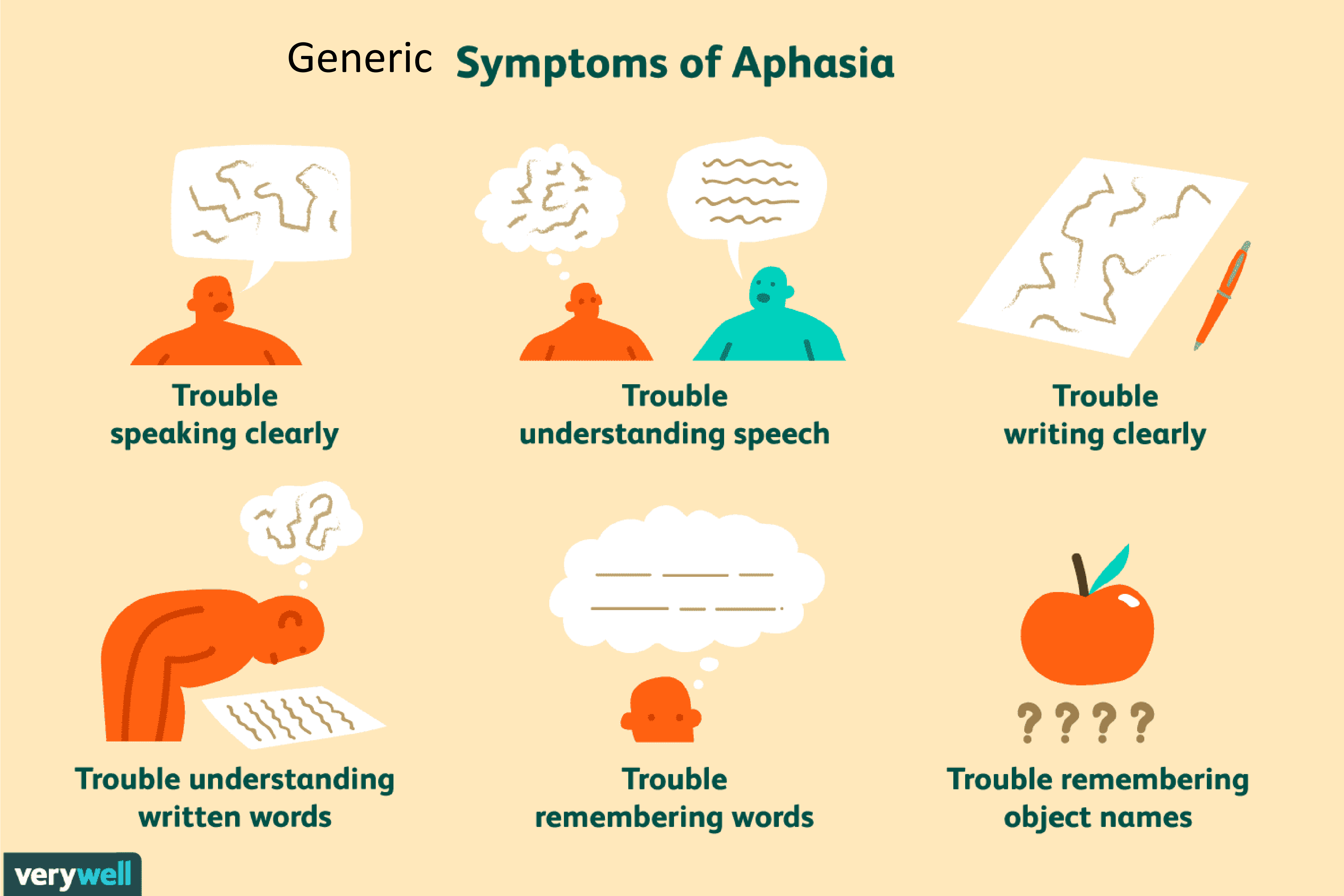
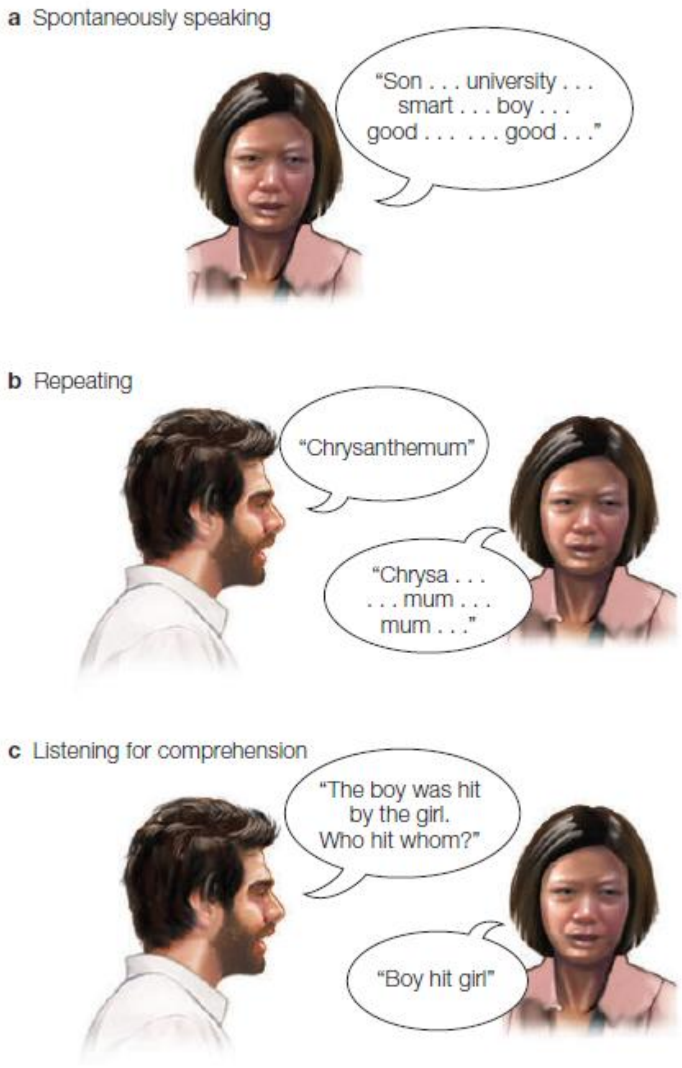
planning of speech movements

Wernicke's Aphasia
- Comprehension difficulties
- Fluent (sometimes excessive), word finding difficulties, excess of grammatical words but paucity of meaning; some syntactic difficulties
- ability to grasp the meaning of spoken words and sentences is impaired


Generic Symptoms of Aphasia
Trouble speaking clearly
Trouble understanding speech
Trouble writing clearly
Trouble understanding written words
Trouble remembering words
????
Trouble remembering object names
verywell

Broca's Aphasia



Broca's Aphasia

Cookie jar...fall over... chair...water....

Paucity of words

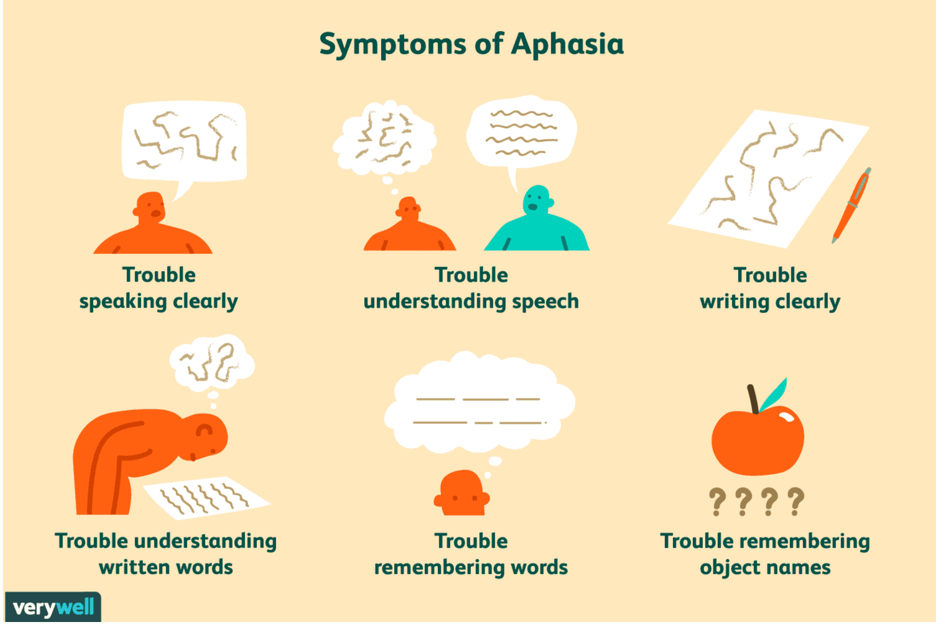
Wernicke's Aphasia

Well this is...mother is away here working her work out o' here to get her better, but when she's looking, the two boys look in the other part. One their small tile into her time here. She's working another time because she's getting to. So two boys work together and one is sneakin' around here, making his work an' his further funnas his time he had.

Paucity of meaning

I want an
I want an... ?

Anomia



Symptoms of Aphasia
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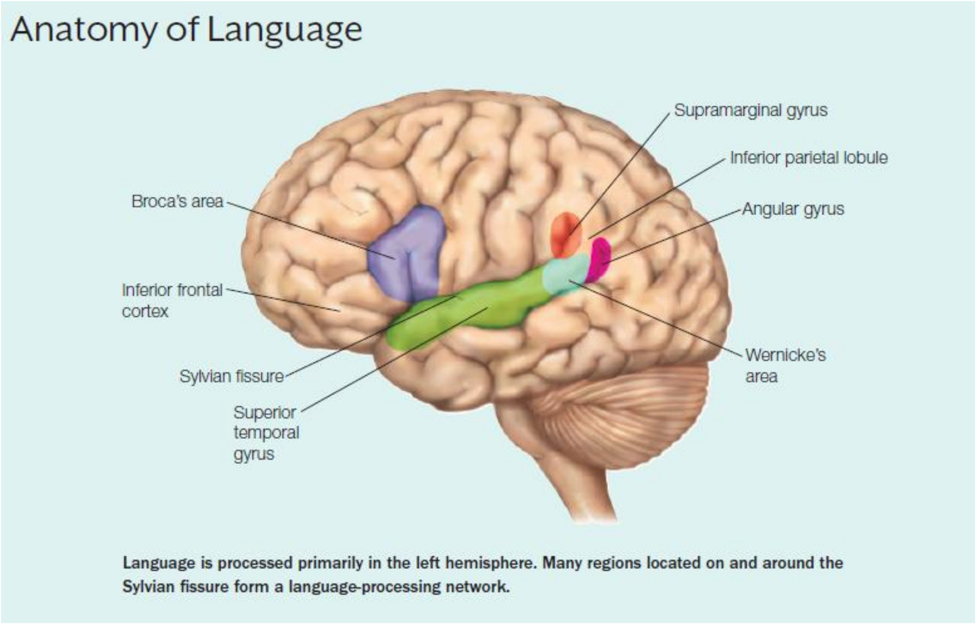
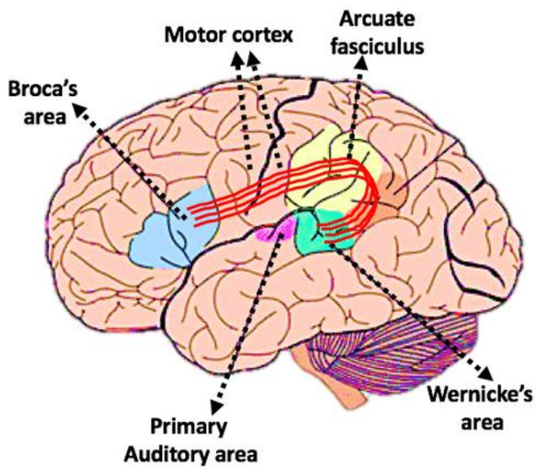


Anatomy of Language
Supramarginal gyrus
Inferior parietal lobule
Angular gyrus
Broca's area
Inferior frontal cortex
Sylvian fissure
Superior temporal gyrus
Wernicke's area
Language is processed primarily in the left hemisphere. Many regions located on and around the Sylvian fissure form a language-processing network.



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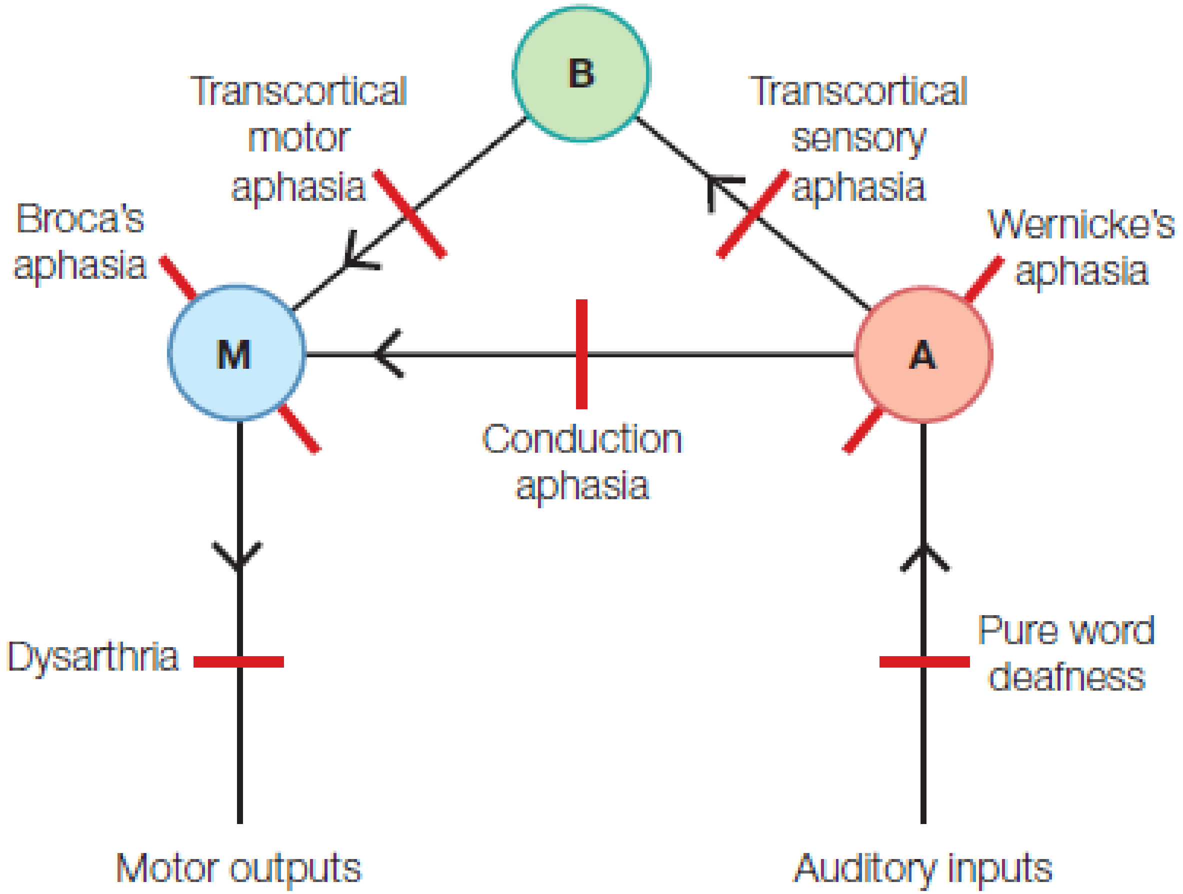
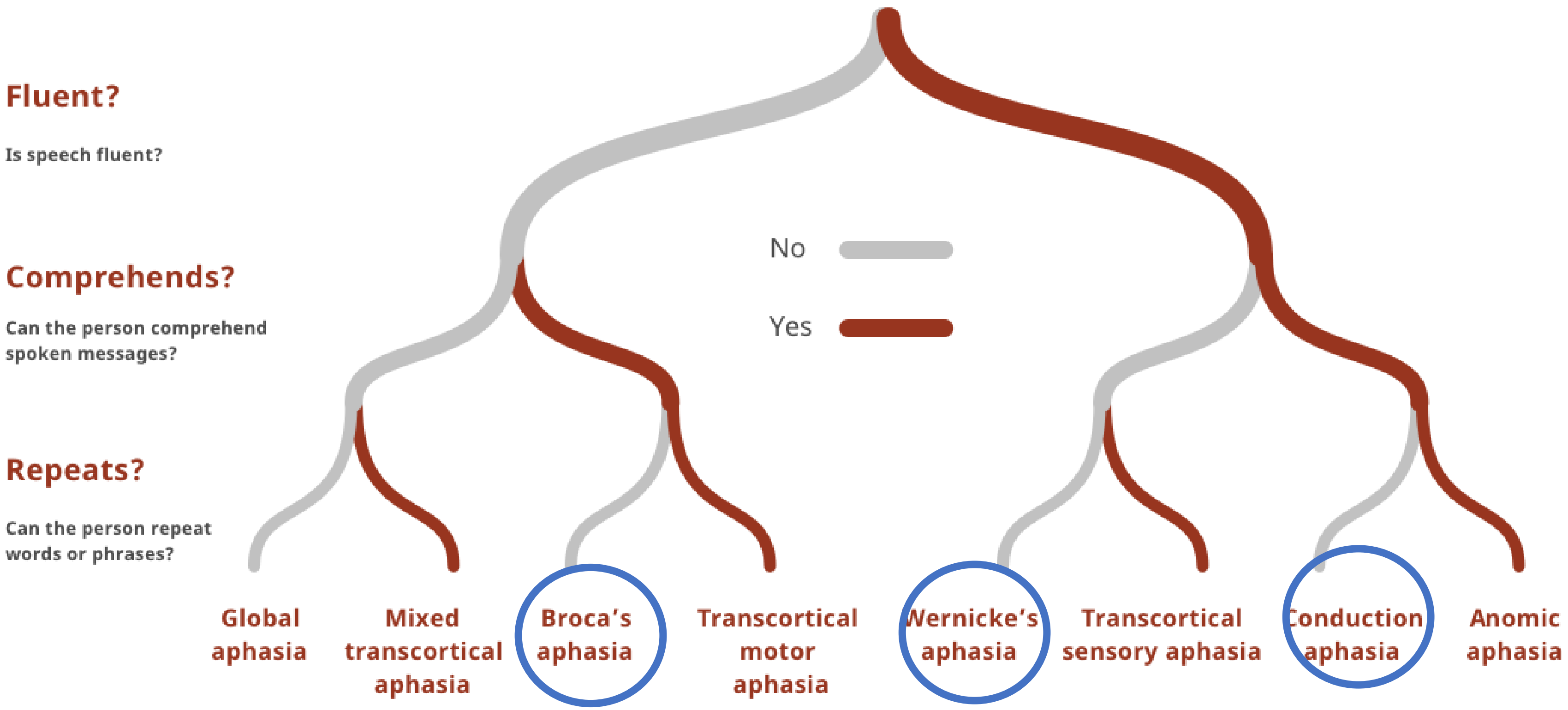
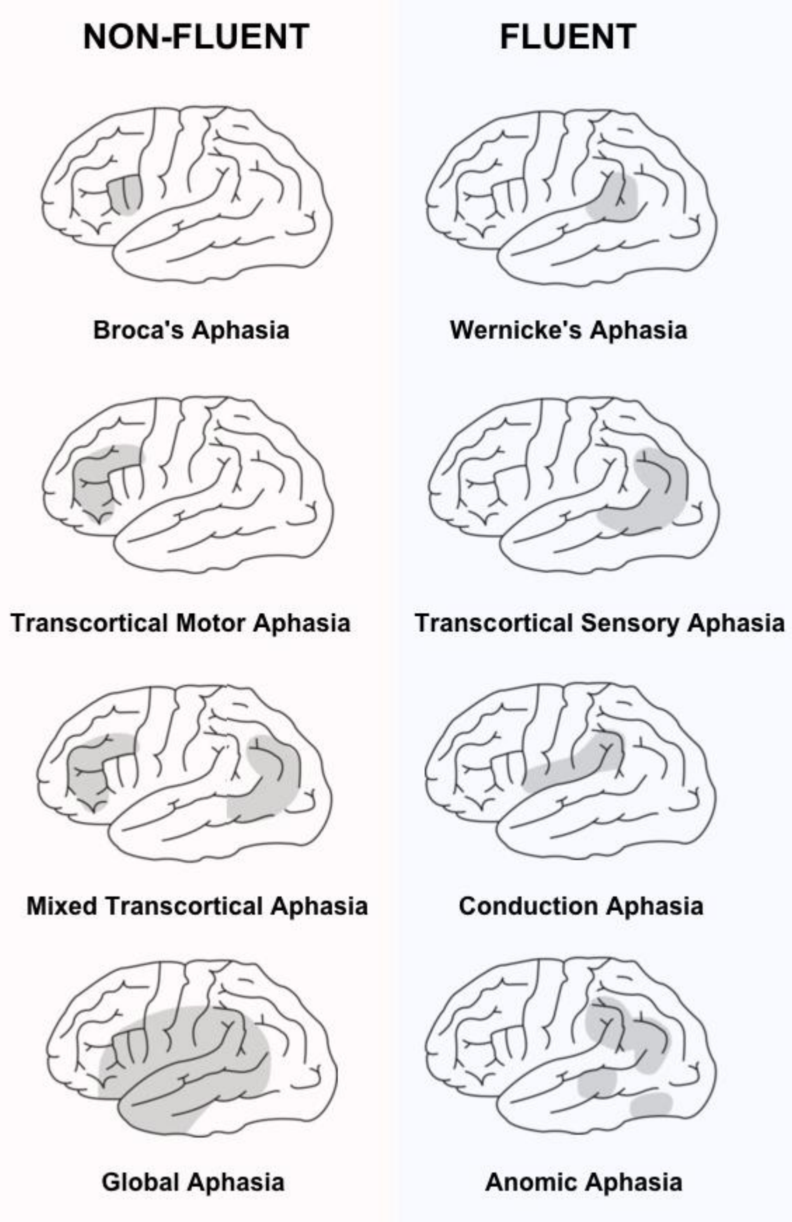


Types of Aphasia



www.aphasia.org



Language deficits can vary a lot

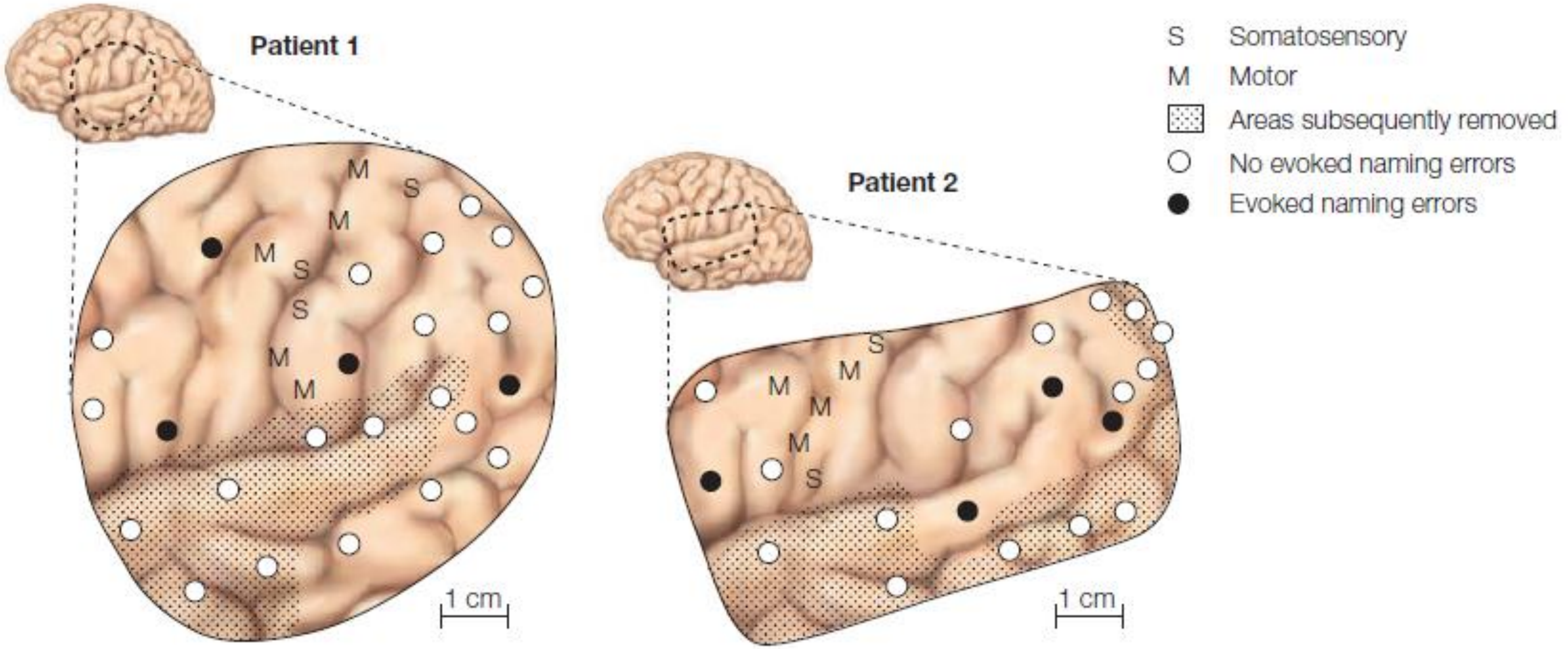


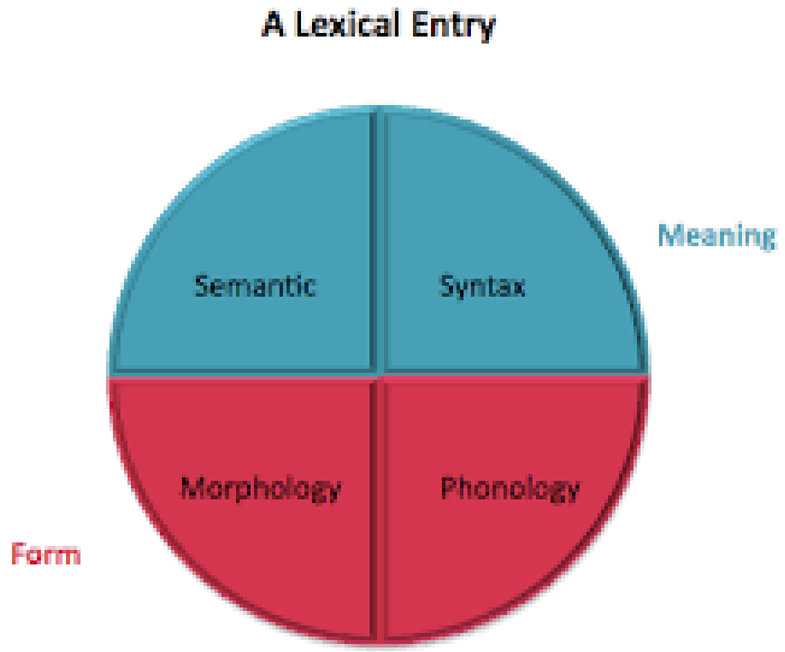
FIGURE 11.1 Regions of the brain of two patients studied with cortical-stimulation mapping. Stimulating the regions of the patients' brains indicated by black dots evoked language errors. These regions implicated as being involved in language were then mapped. Stimulating the regions indicated by white dots did not evoke language errors. The crosshatched areas were later surgically removed.

Mental Lexicon

A word in a spoken language has two properties:

- A meaning and a **phonological** (sound-based) **form**.
- A word in a written language also has an **orthographic** (vision-based) **form**.

Mental Lexicon—
a mental store of information about words that includes semantic information (the words' meanings), syntactic information (how the words combine to form sentences), and the details of word forms (their spellings and sound patterns).



argep

car ucrtk

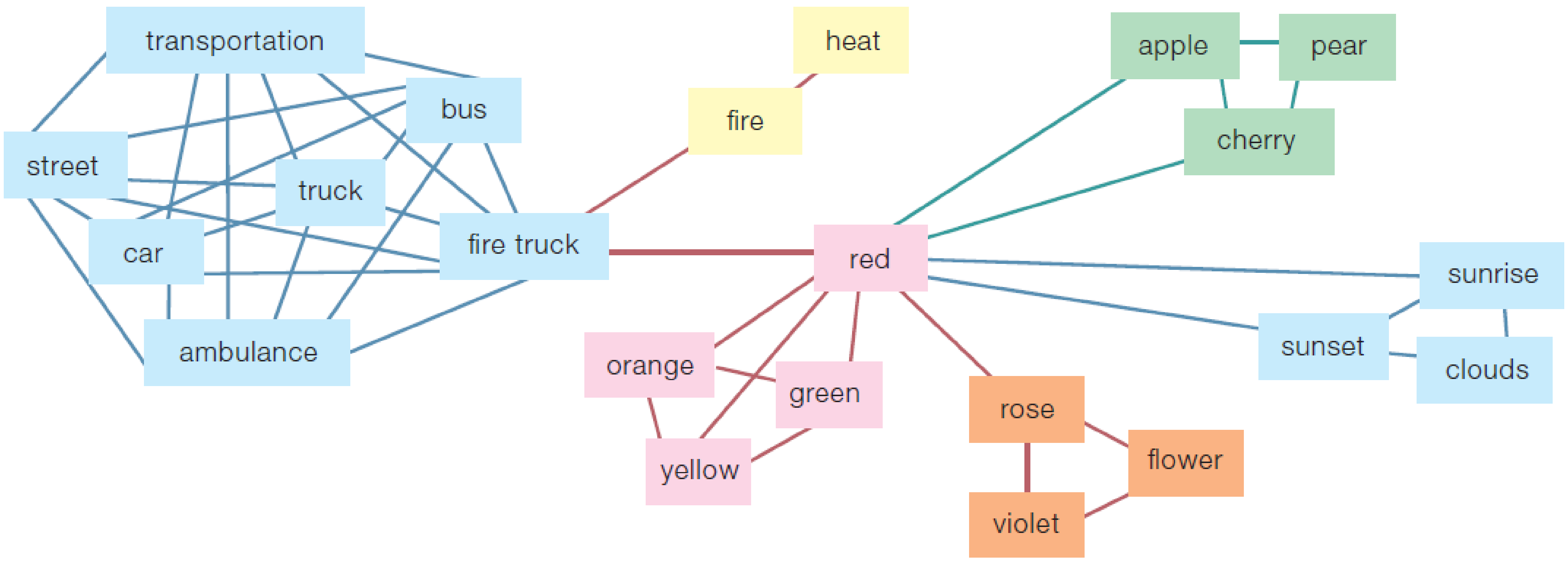


FIGURE 11.6 Semantic network.
Words that have strong associative or semantic relations are closer together in the network (e.g., *car* and *truck*) than are words that have no such relation (e.g., *car* and *clouds*). Semantically related words are colored similarly in the figure, and associatively related terms (e.g., *fire truck* and *fire*) are closely connected.

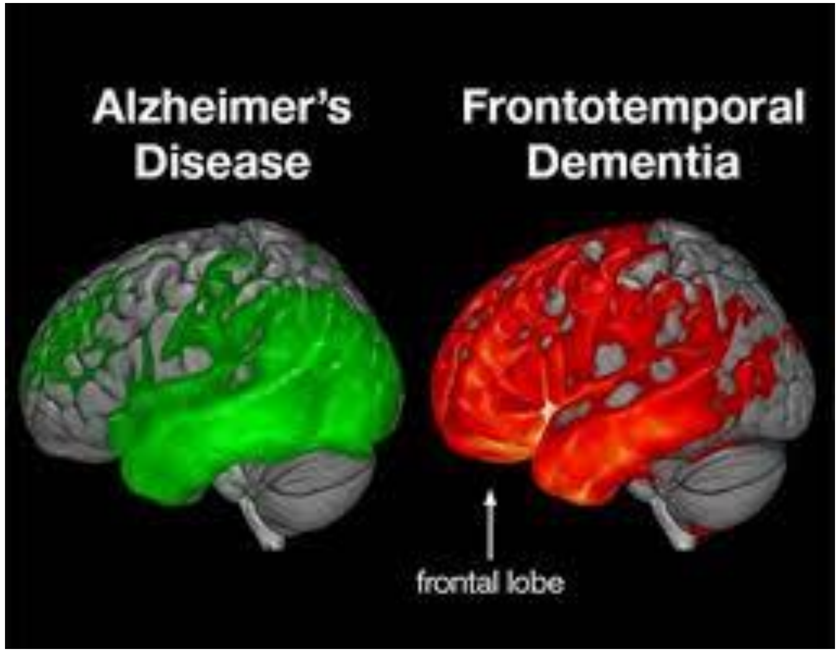
Support for this model
Semantic dementia – animal/dog (not ape)

Organization of the Mental lexicon of our language → semantic network

Semantic dementia

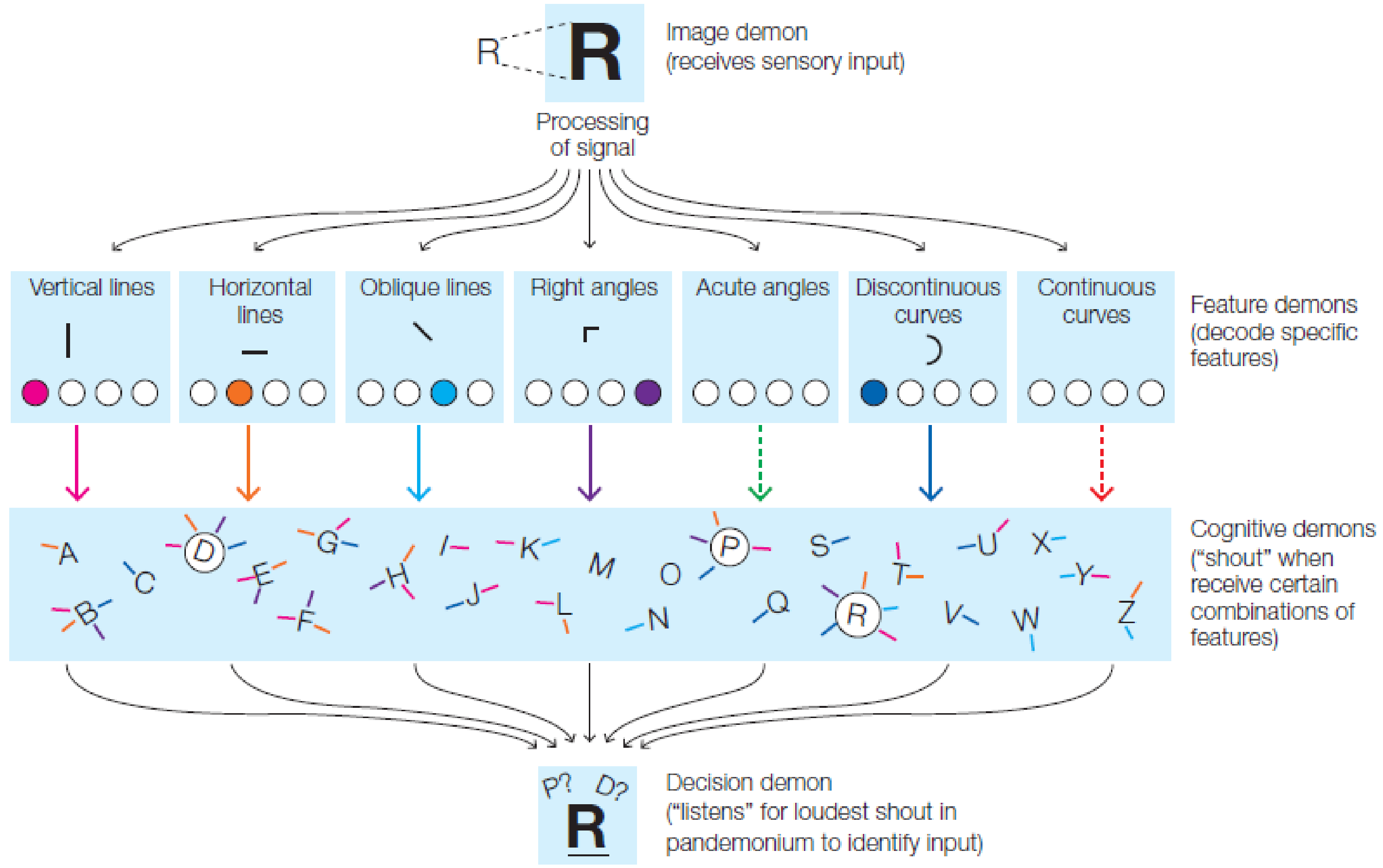
difficulty to understand words and their meanings, difficulty finding words and name objects

Can also be known as FrontoTemporal Dementia



Semantic dementia – animal/dog (not ape)

Letter recognition (feature recognition)



1959

- Bottom – up processing
- Single letter at a time (serial processing)

Letter recognition (feature recognition)

McClelland and Rumelhart model (1981)

- processes can take place in parallel such that several letters can be processed at the same time
- top-down information of the words can either activate or inhibit letter activations, thereby helping the recognition of letters.

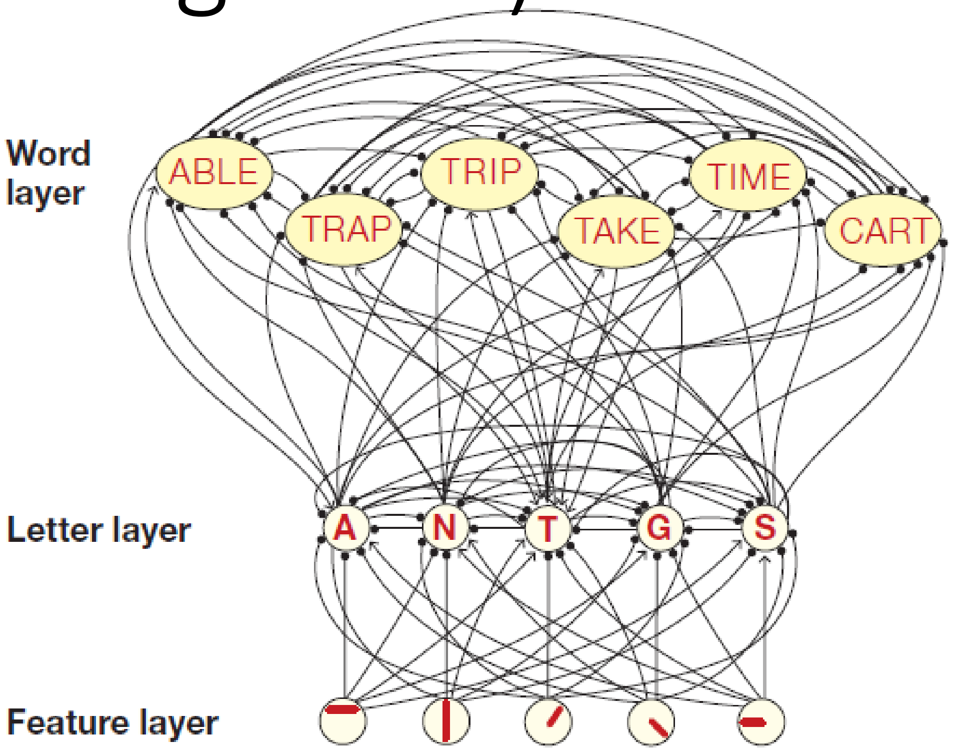
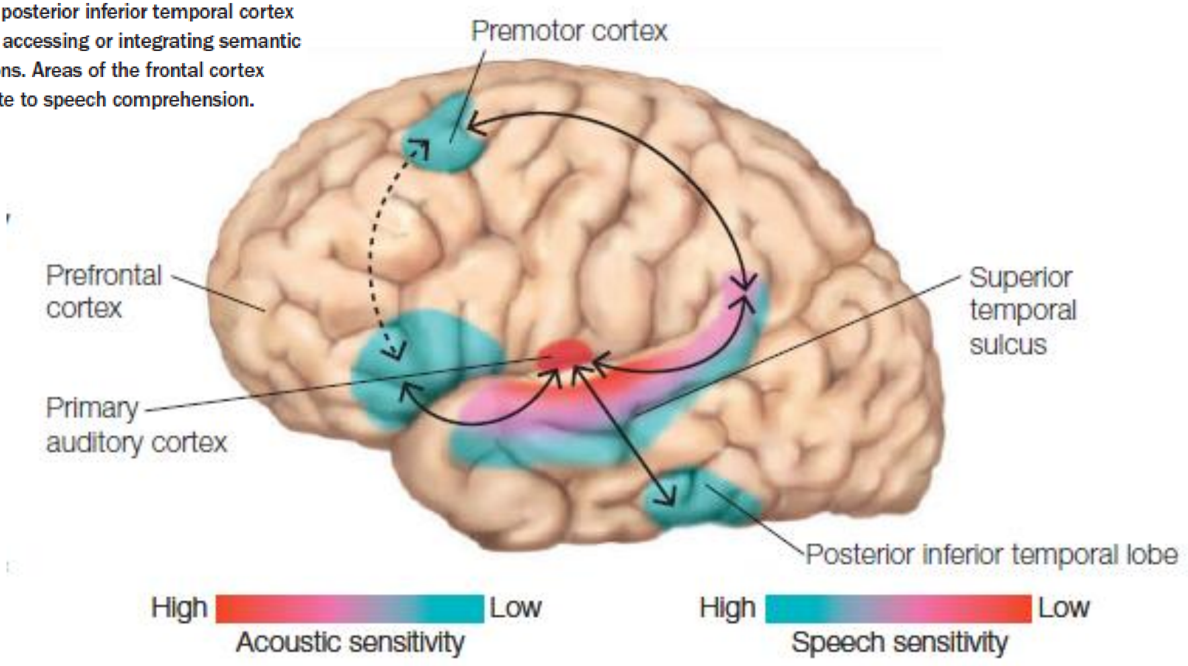
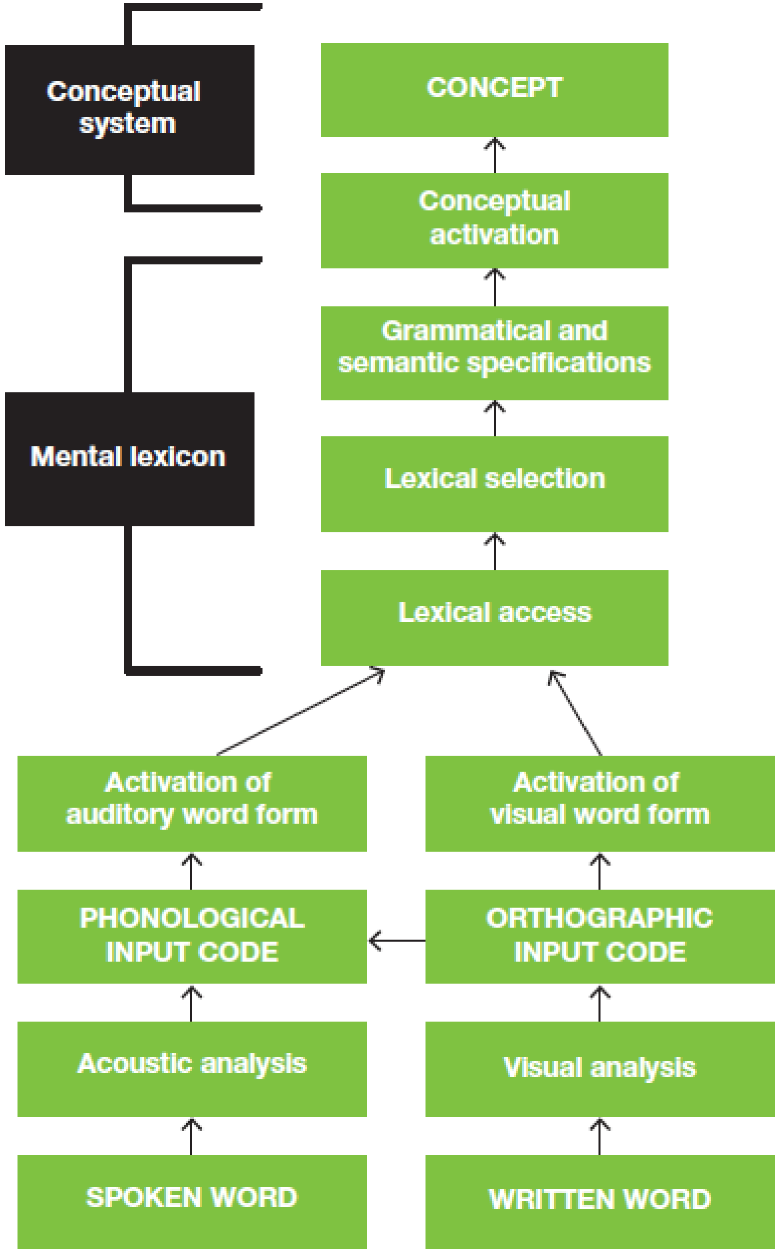


FIGURE 11.16 Fragment of a connectionist network for letter recognition.
Nodes at three different layers represent letter features, letters, and words. Nodes in each layer can influence the activational status of the nodes in the other layers by excitatory (arrows) or inhibitory (lines) connections.

Speech comprehension

FIGURE 11.12 Hierarchical processing is a key organizational aspect of the human cortical auditory system.
Multiple parallel processing pathways radiate outward from primary auditory areas to regions of motor, premotor, and prefrontal cortex. Acoustic sensitivity is highest in primary auditory cortex (Heschl's gyrus; red spot) and is activated by all auditory inputs. Acoustic sensitivity decreases moving anteriorly, inferiorly, and posteriorly away from primary auditory cortex, while intelligibility of the speech increases. Anterior and posterior regions of the superior temporal sulcus are increasingly speech specific. The left posterior inferior temporal cortex is involved in accessing or integrating semantic representations. Areas of the frontal cortex also contribute to speech comprehension.





Word recognition

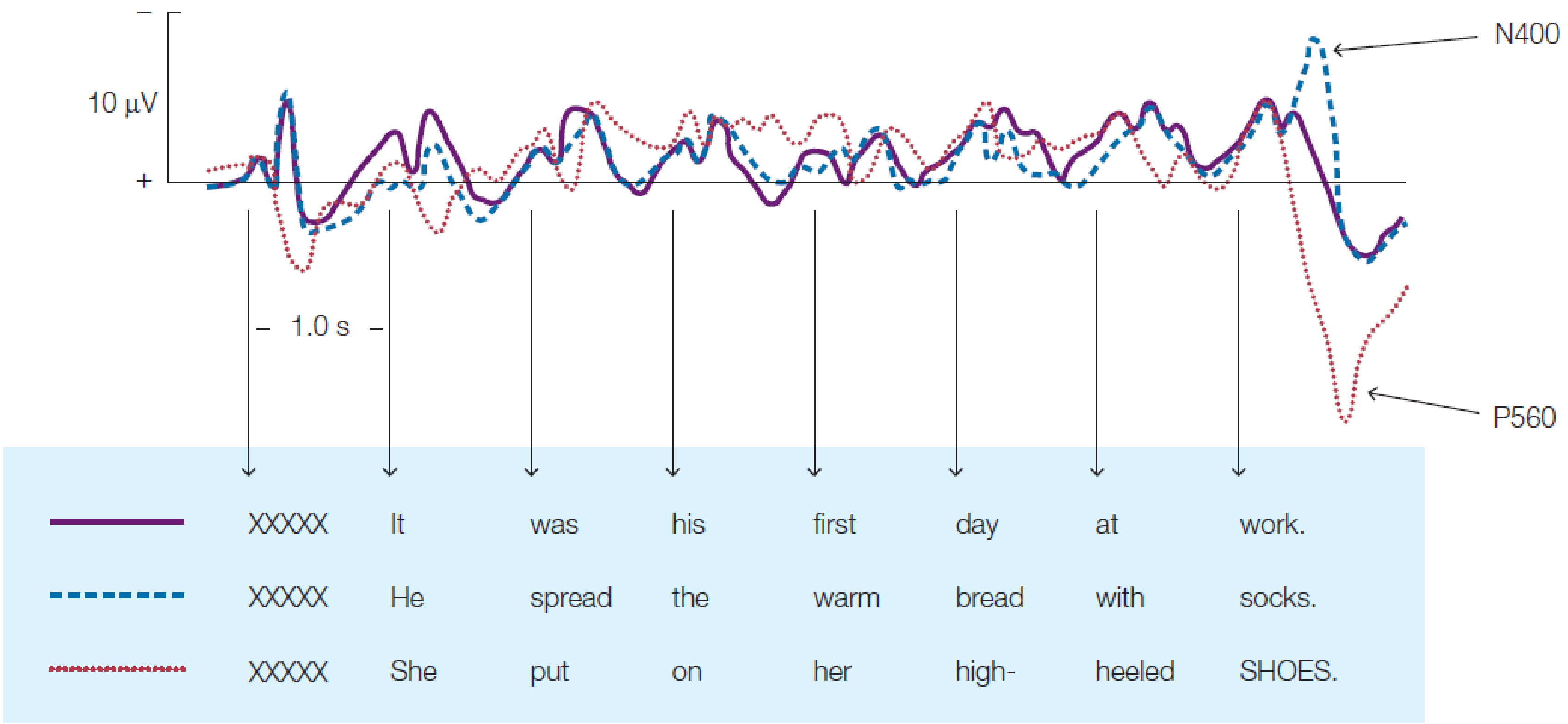
Auditory Word Recognition

- Clearly, we use **top-down processing**
- The acoustic signal alone is often just **not enough**
  - Record people saying:
    - Predictable: ***A stitch in time saves nine.***
    - Unpredictable: ***The next number will be nine.***
  - The ***nine*** spliced out of the predictable context is often unintelligible in isolation
- **So**, people use **context**
  - How and when???

The tall man planted a tree on the bank

bank

“After pulling the fragrant loaf from the oven, he cut a slice and spread the warm bread with socks.”



Also observed for context in stories For example, in a story about a man who had become a vegetarian, the last sentence could be “He went to a restaurant and ate meat that was well prepared.”

FIGURE 11.19 ERPs reflecting semantic aspects of language.
ERP waveforms differentiate between congruent words at the end of sentences (*work* in the first sentence) and anomalous last words that do not fit the semantic specifications of the preceding context (*socks* in the second sentence). The anomalous words elicit the N400 response. Words that fit into the context but are printed with all capital letters (*SHOES* in the third sentence) elicit a positive wave (P560) and not the N400, indicating that the N400 is not generated simply by surprises at the end of the sentence.

Word comprehension in Aphasia

- patients with left -hemisphere strokes resulting in severe aphasia (low comprehenders)
- or mild aphasia (high comprehenders)
- control patients with right-hemisphere strokes and no aphasia,
- healthy age-matched participants.

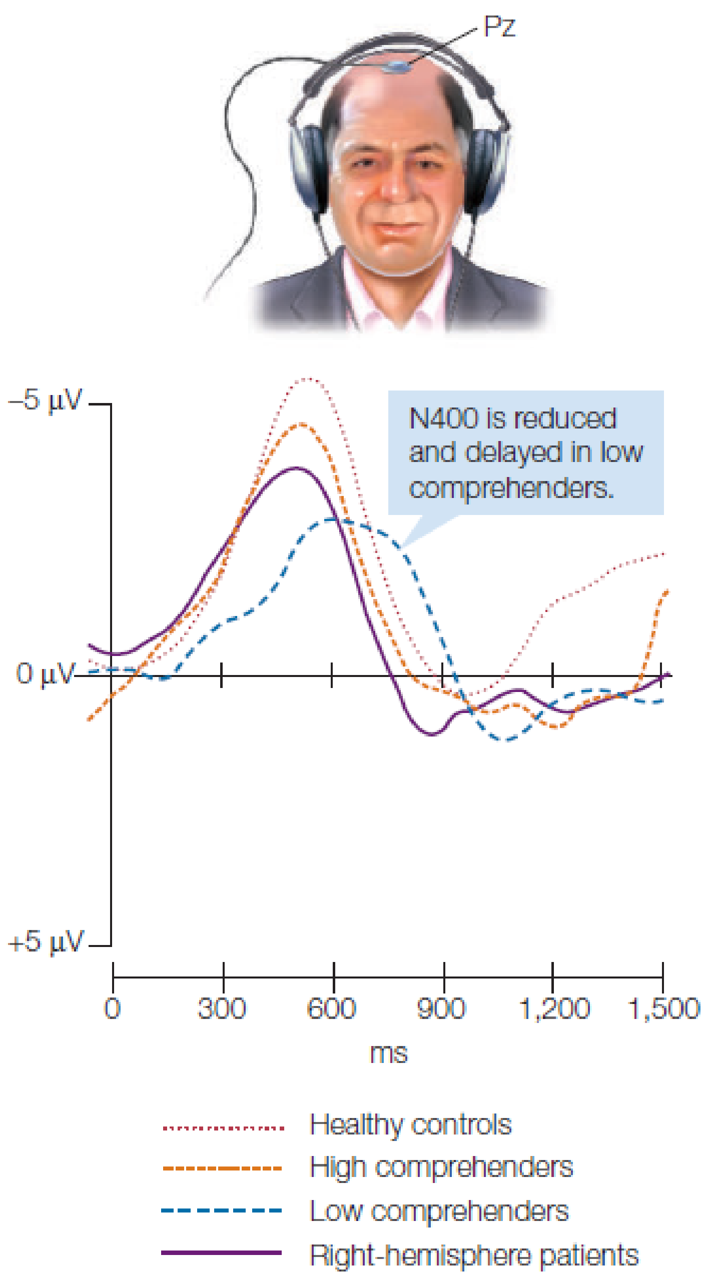


FIGURE 11.20 The N400 response to different anomalous words at the end of a sentence.

Syntax/grammar processing

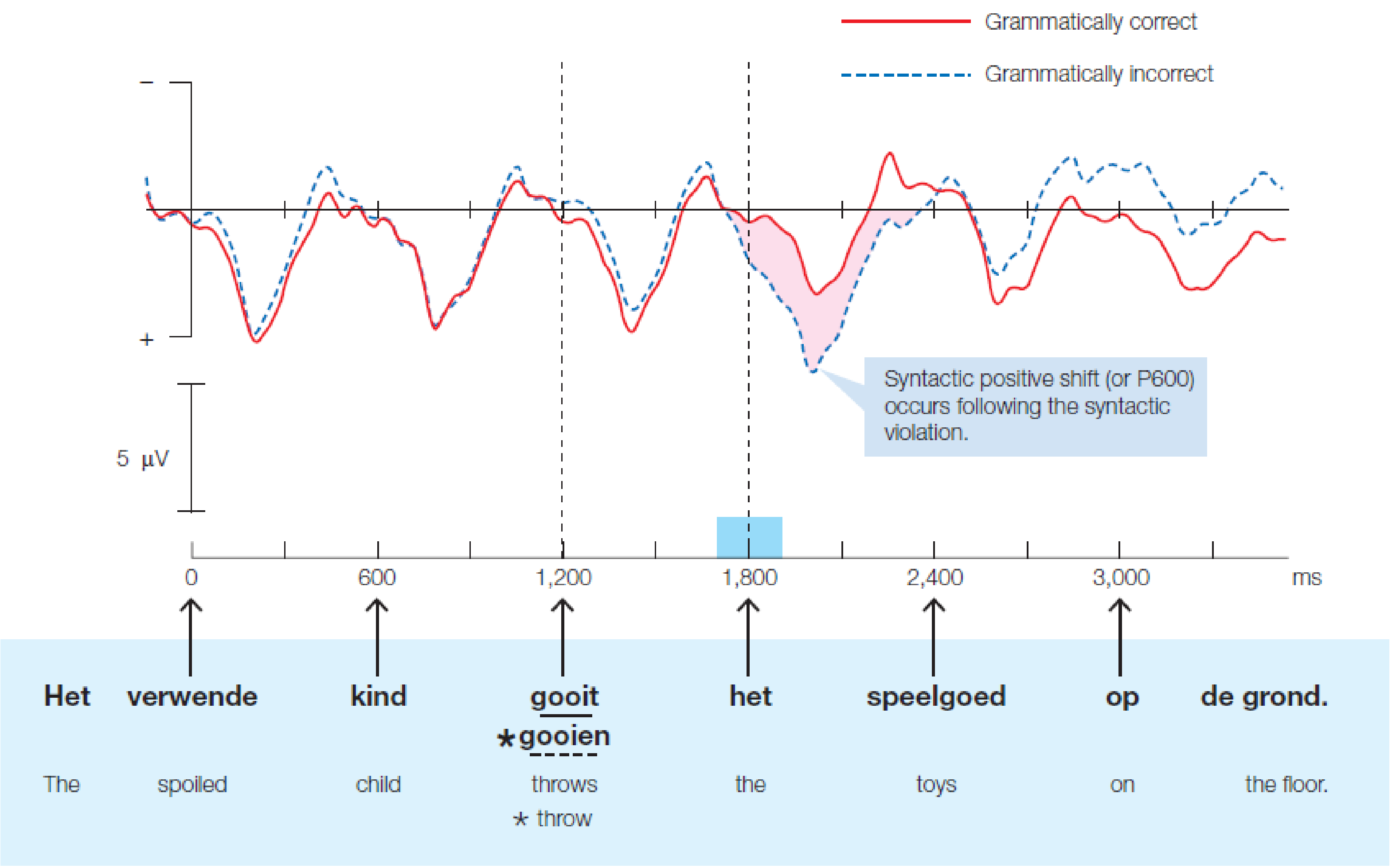
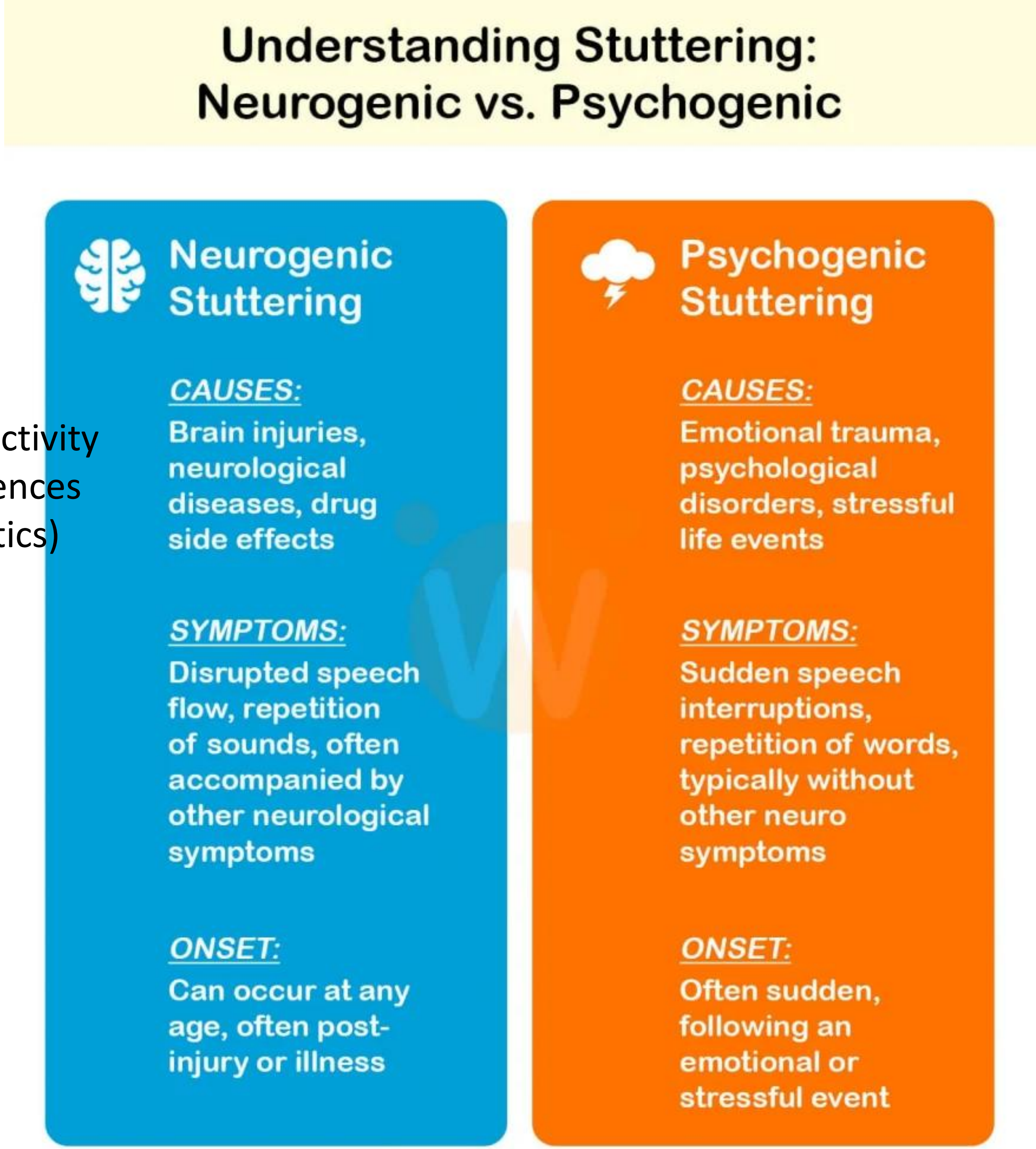


FIGURE 11.21 ERPs reflecting grammatical aspects of language.
ERPs from Pz, a midline parietal scalp site, in response to each word of a sentence that is syntactically anomalous (dashed waveform) versus one that is syntactically correct (solid waveform). In the anomalous sentence, a positive shift (shaded) emerges in the ERP waveform at about 600 ms after the syntactic violation. It is called the syntactic positive shift (SPS), or P600.

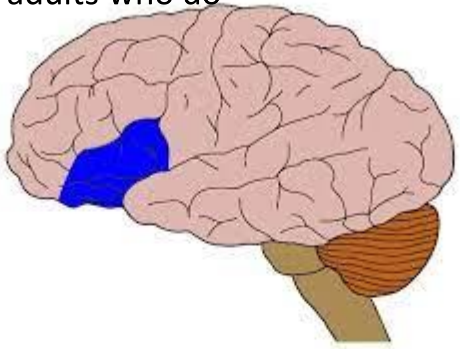
Stuttering?

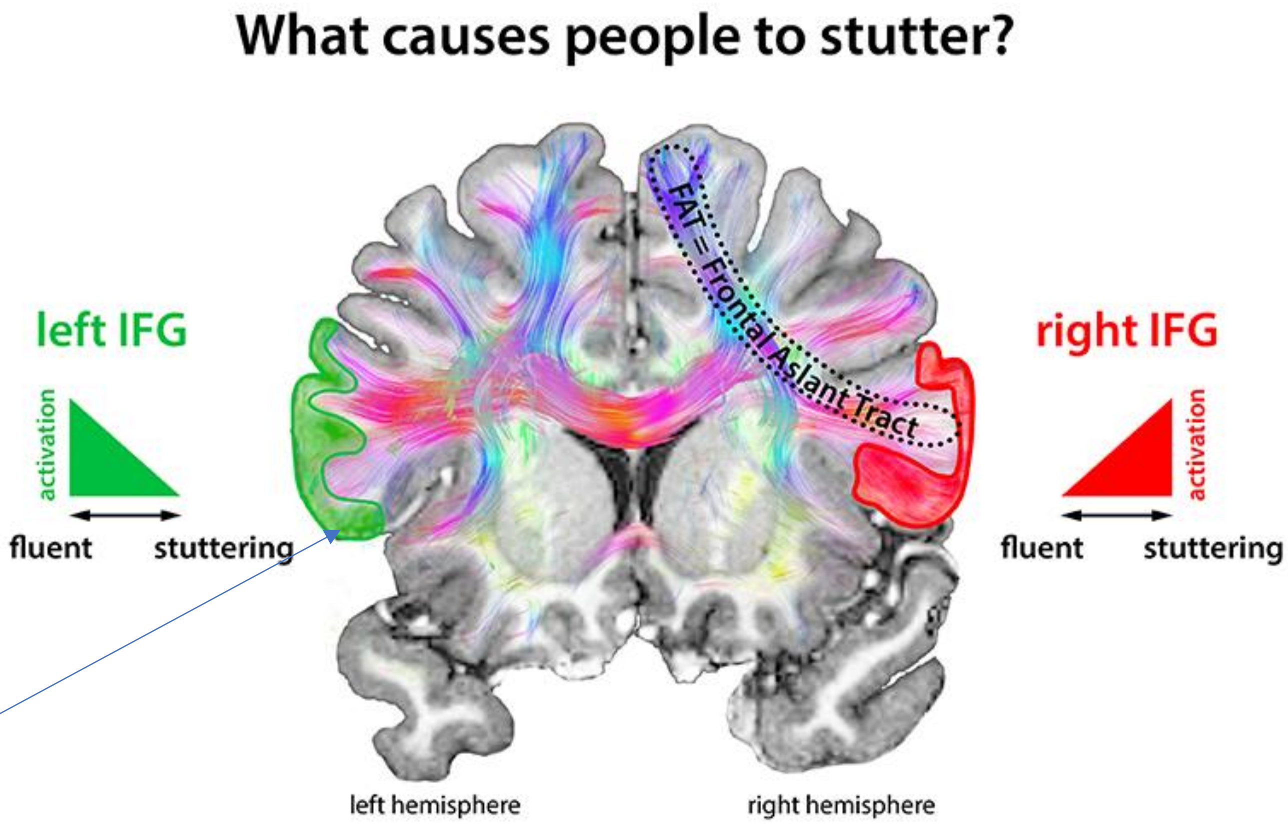
Brain connectivity differences (genetics)



- problems with normal fluency and flow of speech
- difficulty uttering certain sounds or starting a sentence
- genetics, language development, environment, as well a brain structure and function
- Treatment – speech therapy – awareness of motor activity while speaking and slowing down speed

Adults who stutter show less activity in the left-hemisphere areas that support speech production and more activity in the right hemisphere than adults who do not stutter.





Typically, the right Inferior Frontal Gyrus (IFG) stops the flow of speech, whereas the left one supports it. In people who stutter, these two areas are conversely activated: The right IFG is overactive and shows tightened connections with the frontal aslant tract (FAT), which is a sign of a strengthened movement inhibition. This interrupts the flow of speech and might inhibit activity in the left IFG. The stronger the frontal aslant tract (FAT), the more severe the stuttering

https://www.cbs.mpg.de/stuttering-in-the-brain

Dyslexia?

Dyslexia – deficit in reading

Under 5	5-13	13 and up
Mixing up letters when pouncing word, i.e. saying biving doard instead of diving board	Struggling with math word problems	Trouble understanding phrases, jokes or idioms
Problem with learning new vocabulary words	Problem recalling simple facts and numbers	Trouble learning a different language
Trouble recognizing the alphabet or alphabet sounds	Trouble with using writing tools, i.e. pens	Problems reading aloud and with retelling the main points of a story
Trouble learning familiar word sequences, i.e. the name of the months in a year or the days of the week	Trouble with understanding spelling rules, i.e. "I" before "E" except after "C"	Reading below grade level even with average intelligence
	Trouble with understanding new knowledge	Trouble with time management

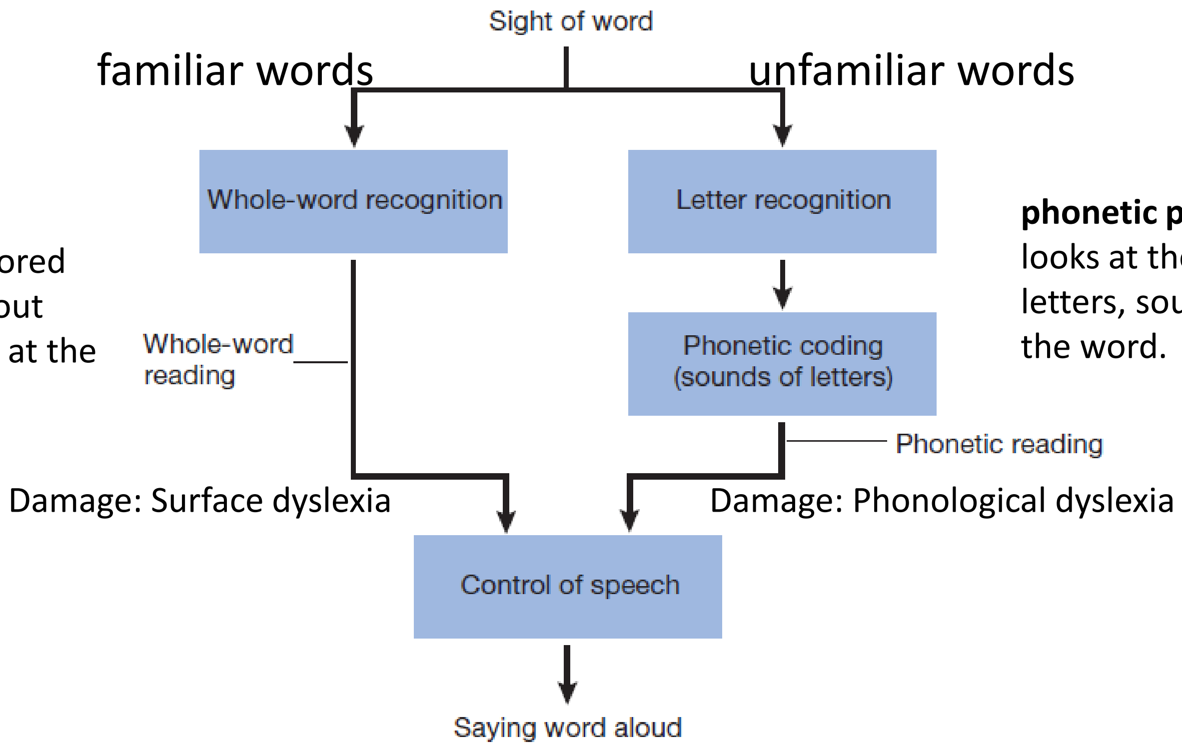
- Problems in identifying speech sounds and learning how they relate to letters and words (decoding).
- Developmental or acquired (brain injury)

Dyslexia: Myths and Misconceptions

https://sarahsnippets.com/dyslexia-myths-and-misconceptions/

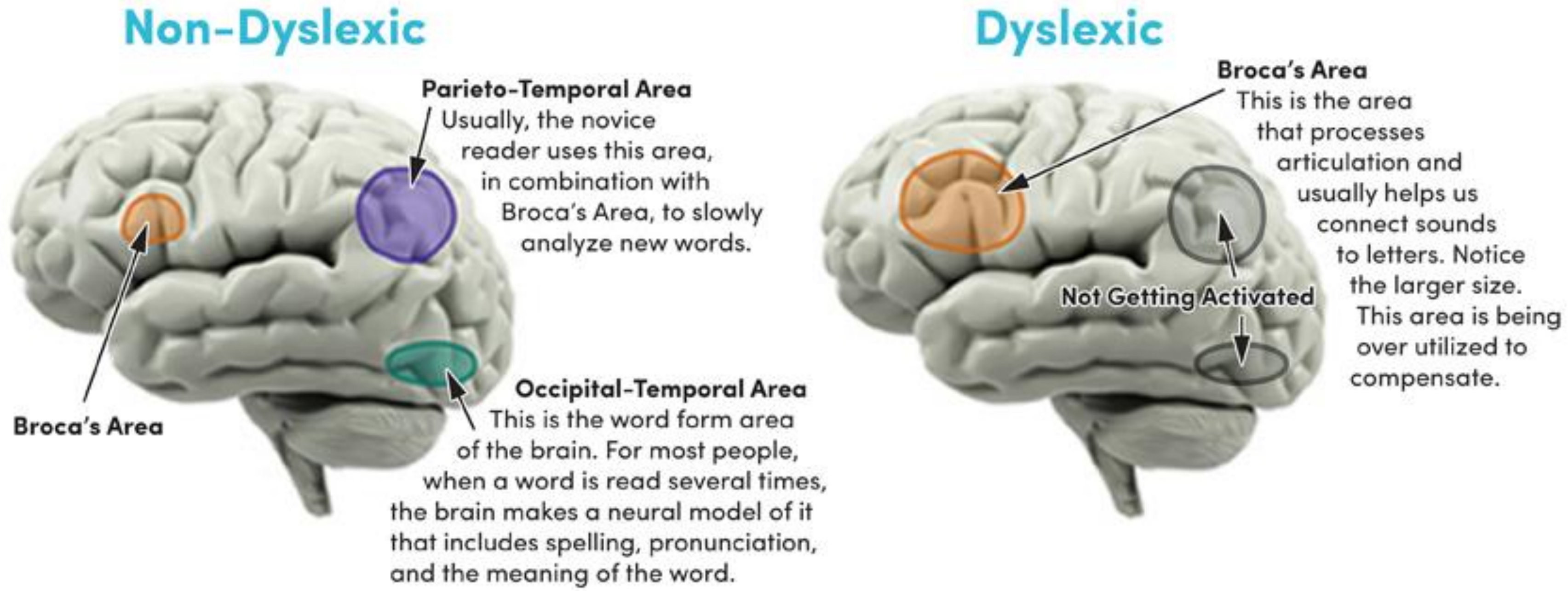
Different ways of reading

lexical procedure - based on specific stored information that has been acquired about written words: The reader simply looks at the word, recognizes it, and says it.

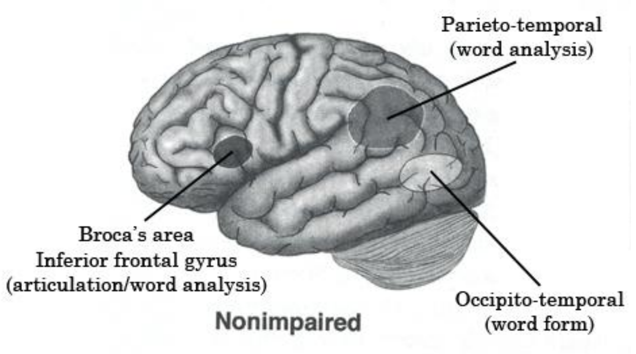


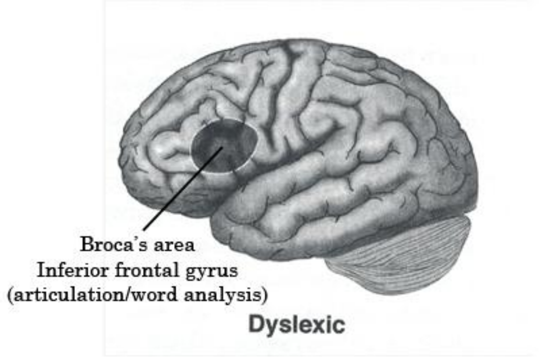
phonetic procedure: The reader looks at the word, recognizes the letters, sounds them out, and says the word.

NON-DYSLEXIC BRAIN vs. DYSLEXIC BRAIN WHEN READING



Research in neuroscience reveals that the brain functions differently in people with dyslexia than those without it. These structural and neural differences make it more difficult for people with dyslexia to read, spell and write. For example, in the left brain hemisphere, three dominant areas of the brain are usually activated for reading, but in those with dyslexia, only one area of the brain is being stimulated.



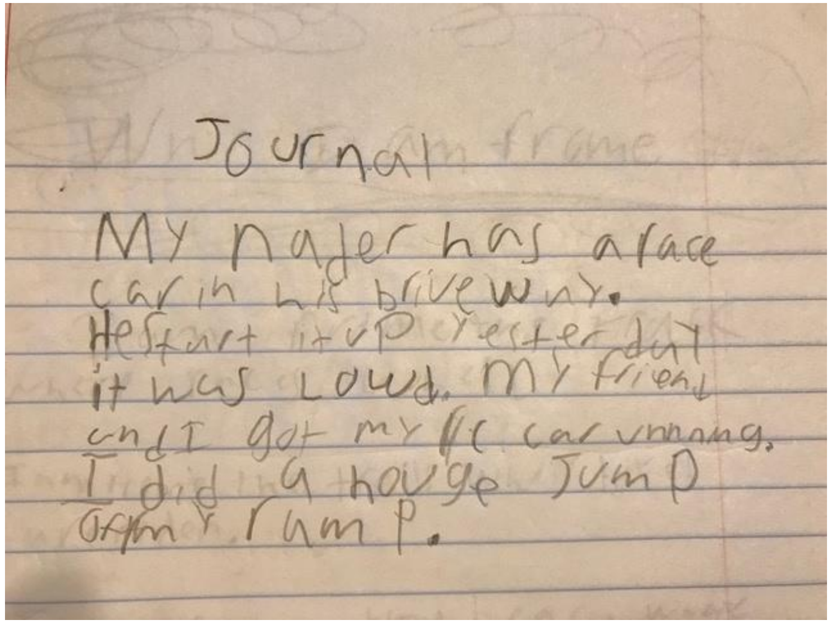


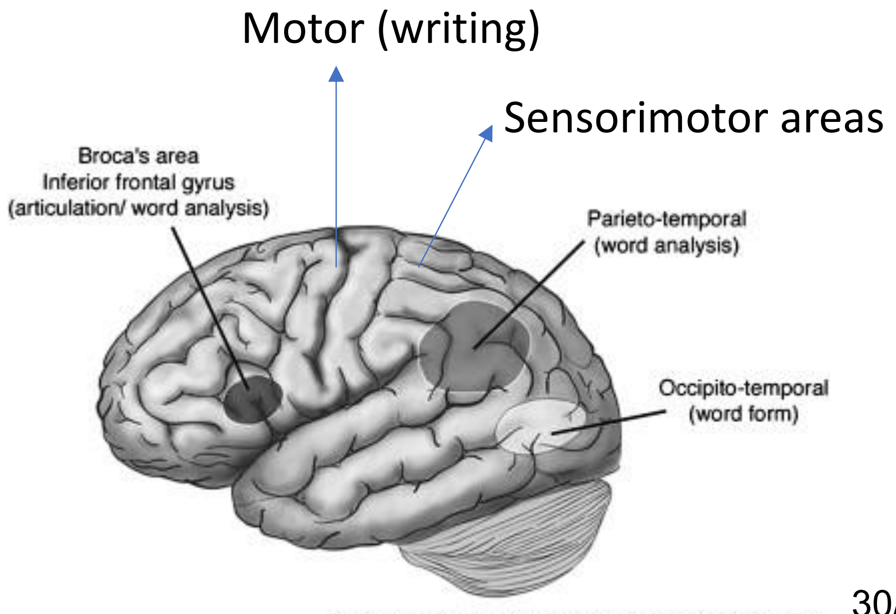
Dysgraphia commonly accompanies dyslexia.

Dysgraphia – deficit in writing

Difficulty in converting spoken sounds into written words
Difficulty in fine motor skills

- Difficulty visualizing letter formation beforehand
- Poor legibility
- Poor spatial planning on paper
- Difficulty writing and thinking at the same time (creative writing, taking notes)
- Handwriting abilities that may interfere with spelling and written composition
- Difficulty understanding homophones and what spelling to use
- Having a hard time translating ideas to writing, sometimes using the wrong words altogether
- May feel pain while writing (cramps in fingers, wrist and palms





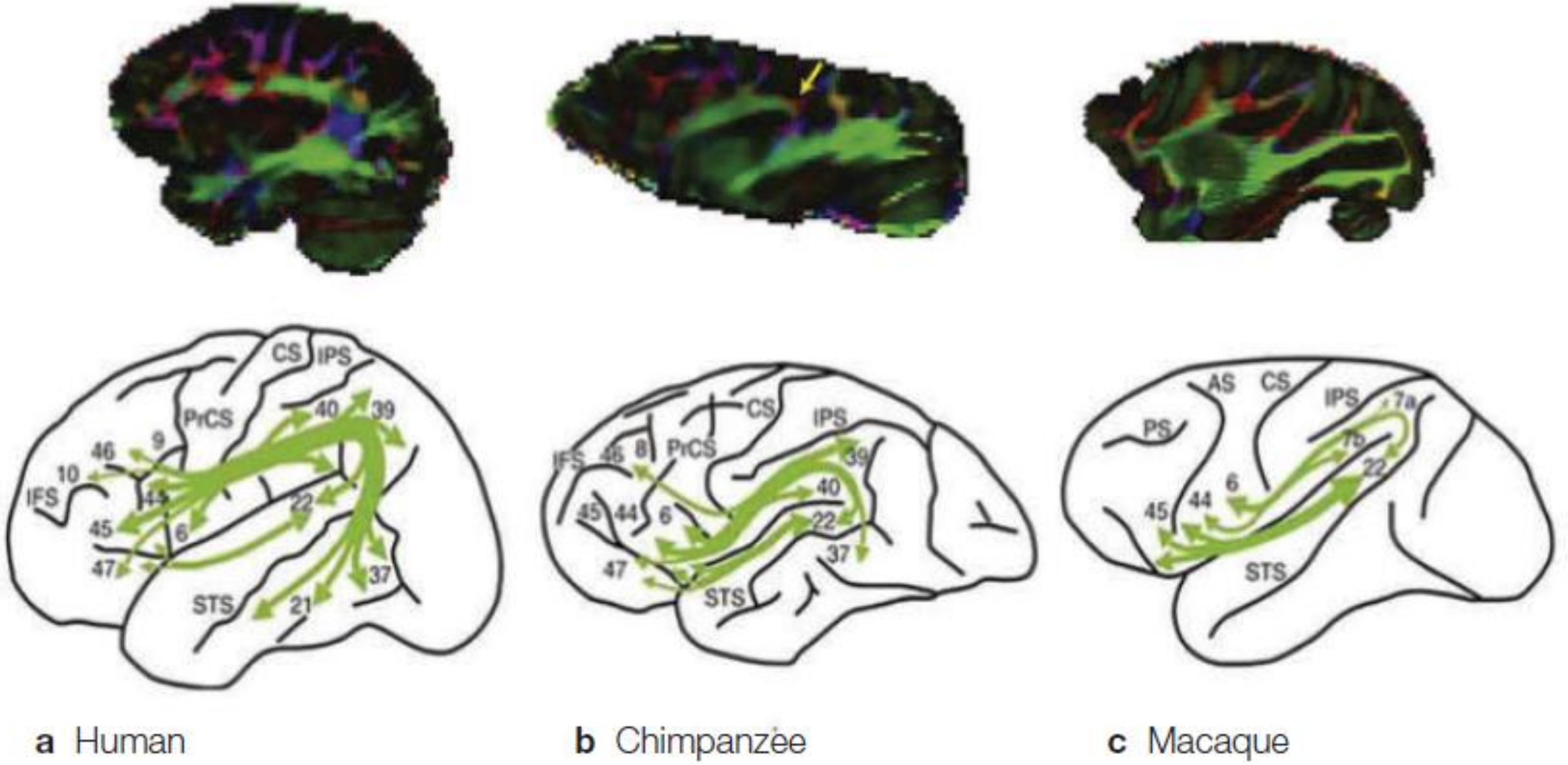
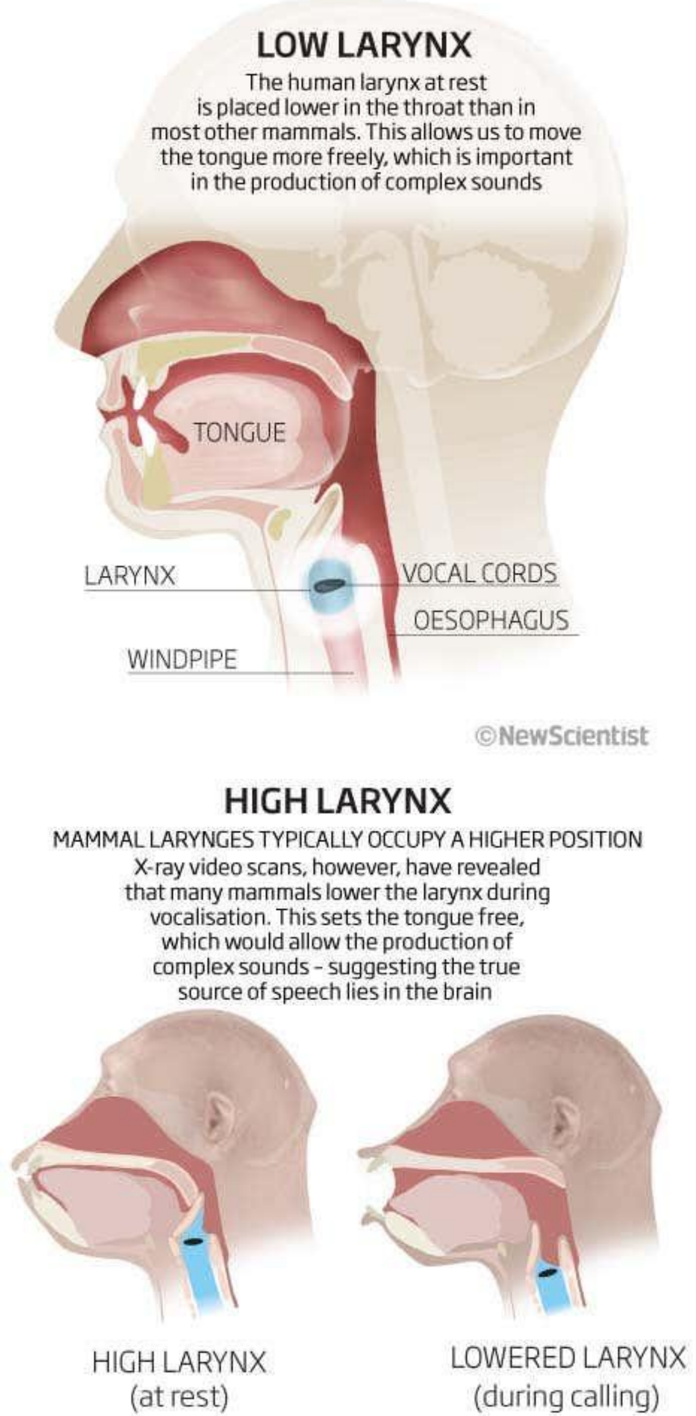
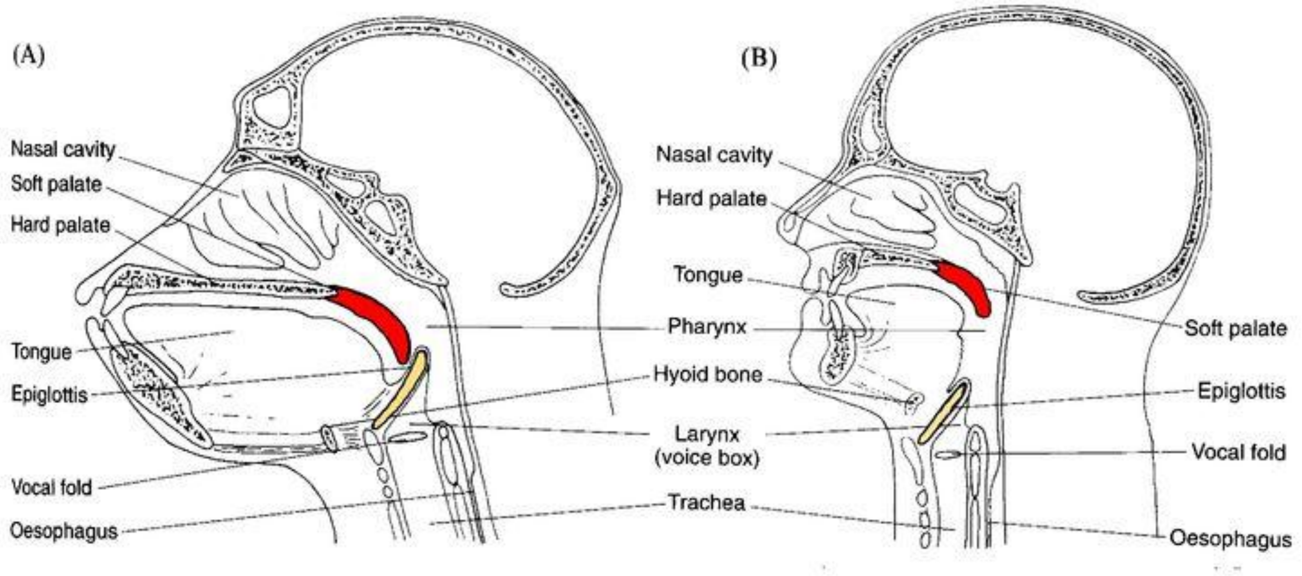


FIGURE 11.30 Neuroanatomy of the human left-hemisphere perisylvian language system compared to chimpanzees and macaques.

DTI images (top) and network models (bottom). **(a)** Humans have robust interconnectivity of the inferior frontal cortex, inferior parietal cortex, and temporal cortex, especially lateral and inferior temporal cortex by massive projections of the arcuate fasciculus. **(b–c)** The white matter tracts of the chimpanzee and the macaque monkey show greatly reduced or absent projections into lateral and inferior temporal cortex. CS = central sulcus; IFS = inferior frontal sulcus; IPS = intraparietal sulcus; PrCS = precentral sulcus; STS = superior temporal sulcus.



The descended larynx



Other mammals / Human infants

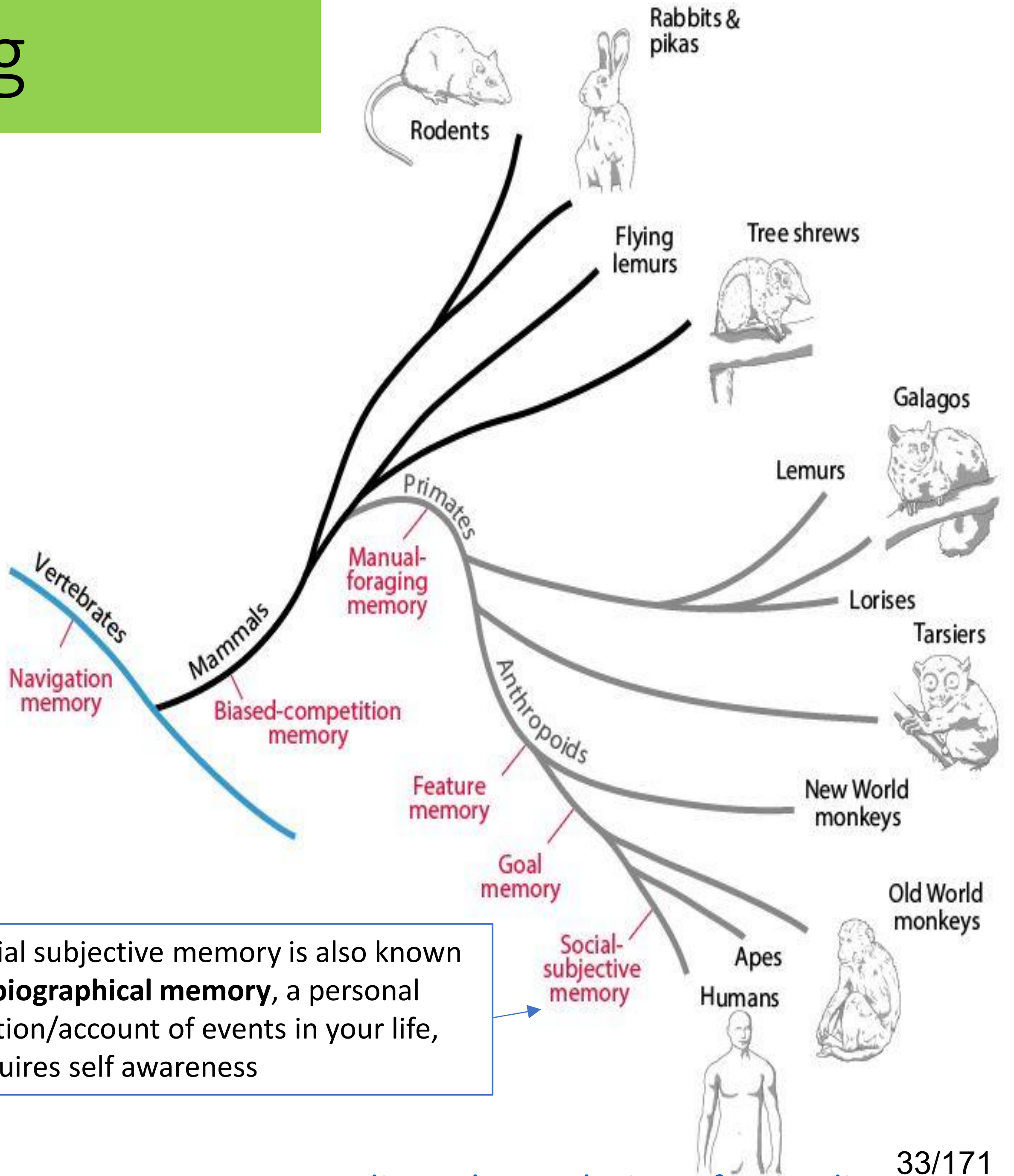
Humans (Adult)

Episodic Future Thinking

As human beings, we don't just learn and remember information. We make use of our experiences.

- **Planning the future** – imagine or simulate future scenarios or events using past experiences.
- **Predicting the future** – using past experiences to make novel inferences and solve problems by reorganizing memory networks
- **Social relationships** – evaluating, predicting social behaviour in others and maintaining relationships by remembering whether they were good (cooperative) or bad (aggressive) to you.
- **Language (refer to events)** – remembering the meaning and context of words/phrases/semantic knowledge
- **Self-awareness / autonoetic consciousness** – the ability to be aware of yourself, that you know what you know, it a special trait that arises due to episodic memory

This social subjective memory is also known as **autobiographical memory**, a personal recollection/account of events in your life, that requires self awareness



Source + Extra Reading: The evolution of episodic memory

The cognitive neuroscience of human memory

cognitive neuroscience

What is memory?

- **Memory**: the ability to store and retrieve information over time
- There are three key functions of memory:
    - **Encoding:** the process by which we transform what we perceive, think, or feel into an enduring memory
    - **Storage:** the process of maintaining information in memory over time
    - **Retrieval:** the process of bringing to mind information that has been previously encoded and stored

What are some questions you have about memory and how it works?

- Why do we remember some events but not others?
- Why do we forget? Can we intentionally forget?
- What causes deja vu?
- What aspects of our memory system change as we grow old?
- Why is it that in some memory disorders, people do not forget some types of information?
- What causes Alzheimer's? What can we do to protect against it?
- Can we grow new neurons in the brain to aid memory and other functions?

Examples of memory loss

- Clive Wearing: https://www.youtube.com/watch?v=Vwigmktix2Y

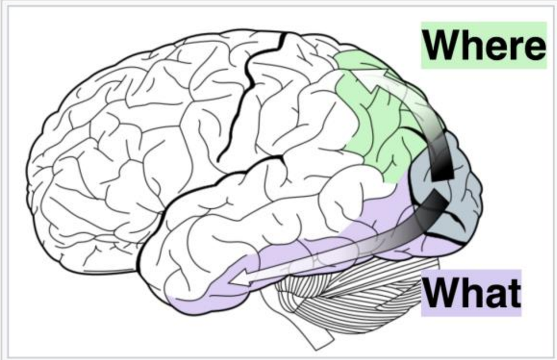
~~8:31 AM: Now I am really, completely awake.~~

~~9:06 AM: Now I am perfectly, overwhelmingly awake.~~

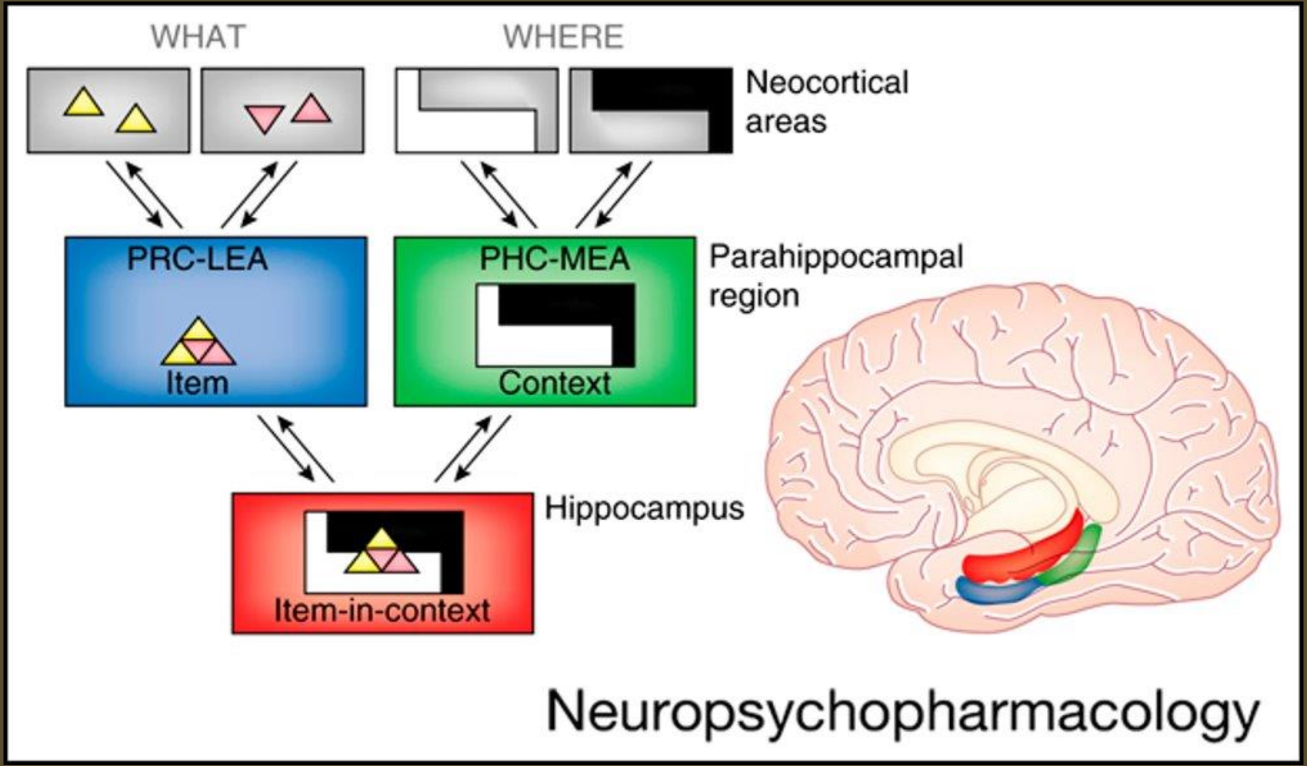
9:34 AM: Now I am superlatively, actually awake.

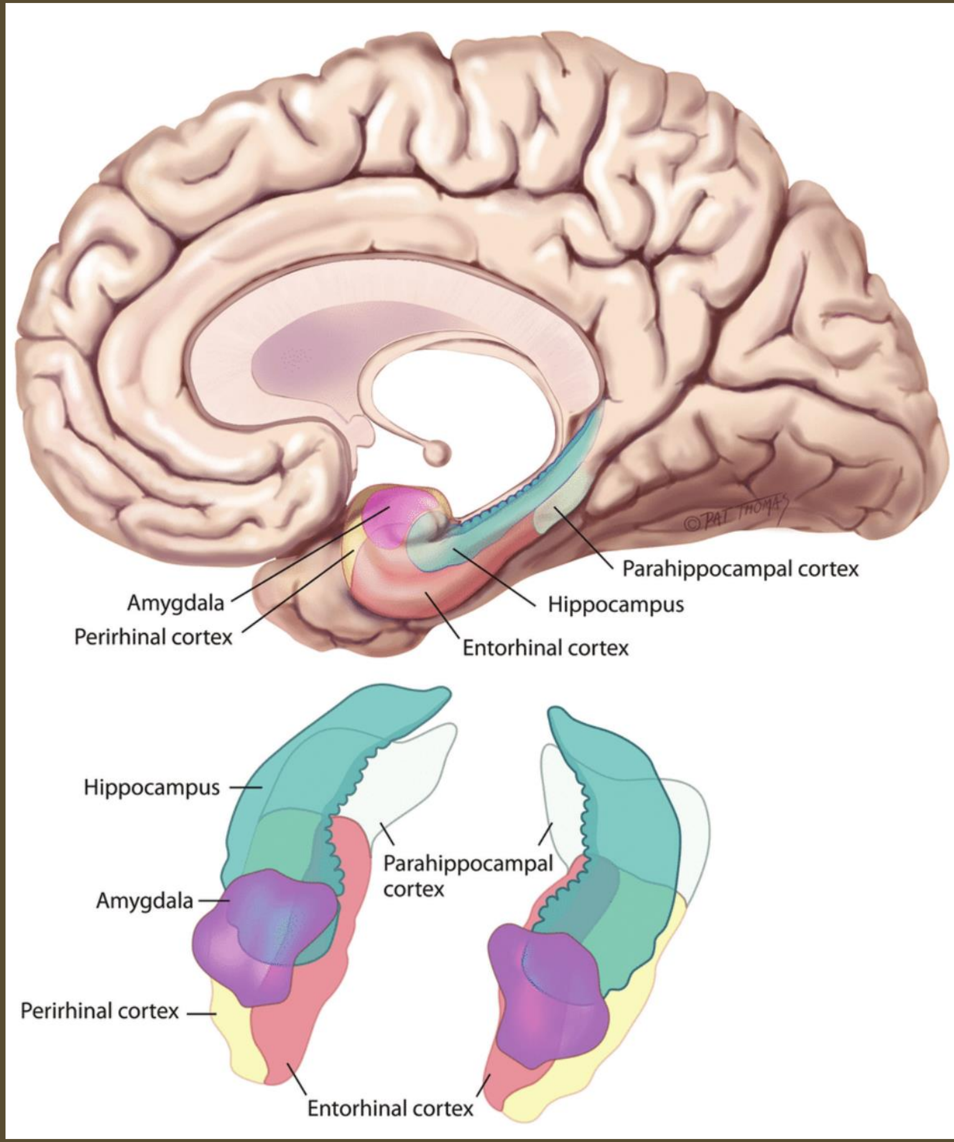
Neocortex vs the hippocampus (subcortical structures)

- Medial temporal lobe system (Eichenbaum et al., 2007)



The dorsal stream (green) and ventral stream (purple) are shown. They originate from a common source in the visual cortex





Medial Temporal Lobe

Examples of superior memory

- Highly superior autobiographical memory
- https://www.youtube.com/watch?v=wliStZc_sa4
- https://www.youtube.com/watch?v=en23bCvp-Fw

Observations about HSAM

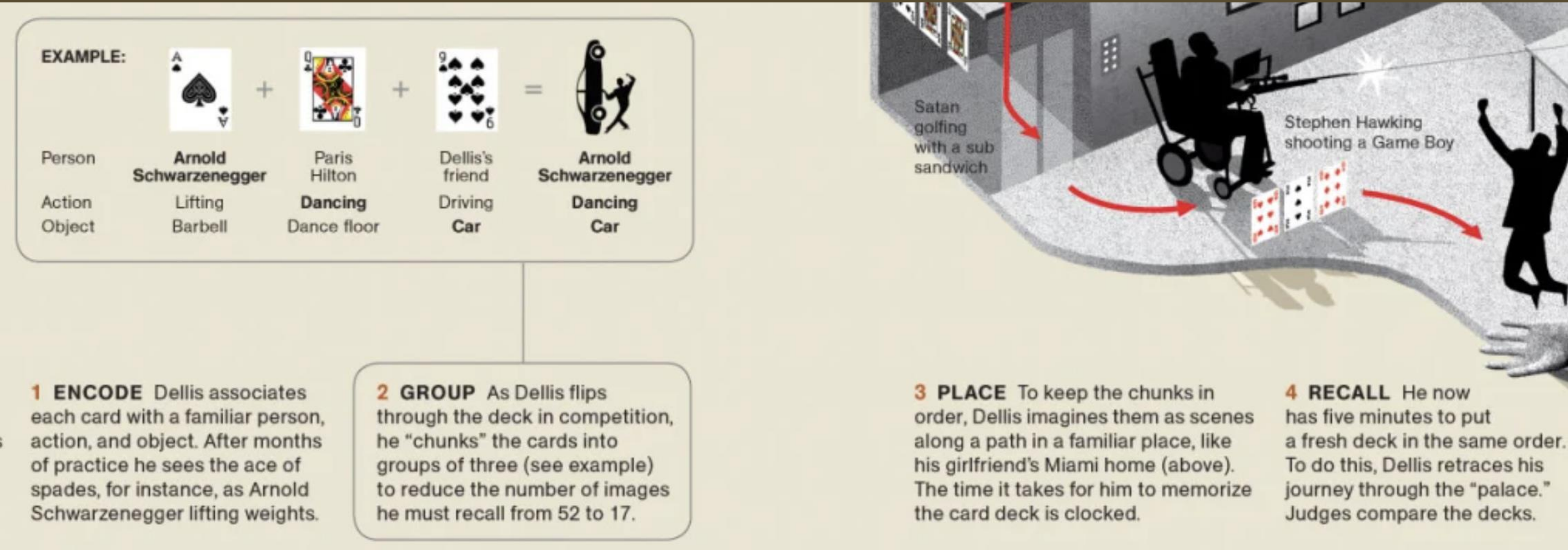
- OCD-like
- Adaptive nature of memory: can forgetting have a beneficial role? Is HSAM a boon or a curse? What would it be for you?
- Organizing memories everyday: semantic? According to the calendar and by anchoring to major events, etc..
- Bigger temporal lobe, caudate nucleus, but chicken or egg problem – This is a cog neuro course but often it is very difficult to infer causation from the brain alone.
- Memory access: was it direct and immediate? Or did they seem to take some time to logically arrive at the date? Well, there are theories about this made based on lab experiments.

We lie in between, we sometimes forget, sometimes remember really well, ..

MEMORY DOES NOT ARISE ONLY OUT OF THE BRAIN!

DEPENDENCE ON CONTEXT.

Memory champion – 3 pm KRB



https://benmeer.com/newsletter/memory-palace/

How are memories organized?

- Space
- Time
- Semantic
- Other contextual features

How do we study such questions in a careful manner?

Laboratory memory experiments

Memory Test

- Bed
- Sheets
- Xylophone
- Pillow
- Dream
- Rest
- Tired
- Snore
- Yawn
- Darkness
- Blanket
- Couch

READY

SET

Have you seen this word? How confident are you?

- Sheets?
- Sleep?
- Dream?
- Mattress?
- Snore?

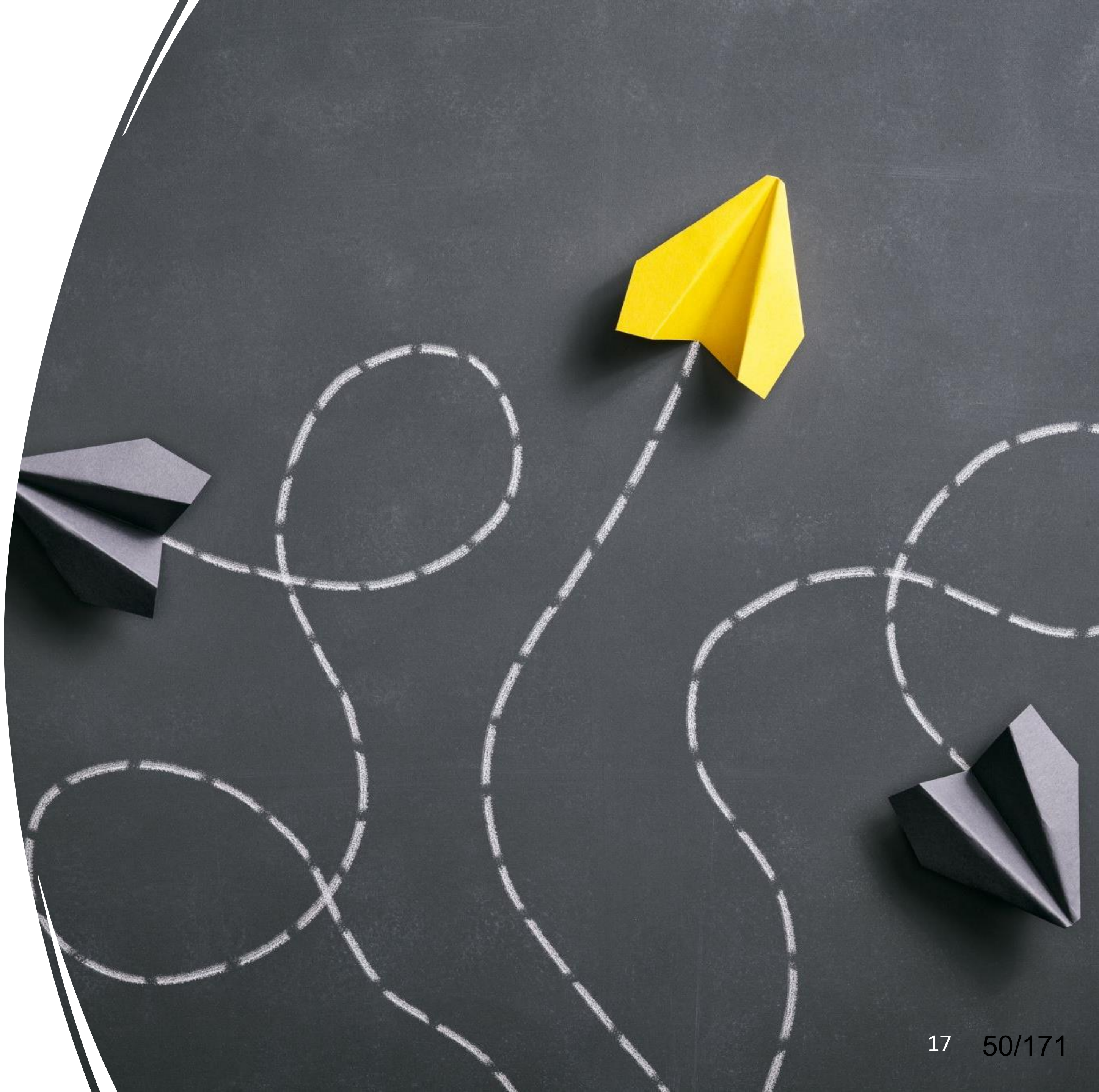
False memories: due to semantic structure and activation of semantic associates

- We tend to organize memories by their meanings (semantics)
- This can sometimes lead to errors such as the one we just saw

Different tests used in experiments to get at different neural processes underlying memory

- Recall the words in the same order: serial recall
- Recall the words in any order you like: free recall
- Pants: Did you see this word on the list? Yes or not?: Recognition memory test

Let's start with a free recall task



COUCH

ORANGE

BOOK

APPLE

PARK

PHONE

BANANA

BOTTLE

GRAPE

PLANT

DESK

PEACH

$$35 + 28 = ?$$

$$47 + 15 = ?$$

32 + 27 = ?

Write down the words you saw in any order you like

INTENTIONALLY LEFT BLANK

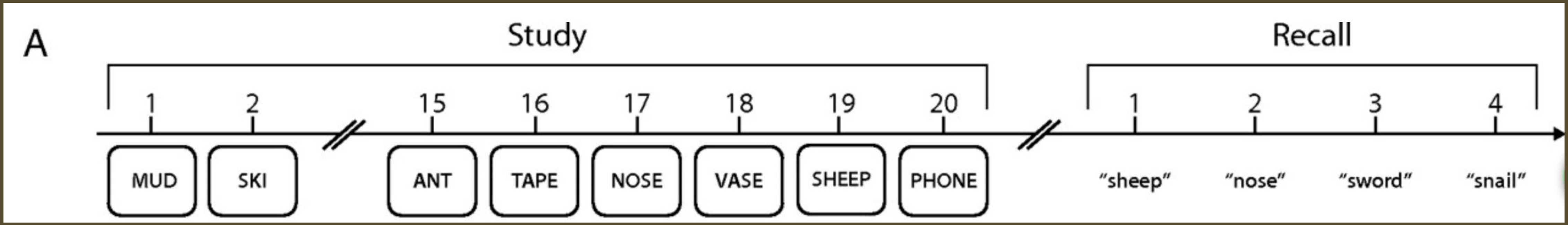
Recall: Temporally contiguous?

COUCH
ORANGE
BOOK
APPLE
PARK
PHONE
BANANA
BOTTLE
GRAPE
PLANT
DESK
PEACH

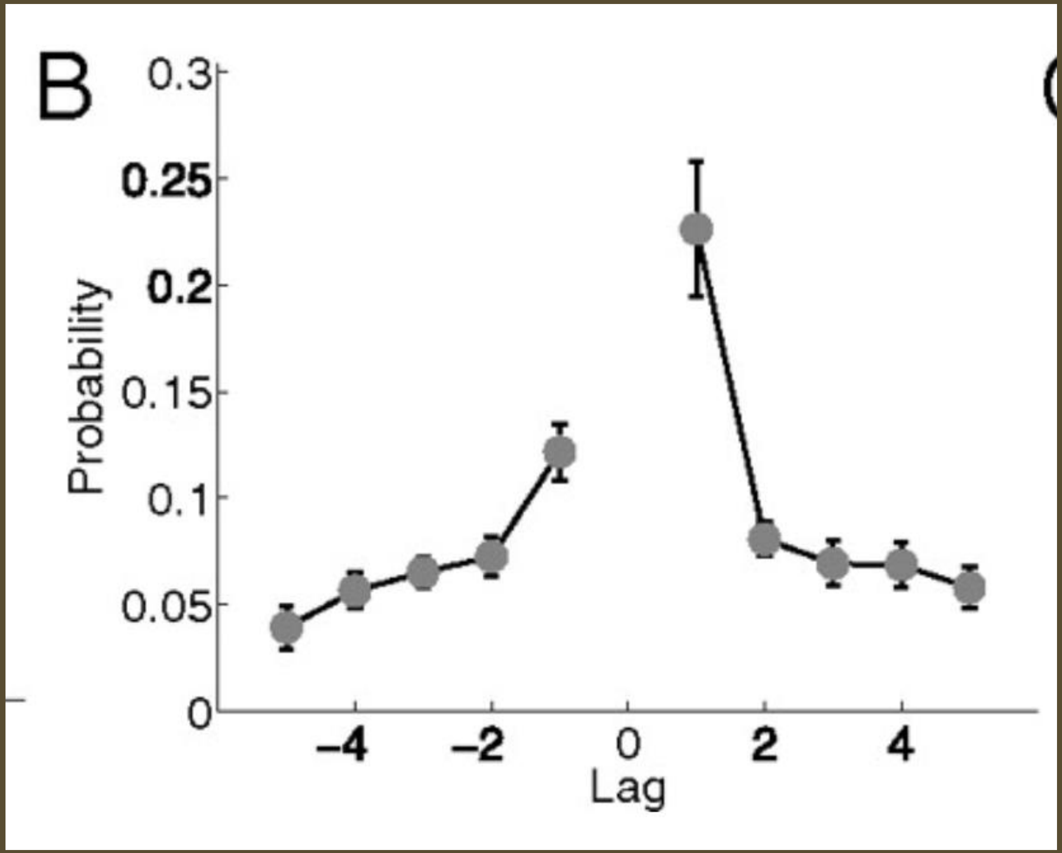
Recall: Grouped by semantic category?

COUCH
ORANGE
BOOK
APPLE
PARK
PHONE
BANANA
BOTTLE
GRAPE
PLANT
DESK
PEACH

Free Recall

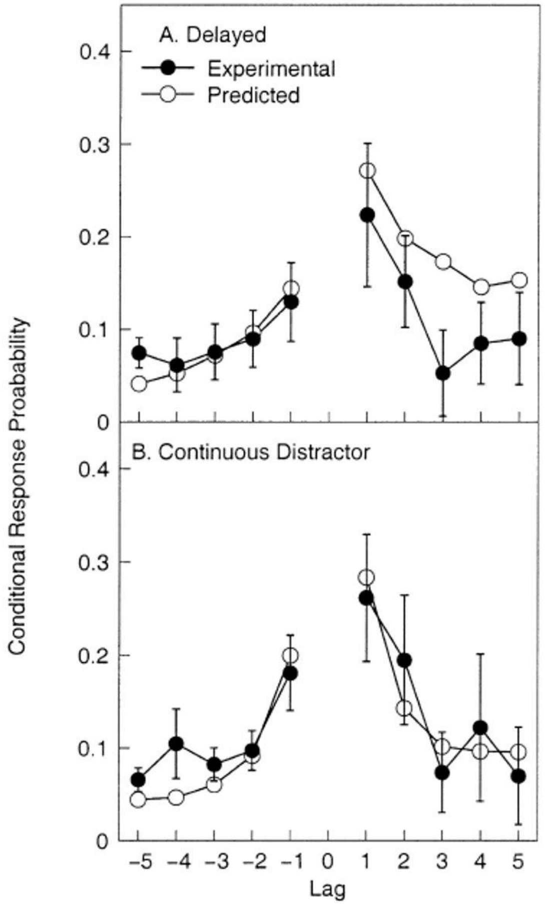

A
Study
Recall
1
2
15
16
17
18
19
20
MUD
SKI
ANT
TAPE
NOSE
VASE
SHEEP
PHONE
1
2
3
4
"sheep"
"nose"
"sword"
"snail"

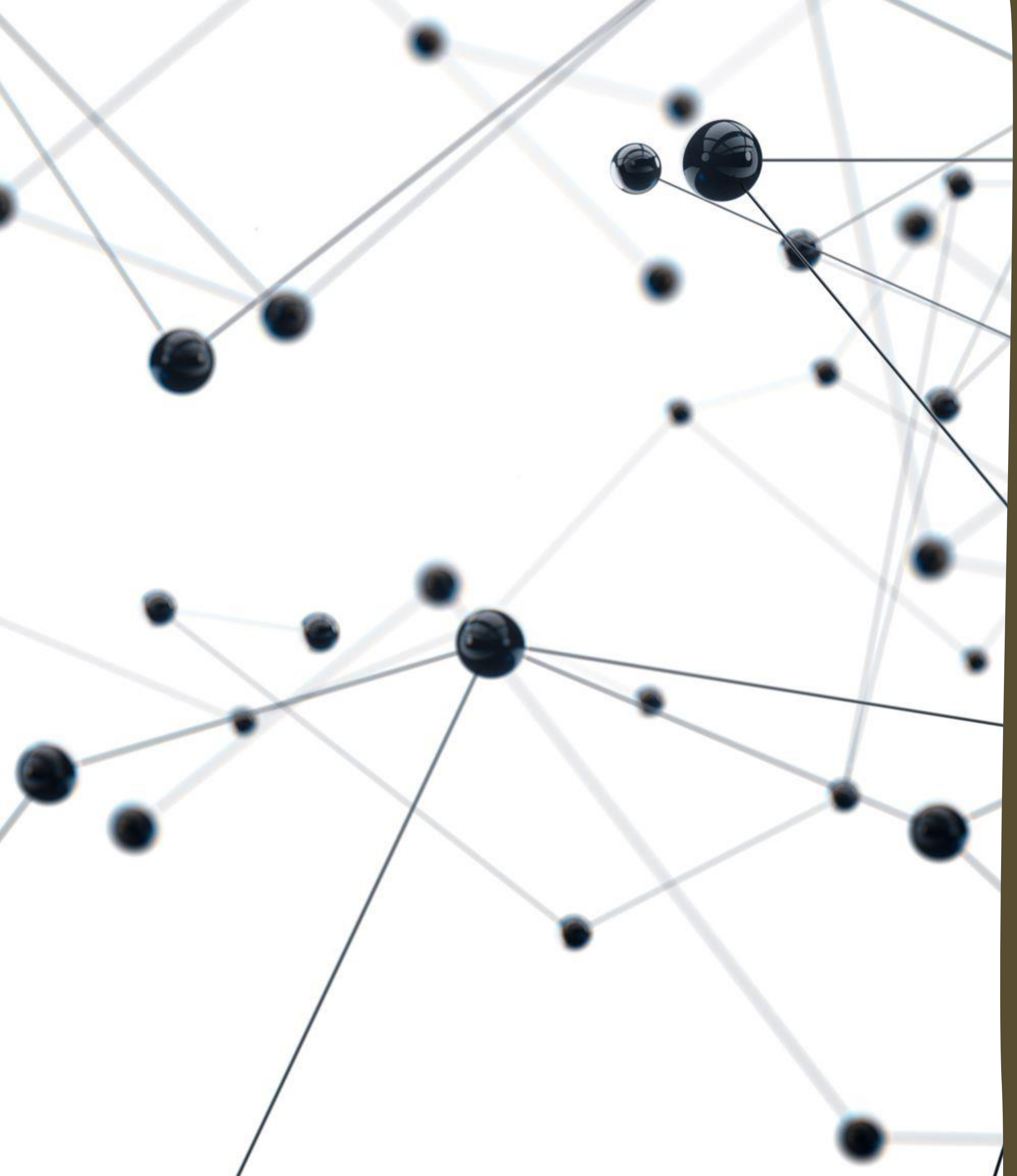
Lag-conditional response probability plot of free recall data: Indicates that we organize memories by their time of occurrence



Episodic memory retrieval is a cue-dependent process

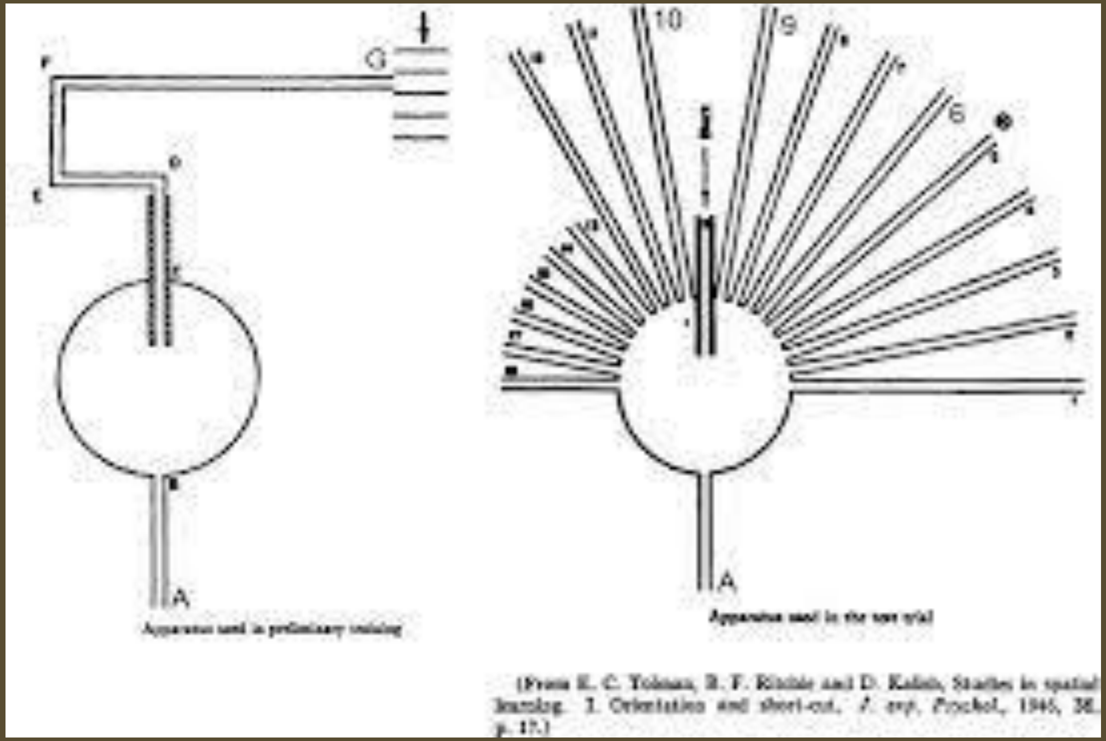
- Reflects:
  - semantic relatedness
  - Temporal contiguity



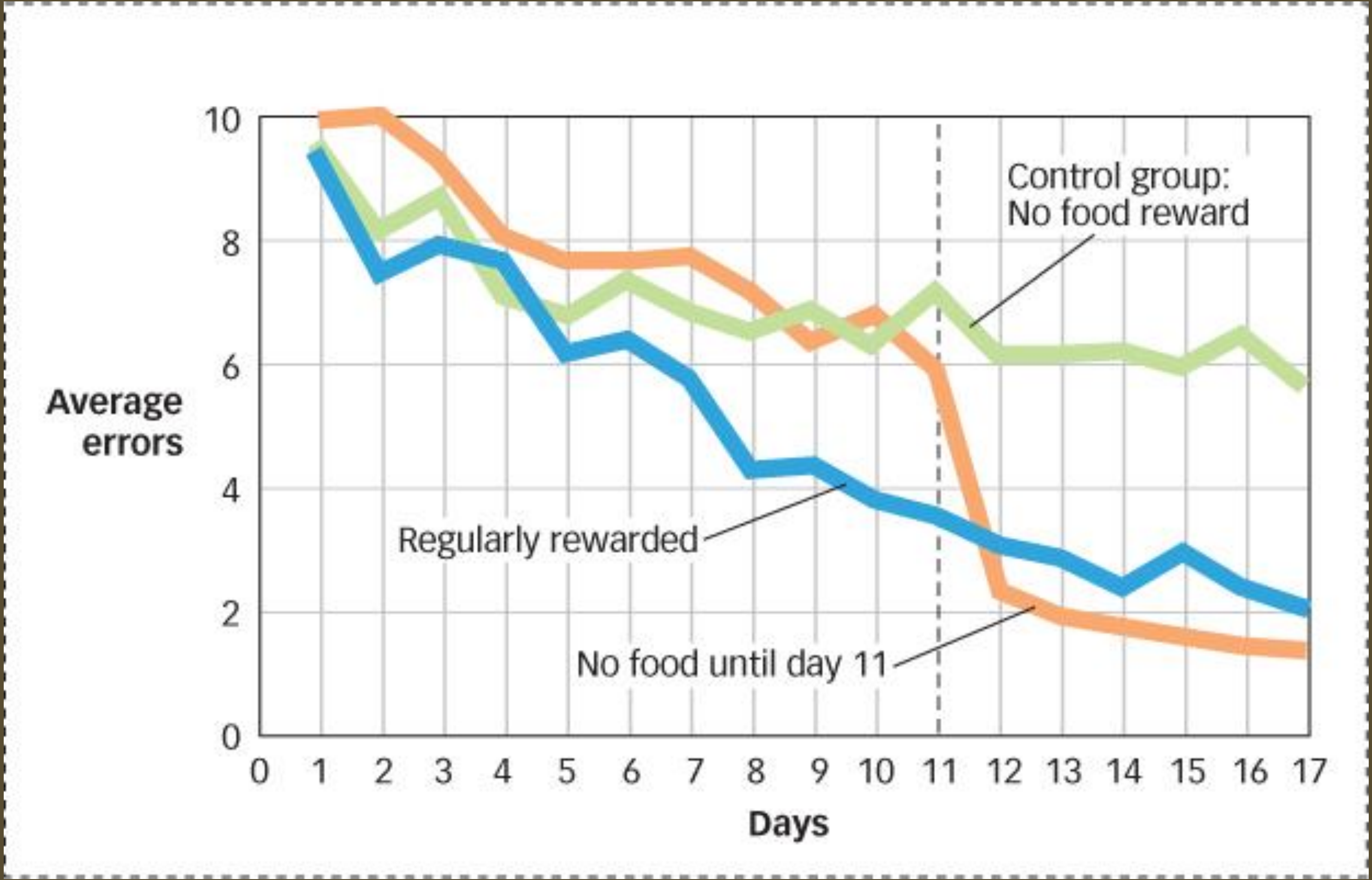


- Therefore, we organize memories based on where they occurred (space), when they occurred (time), their meanings (semantics), etc.
- What are the brain and neuronal bases for these different aspects (space, time, semantics)?

Cognitive Maps: Tolman et al. 1946



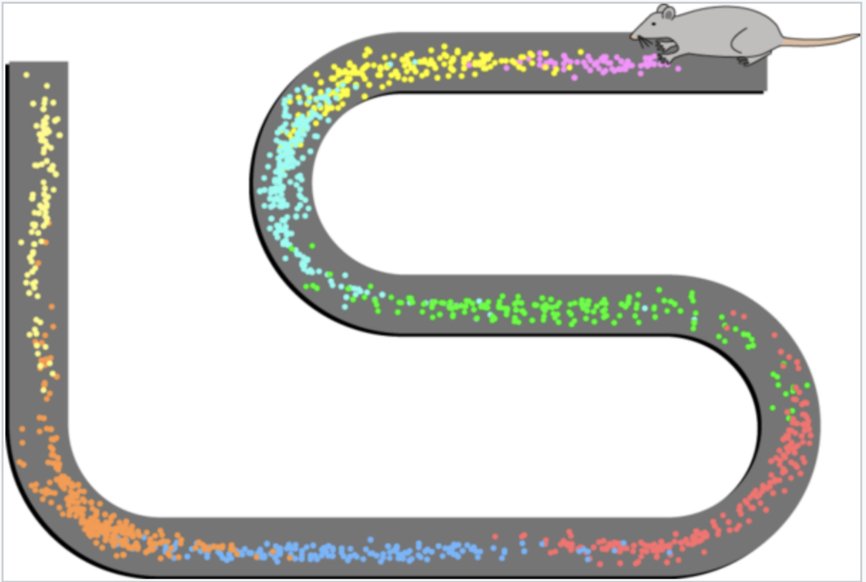
Latent Learning in a Maze



Space and memory: Place Cells!

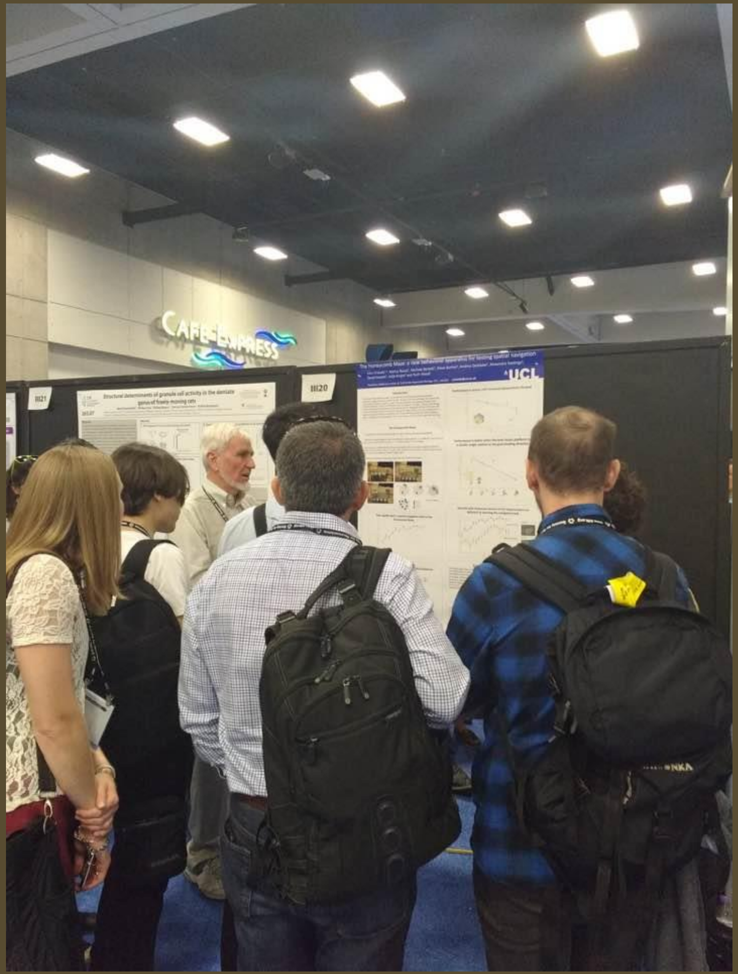
Won the 2014 Nobel prize for physiology – John O'Keefe!

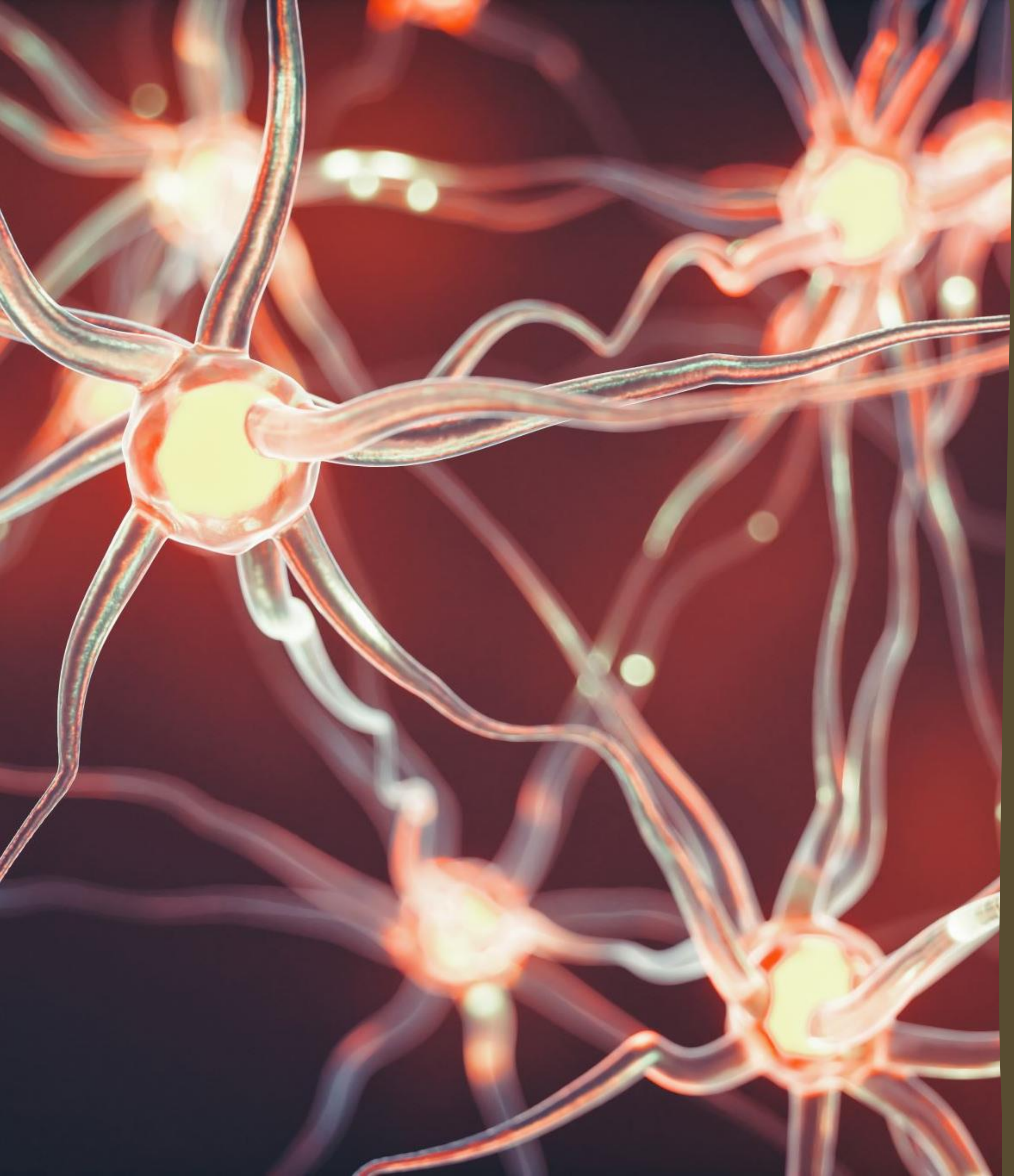
Video: https://www.youtube.com/watch?v=lfNVv0A8QvI&ab_channel=mwlmovies



Spatial firing patterns of 8 place cells recorded from the CA1 layer of a rat. The rat ran back and forth along an elevated track, stopping at each end to eat a small food reward. Dots indicate positions where action potentials were recorded, with color indicating which neuron emitted that action potential.

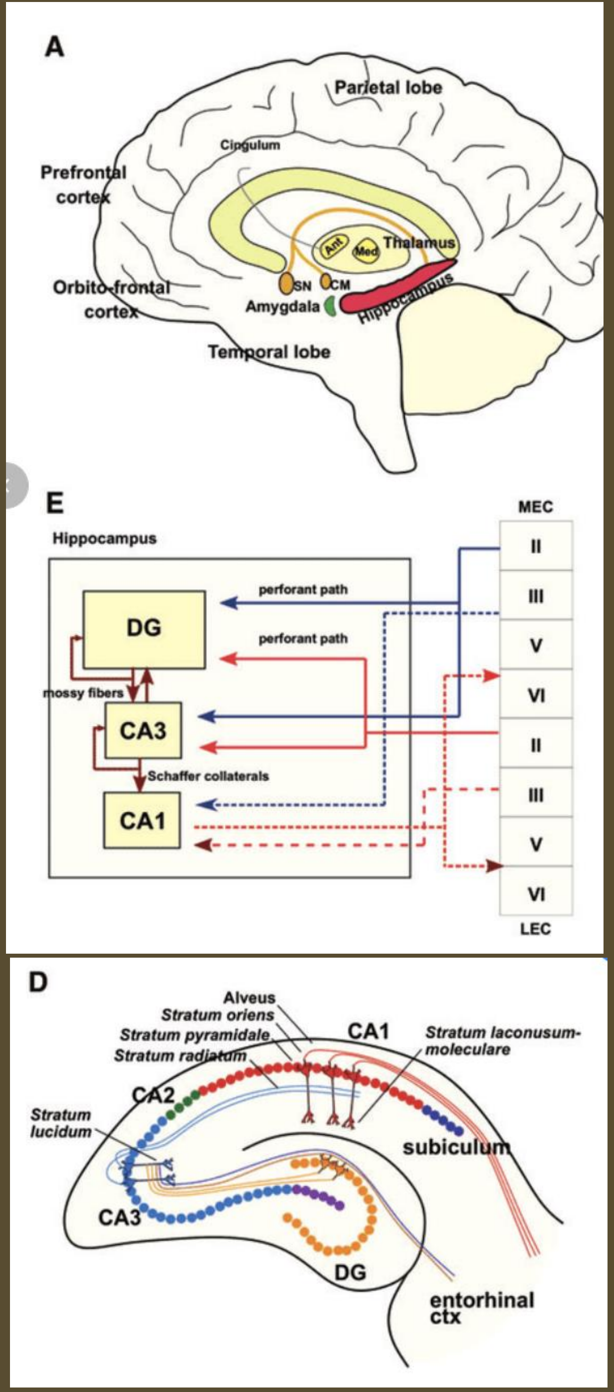
SfN - 2016





How do place cells come about?

- Unlike basic sensation, we do not have receptors for space!
- So how do these neurons know to fire at different locations?



To solve this mystery of how place cells arise, we can do lesion experiments (ablation studies)

- Brun et al., 2002: cut all within-hippocampus connections. E.g. no input to CA1 from CA3
- Place cells within CA1 continue to work!
- Did fine on associative spatial recognition.
- Impaired performance on spatial recall and navigating to specific places.
- CA3-CA1 connections therefore are necessary for recall but not associative recognition or the development of stable place cell fields.

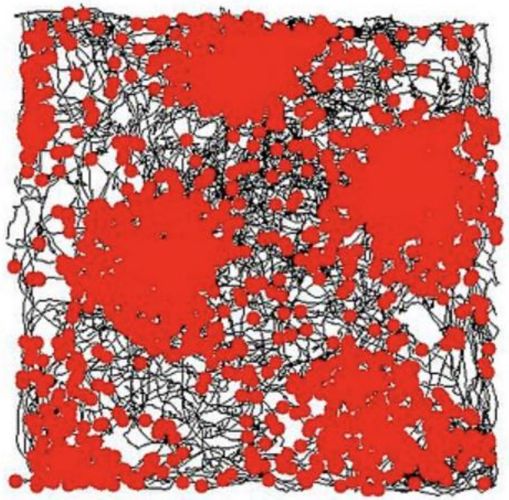
https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC6761599/

If the internal circuitry of the hippocampus is not the primary driver of place cells, we may have to look elsewhere

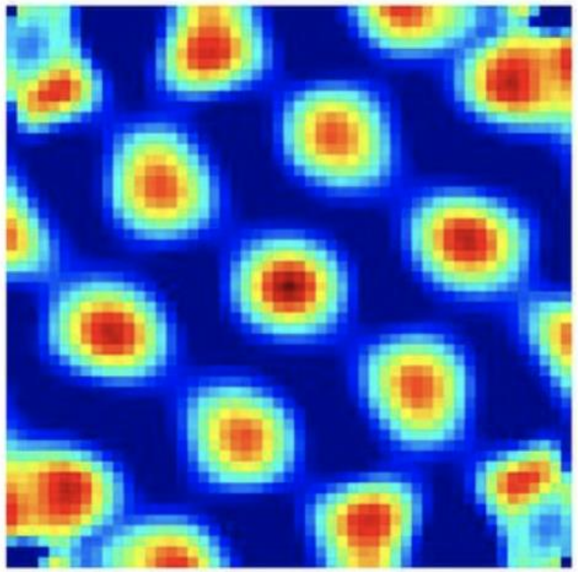
- The entorhinal cortical projections into the hippocampus?
- So people started looking at neurons in the entorhinal cortex.

More about space and memory: Grid Cells in the entorhinal cortex!

Also won the 2014 Nobel prize for physiology!



Trajectory of a rat through a square environment is shown in black. Red dots indicate locations at which a particular entorhinal grid cell fired.



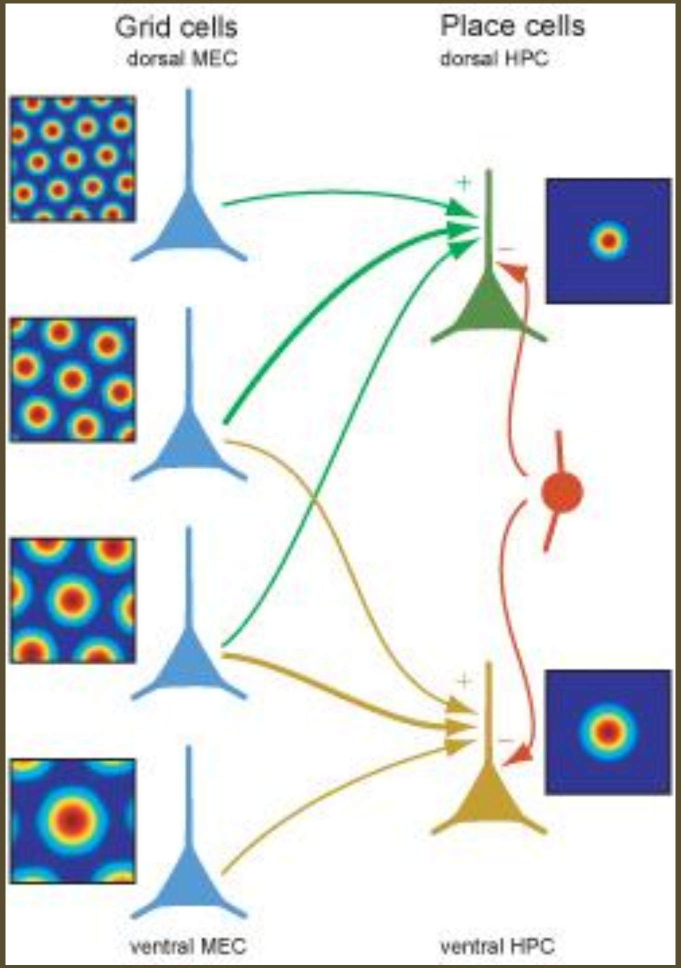
Spatial autocorrelogram of the neuronal activity of the grid cell from the first figure.

Images: Wikipedia

The relationship between place cells and grid cells

If hippocampal place cells are driven by periodic grid cells, why aren't place cells also periodic?

Ans: could lie in the variation of orientation and scale of the grid cells that project to each hippocampal place cell: linear summation would result in place fields that repeat over much larger spatial scales than can be measured in the lab!



Images: Wikipedia

Do grid cells drive place cells? Still an open question.

What do grid cells contribute to place cell firing?

Daniel Bush,[1,2] Caswell Barry,[3] and Neil Burgess[1,2]

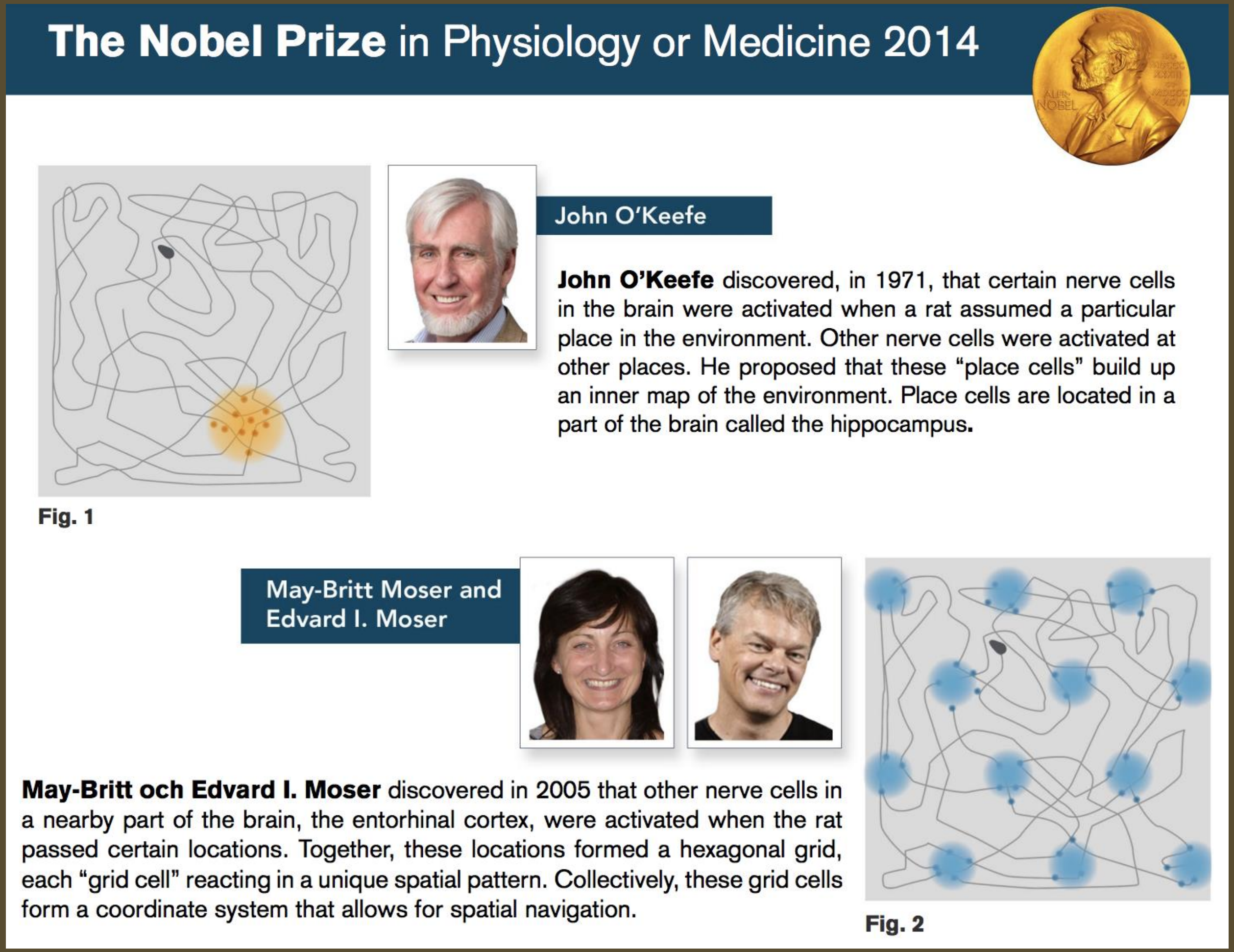
Author information Copyright and License information Disclaimer

Abstract

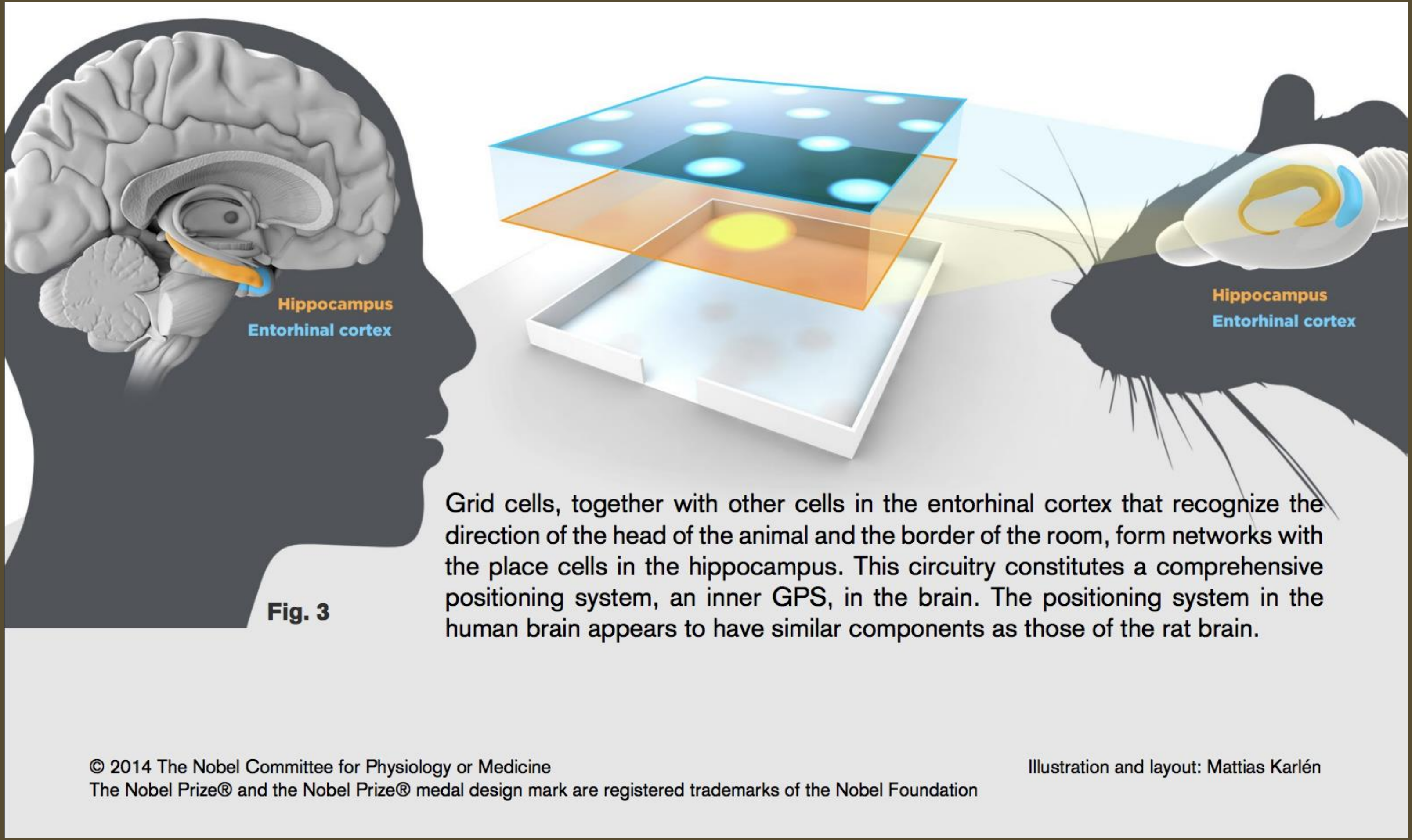
Go to:

The unitary firing fields of hippocampal place cells are commonly assumed to be generated by input from entorhinal grid cell modules with differing spatial scales. Here, we review recent research that brings this assumption into doubt. Instead, we propose that place cell spatial firing patterns are determined by environmental sensory inputs, including those representing the distance and direction to environmental boundaries, while grid cells provide a complementary self-motion related input that contributes to maintaining place cell firing. In this view, grid and place cell firing patterns are not successive stages of a processing hierarchy, but complementary and interacting representations that work in combination to support the reliable coding of large-scale space.

An internal GPS system: hippocampus + entorhinal cortex

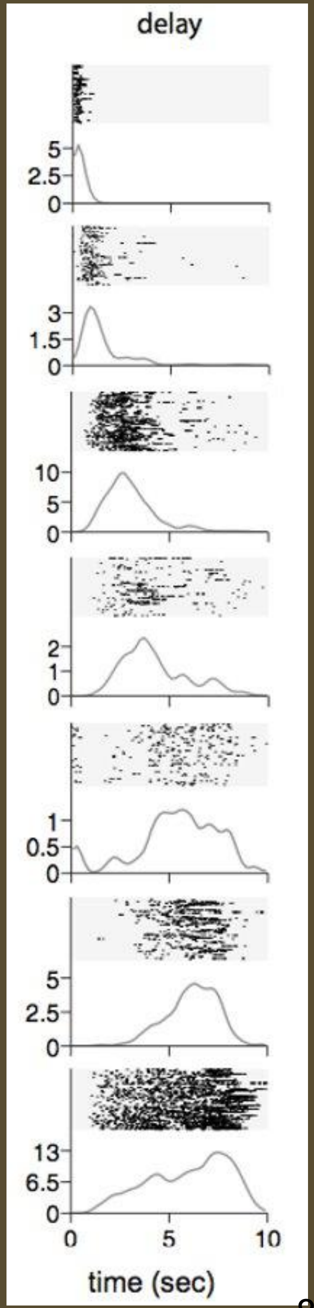


The internal GPS system: place cells, grid cells, head direction cells, boundary cells...

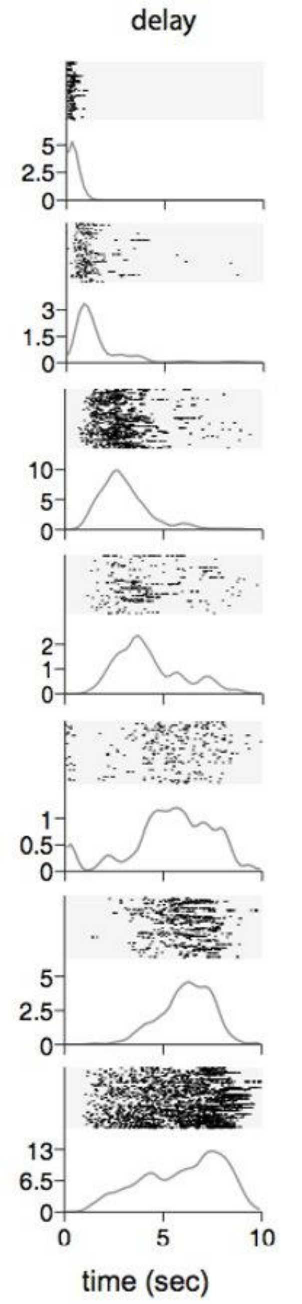


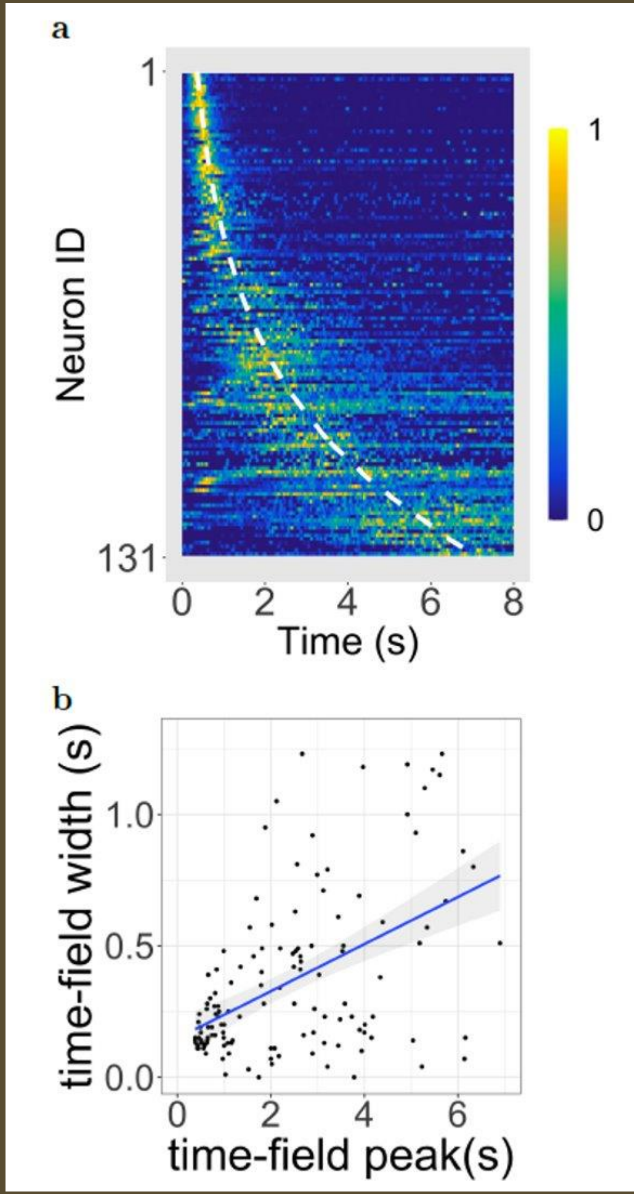
Time and memory: Time Cells!

- Neurons that fire at specific times within a blank delay period: time cells (MacDonald, Lepage, Eden, Eichenbaum, 2011, *Neuron*).
- Delayed match-to-sample experiment



Time and memory: Time Cells!





Time cells and place cells: Hippocampus

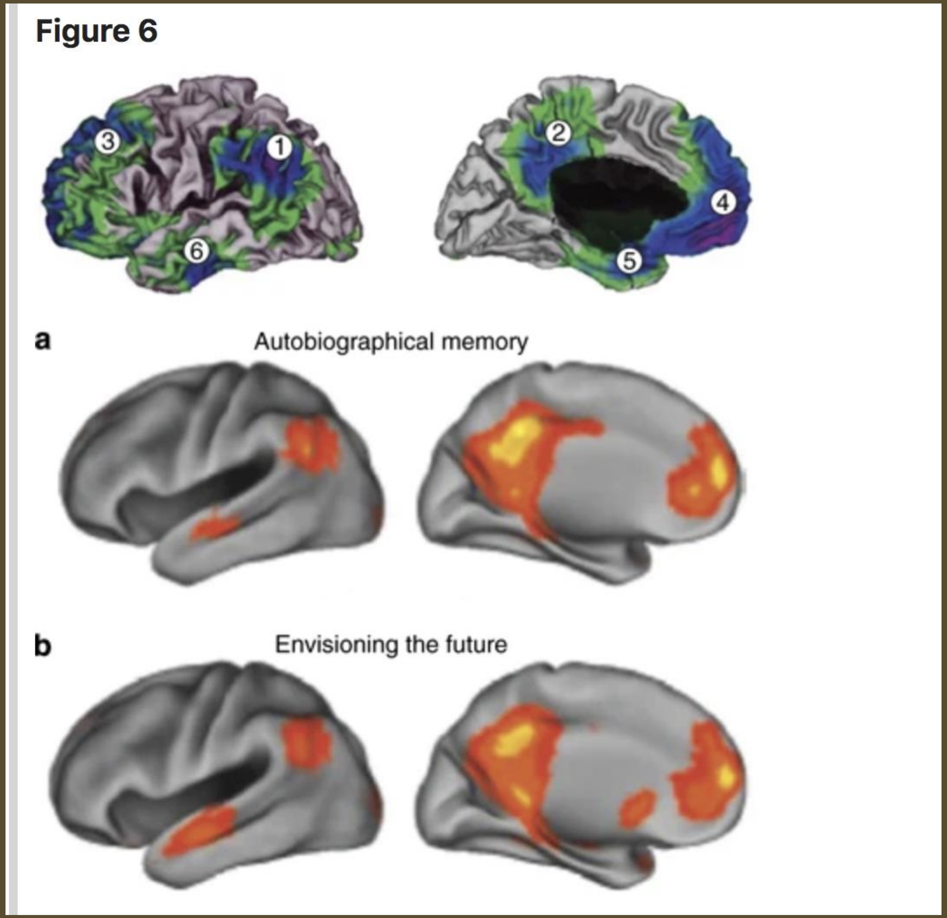
Grid cells and others: in nearby areas such as the entorhinal cortex

- However, there's more to memory than the hippocampus and surrounding structures!
- Humans have the most developed neocortex.
- Surely, the neocortex must be doing some heavy lifting!

The default mode network (DMN)

- Parietal Posterior Cingulate/precuneus
- Dorsolateral prefrontal
- Medial prefrontal
- Medial temporal
- Rostrolateral temporal

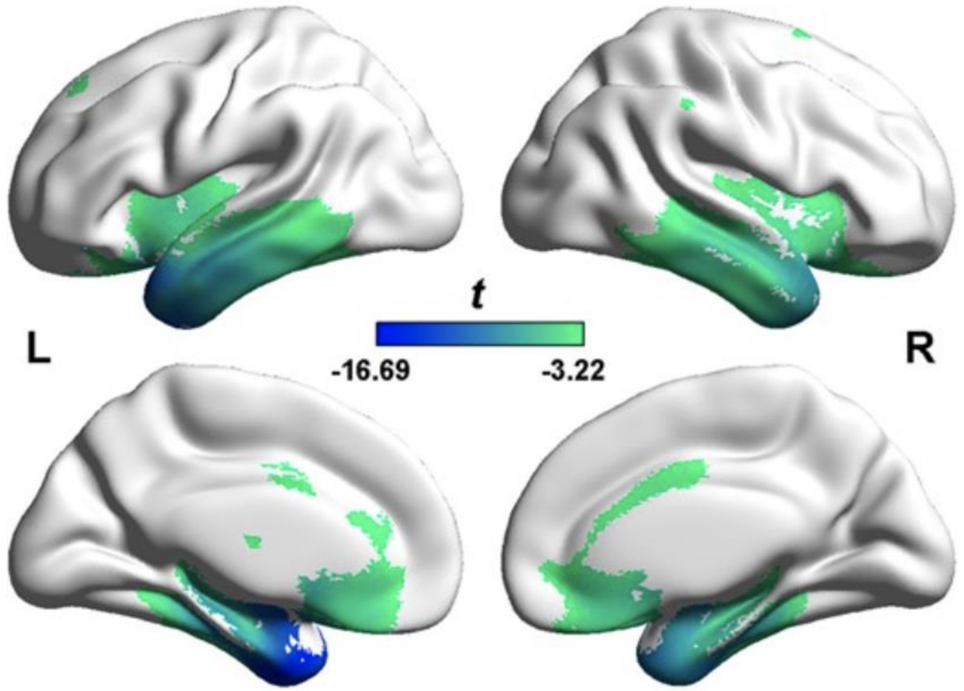
- Typically deactivates in many types of tasks but activates above baseline in autobiographical memory search and future thinking
- Alzheimer's... some of the first nodes to be affected.



Semantics

Most gray matter volume difference in the ATL (anterior temporal lobe).

Figure 1

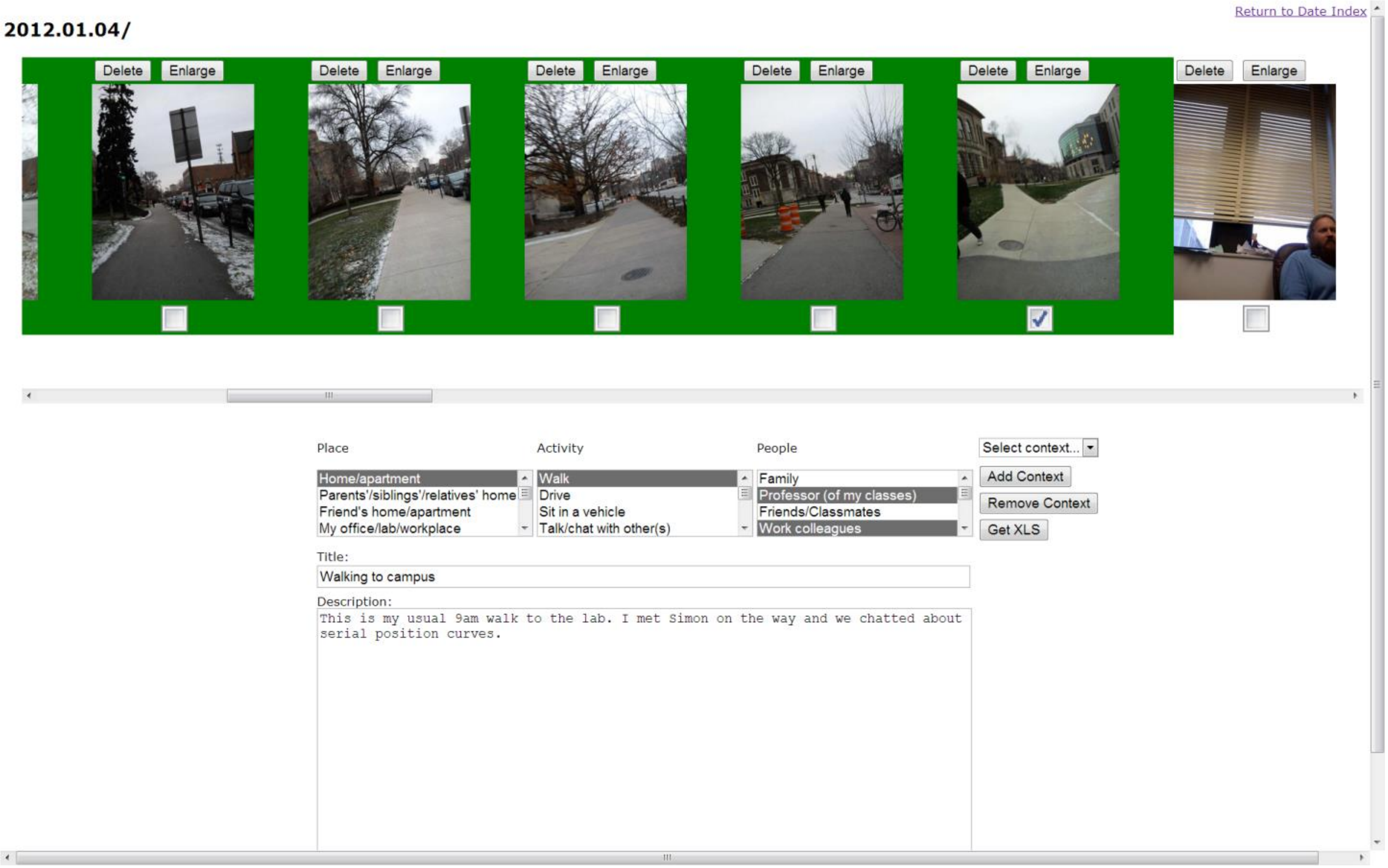


Open in new tab

Download slide

Atrophy map of the semantic dementia patients. The figure shows the areas with significant differences in grey matter volume between the semantic dementia patients and healthy control subjects (FDR-corrected *q*<0.01).

Space and time in the real world: Experience Sampling



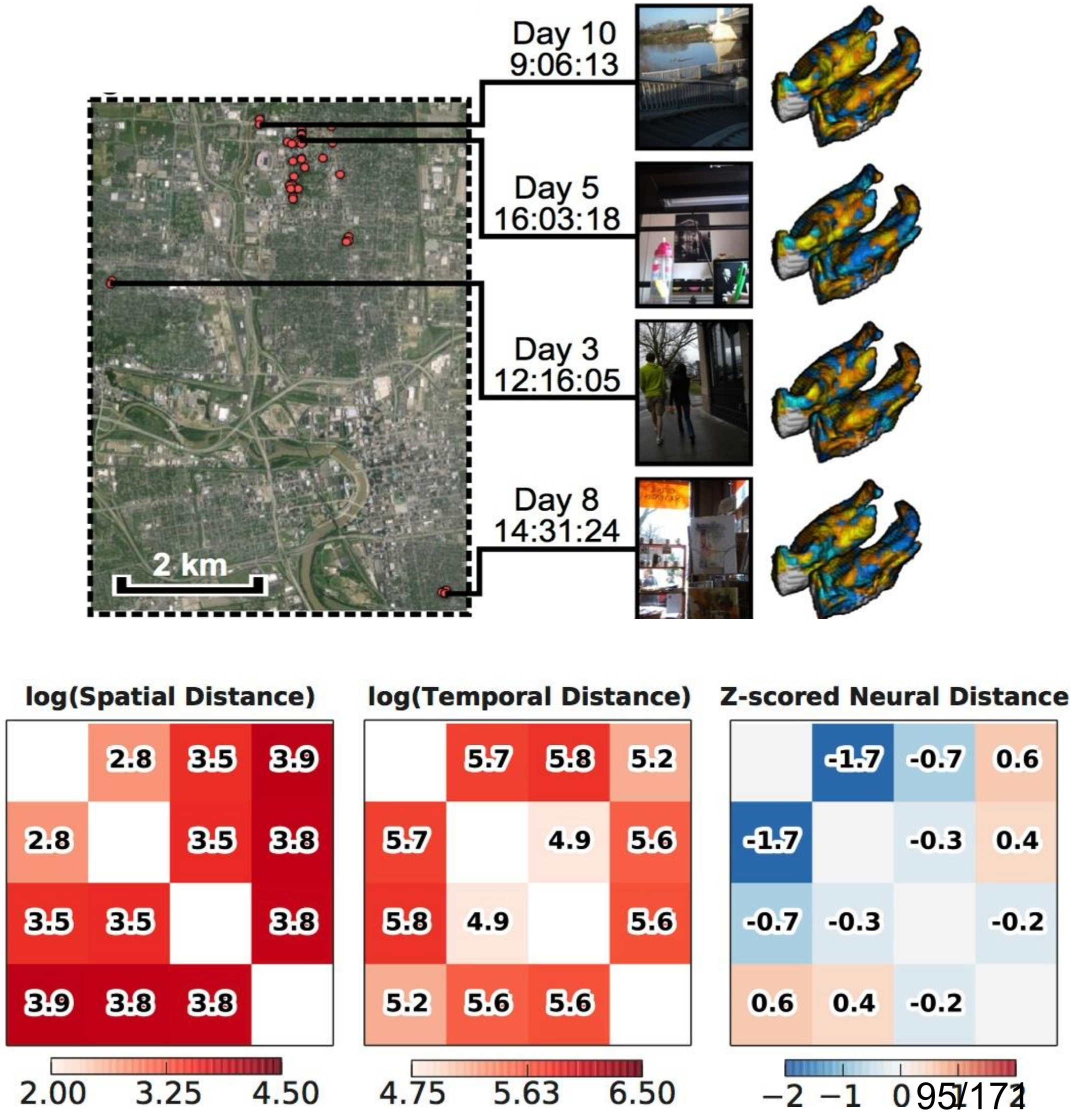
- Images
- Accelerometry
- GPS
- Obfuscated audio
- Orientation
- Time

Dennis, Yim, Garrett, Sreekumar, Stone, *Behavior Research Methods*, 2019.

Tracking space and time in the human brain

Experience Sampling
(2-4 weeks)

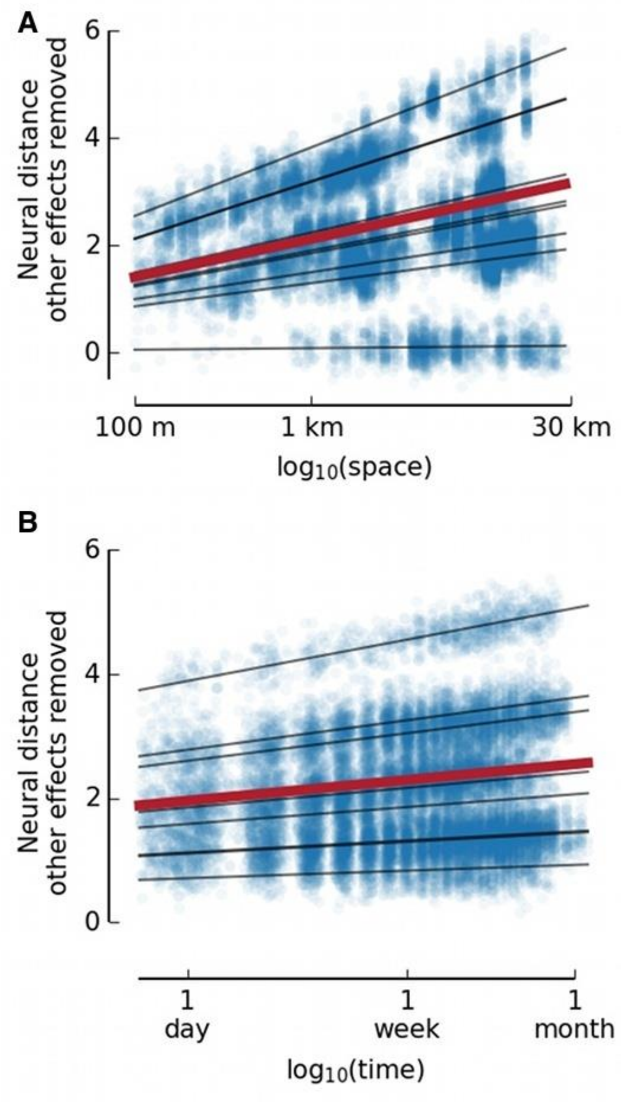
Reminiscence Task
in fMRI



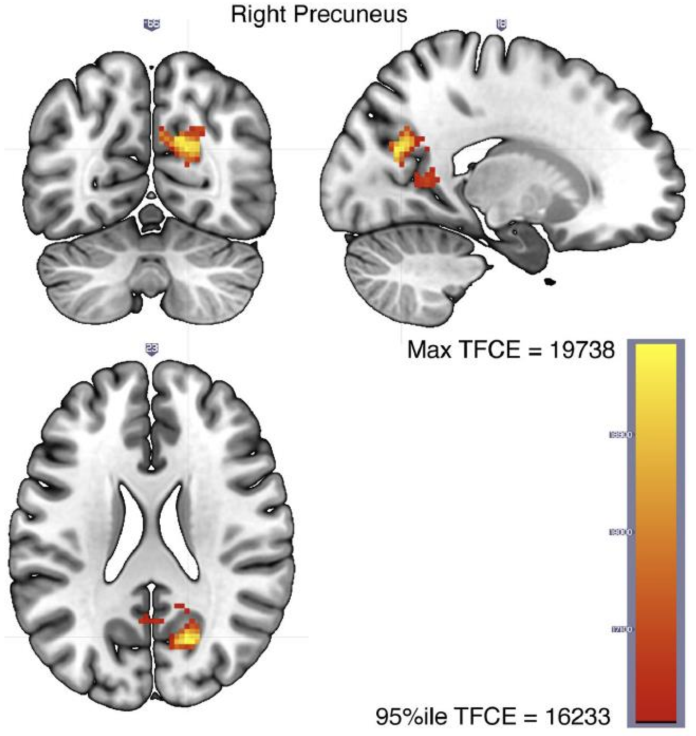
Nielson, Smith, Sreekumar, Dennis, & Sederberg, 2015, *PNAS*
Sreekumar, Nielson, Smith, Dennis, & Sederberg, 2018, *Scientific Reports*

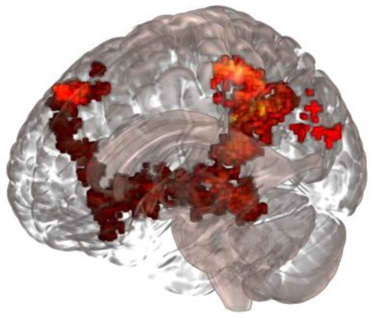
Mapping context similarity to neural activation patterns

Spatial and temporal contexts



Personal semantic contexts



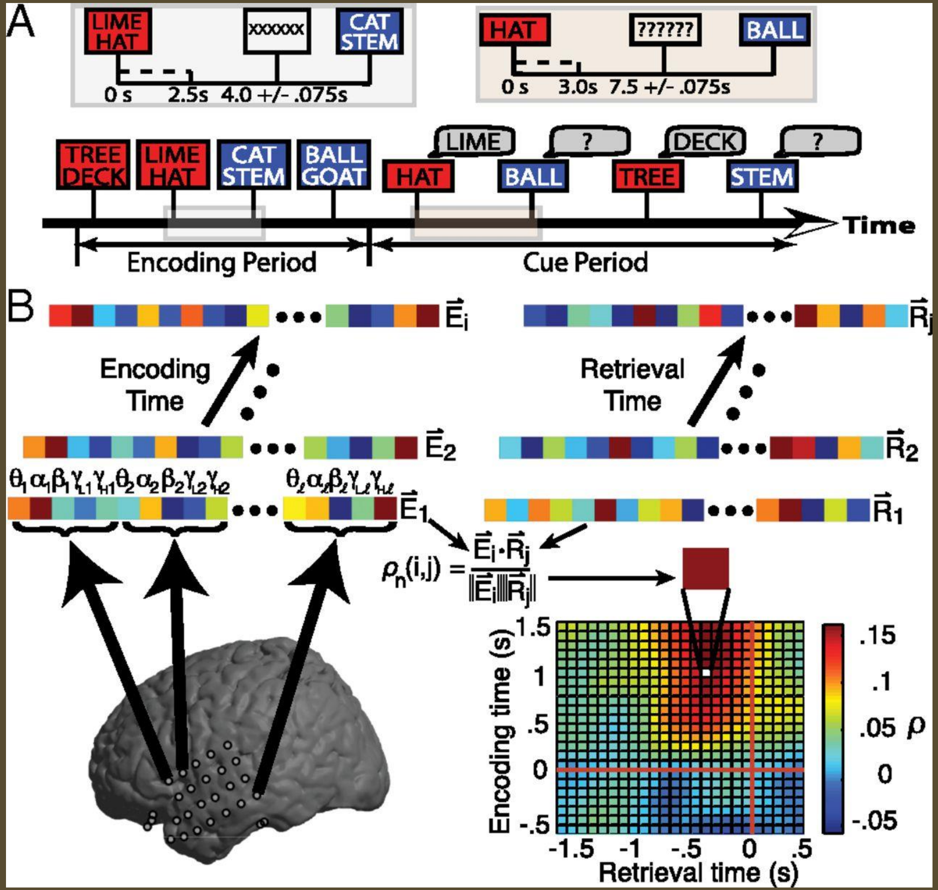


Nielson, Smith, Sreekumar, Dennis, & Sederberg, 2015, *PNAS*

Sreekumar, Nielson, Smith, Dennis, & Sederberg, 2018, *Scientific Reports*

What happens in the brain when you remember?

- Neural patterns that were present at encoding tend to be "reinstated"



Robert B. Yaffe et al. PNAS 2014;111:52:18727-18732

The "engram"

- Richard Semon, evolutionary zoologist: 1904 coined the term
- Experience --> enduring chemical and physical changes in the brain
- Reactivation of this "engram" in the brain --> memory

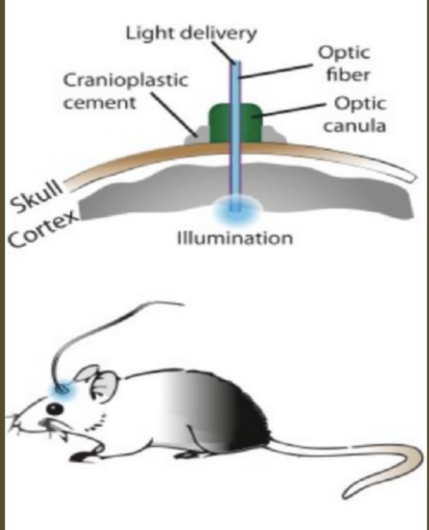
https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC7577560/
Highly recommended paper to read.

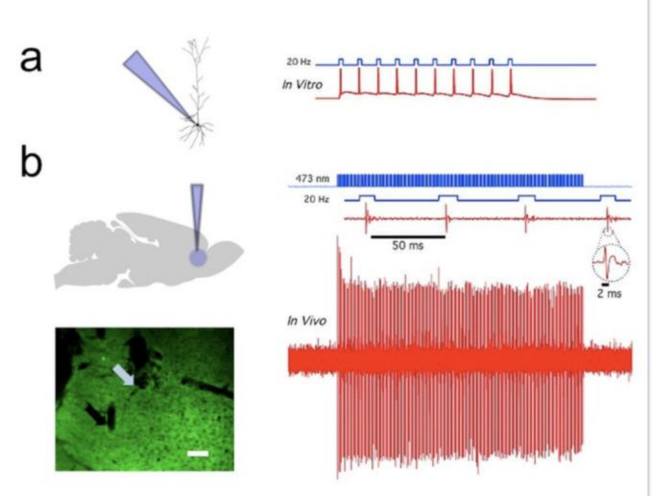
Karl Lashley – The search for the memory engram, a failed attempt after 30 years of looking!

- Rats
- Trained on mazes
- Removed different cortical regions
- Varying sizes
- Size of region removed correlated with memory impairment but the location did not
- Lashley gave up and called the engram "elusive"

Next in the search of the engram: Donald Hebb

- Lashley's student
- Cell assembly theory: interconnected neurons that are co-active during an experience form a "cell assembly".
- Connections get strengthened with sufficient activity within the assembly
- "Neurons that fire together, wire together" - Hebbian rule.
- Cell assembly: capable of pattern completion (partial input)
- Cell assembly: graceful degradation of a memory if part of the assembly is destroyed





We finally have the technology to look for these assemblies at the level of single neurons

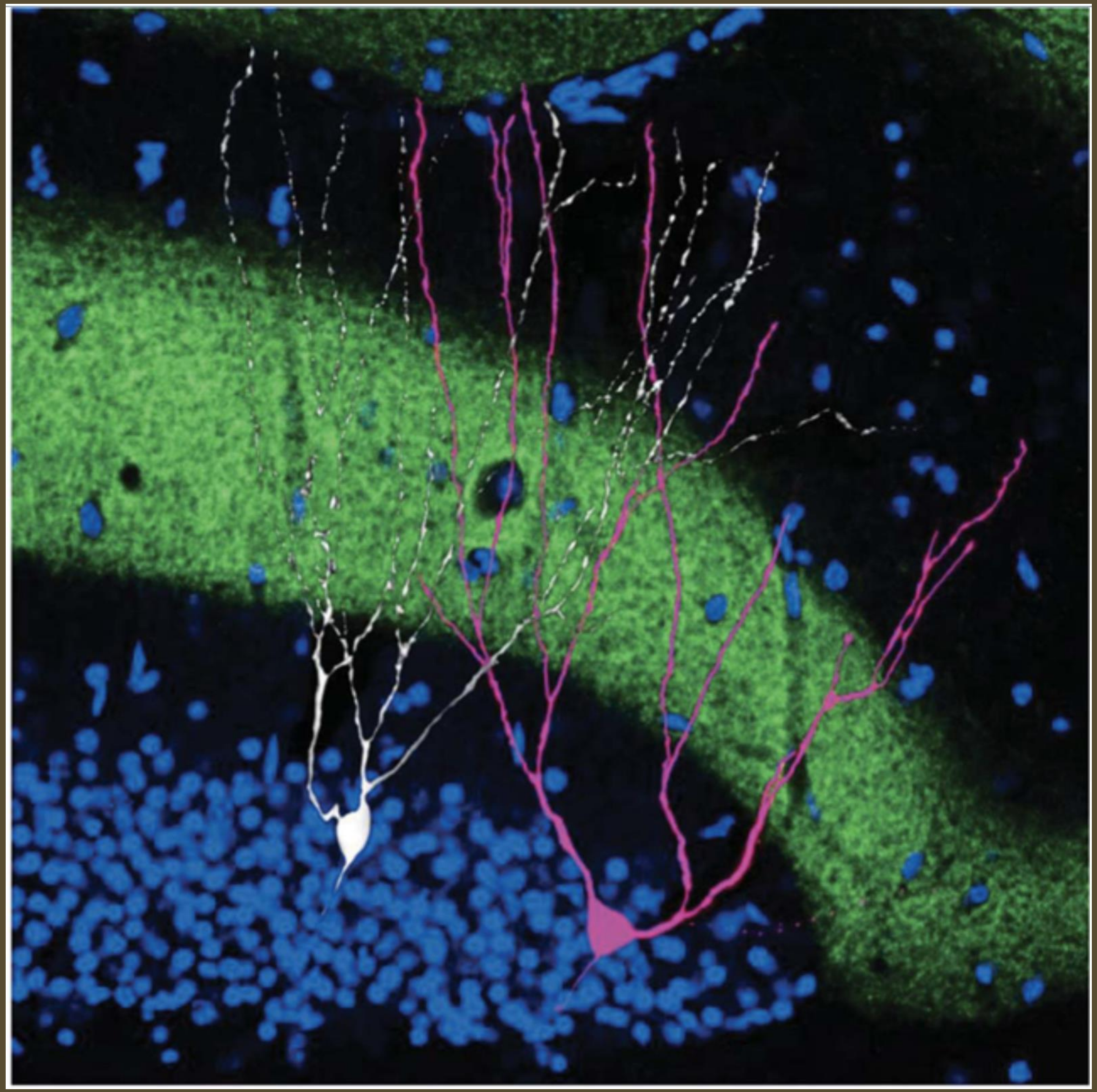
- Optogenetics.
- Predisposing certain neurons to be incorporated into engrams using neurotropic viruses that increase excitability of neurons.
- And many more..

Images: Wikipedia

Engram cell (pink)

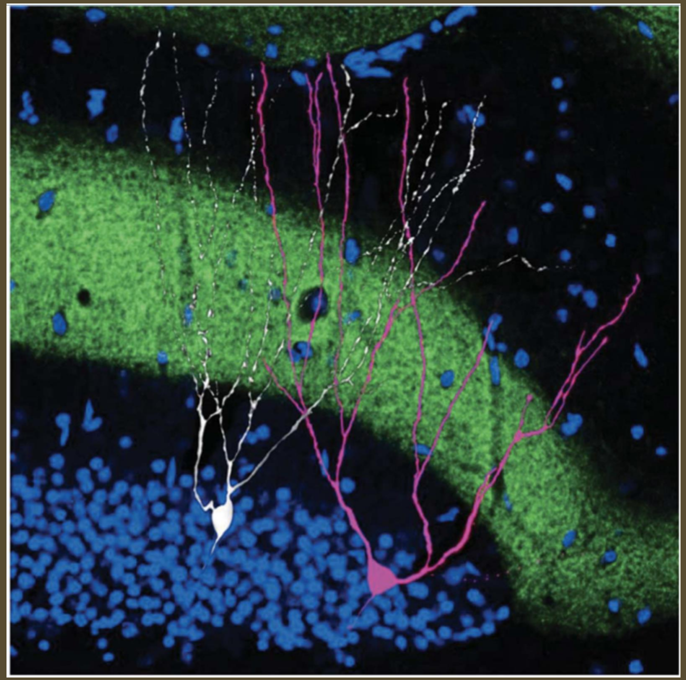
Engram cells are:

1. activated by a learning experience
2. physically or chemically modified by the learning experience
3. reactivated by subsequent presentation of the stimuli present at the learning experience (or some portion thereof), resulting in memory retrieval.



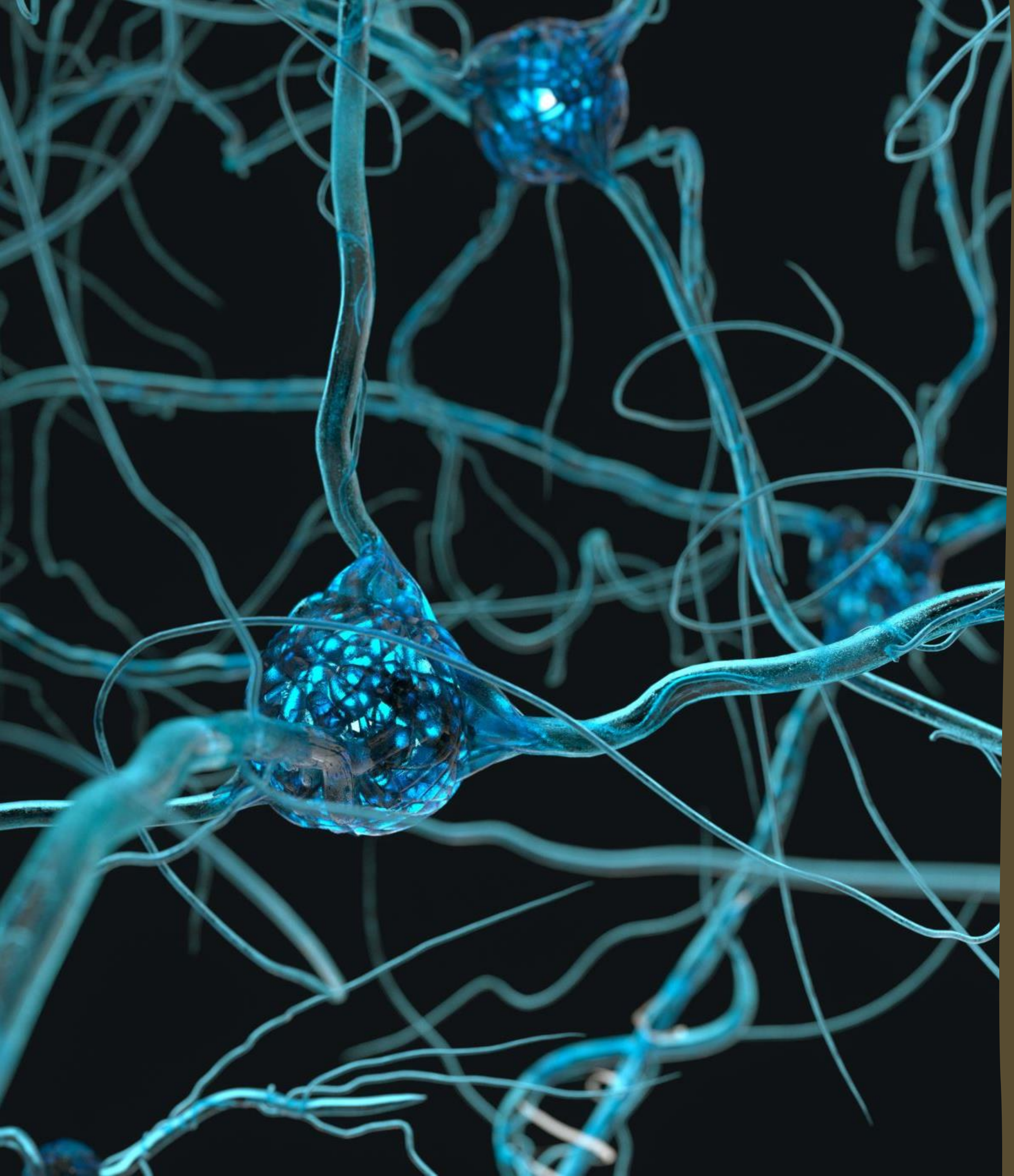
https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC7577560/

Engram cells: Evidence?



1. The same (or overlapping) cell populations are activated both by an experience and by retrieval of that experience with long-lasting changes in these cells.
2. Loss-of-function studies should show that impairing engram cell function after an experience impairs subsequent memory retrieval.
3. Gain-of-function studies should show that artificially activating engram cells induces memory retrieval, in the absence of any natural sensory retrieval cues.
4. Mimicry studies should artificially introduce an engram of an experience that never happened into the brain and show that rodents use the information of an artificial engram to guide behavior.

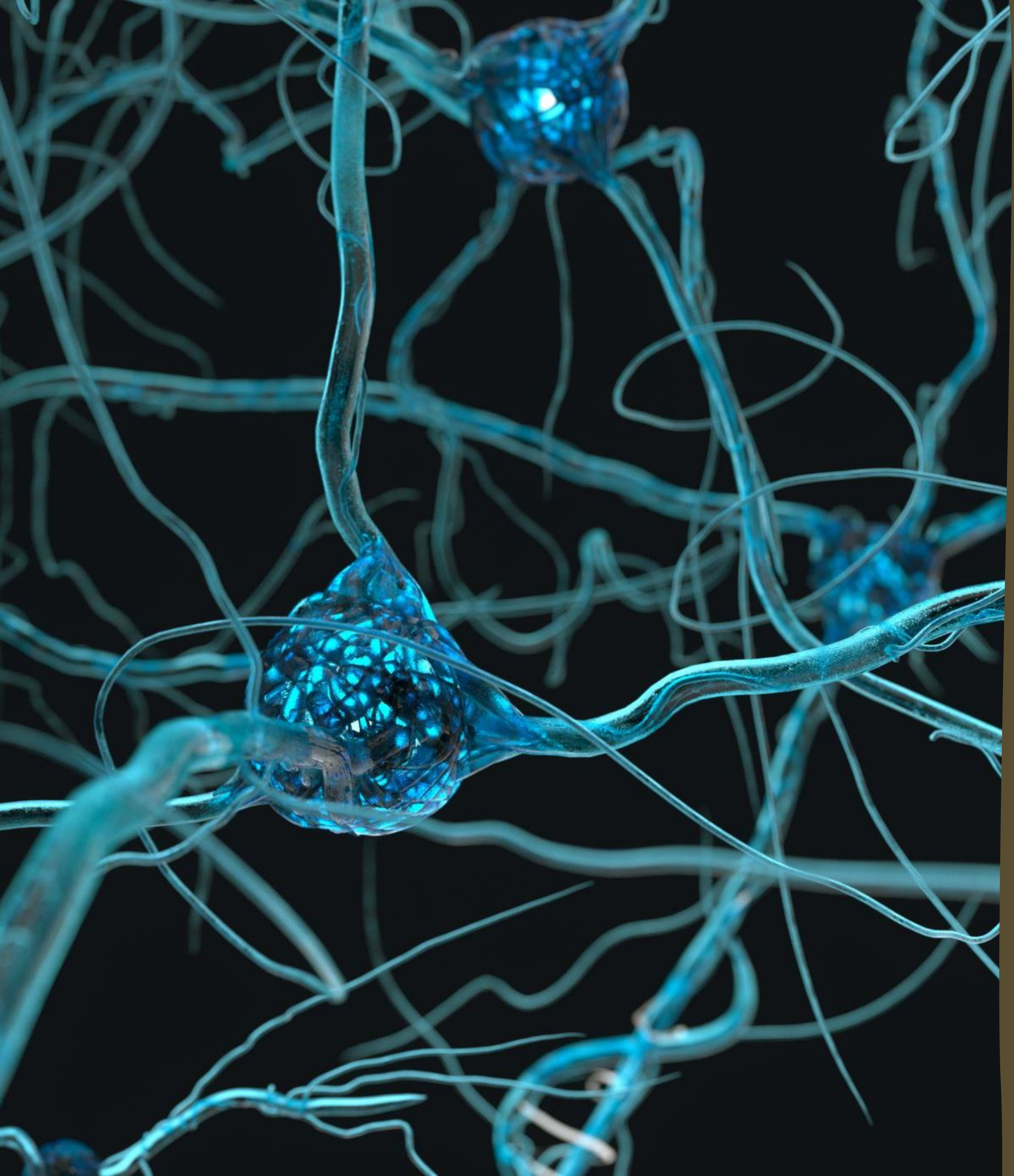
https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC7577560/



Some new evidence for memory "engrams"

1. Reactivation of neurons involved in the original experience

- "Tag" neurons active during a memory task
- Later: the tagged neurons are more active than others during remembering

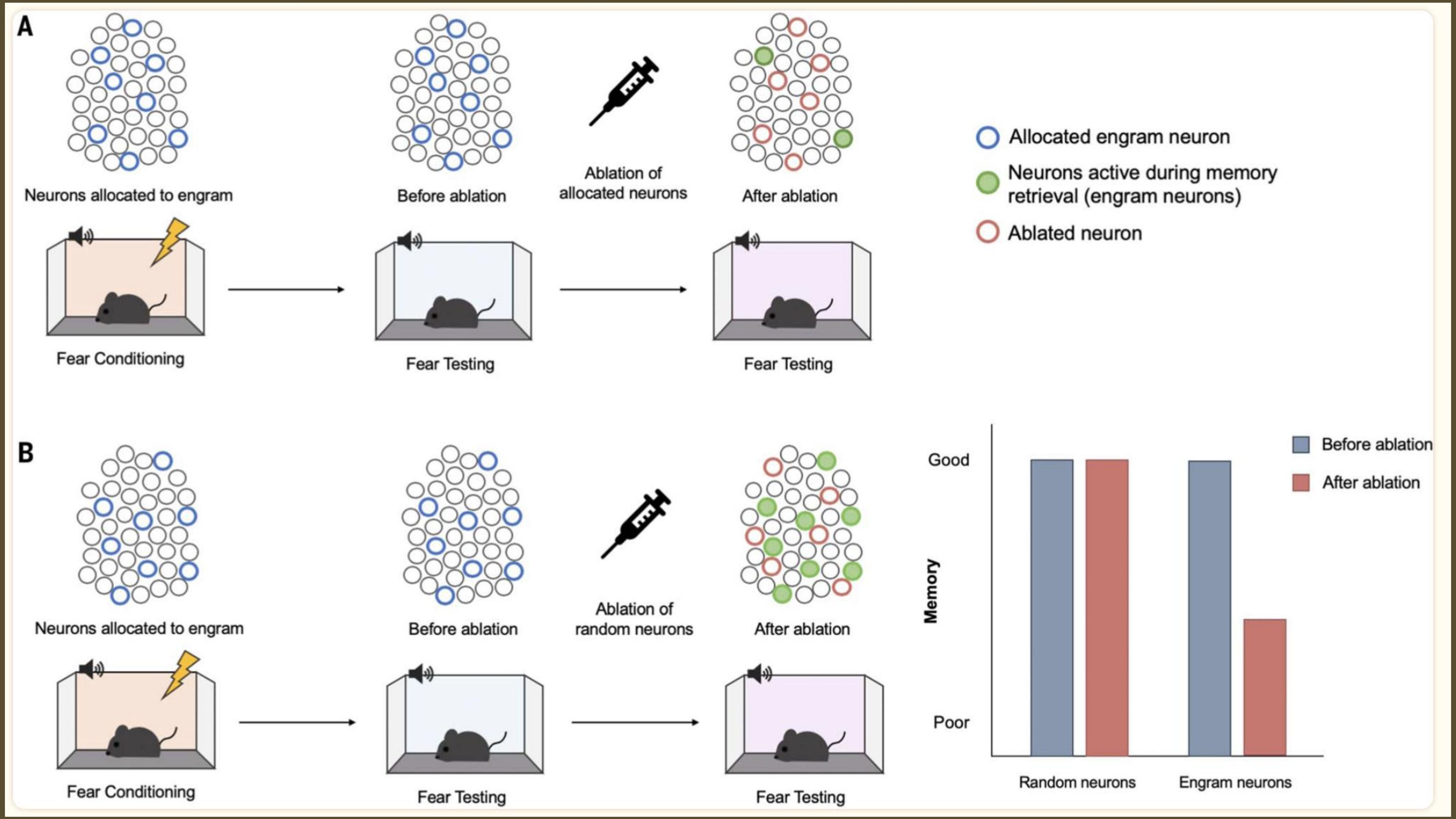


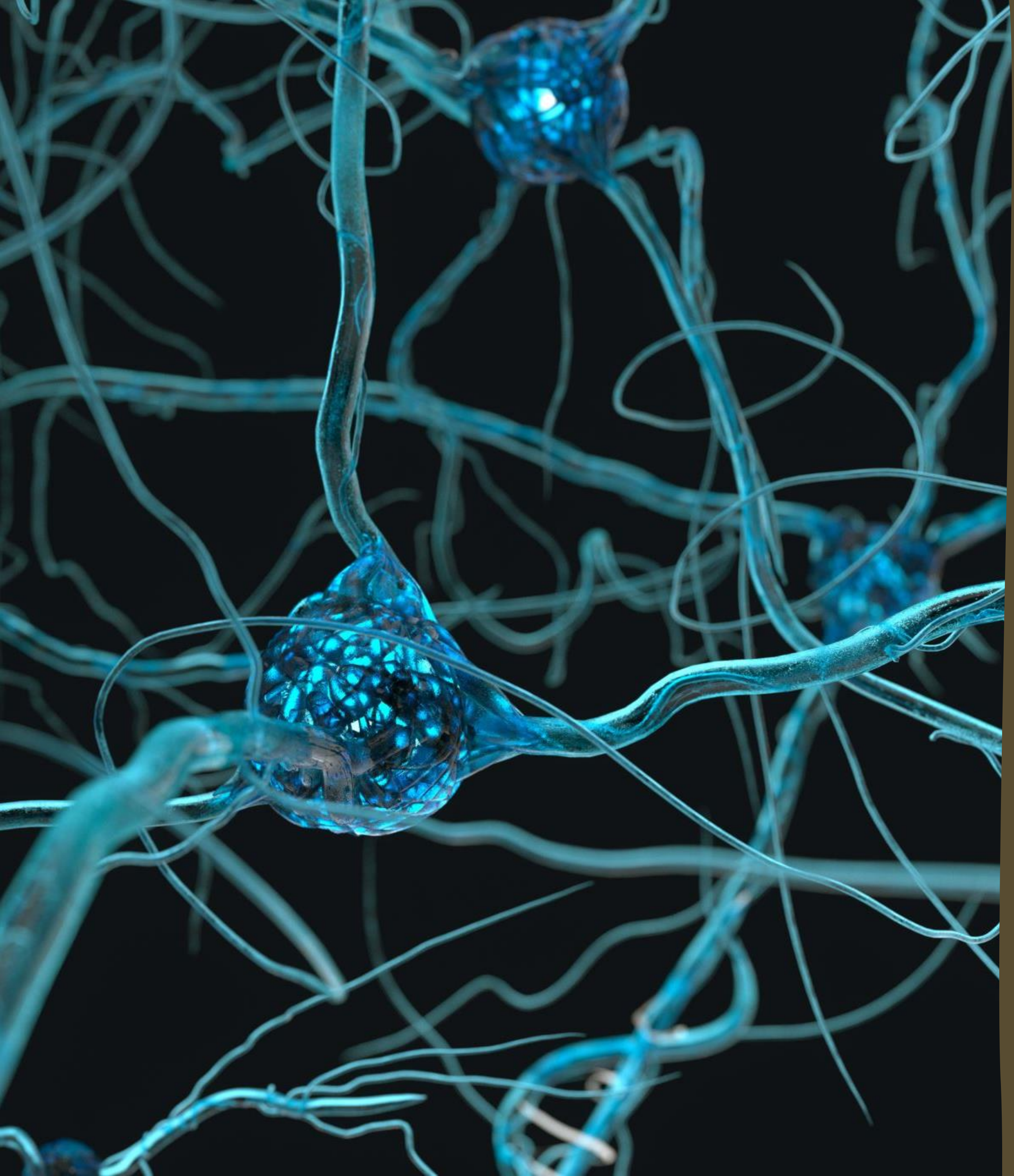
Some new evidence for memory "engrams"

2. Loss of function studies:

- some cells biased for inclusion into an engram using neurotropic viruses that express CREB (increases neuronal excitability).
- A fear memory was induced (loud tones --> freezing behavior)
- Later, when the engram cells were ablated, the mice stopped freezing --> their fear memory was erased!

Silence an engram, erase a fear memory!
Sheena Josselyn et al., Science, 2009





Some new evidence for memory "engrams"

3. Gain of function studies:

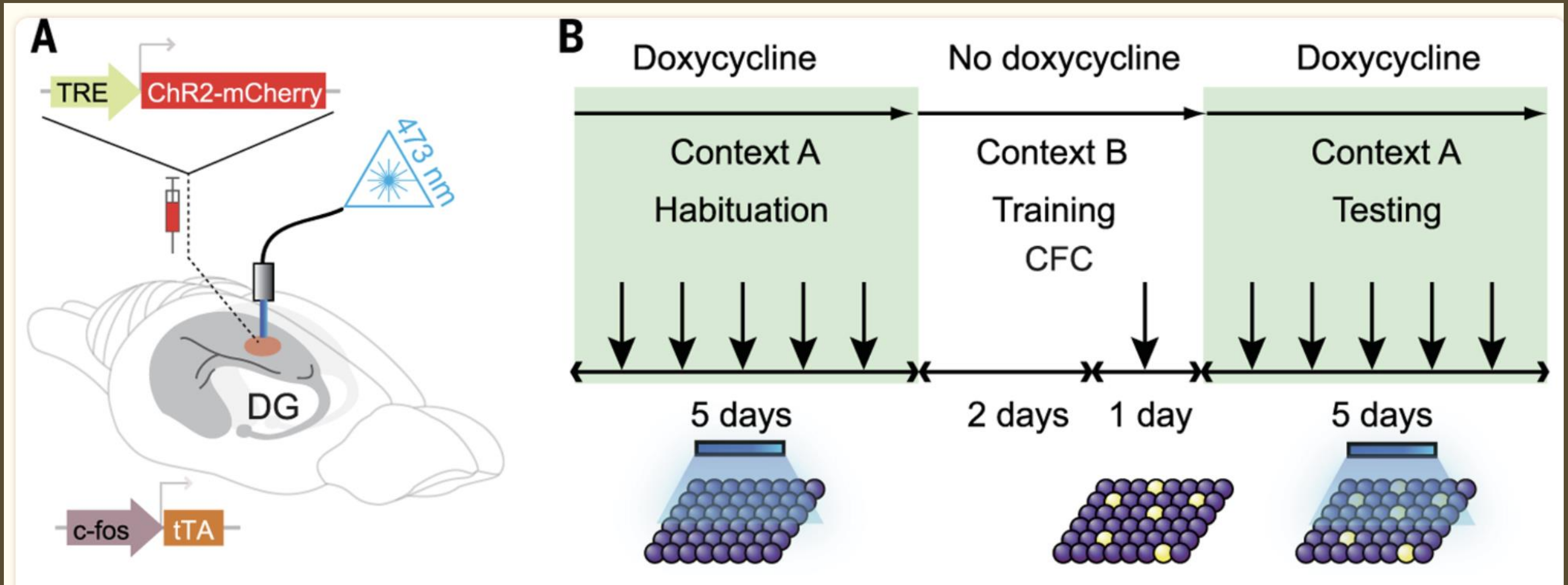
- Can I reactivate engram cells in your brain and make you think or remember a specific experience for which you have no other cue from the environment or otherwise?
- Liu X et al., Optogenetic stimulation of a hippocampal engram activates fear memory recall. *Nature* 484, 381–385 (2012).

Inducing an artificial memory

Habituation in context A

Context B = foot shocks and tag this fear engram cell population

Bring back to context A. Photostimulate: rats suddenly have fear memory in context A.



Can you implant a memory?!

If engrams exist, how would we go about attempting this?

Can you implant a memory?!

Published in final edited form as:
Nat Neurosci. 2019 June ; 22(6): 933–940. doi:10.1038/s41593-019-0389-0.

Memory formation in the absence of experience

Gisella Vetere[1,10], Lina M. Tran[1,2], Sara Moberg[1], Patrick E. Steadman[1,3], Leonardo Restivo[1], Filomene G. Morrison[4,5], Kerry J. Ressler[6], Sheena A. Josselyn[1,2,3,7,8,*], Paul W. Frankland[1,2,3,7,9,*]

- Instead of using external stimuli for creating memories, can you use entirely intracranial means? That is, activating neurons that supposedly respond to different stimuli, and then try to form engrams?
- Odor + shock (external pairing, typical experiments)
- Here: optogenetically stimulate olfactory neurons + modulate inputs to ventral tegmental area known to mediate aversion or reward
- Now you can give this rat a certain neutral odor, never before trained externally, but it will exhibit aversion/attraction to it.

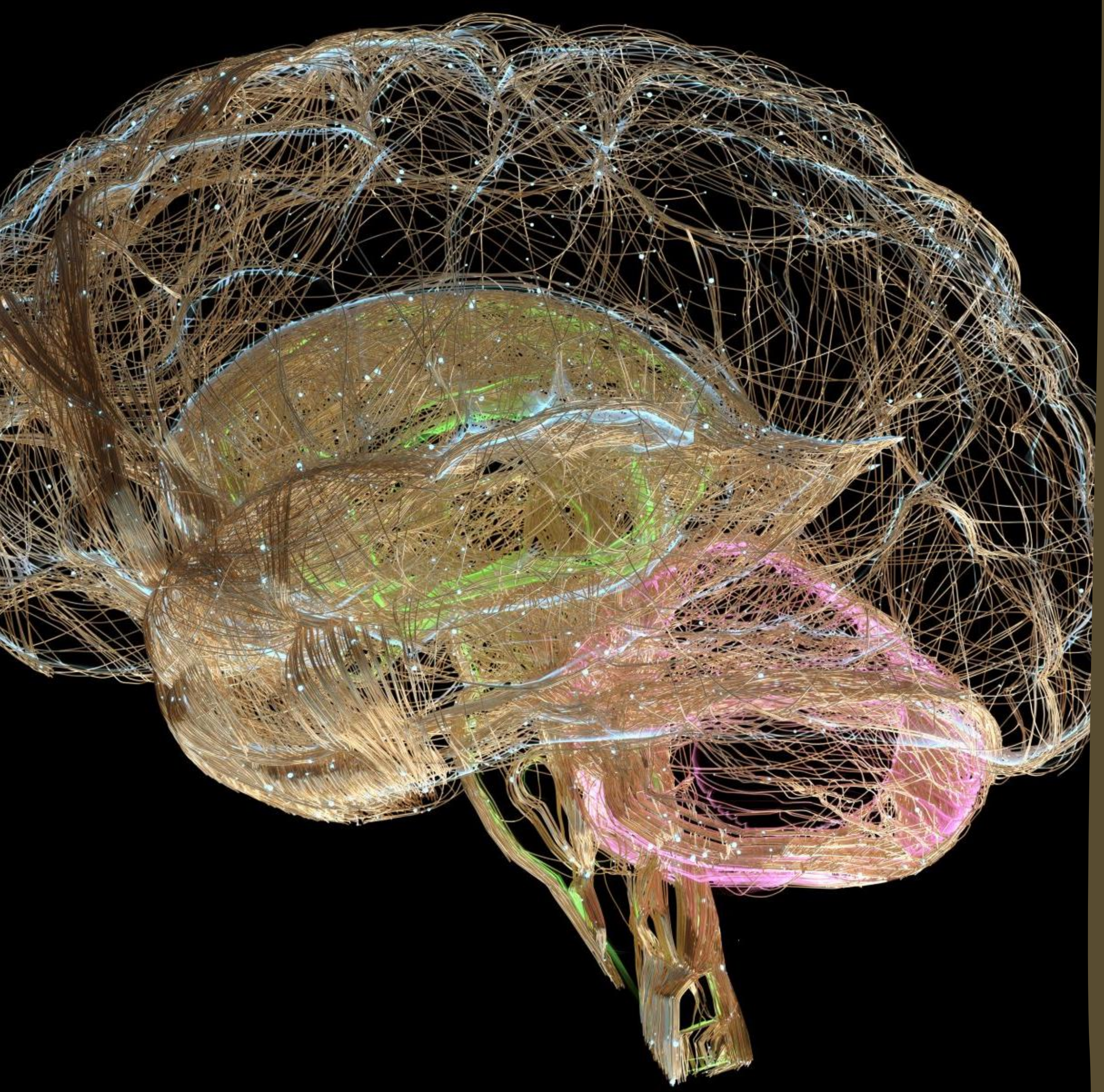
Engrams: Current Status

There is evidence that they exist

Lashley probably didn't use the right tasks and didn't look in the right brain regions

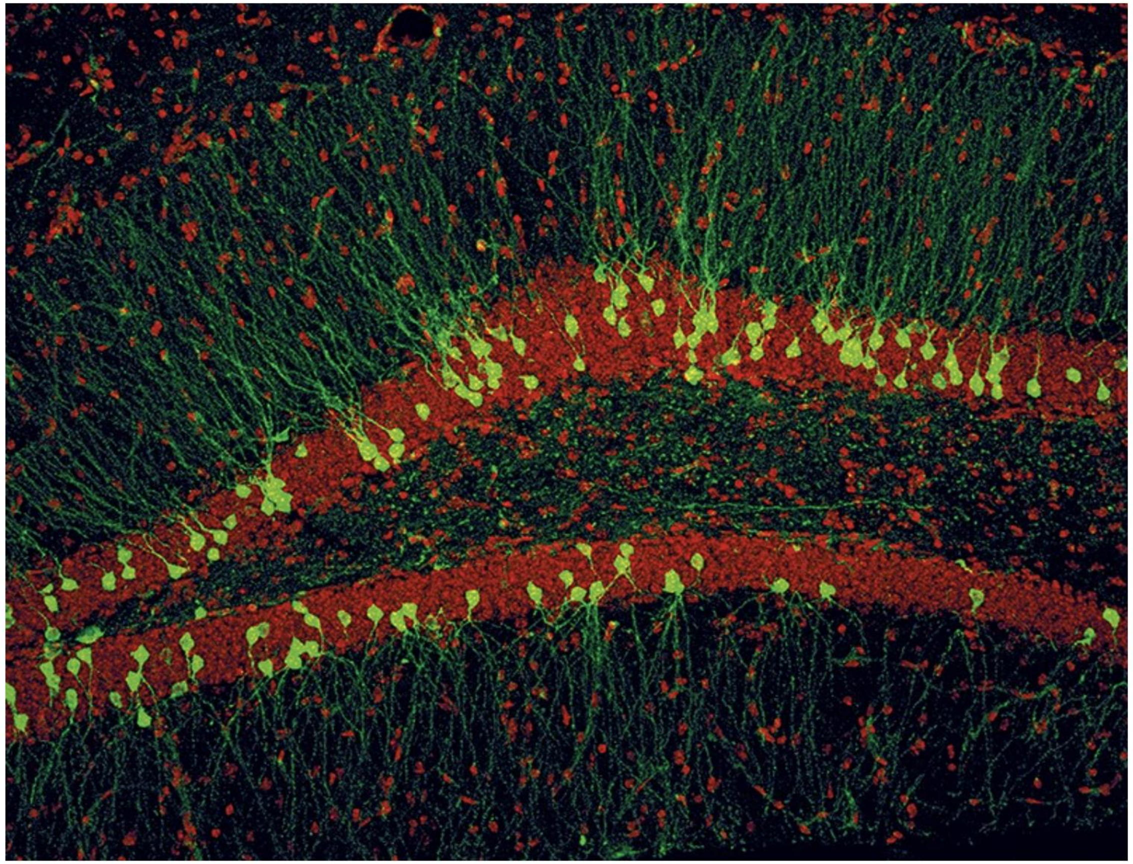
Neurobiology of memory

- Focuses primarily on how we remember
- However, how and why we forget are equally important to study!



More on forgetting

- Interference
- Decay
- Other reasons..
- Controlled forgetting by the brain?! Brains may be wired to forget!
- HSAM - obsessive
- SDAM – good at abstract thinking (Brian Levine: read more here https://www.nature.com/articles/d41586-019-02211-5)



The integration of new neurons (green) into the hippocampus (red bands) degrades stored memories. Credit: Jagroop Dhaliwal

Neurogenesis

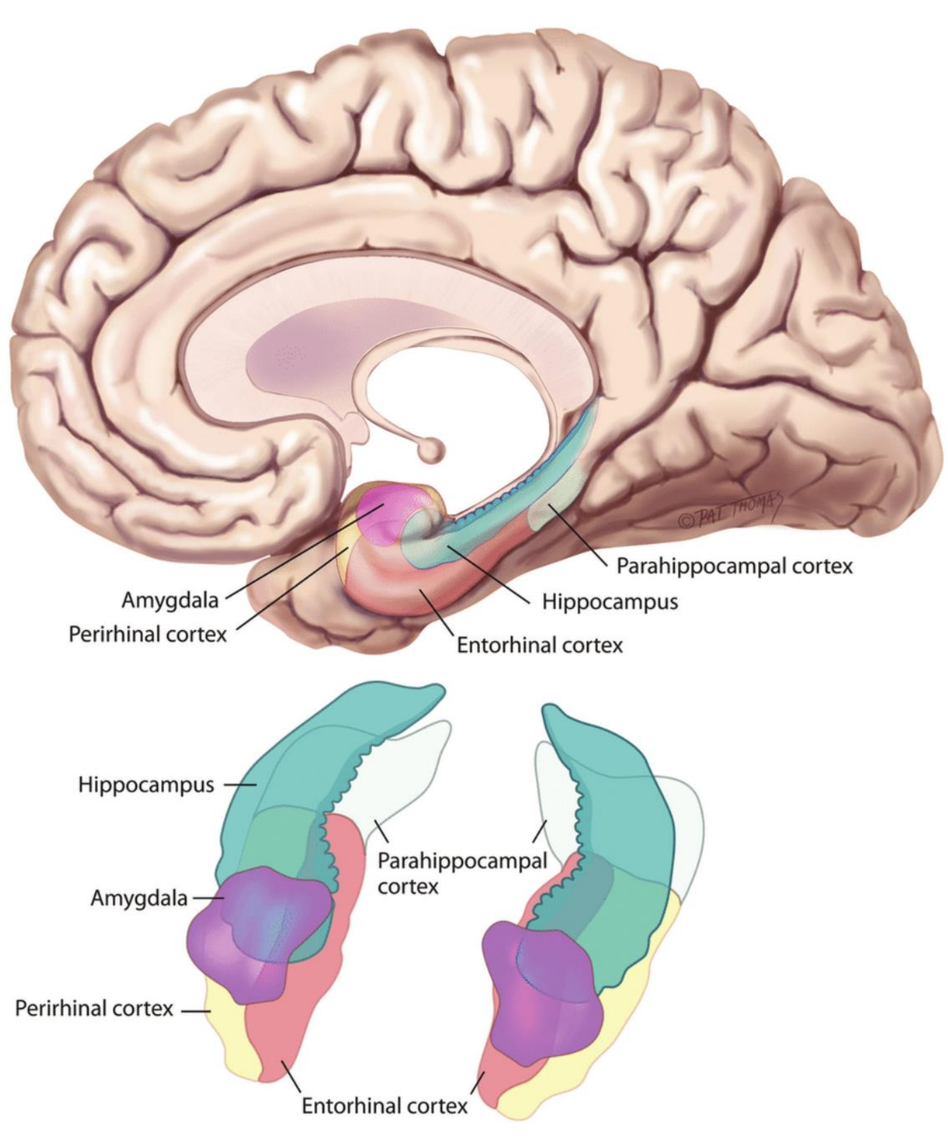
- https://www.nature.com/articles/d41586-019-02211-5

The brain after COVID-19: Compensatory neurogenesis or persistent neuroinflammation?

Elkhonon Goldberg • Kenneth Podell • Daniel K. Sodickson • Els Fieremans

Final picture of memory in the brain and open questions

- Context and items --> memory
- Memory disorders
- Extreme memory ability
- Space
- Time
- Cognitive Maps
- Engrams
- Distributed engrams
- How do they communicate with each other?



Social Cognition and Consciousness

Phineas Gage

1848, age 25

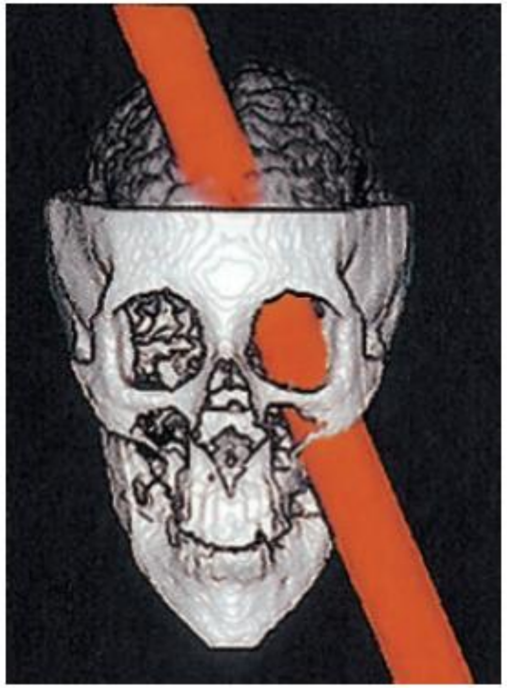
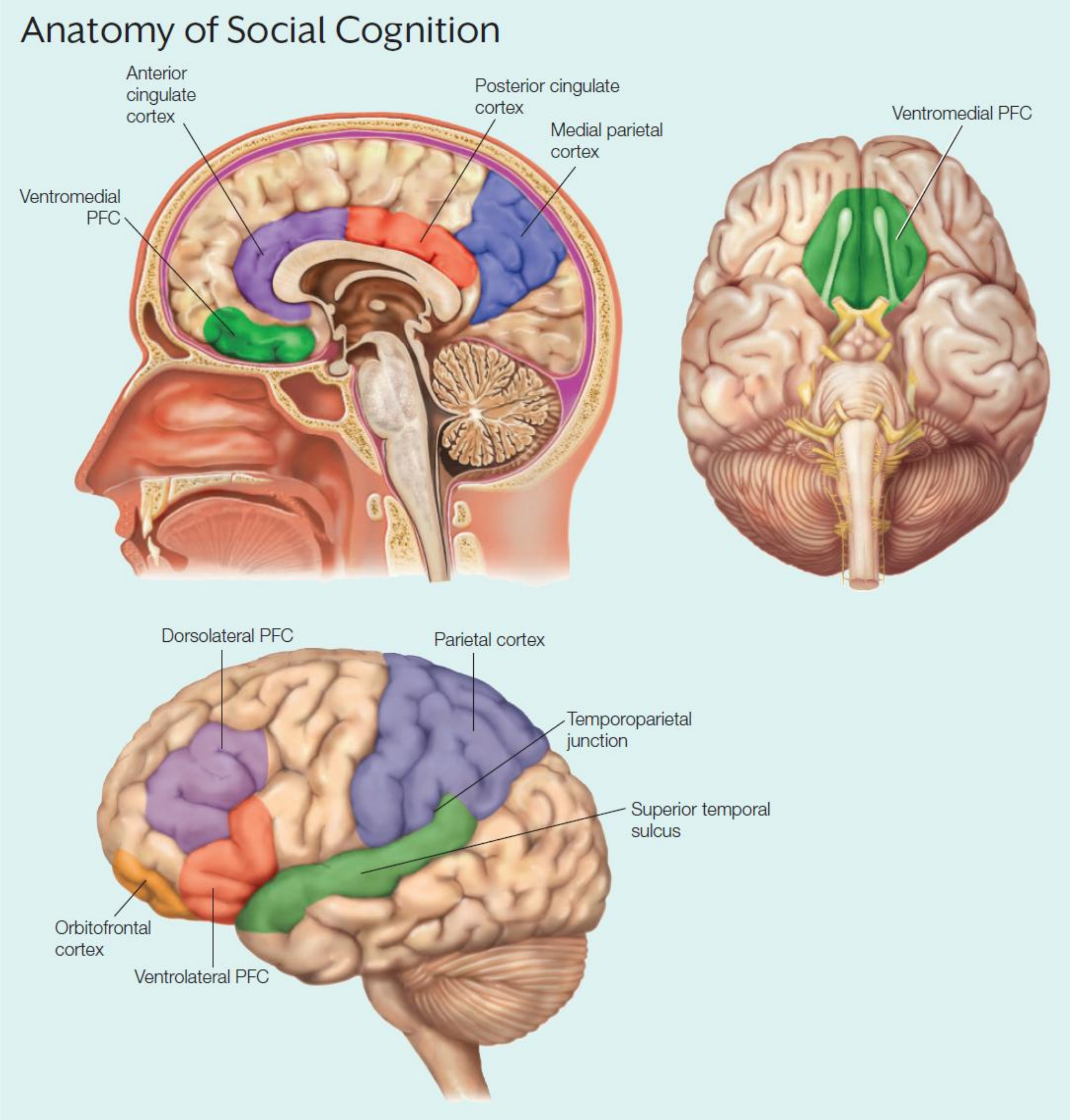


FIGURE 13.1 Computer re-construction of Phineas Gage's injury.
The tamping iron entered Gage's brain just below the left eye and exited from the top of the head. It destroyed much of the medial region of the prefrontal cortex.



- The prefrontal cortex continues to develop through adolescence.
- Social isolation and lack of social play during childhood and adolescence have negative impacts on the neuronal development of areas that support social behavior, resulting in social behavioral deficits that last into adulthood.
- Social stress during childhood affects the neuronal development of the brain.
- Social stress in adults contributes to neural degeneration.

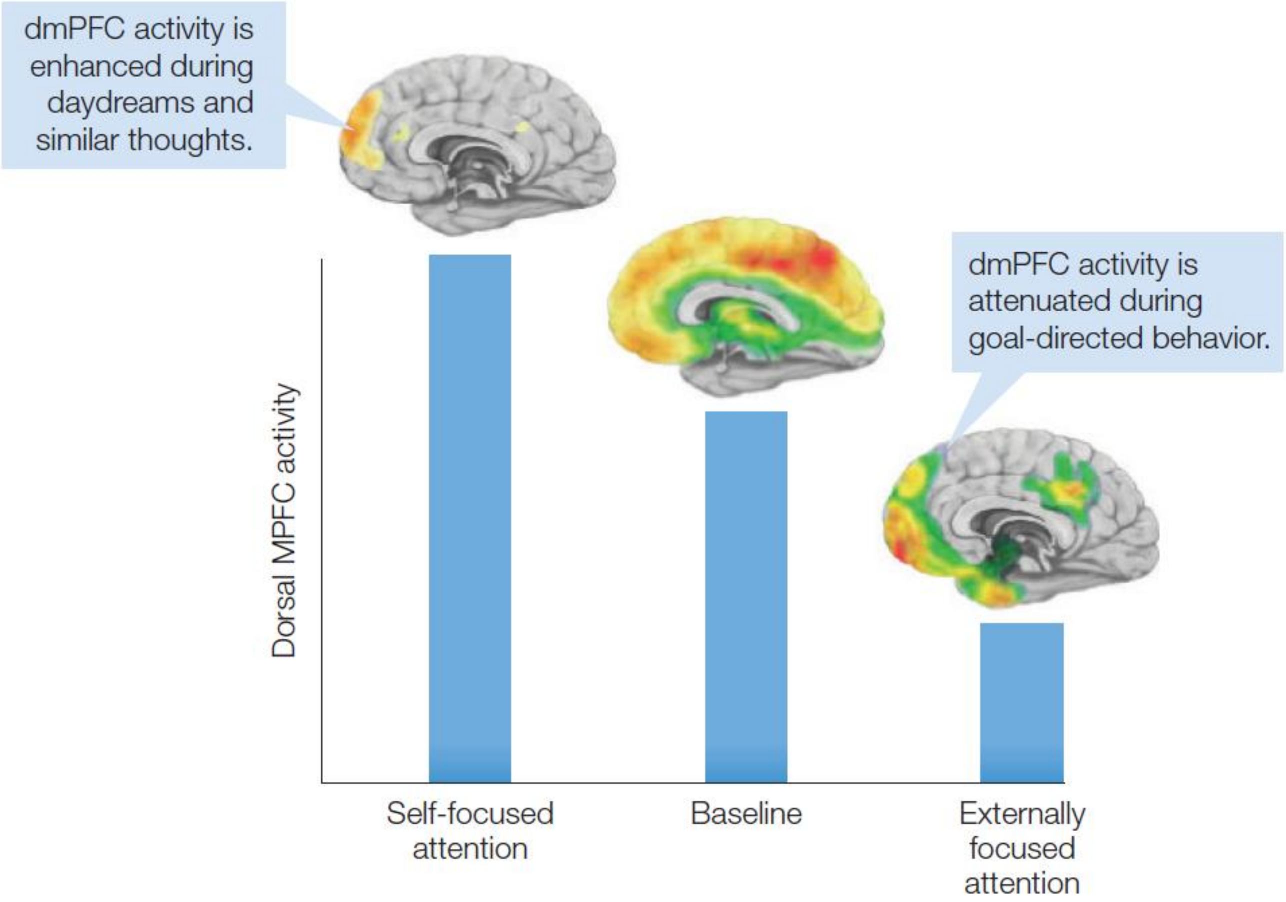
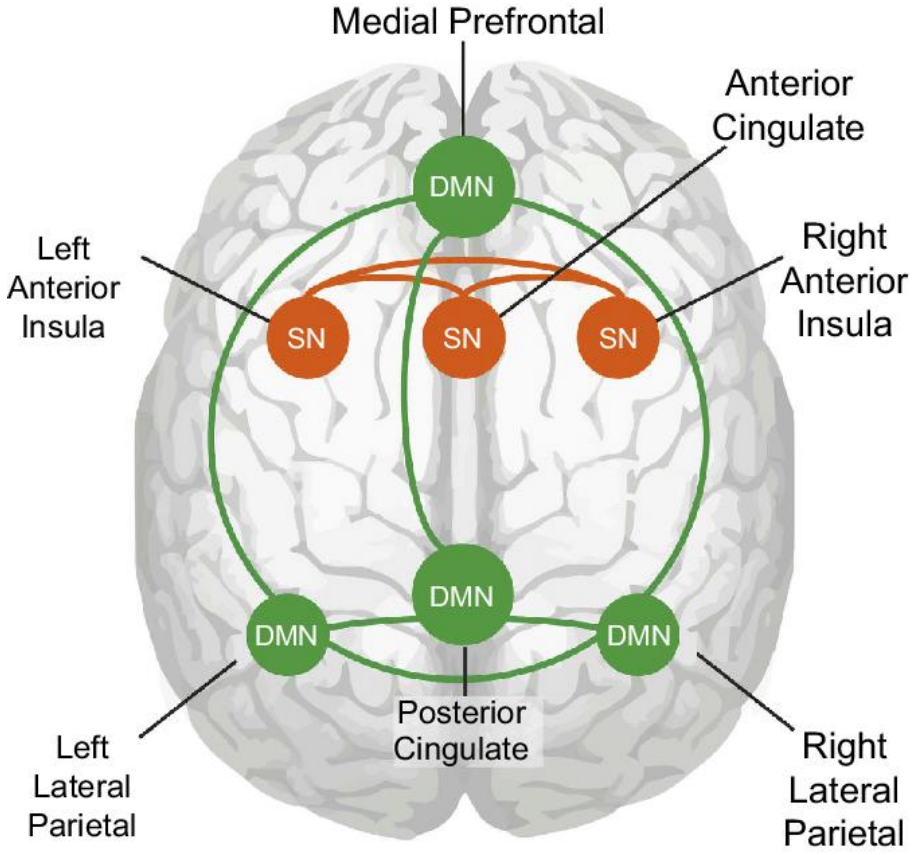


FIGURE 13.5 Focus inward is accompanied by increased dmPFC activity. Activity in the dorsomedial prefrontal cortex (dmPFC) increases during tasks that involve self-referential mental activity or self-focused attention and decreases during tasks that involve externally focused attention. This finding is consistent with the observation that during goal-directed behaviors, self-focused attention decreases, and it also indicates that at baseline, some degree of self-referential mental activity should be engaging this region—a suggestion that has been supported by functional imaging data.

Default mode network

The default network is strongly active when we are engaged in self-reflective thought and judgment assessments that depend on social and emotional content.



Van Ettinger-Veenstra et al., 2013

https://news.usc.edu/90485/belief-in-core-values-triggers-a-default-mode-network-in-the-brain/

O'Reilly, 2010

1. A ventral–dorsal gradient organized in terms of maintenance and manipulation, such as the ventral and dorsal visual pathways for "what" versus "how" abstraction

2. An anterior–posterior gradient that varies in abstraction, where the more abstract representations engage the more anterior regions (e.g., frontal pole), and the less abstract engage more posterior regions of the frontal lobes. (we might think of the most posterior part of the frontal lobe, the primary motor cortex, as the point where abstract intentions are translated into concrete movement)

3. A lateral–medial gradient related to the degree to which working memory is influenced by information in the environment (more lateral) or information related to personal history and emotional states (more medial). In this view, lateral regions of the PFC integrate external information that is relevant for current goal-oriented behavior, whereas more medial regions allow information related to motivation and potential reward to influence goal-oriented behavior.

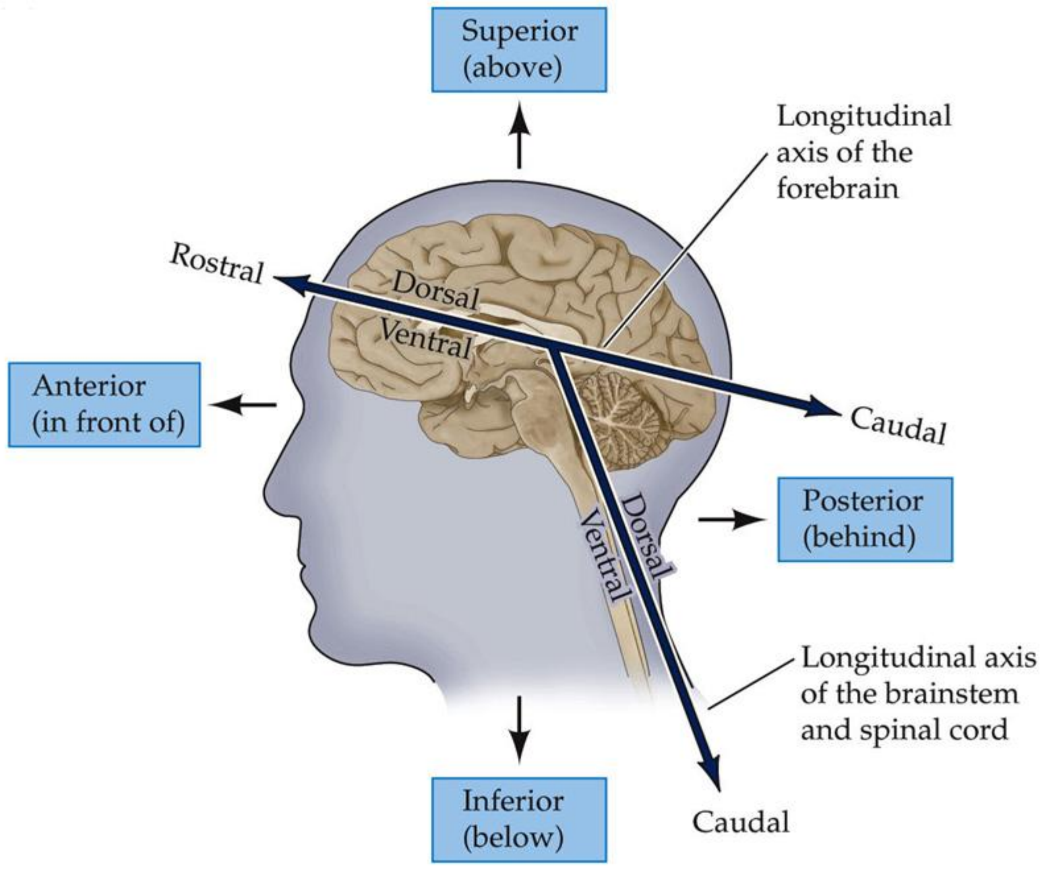
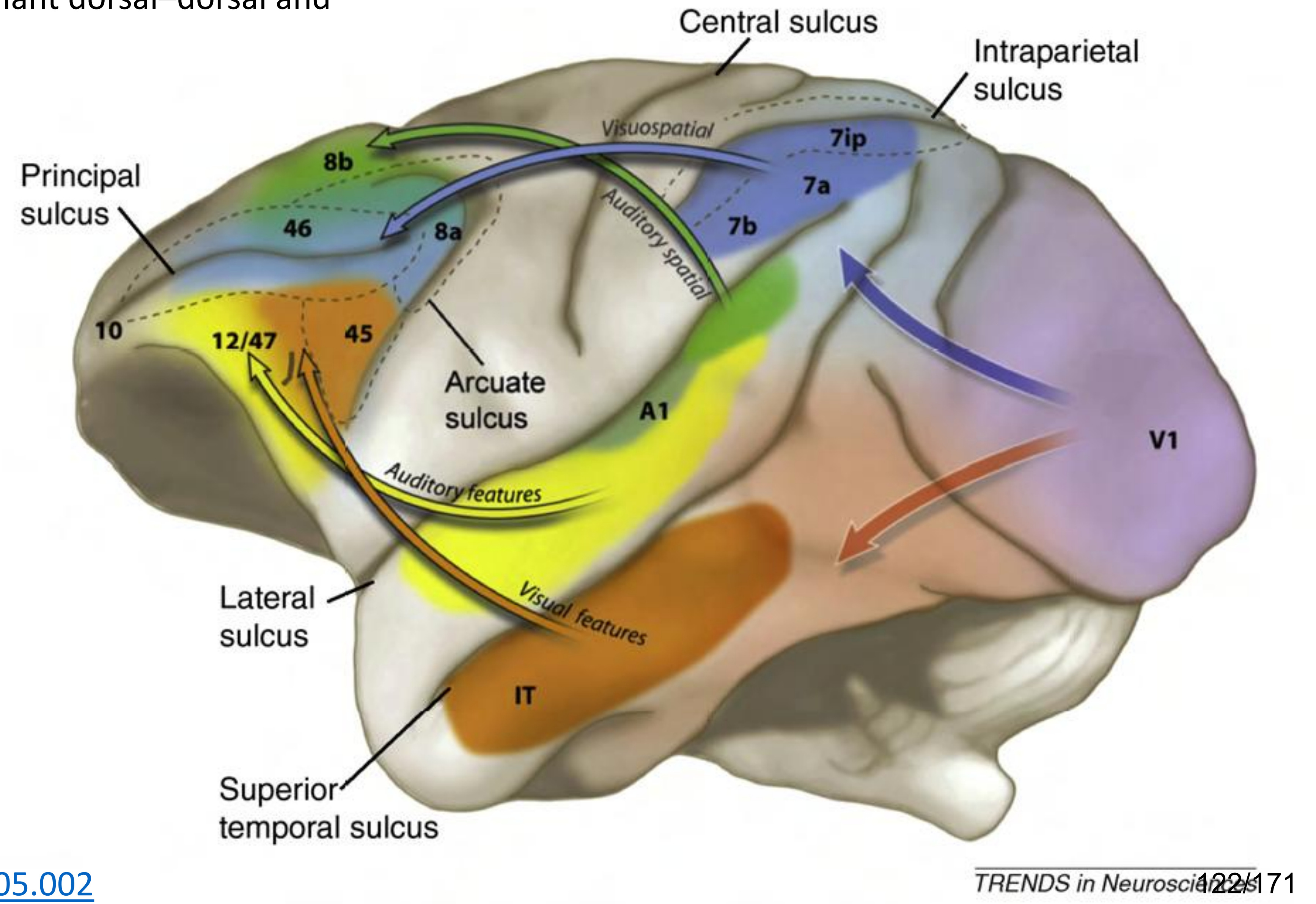


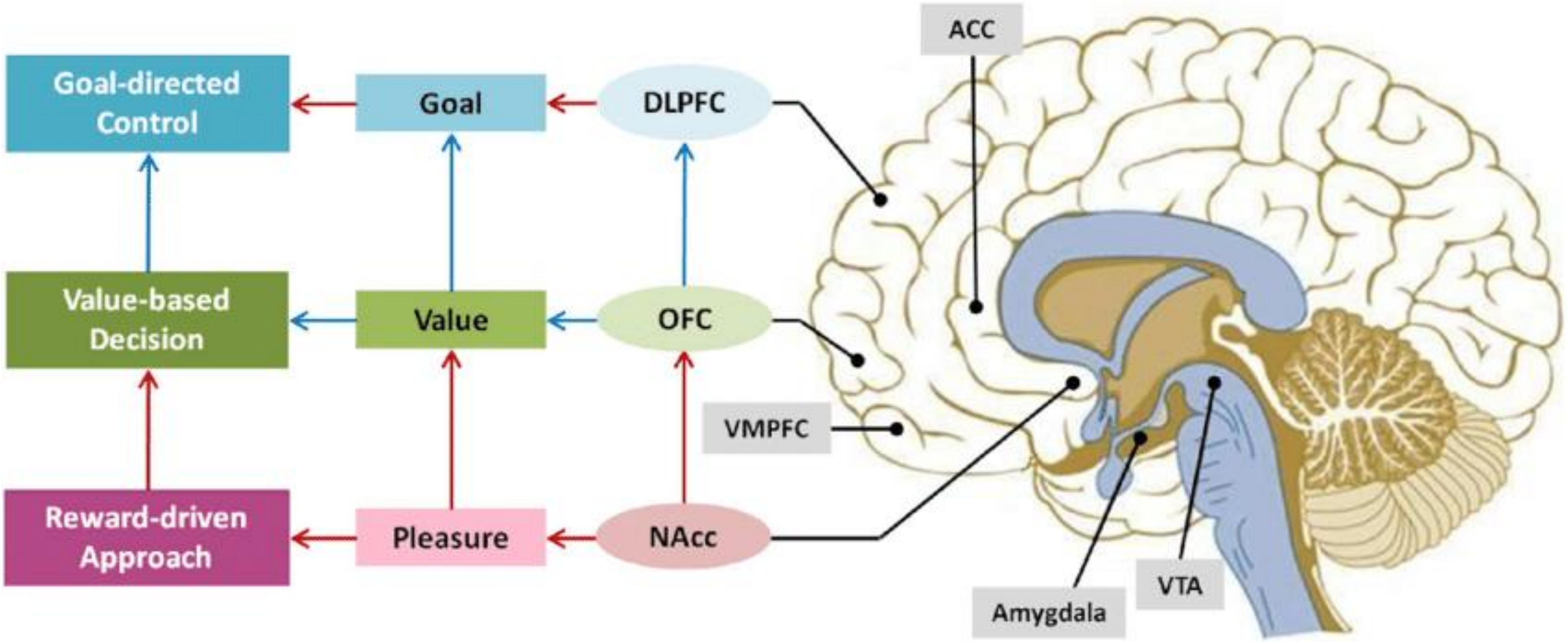
Figure 1.3. Conventions for specifying location in the human CNS. Note the flexure in the long axis of the nervous system near the junction of the midbrain and diencephalon. (Figure A1A from Neuroscience, 6th Ed.; after original from N.B. Cant)

https://sci-hub.st/10.1016/j.tins.2010.05.002

Summary of anatomical connectivity (in the macaque, where most of the anatomical work has been done) suggesting that dorsal versus ventral distinctions in posterior cortex should influence prefrontal cortex, due to dominant dorsal–dorsal and ventral–ventral connectivity.

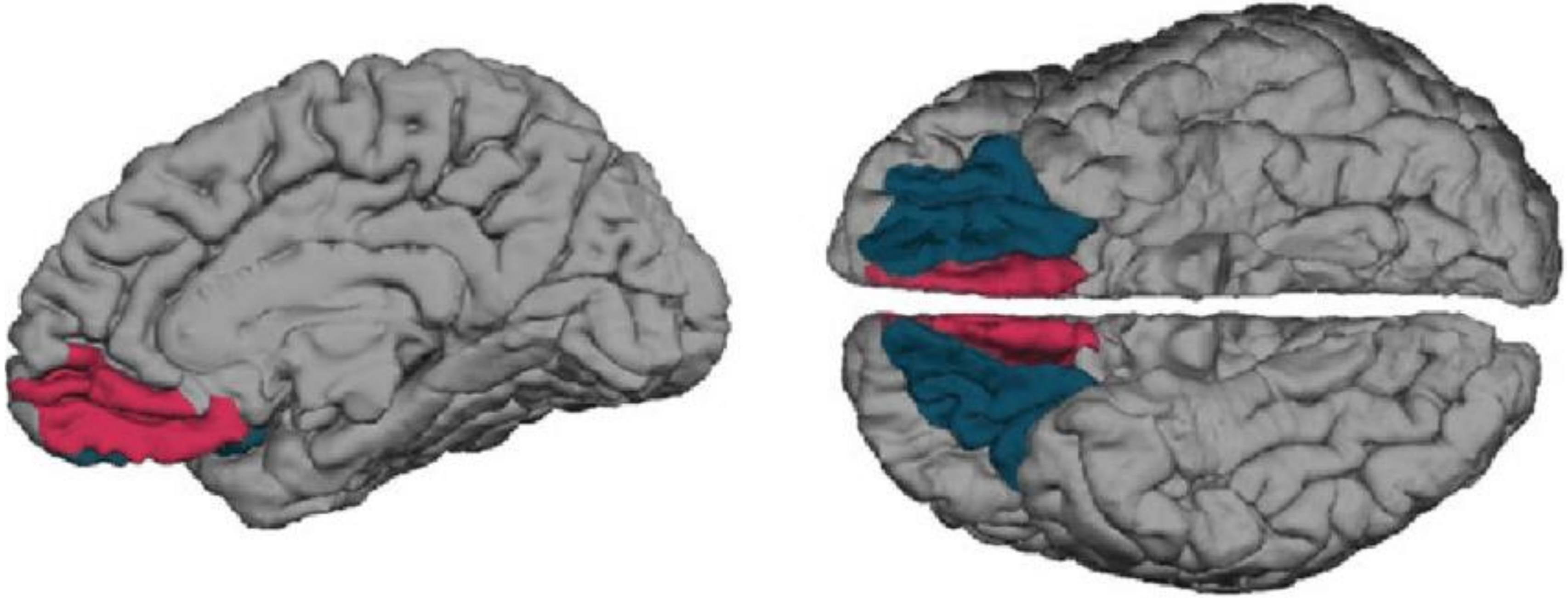


https://sci-hub.st/10.1016/j.tins.2010.05.002



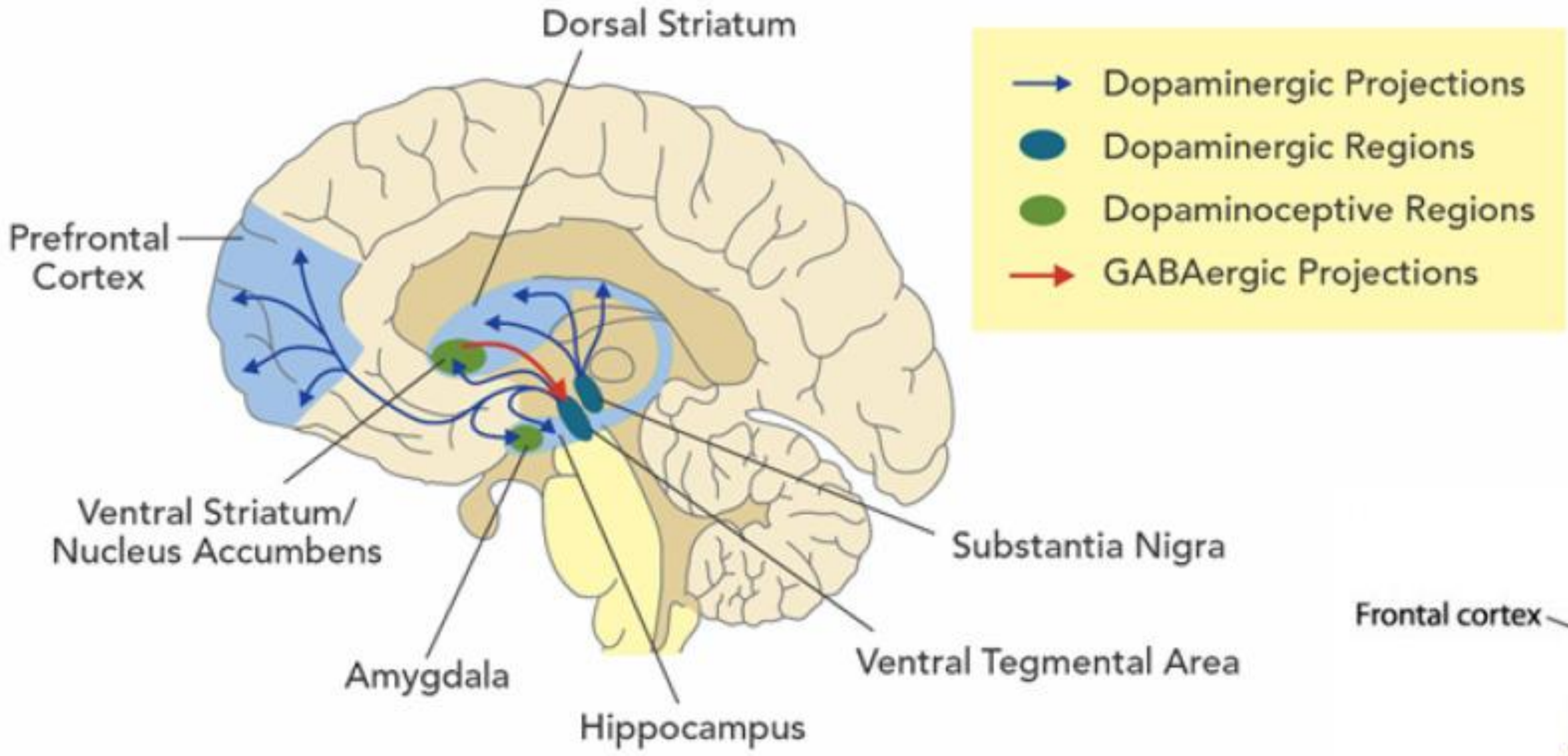
Kim et al., 2013, Frontiers in Psychology

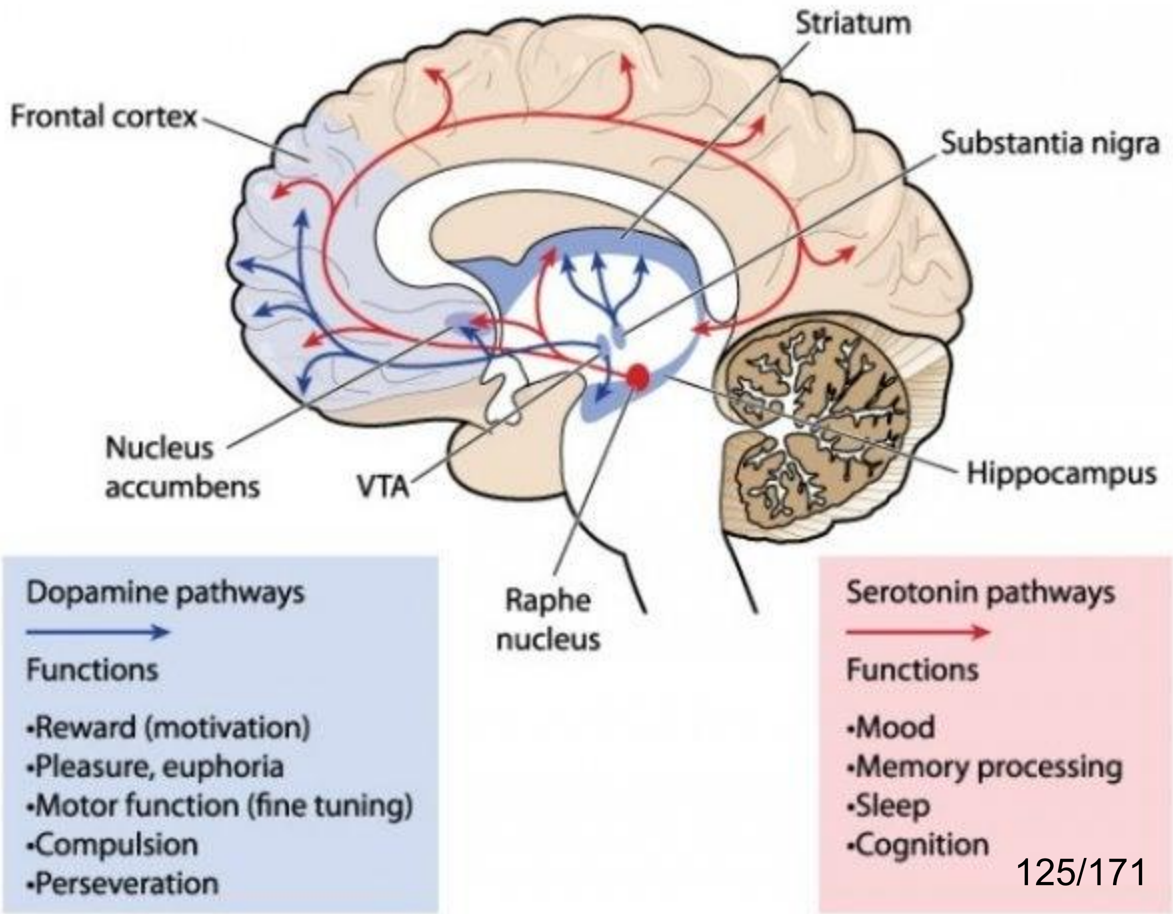
ventro-medial PFC

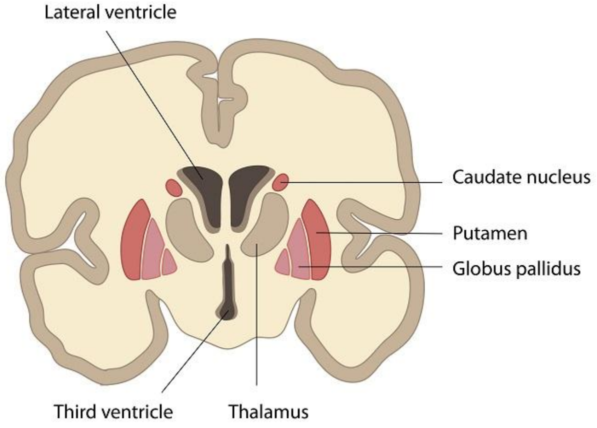


vmPFC uses contextual information to guide behavior, particularly in situations of ambiguity or conflict

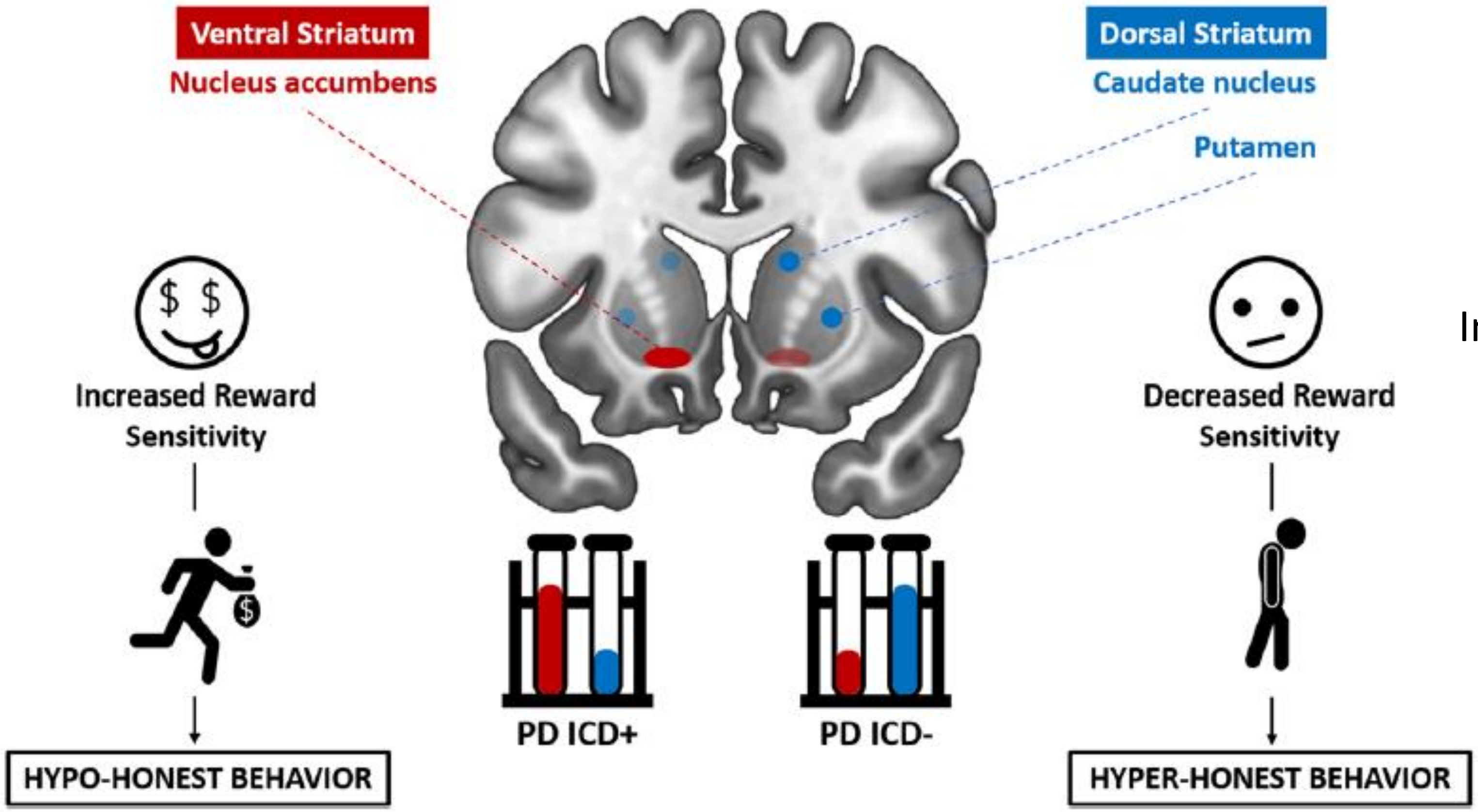
https://pmc.ncbi.nlm.nih.gov/articles/PMC8425341/


Dorsal Striatum
Dopaminergic Projections
Dopaminergic Regions
Dopaminoceptive Regions
GABAergic Projections
Prefrontal Cortex
Ventral Striatum/ Nucleus Accumbens
Substantia Nigra
Ventral Tegmental Area
Amygdala
Hippocampus


Striatum
Frontal cortex
Substantia nigra
Nucleus accumbens
VTA
Hippocampus
Raphe nucleus
Dopamine pathways
Functions
•Reward (motivation)
•Pleasure, euphoria
•Motor function (fine tuning)
•Compulsion
•Perseveration
Serotonin pathways
Functions
•Mood
•Memory processing
•Sleep
•Cognition


Lateral ventricle
Caudate nucleus
Putamen
Globus pallidus
Third ventricle
Thalamus

External reward



Internal reward

- dopaminergic hyperactivity
- (impulse control disorders/addiction/gambling)
- enhanced novelty-seeking,
- risk-proneness,
- impulsivity, and
- reward sensitivity

- dopaminergic hypo-activity
- (Parkinson’s)
- implying enhanced harm avoidance,
- risk aversion,
- non-impulsivity, and
- reduced reward sensitivity

https://www.nature.com/articles/s41531-021-00167-w

Ponsi et al., 2021, Nature

How do we plan our goals?

Mental Time Travel

1) Remember our past – The nature of information processing, in the internal circuits in the hippocampus, allow our past experiences to be retrieved with exceptional detail, as though we were reliving those moments.

- Adaptive advantage of episodic memory - it allows us to learn from the same event more than once. We can mentally revisit events and compare them to similar and related episodic memories.

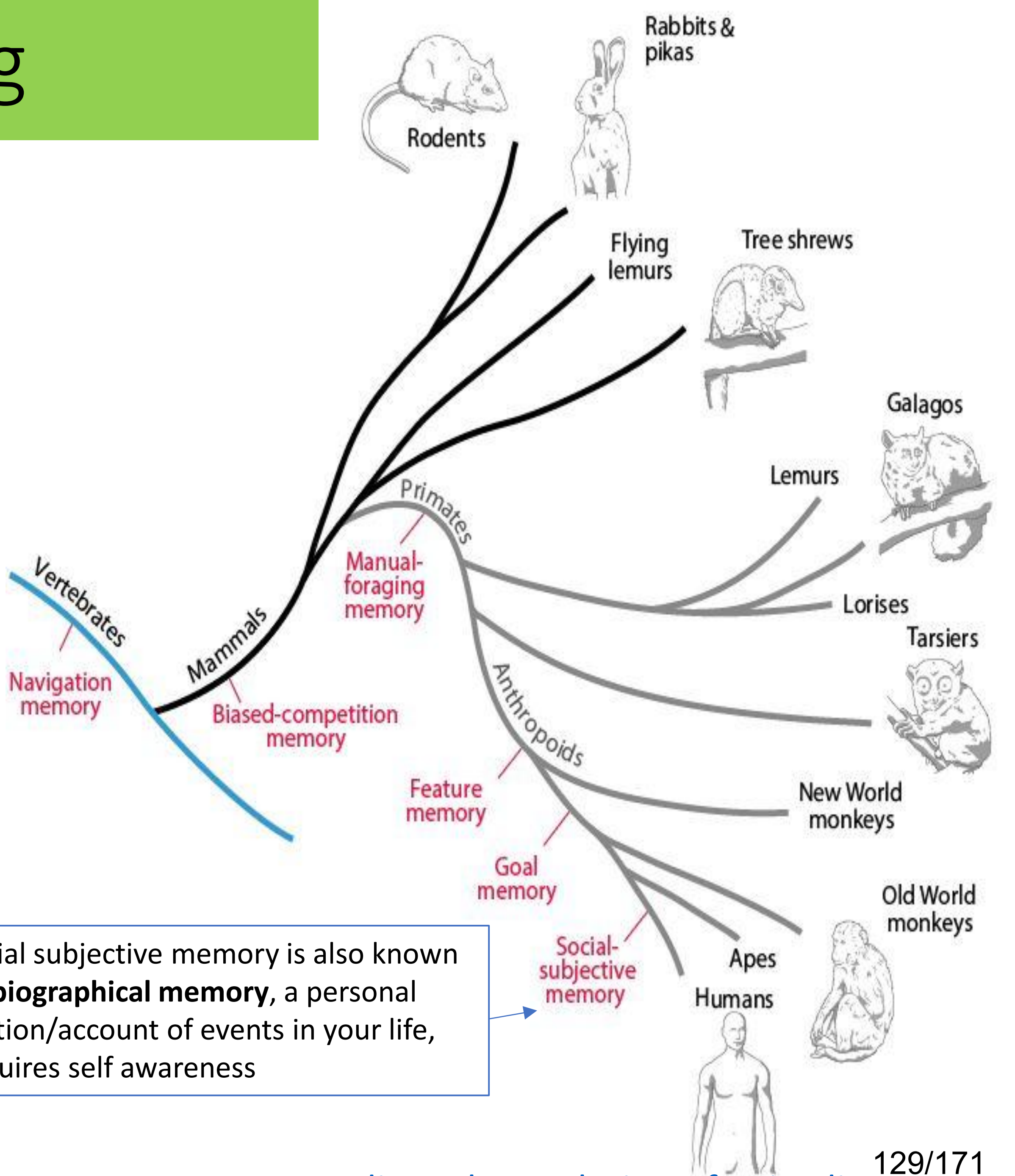
2) Simulate the Future – By using our past experiences, we can construct or simulate future scenarios, predict outcomes in novel circumstances.

Episodic Future Thinking

As human beings, we don't just learn and remember information. We make use of our experiences.

- **Planning the future** – imagine or simulate future scenarios or events using past experiences.
- **Predicting the future** – using past experiences to make novel inferences and solve problems by reorganizing memory networks
- **Social relationships** – evaluating, predicting social behaviour in others and maintaining relationships by remembering whether they were good (cooperative) or bad (aggressive) to you.
- **Language (refer to events)** – remembering the meaning and context of words/phrases/semantic knowledge
- **Self-awareness / autonoetic consciousness** – the ability to be aware of yourself, that you know what you know, it a special trait that arises due to episodic memory

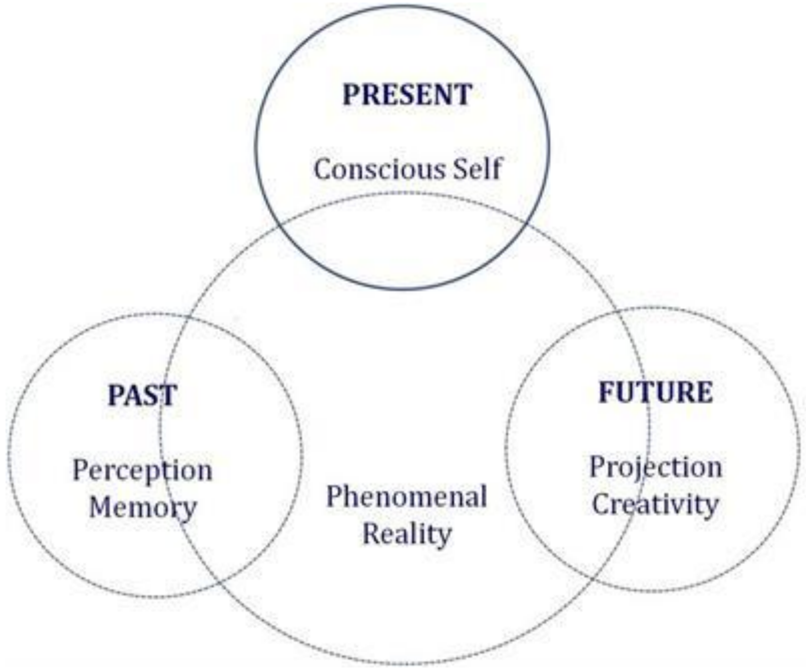
This social subjective memory is also known as **autobiographical memory**, a personal recollection/account of events in your life, that requires self awareness



[Source + Extra Reading: The evolution of episodic memory]

Mental time travel

- Past – present – future (episodic memories)

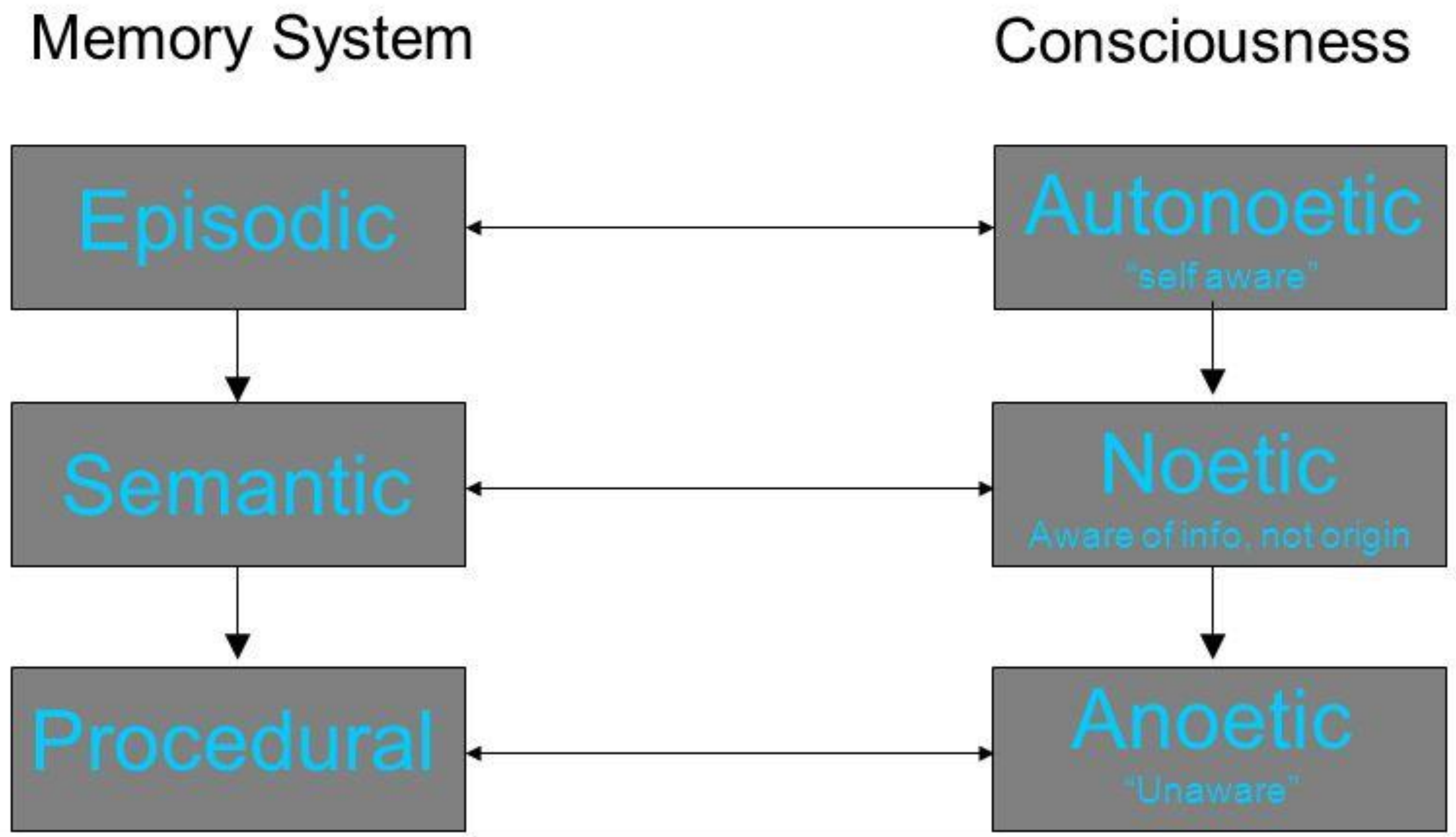


HM – sentient but no conscious experience (Long term memory)

Fig, Dresp-Langley, 2022

Memory and Consciousness

The relationship between types of LTM and varieties of consciousness (Tulving, 1985).



functional coupling of brain areas in aware/conscious states is energetically highly cost-intensive but is yet seen in a simpler form in other species

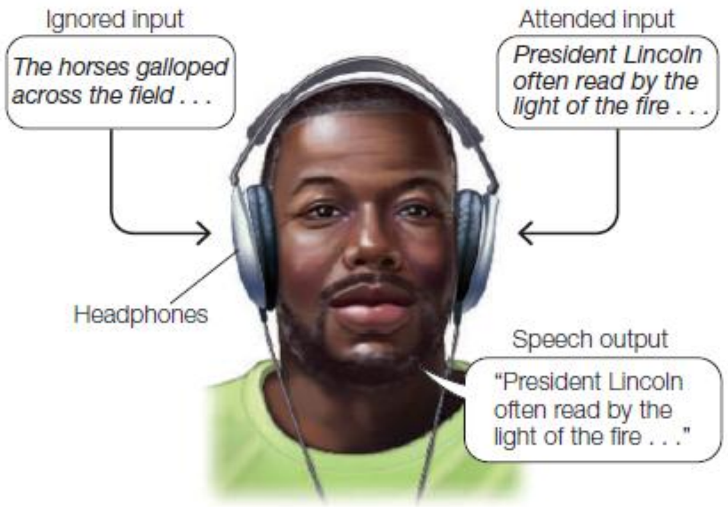
https://www.frontiersin.org/journals/systems-neuroscience/articles/10.3389/fnsys.2022.941534/full

- Consciousness may have something to do we how we perceive our world.

- What modulates our perception?

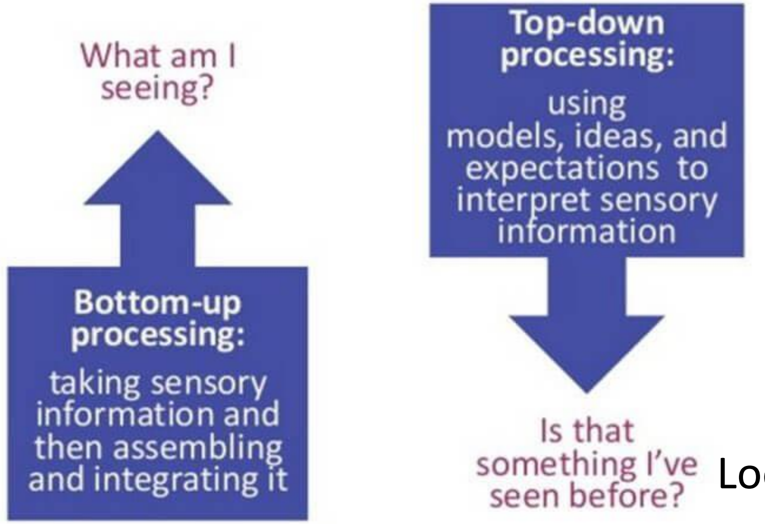
- Can attention influence perception?

FIGURE 7.10 Auditory selective attention in a noisy environment. The cocktail party effect of Cherry (1953), illustrating how, in the noisy, confusing environment of a cocktail party, people are able to focus attention on a single conversation, and, as the man in the middle right of the cartoon illustrates, to covertly shift attention to listen to a more interesting conversation than the one in which they continue to pretend to be engaged.



Cocktail Party Effect

- At what stage does attention influence perception?



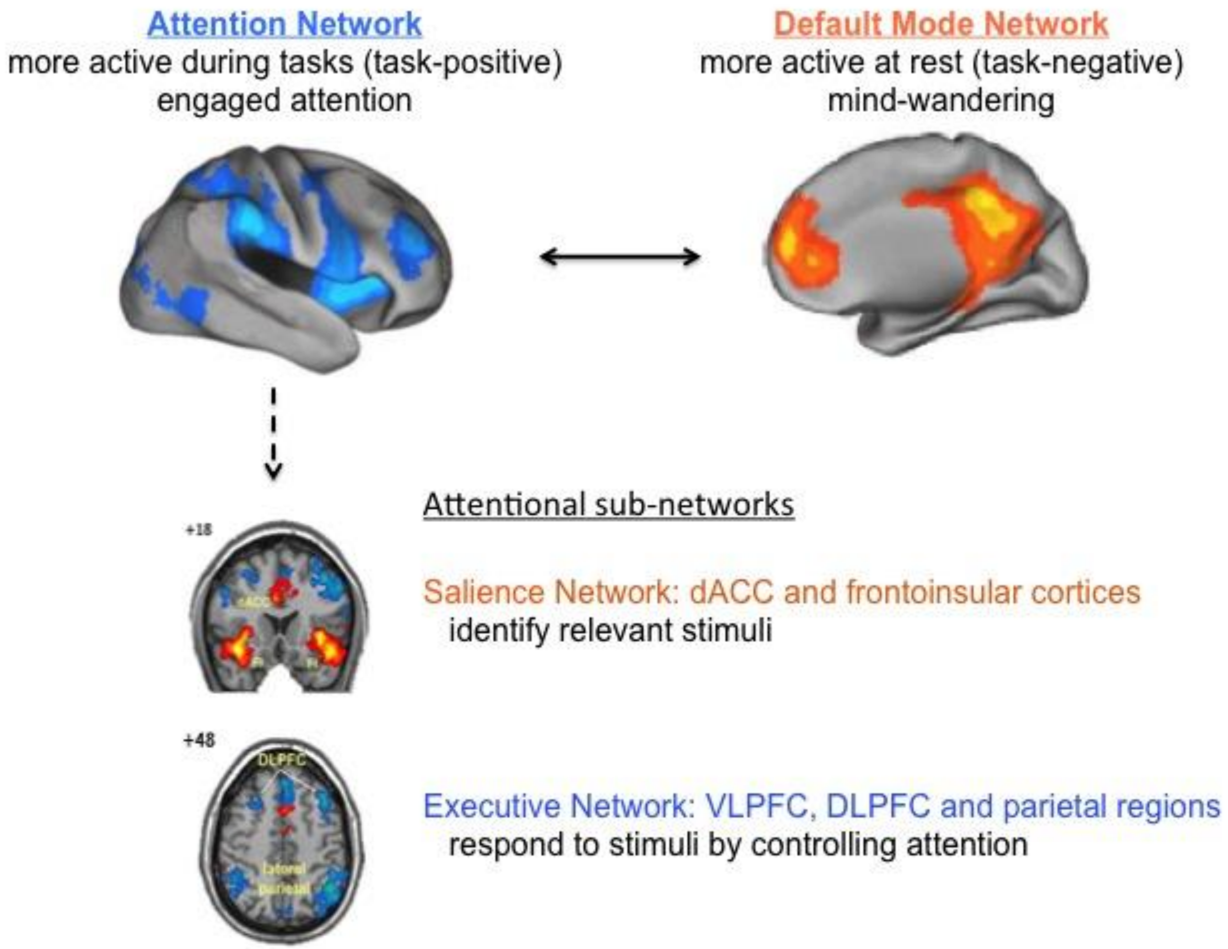
Look for an animal

Top down – goal/thought/experience driven
Bottom up – stimulus driven

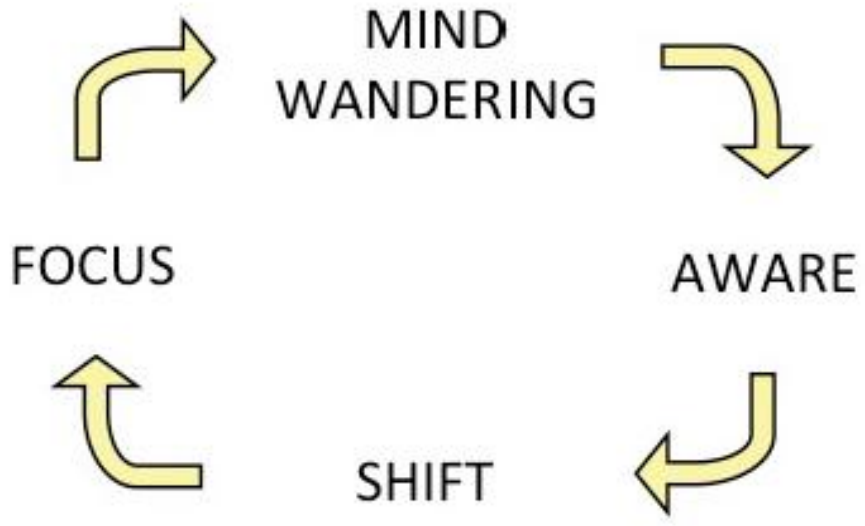
- Where does top-down and bottom up processing meet or interact in the brain?
- At what stage does attention influence perception?

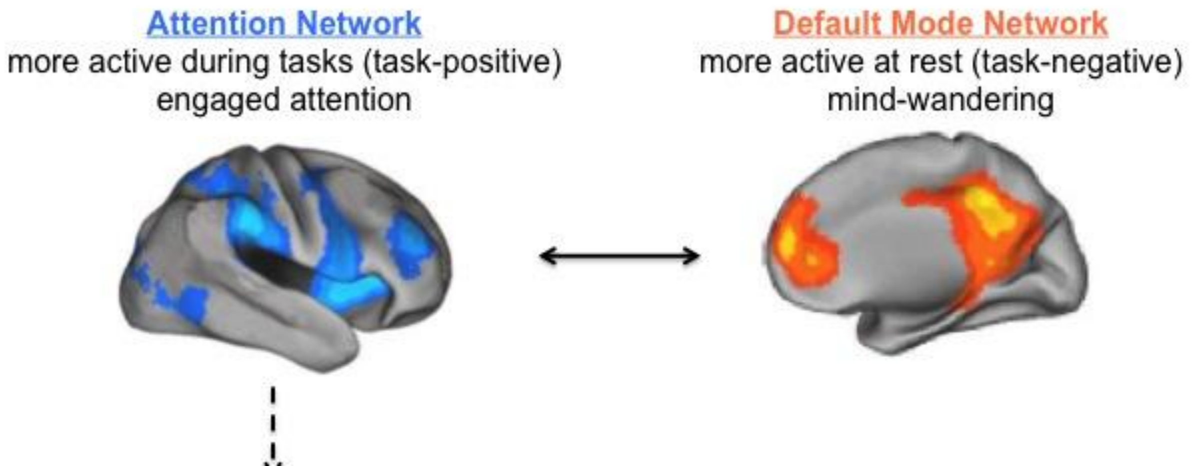
- Can answering this question help to understand how our brain becomes conscious?

Where is attention in the brain?



When attempting to sustain focus on an object (FOCUS), an individual inevitably loses this focus and experiences wandering of attention (MIND WANDERING). At some time during mind wandering, the practitioner becomes aware that his/her mind is not on the object (AWARE), at which point he/she disengages from the current train of thought and shifts attention back to the object (SHIFT), where it stays focused again for some period of time (FOCUS). The cycle iterates repeatedly over a session of Focused Attention meditation.



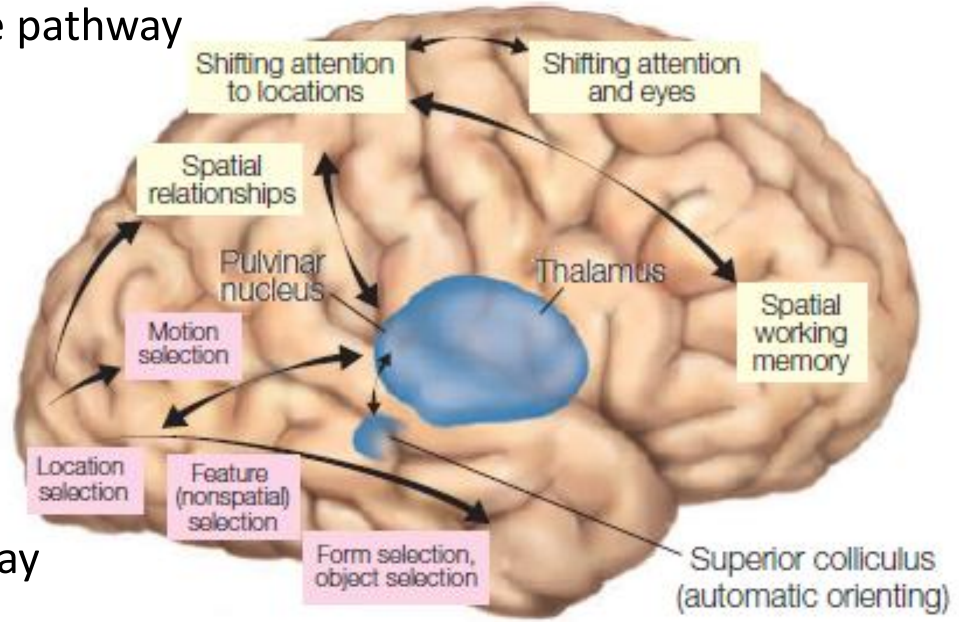


To perceive sensory information, do you have to be aware of it?

Is neglect following brain damage a deficit in perception, attention, or awareness? How would you test this?

P.S. was presented simultaneously with two line drawings of a house, in one of which the left side was on fire. She judged that the drawings were identical; yet when asked to select which house she would prefer to live in, she reliably chose the house that was not burning.

Where pathway



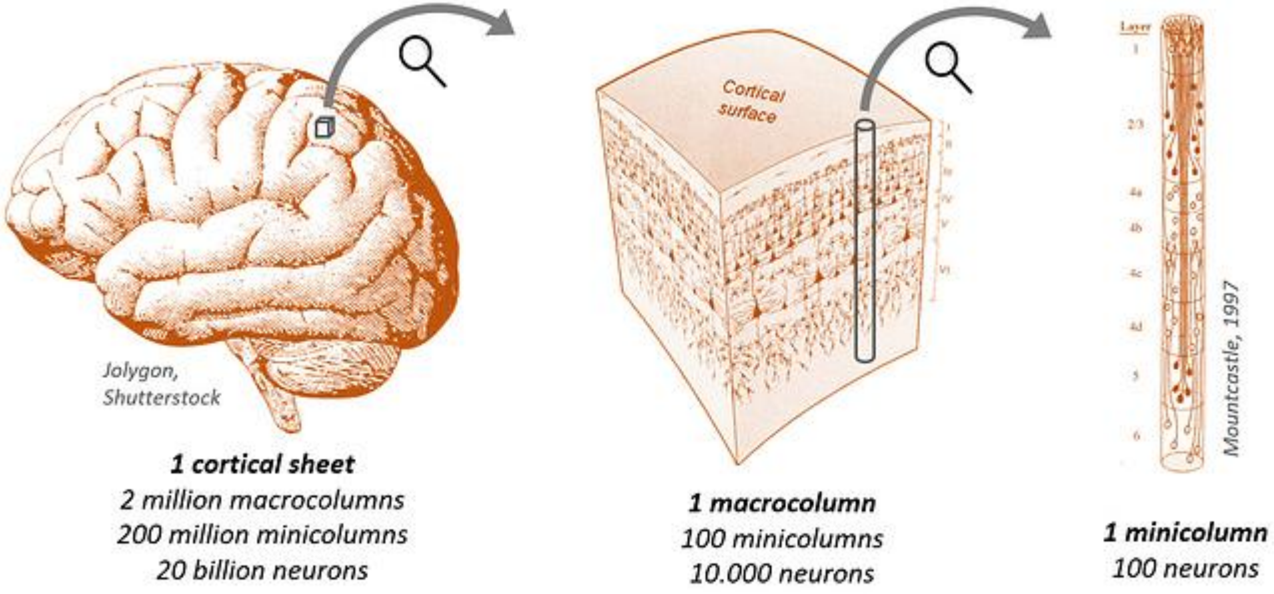
What pathway

FIGURE 7.39 Sources and sites of attention.
Model of executive control systems, showing how visual cortex processing is affected by the goal-directed control of a network of brain areas.

The brain is receiving the information yet cannot “perceive” it

Where in the brain does physical/sensory perception become a mental perception?

- Can consciousness be explained by the way we access information in the brain?



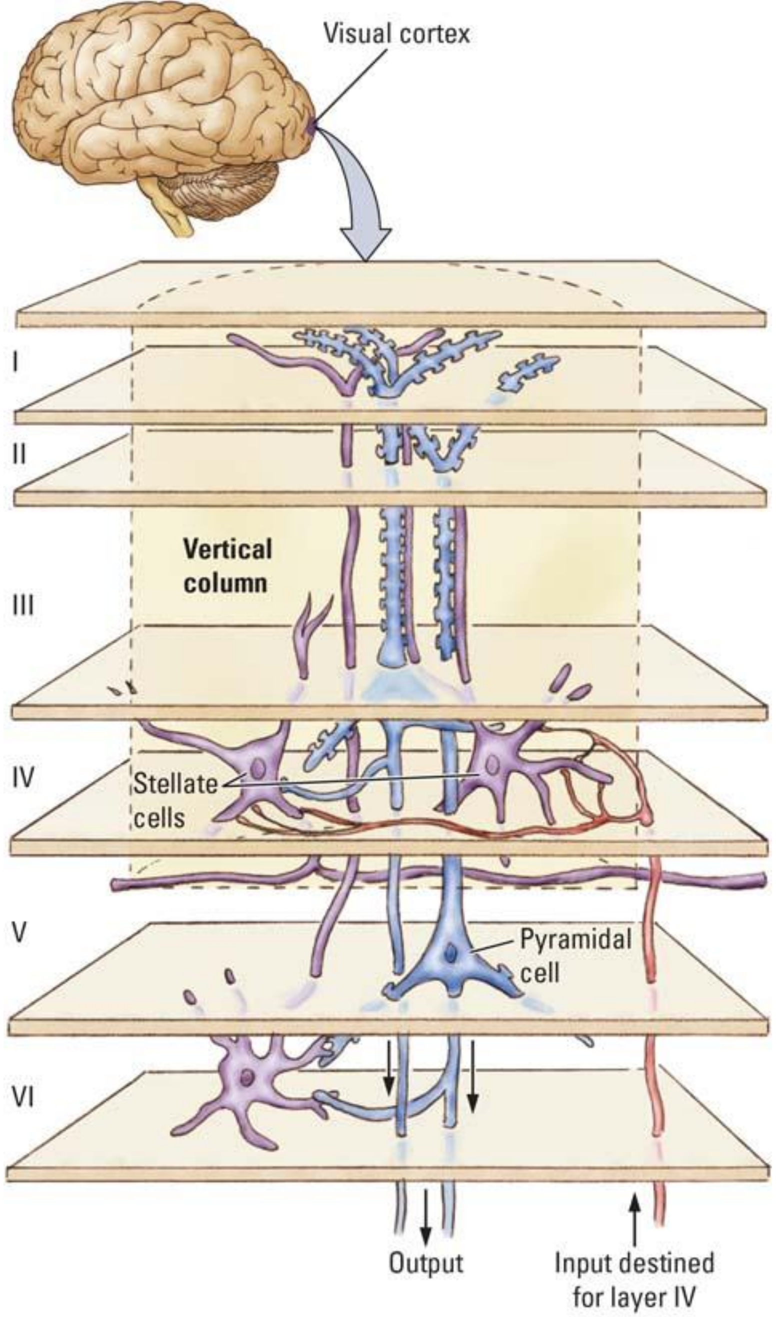
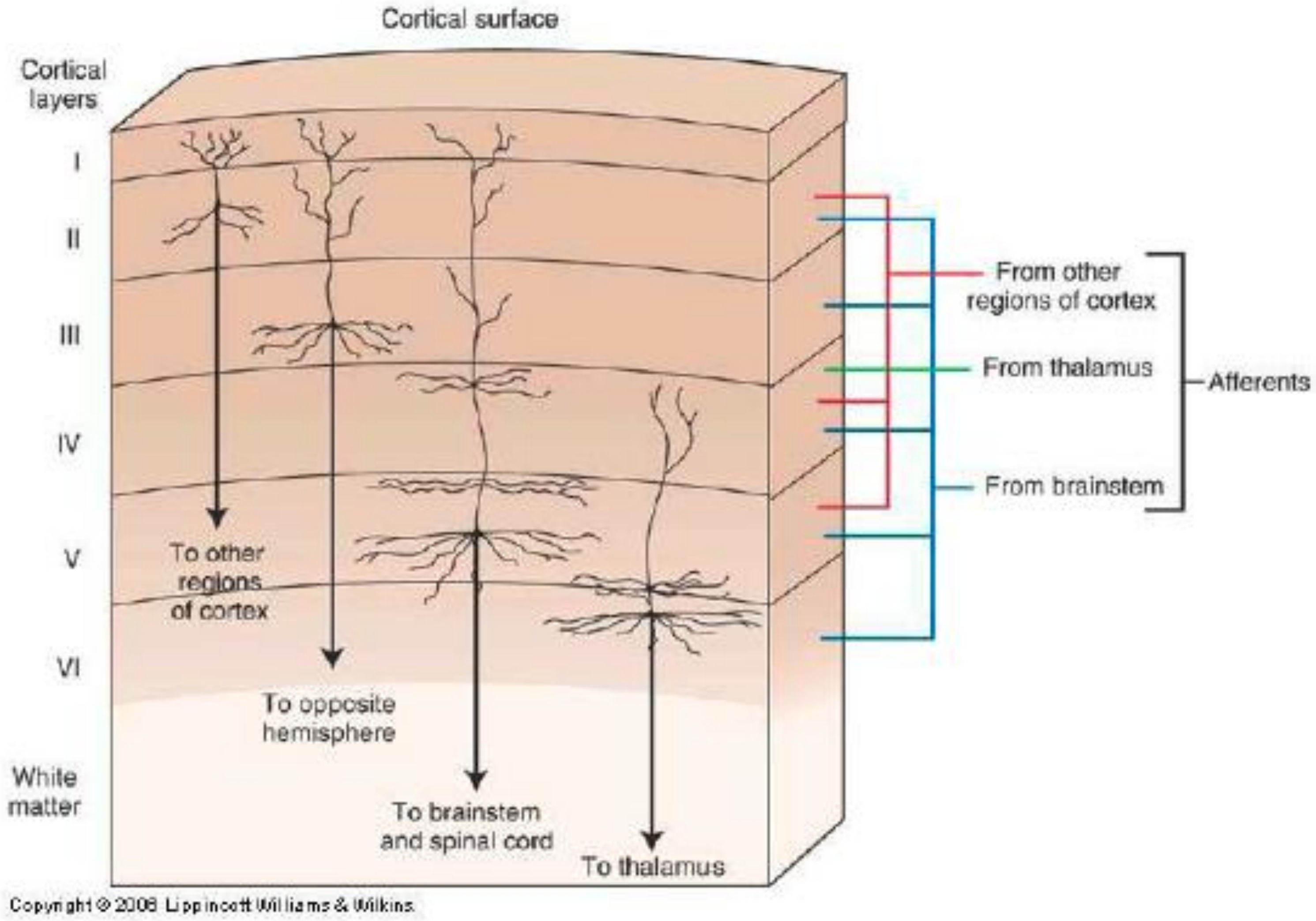


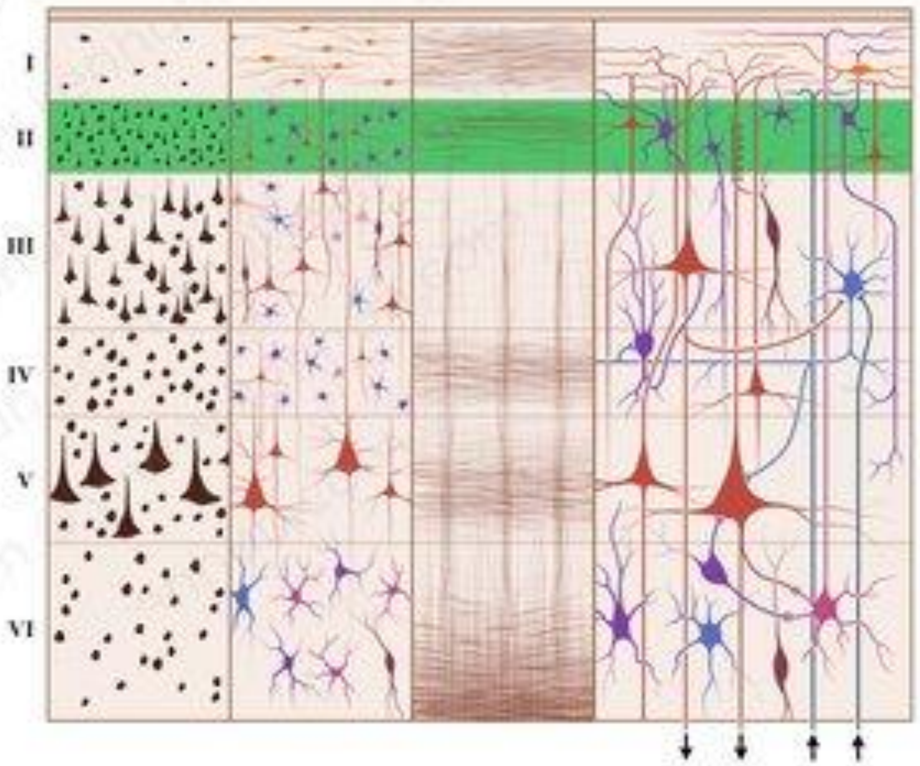
Figure 9.33
Kolb/Whishaw/Teskey, *Intro to Brain & Behavior*, 5e, © 2016 Worth Publishers
Information from J. Szentagothai (1975). The "module-concept" in cerebral architecture. *Brain Research*, 95, p. 490

Neural Circuit in a Column in the Visual Cortex In this three-dimensional view, sensory inputs enter the cortical column at layer VI (bottom) and terminate on stellate cells in layer IV that synapse with pyramidal cells in layers III and V. The information flow is vertical. Axons of the pyramidal cells leave the column to join other columns or structures.

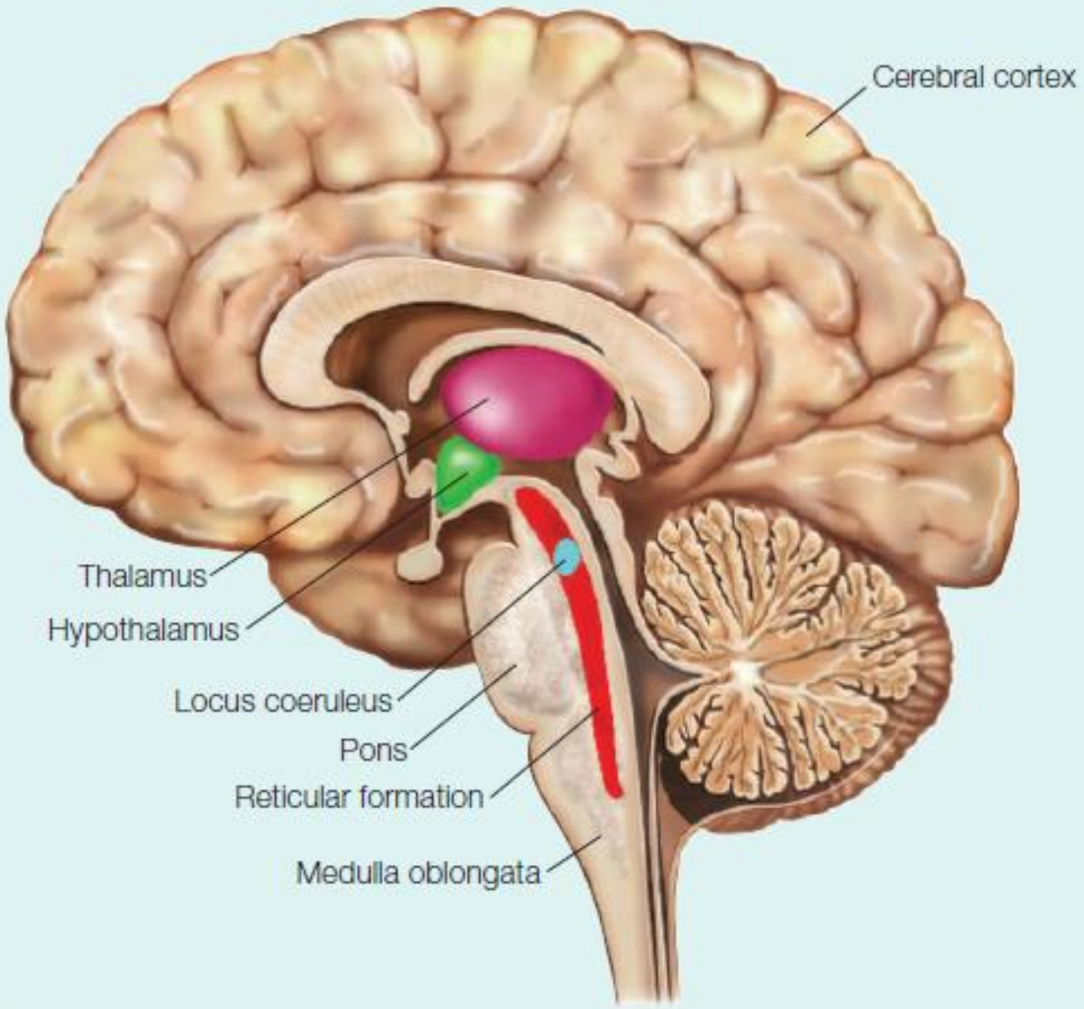


Layered architecture of the brain

- The brain is receiving the information yet cannot "perceive" it
- Layered architecture of the brain?
- Layers of neurons that process sensory information are intact
- Layers that receive the processed sensory information and control the relay of that information are not intact



Anatomy of Consciousness



The cerebral cortex, thalamus, brainstem, and hypothalamus are largely responsible for the conscious mind.

Processing in the brainstem and thalamus is sufficient for an organism to be alive, awake, alert, and aware of the current moment and place.

- The reticular activating system is involved with arousal, regulating sleep–wake cycles, and mediating attention.
- The contents of our conscious experience are expanded by processing in the cerebral cortex.

Levels of awareness

- Coma (brain is alive) –external world not communicating with the internal world
- unresponsive wakefulness syndrome (UWS) – open eyes but show only reflex behavior – spinal nerve circuit
- minimally conscious state (MCS) patients -who show localization to pain and non reflex movement.
    - they will visually fixate on or pursue a stimulus, or will follow simple commands like “squeeze my hand”
- Locked in syndrome (LIS) –
    - lesion to the ventral part of the pons
    - unable to move any muscle but is fully conscious and has normal sleep–wake cycles.
    - ability to voluntarily blink an eyelid or make very small vertical eye movements
- Subconscious (background activity in the brain, memory, biases)
- Other factors that can alter consciousness?

Levels of Awareness

- Awake
- Sleep
- Sleepwalking
  - half the brain is awake
  - Complex motor behavior and emotion generation are active—the cerebellum, posterior cingulate cortex (important for monitoring functions), and brainstem
  - frontal lobe that are involved in planning, attention, judgment, inhibition of automatic responses, recognition of emotional expressions, and emotion regulation are asleep, along with the parietal association cortex
  - the cortex, anterior cingulate cortex (important for cognitive control and emotional regulation), and cerebrum are asleep.

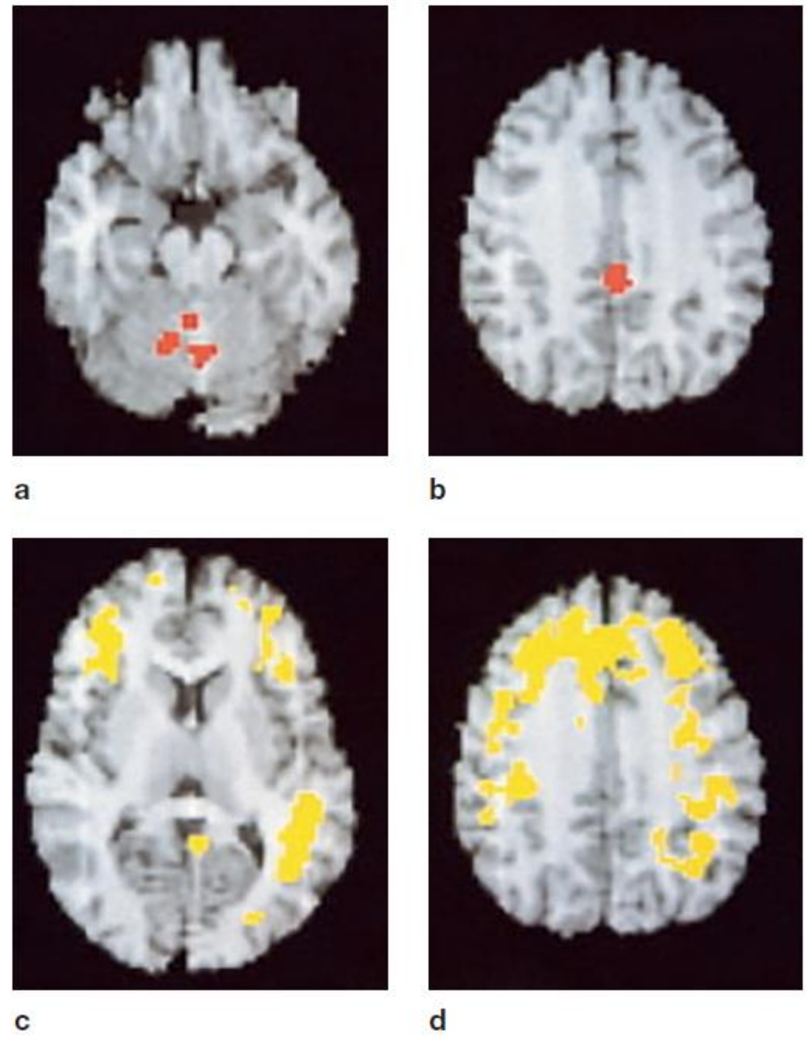


FIGURE 14.8 Neuroimaging findings during sleepwalking. Areas in red indicate 25% more blood flow during a sleepwalking episode than in quiet Stages 3 to 4 NREM sleep in cerebellum **(a)** and posterior cingulate cortex **(b)**. **(c, d)** Areas in yellow are deactivated during sleepwalking compared to normal wakeful volunteers. Large areas of frontal and parietal association cortices remain deactivated during sleepwalking.

Non-conscious or Sub-conscious processing

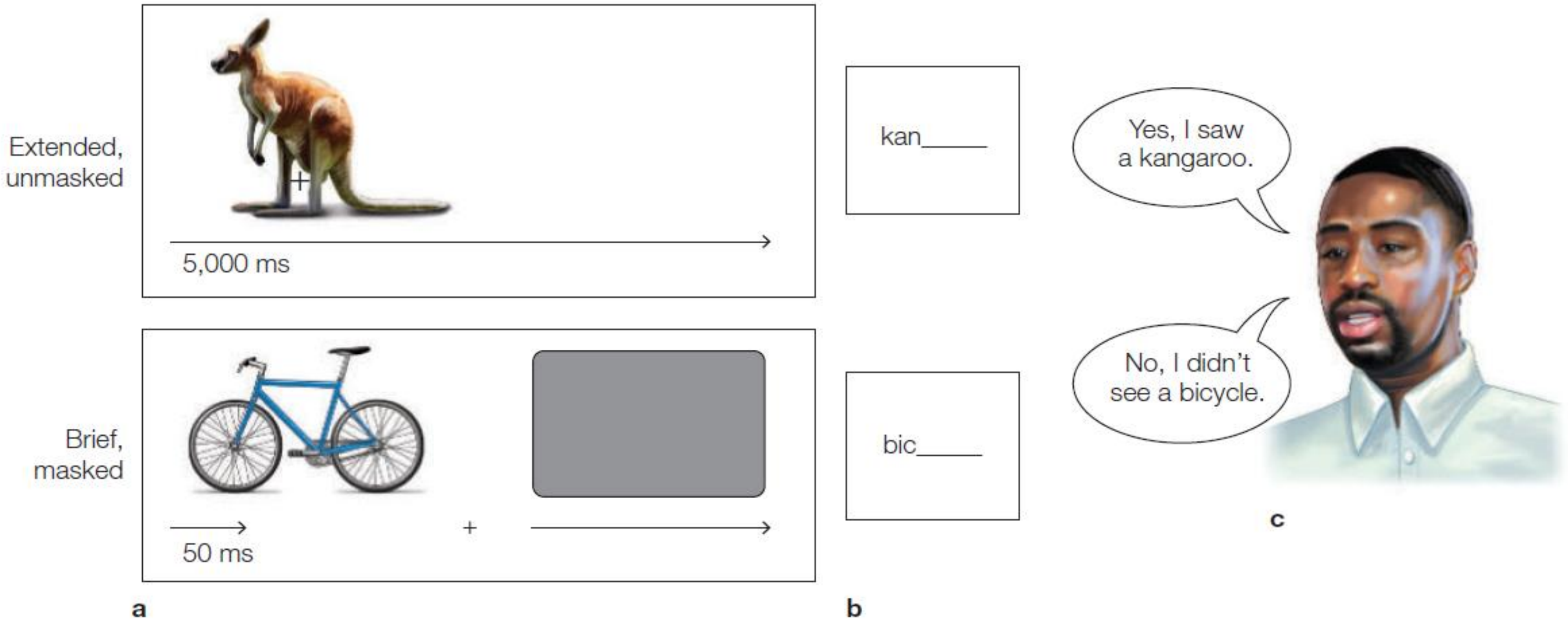


FIGURE 14.19 Picture-to-word priming paradigm.
(a) During the study, either extended and unmasked (top) or brief and masked (bottom) presentations were used. **(b)** During the test, participants were asked to complete word stems ("kan" and "bic" in this example). Priming performance was identical between extended and brief presentations. **(c)** Afterward, participants were asked whether they remembered seeing the words as pictures. Here, performance differed: Participants usually remembered seeing the extended presentations but regularly denied having seen the brief presentations.

Non-conscious or Sub-conscious processing

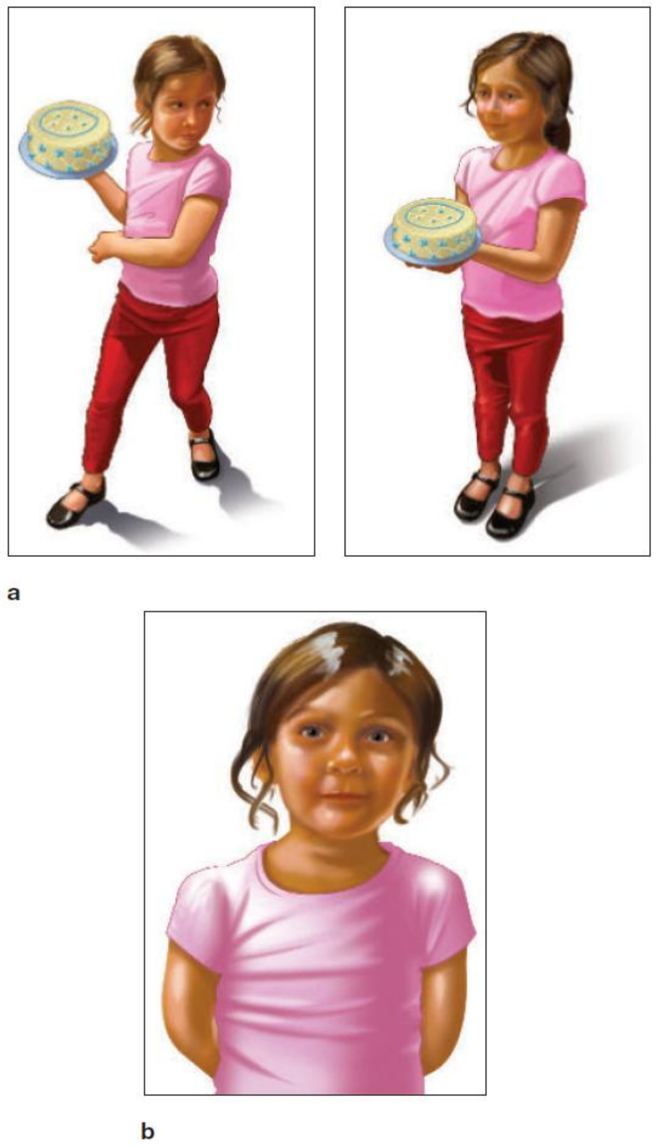


FIGURE 14.18 Testing subliminal perception.
(a) A participant is quickly shown just one picture of a girl, similar to these images, in such a way that the participant is not consciously aware of the picture's content. The participant is then shown a neutral picture **(b)** and is asked to describe the girl's character. Judgments of the girl's character have been found to be biased by the previous subthreshold presentation.

- Can information or knowledge or ability be transferred from conscious to non-conscious?

- E.g. car driving, playing chess, playing a musical instrument

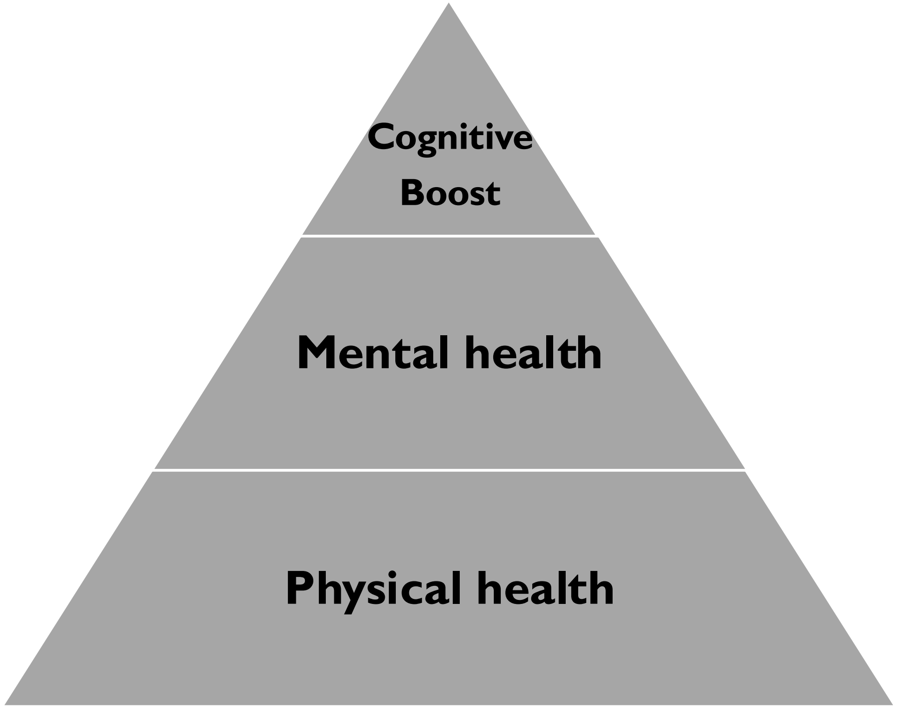
Subjective experience

- Subjective experience – qualia or qualitative nature of an experience
- Sentience – ability to sense or feel

- Deafness, blindness – sentience is intact, conscious experience of a particular sense is absent
- Damage to Wernicke's area – cannot comprehend speech but understand facial expressions and intentions of others.
- Chat GPT?

NEURODEVELOPMENT AND ROLE OF EPIGENETICS

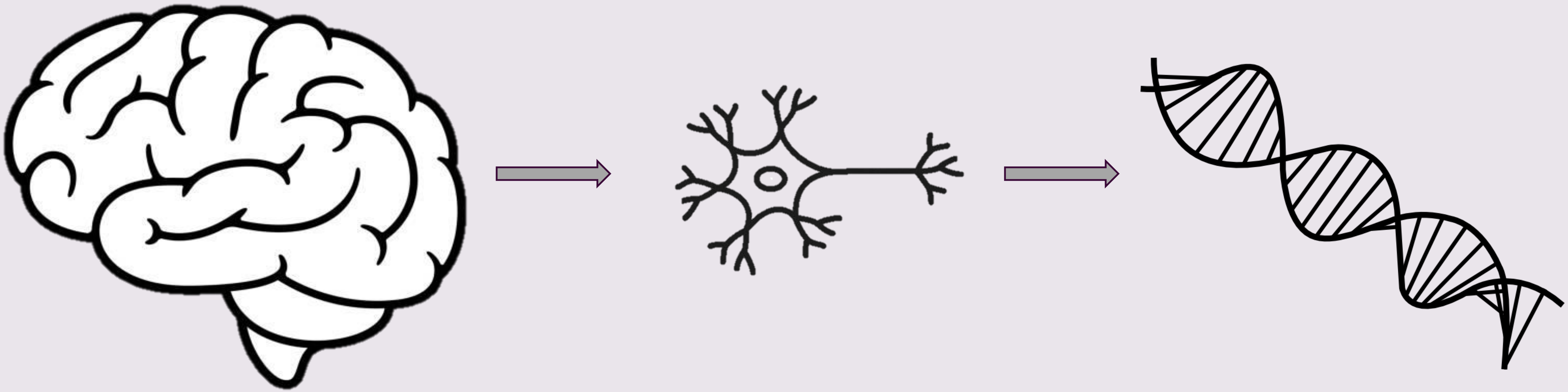
Vaishnavi Kodakandla


Cognitive
Boost
Mental health
Physical health

WHY DOES THAT HAPPEN?

How does an external action change how we feel?

OUR BRAIN…



OUR BRAIN FORMS CONNECTIONS AND UNDERGOES CHANGES THROUGHOUT LIFE

Neurodevelopment is a term that refers to the brain's development of these systems or networks.

It encompasses a complex series of processes that begin in embryonic stages and continue throughout the lifespan.

During the developmental period from infancy through adolescence, neurodevelopment and behavior are intricately related.

It is responsible for:
Structural consolidation
Skill acquisition

Neural and cognitive development have a parallel growth.

The structural architecture, cytological connections, and precise timing of development
play a crucial role in ensuring optimal growth and function.

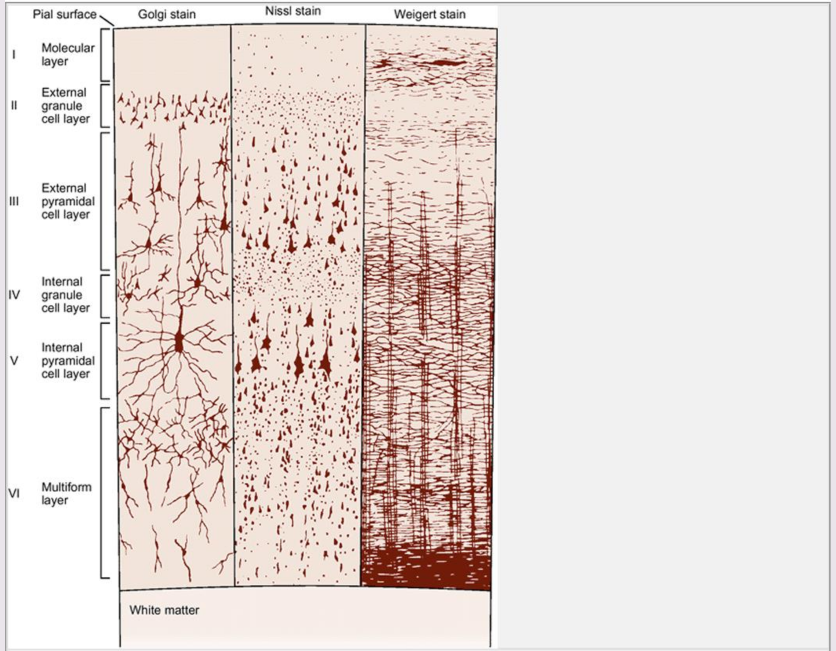


Figure 17-6 The neurons of the cerebral cortex are arranged in distinctive layers. The appearance of the cortex depends on what is used to stain it. The Golgi stain reveals neuronal cell bodies and dendritic trees. The Nissl method shows cell bodies and proximal dendrites. A Weigert stain for myelinated fibers reveals the pattern of axonal distribution. (From Heimer 1994.)

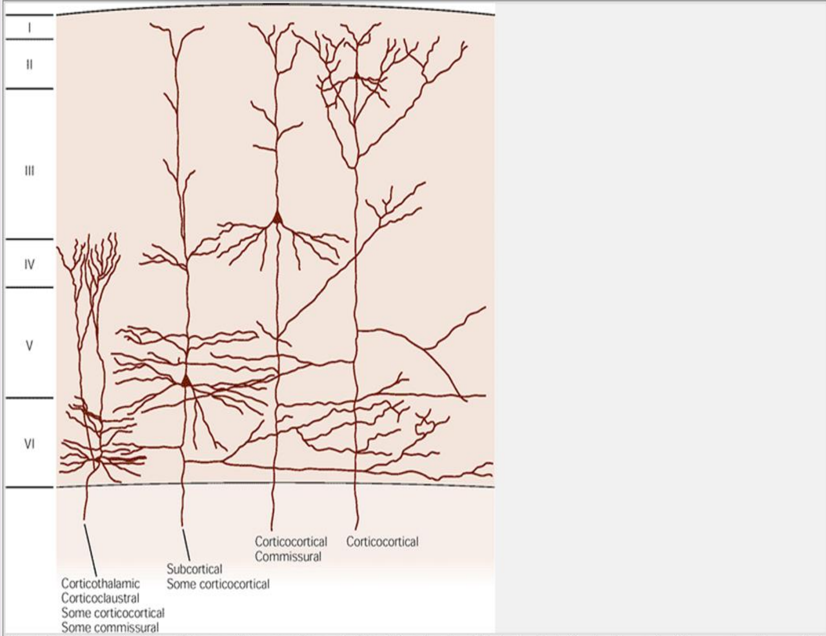


Figure 17-8 Neurons in different layers of the neocortex project to different parts of the brain. Projections to other parts of the neocortex, the so-called corticocortical or associational connections, arise primarily from neurons in layers II and III. Projections to subcortical regions arise mainly from layers V and VI. (From Jones 1986.)

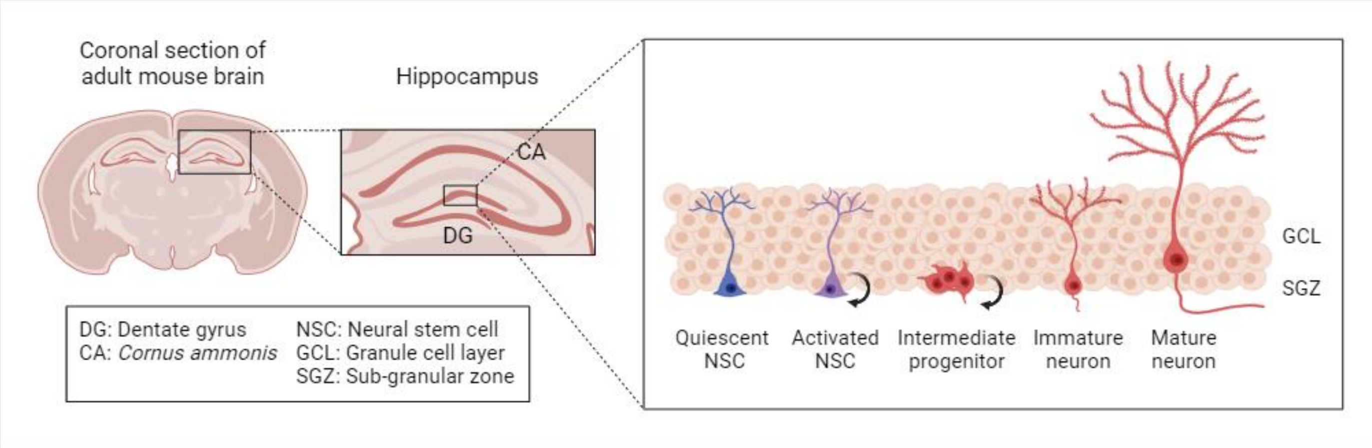
Developmental Stage	Life Stage	Key Processes	Description
Neurogenesis	Prenatal (3rd–4th week of gestation to mid-pregnancy)	Formation of neurons	Neurons are generated from neural stem cells in the ventricular zone of the neural tube. **The majority of neurons are created before birth.**
Neuronal Migration	Prenatal (6th week to birth, peak at 3–5 months gestation)	Movement of neurons to their destined locations	Neurons migrate along radial glial cells to form the six-layered structure of the cerebral cortex. **Defects in migration can lead to conditions like lissencephaly**.
Differentiation	Prenatal (mid-gestation) & continues postnatally	Specialization of neurons	Neurons develop into different types (excitatory, inhibitory, sensory, motor) and establish their functions based on genetic and environmental signals.
Synaptogenesis	Late prenatal to early postnatal (begins around 20 weeks gestation, peaks at 2–3 years postnatally)	Formation of synapses	Connections between neurons are established, allowing communication between different brain regions. This process continues into adulthood but is most intense in early childhood.

(Tierney, A. L., & Nelson III, C. A., 2009)

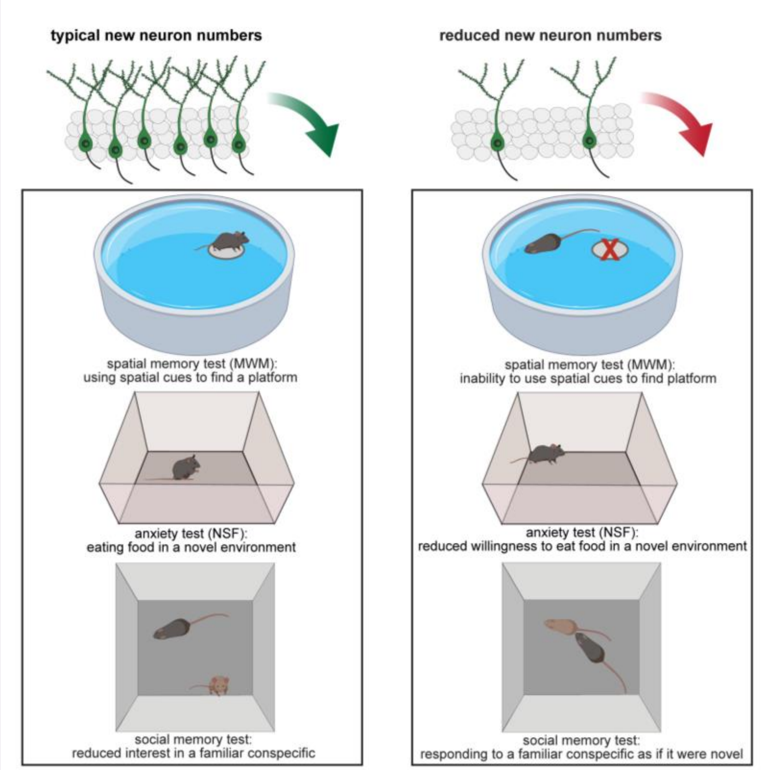
Developmental Stage	Life Stage	Key Processes	Description
Myelination	Prenatal (starts ~24 weeks gestation) to adulthood (peaks in infancy and adolescence)	Development of myelin sheath	Myelin, a fatty substance, wraps around axons to increase the speed of electrical signals. Begins in the spinal cord and moves toward the brain. **The prefrontal cortex is myelinated last.**
Synaptic Pruning	Early childhood to adolescence (peaks between 2–10 years, continues into early adulthood)	Elimination of excess synapses	Synapses that are rarely used are removed to make brain networks more efficient. "Use it or lose it" principle applies. **Over-pruning is linked to disorders like schizophrenia.**
Experience-Dependent Plasticity	Throughout life (most prominent in early childhood)	Modification of neural circuits based on experience	The brain adapts to environmental inputs like learning a language, social interactions, or skill acquisition. Highly active in early childhood but continues throughout life.

(Tierney, A. L., & Nelson III, C. A., 2009)

NEURAL DEVELOPMENT CONTINUES INTO ADULTHOOD

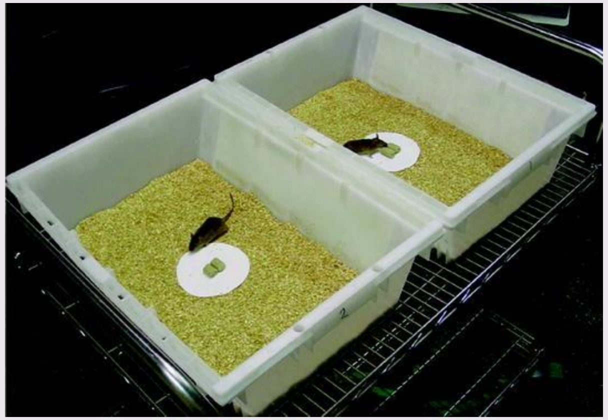


The subgranular zone of the dentate gyrus (DG) of the adult brain of mice hosts a niche of neural stem cells (NSCs).



Compared to rodents with typical numbers of new neurons (left), rodents with reduced adult neurogenesis (right) are impaired cognitively.

Heren, they are unable to locate the location of a hidden platform in the Morris water maze.



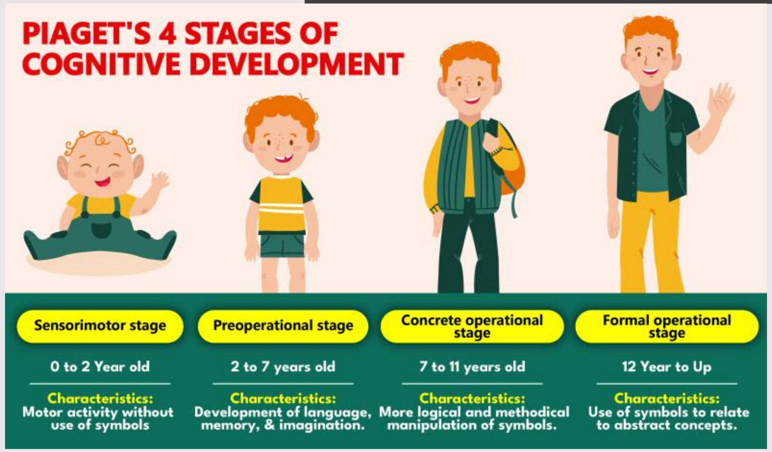
High latency to eat ~ more anxious

They also show Atypical responses in anxiety tests- different latencies to approach food in the novelty suppressed feeding task

They also display impaired social cognition- inability to recognize previously encountered mice in a social interaction test.

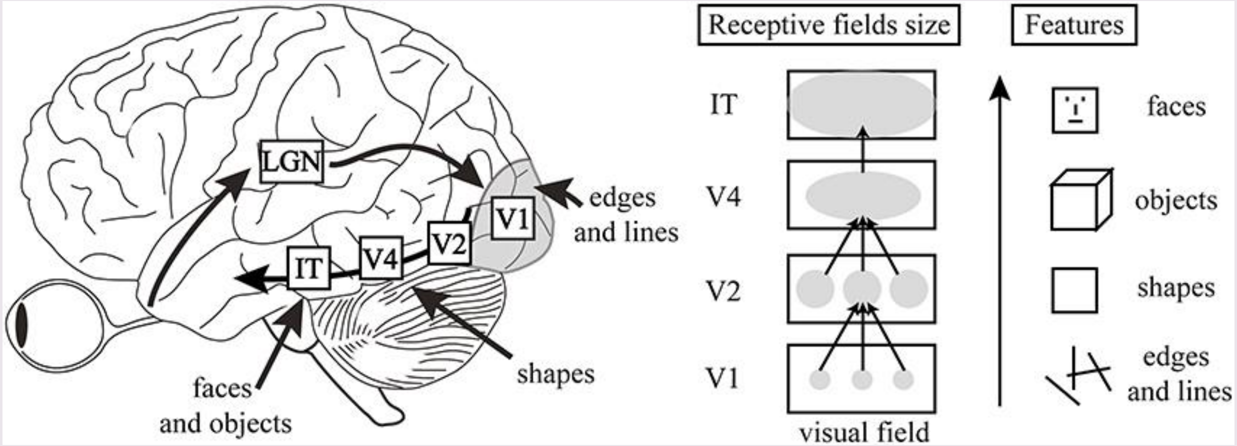
(Cope, E. C., & Gould, E., 2019)

THERE ARE PRINCIPLES THAT GOVERN THIS DEVELOPMENT



Discontinuity- where qualitative changes occur at different developmental stages

Gene-environment interaction- which balances genetic predispositions with environmental influences



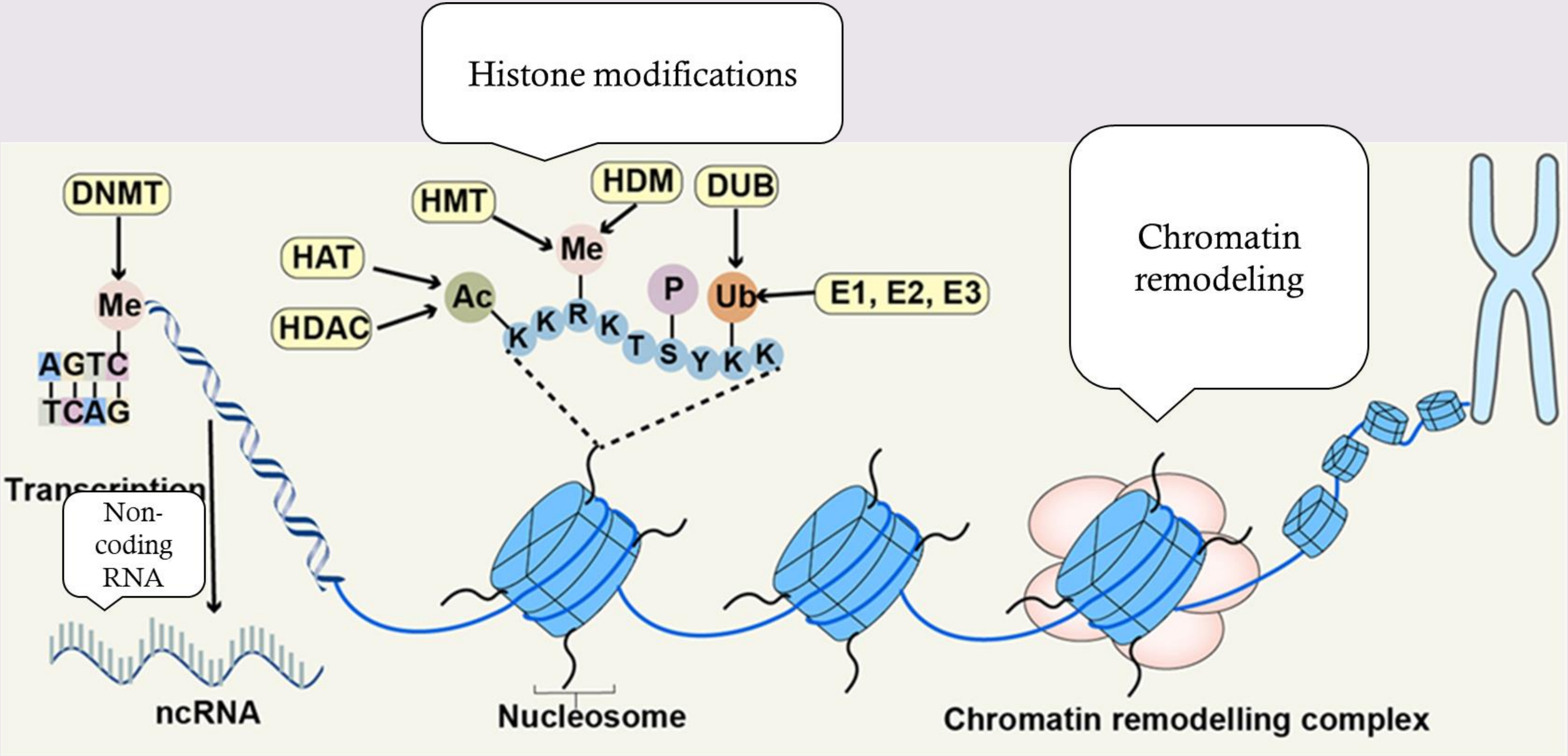
Hierarchy- reflecting the orderly organization of brain structures and functions over time

(Pérez, E. & Capilla, A., 2011)

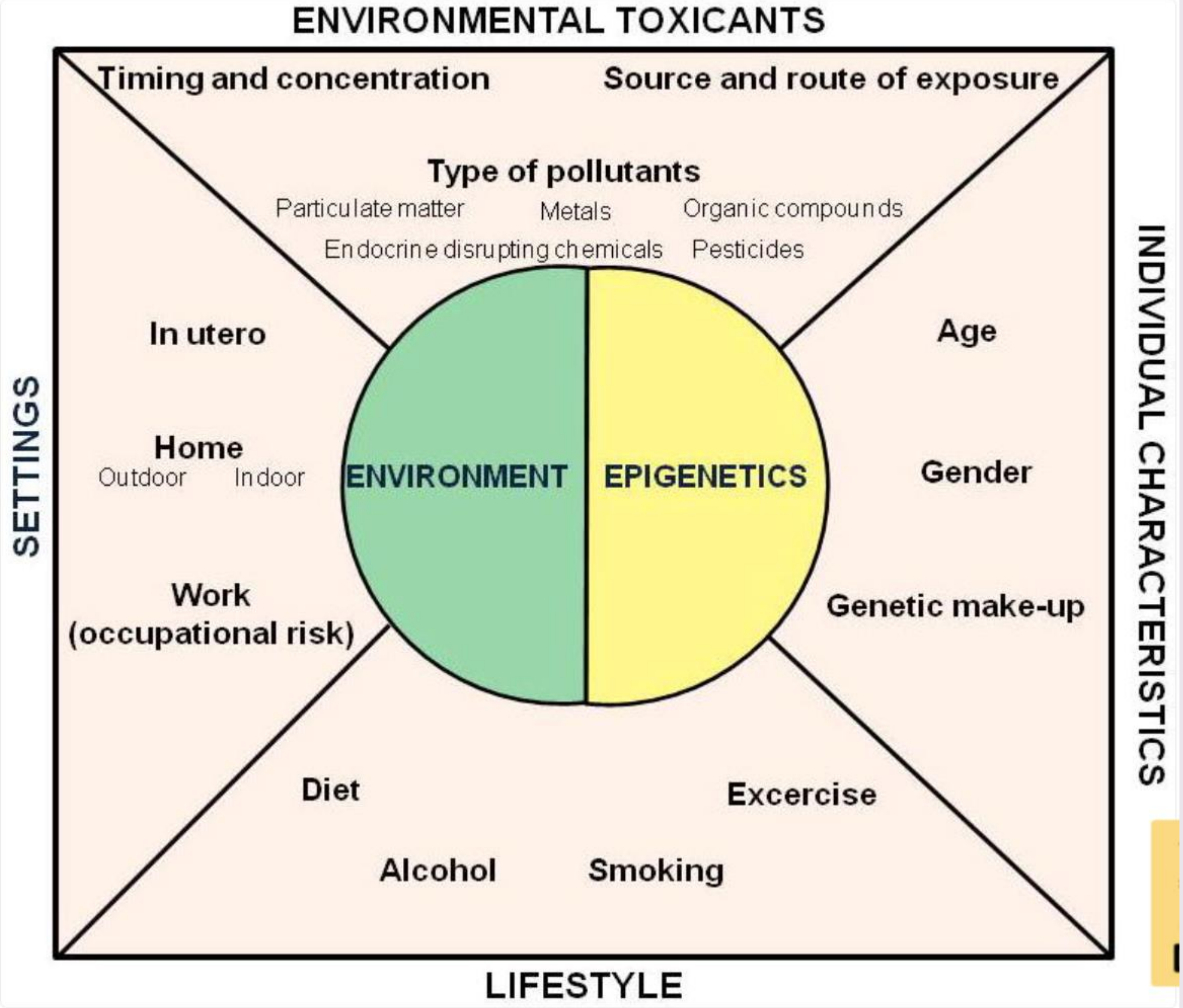
Genes are responsible for the manifestation of such an intricate development and organisation.

Environmental factors can influence the expression of these genes. **Epigenetic mechanisms** represent a crucial link between environmental experiences and gene expression in the nervous system.

Unlike genetic mutations that alter DNA sequences, epigenetic modifications regulate which genes are expressed or silenced without changing the underlying genetic code.



Systems that modify gene expression


ENVIRONMENTAL TOXICANTS
Timing and concentration
Source and route of exposure
Type of pollutants
Particulate matter
Metals
Organic compounds
Endocrine disrupting chemicals
Pesticides
SETTINGS
In utero
Home
Outdoor
Indoor
Work
(occupational risk)
ENVIRONMENT
EPIGENETICS
INDIVIDUAL CHARACTERISTICS
Age
Gender
Genetic make-up
Diet
Excercise
Alcohol
Smoking
LIFESTYLE

EPIGENETIC EFFECTS OF POLLUTION

Heavy metals alter epigenetic **regulation** and may trigger cancer, cardiovascular problems and even neurodegenerative diseases.

Polycyclic aromatic hydrocarbons (PAHs) from coal, fossil fuels, cigarette smoke cause **transgenerational epigenetic changes**, cancer, asthma, and fetal growth impairment.

Bisphenol-A (BPA) is a **xenoestroge**n that induces hypomethylation of specific genes.

Air pollution (PM1, NO2, ozone) → **interferes with T-helper gene expression** → chronic inflammation, asthma, cardiovascular disease.

Endocrine disruptors are exogenous chemicals that mimic or interfere with hormone signaling, often leading to epigenetic changes.

Found in environmental pollutants like **BPA (Bisphenol A)** and **phytoestrogens** in foods such as soy.

Soy Phytoestrogens

Soy-derived phytoestrogens (e.g., **genistein**) have demonstrated protective effects against prostate and breast cancer via epigenetic regulation.

These compounds reverse DNA hypermethylation, restoring the expression of key tumor suppressor genes:

- BRCA1, BRCA2: Critical in breast cancer prevention.
- GSTP1, EPHB2: Linked to prostate cancer suppression.

STRESS AND EPIGENETICS

Oxidative stress:

PUFAs (Polyunsaturated Fatty Acids)- Excessive intake of PUFAs can generate **free radicals**, leading to **oxidative stress** which induces epigenetic alterations that may contribute to chronic diseases like **cancer** and **neurodegeneration**.

Polyphenol-rich foods such as cruciferous vegetables (broccoli, kale) and green tea exhibit protective epigenetic effects.

- These compounds **reduce the activity of DNA methyltransferases (DNMTs),** enzymes responsible for adding methyl groups to DNA.
- Evidence from both *in vitro* (cell culture) and *in vivo* (animal) studies supports their role in preventing aberrant DNA methylation.

Acute Stress:

Acute stress triggers progenitor cell division, aiding **tissue repair** and **maintaining homeostasis**.

This **transient response** is essential for **rapid recovery** from injuries.

Chronic Stress:

Chronic stress **overwhelms renewal systems**, leading to epigenetic abnormalities.

Sustained inflammation and oxidative stress cause **DNA damage, promoting tumorigenesis.**

These changes foster the evolution of a tumor microenvironment, supporting abnormal cellular growth.

Chronic stress is also linked to neurodegeneration, with epigenetic alterations contributing to diseases like Alzheimer's.

Psychological Stress

Psychological stress can leave lasting epigenetic scars.

Glucocorticoid receptor gene promoter in the hippocampus of human suicide victims and controls was examined.

Hypermethylation of the glucocorticoid receptor gene was observed in suicide victims with a history of childhood abuse. This causes impairment in negative feedback regulation of the HPA axis.

No hypermethylation was found in controls or suicide victims without a history of childhood abuse.

Maternal Grooming and Protective Epigenetic Effects

Maternal licking/grooming in rodents triggers serotonin (5-HT) release, initiating downstream signaling that promotes hypomethylation of stress-related genes.

This hypomethylation enhances resilience to stress in offspring, showcasing how nurturing behaviors can positively influence epigenetics.

Condition	Epigenetic Change	Gene Studied	Outcome
Childhood Abuse	Hypermethylation	Glucocorticoid Receptor	Impaired stress response; linked to suicide risk
Maternal Grooming (Positive)	Hypomethylation	Stress-related Genes	Enhanced resilience to stress

(Weaver, I. C, 2007).

EPIGENETICS AND DISEASE

Disorder	Epigenetic Change	Affected Genes	Outcome
Autism Spectrum Disorders	DNA methylation → gene silencing	Retinoic Acid Receptor, BCL2	Impaired brain development
Alzheimer's Disease	Loss of DNA methylation → overexpression	APP	Amyloid plaques, neurofibrillary tangles → dementia
Fragile X Syndrome	Histone deacetylation + DNA methylation → silencing	FMR1	Intellectual disability, autism, hyperactivity, anxiety

SLEEP AND NEUROGENESIS

Impact on Neurogenesis:

Prolonged restriction or disruption of sleep may have cumulative effects, leading to a significant **decrease in hippocampal cell proliferation, cell survival, and overall neurogenesis.**

This can endanger hippocampal integrity, potentially leading to cognitive dysfunction and contributing to the development of mood disorders.