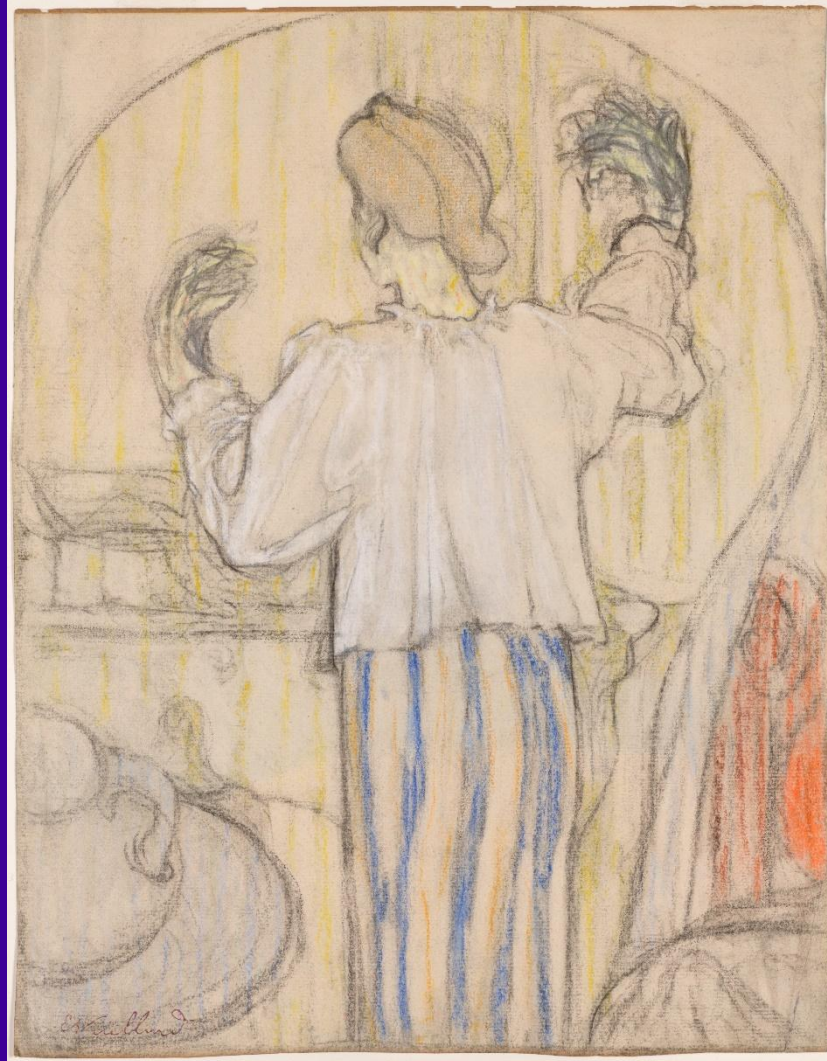


Memory



Joanne Alonso Byars, MD

January 27, 2021

Before we start discussing memory...

It's memory test time!

- Why?
 - Have to test after a delay

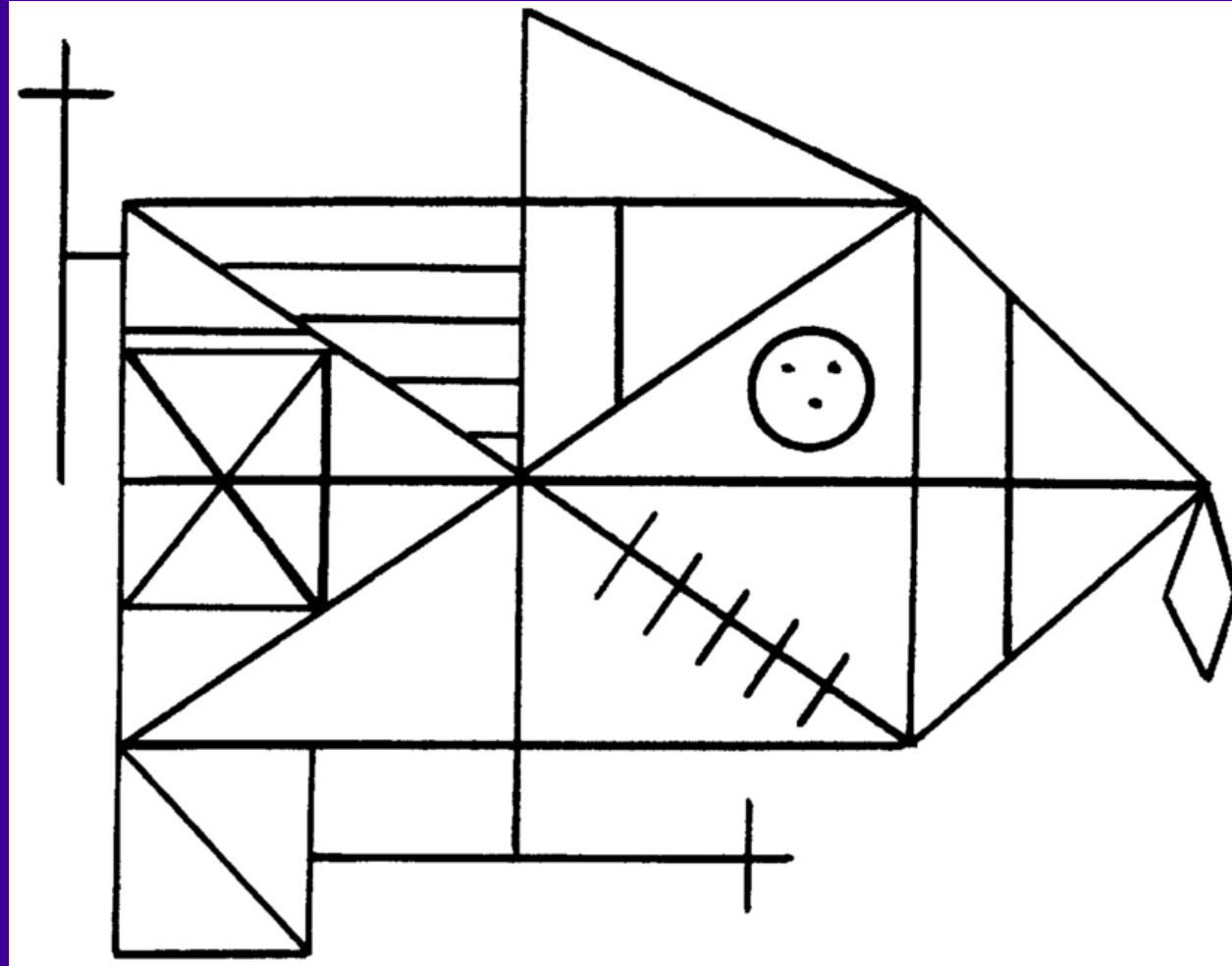


HVLT administration

- Keep score at home!



Rey-Osterreith Complex Figure



ROCF administration

- Copy
- Immediate recall



Now, let's talk about memory!



What is memory?

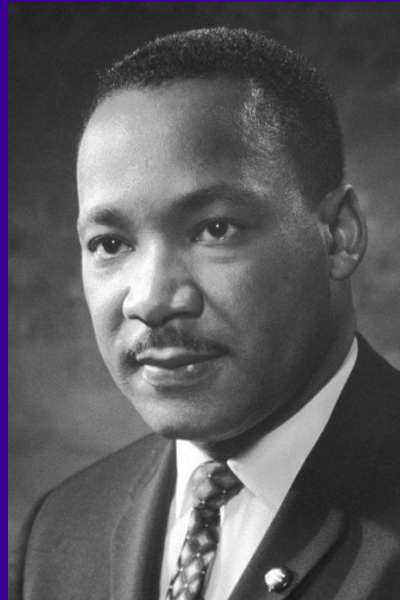
- The ability to encode and store information in the present, and retrieve that information in the future

Types of memory

- 2 types
 - Explicit
 - Implicit



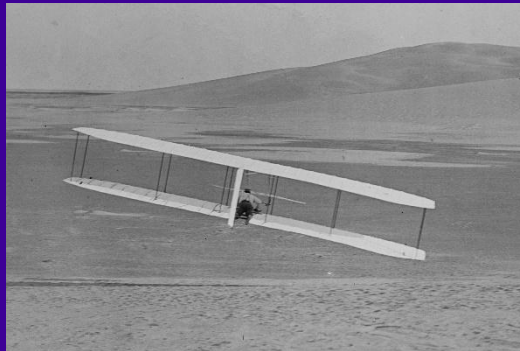
- Explicit:
 - Aka declarative memory
 - Involves conscious recall
 - Can often put into words or draw
 - Who was Martin Luther King, Jr
 - What your wedding was like
 - Involves hippocampus/circuit of Papez



- Implicit:
 - Encompasses:
 - Procedural memory
 - Remembering how to do something
 - How to ride a bike
 - How to swim
 - Classical/operant conditioning
 - Pavlov's dogs, Skinner box
 - Unconscious patterns of interpersonal interaction (maybe)
 - Often hard to put into words or draw
 - Involves basal ganglia and cerebellum (among other structures) At least for motor procedural memories
- This talk focuses on explicit (declarative) memory



- Explicit (declarative) memories come in two types
 - Semantic memory:
 - Facts, things people have told you, things you read in books, things you learned in school
 - Blood supply to the cerebellum
 - Who were the Wright Brothers
 - Episodic memory:
 - Personal experiences
 - What you did after school with your best friend in 5th grade
 - The strangest experience you had in med school



- Semantic memories:
 - Not generally linked to a particular context or emotion
 - Though occasionally can be
 - Feeling sad when thinking about a very sad historical event, even though you didn't personally experience it
 - Remembering where you learned a particularly interesting fact
- Episodic:
 - Often linked to a particular context or emotion
 - But doesn't always have to be
 - Remembering brushing your teeth, but not any one specific time you did it, nor feeling much emotion about it



- Do baby boomers and older remember where they were when they first heard that JFK had been assassinated?
 - If they were living in the US at the time, they probably know exactly where they were and what they were doing, and have some dramatic story about it
 - May remember learning the news as a very shocking and sad moment
- If you're Gen X or later, do you remember where you were when you first heard that JFK had been assassinated?
 - Probably not
 - Maybe in some history class in school, or read a news story on the anniversary, or heard some conspiracy about it
 - Probably don't feel a deep emotional connection to the moment you learned about it
- Episodic for people who lived it, semantic for younger people



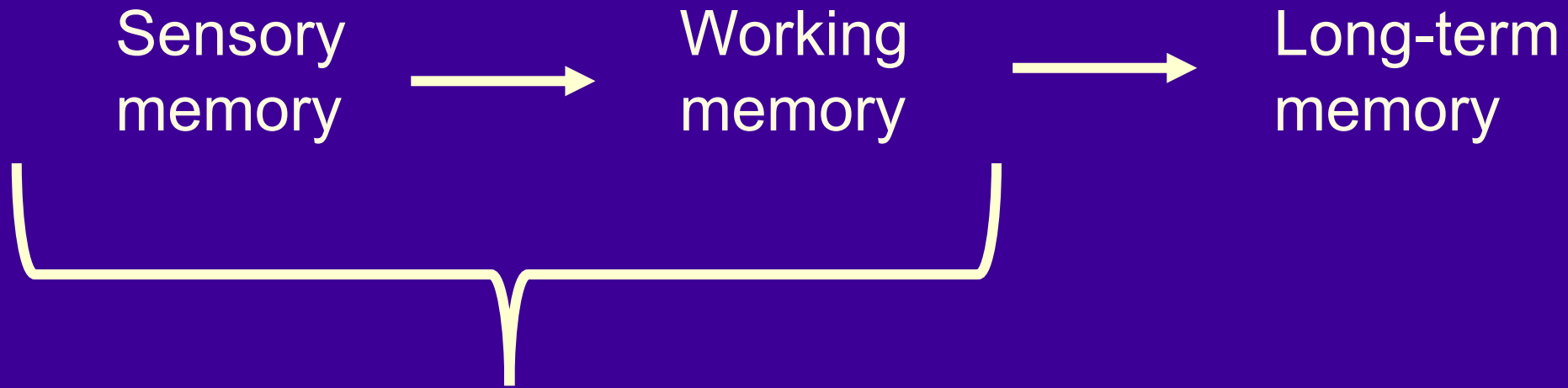
- Modalities of declarative memory
 - Verbal
 - Visual
 - Both
- Semantic visual memory
 - Where California is on a map
- Episodic visual memory
 - What your parents' faces looks like
- A personal (episodic) memory often has both verbal and visual elements
 - The first time you rode a rollercoaster



- Most formal cognitive testing focuses on semantic verbal memory
 - Can test episodic memory by asking about patient's past experiences ("What did you do for Thanksgiving last year?") and checking with family members to see if answer is correct
- Can test visual memory by having patient look at a drawing and then reproduce it from memory, or by hiding objects in the room and having patient find them (also useful in patients with aphasia)



Temporal stages of memory formation



Can also consider these as “attention and concentration”

Sensory memory

- Immediate impressions/sensations of outside world and/or internal states
- Mediated through primary sensory cortices (auditory, visual, somatosensory, etc), visceral/autonomic awareness, and limbic system
- Lasts < 1 sec
- If you pay attention to it, it will pass into working memory



Working memory

- Lasts up to 1 minute
 - Rehearsal or repetition can help retain longer
 - Mentally repeating MRN or (back in the day) a phone number you looked up
- Displaced/lost by new competing stimuli
 - You're trying to remember MRN and you get a text that distracts you
- Processed by prefrontal cortex (L for verbal, R for visual/visuospatial)
- Information is passed from sensory to short-term memory via attention/concentration



How do you turn working memories into long-term memories?

- Repetition/practice
- Association with something meaningful
 - Remembering the types of aphasias
 - Can sit down with aphasia charts and flashcards and test yourself
 - Or can remember patients you personally saw with aphasias, or at least the videos we watched
 - Neurophysiologic process: long-term potentiation
 - Occurs in hippocampus and related brain areas (circuit of Papez)



- What structure(s) do you need to have functioning explicit (declarative) memory?
 - Circuit of Papez



- What structures are in the circuit of Papez?

- Hippocampus
- Fornix
- Mammillary bodies
- Mammillothalamic tract
- Thalamus
 - Specifically the anterior thalamic nucleus

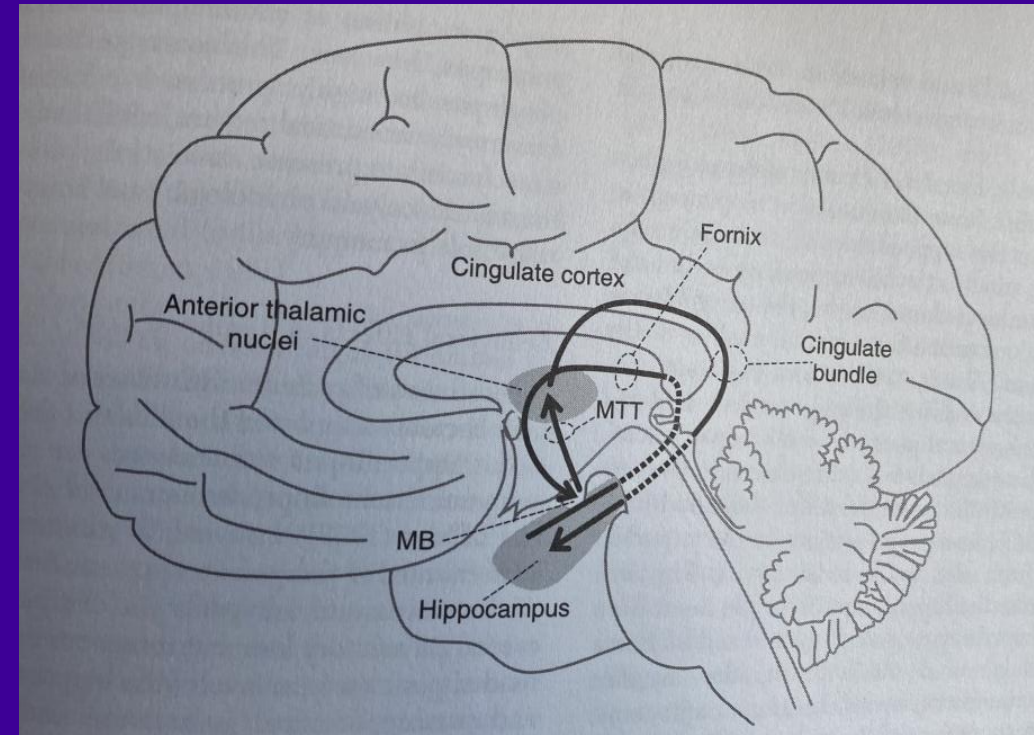
- Cingulate gyrus / cingulum

- Cingulum: the white matter of the cingulate gyrus: a big white matter tract for sending information

- Parahippocampal gyrus

- The part of the medial temporal lobe that goes around the hippocampus

- Hippocampus



Memory storage/consolidation (retention):

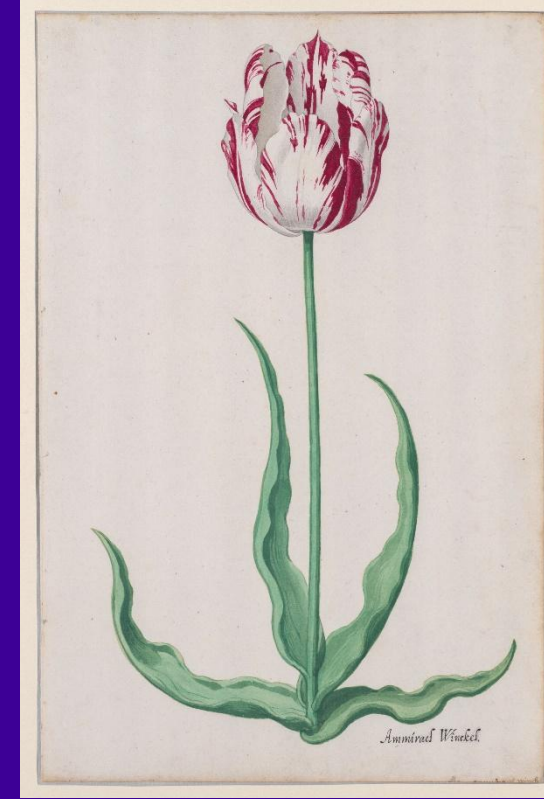
- Hippocampus

Recall:

- Parahippocampal gyrus (part of temporal lobe) and prefrontal cortex

Truly long-term storage:

- In whatever part of the cortex originally processed the external stimuli associated with the memory
 - Occipital lobe for visual stimuli, parietal lobe for tactile stimuli, etc



- Verbal memories are preferentially processed by L hippocampus and associated structures
- Visual memories are preferentially processed by R hippocampus and associated structures
- BUT: not as lateralized as language and hemispatial attention
 - If someone has a lesion destroying the one hippocampus/other associated structures, the other side can take over the job
 - I.e., unilateral hippocampal destruction will NOT give you the memory equivalent of aphasia or neglect



What are some disorders that can damage the different parts of the circuit of Papez (and thus cause memory disorders)?

Mammillary bodies: Thiamine deficiency / WKS

Hippocampus:

- Alzheimer disease
- HSV encephalitis
- Status epilepticus
- PCA stroke
- TBI
- Neurosurgery (H. M.)

Other parts:

- Stroke
- TBI
- Neurosurgery



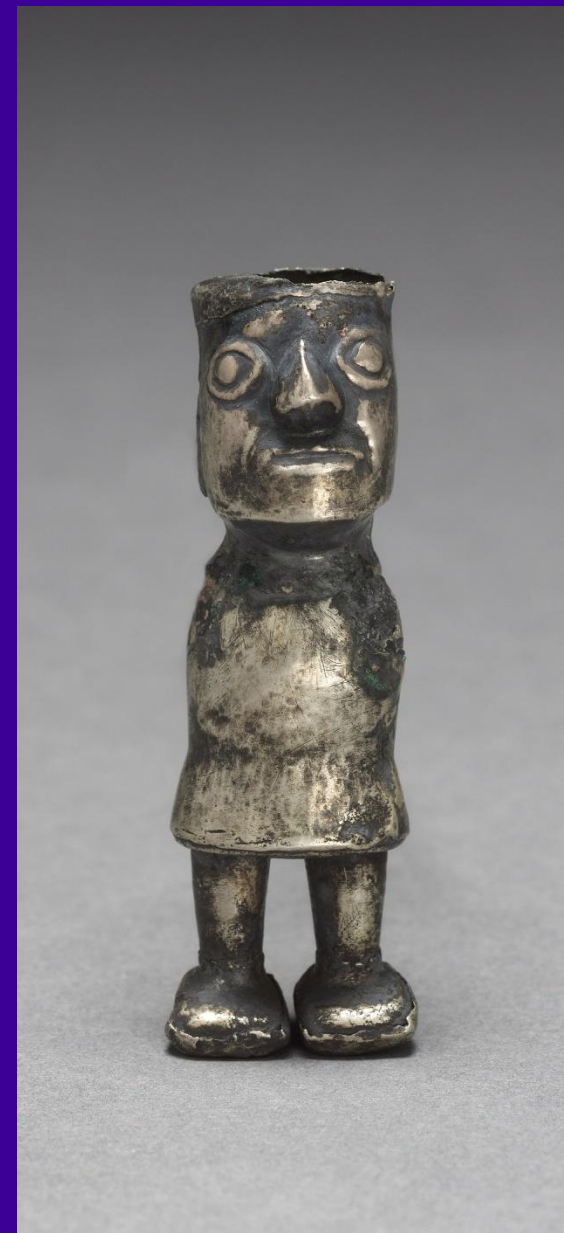
Reversible cause of memory loss:

- Transient global amnesia
 - Etiologies:
 - Migraine
 - Stroke/TIA
 - Seizure
 - Unknown etiologies (but probably related to alterations of blood flow to hippocampus)



Retrospective and prospective memory

- Retrospective (retrograde) memory
 - Remembering things that have already happened or things you have already learned about
 - State capitals
 - The date of your sister's birthday
 - Your wedding
- Prospective (anterograde) memory
 - Remembering new information/things to do in the future
 - Word list items on a neuropsychological test
 - Remembering to buy a birthday present for your sister's upcoming birthday



Damage to retrospective memory: retrograde amnesia

Damage to prospective memory: anterograde amnesia

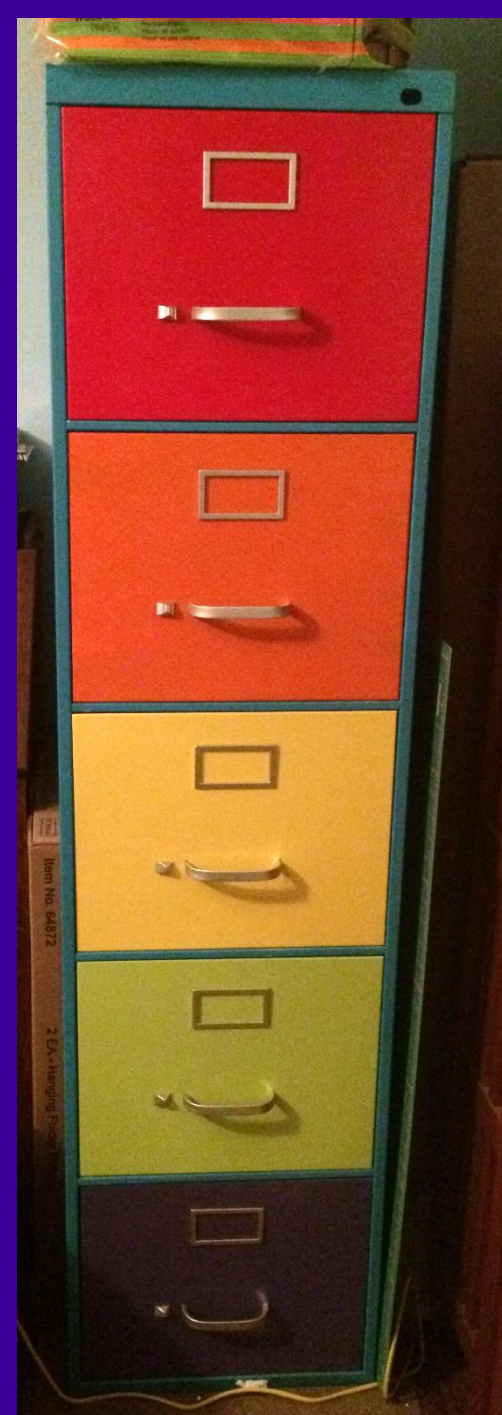


Can you have retrograde amnesia without anterograde amnesia?

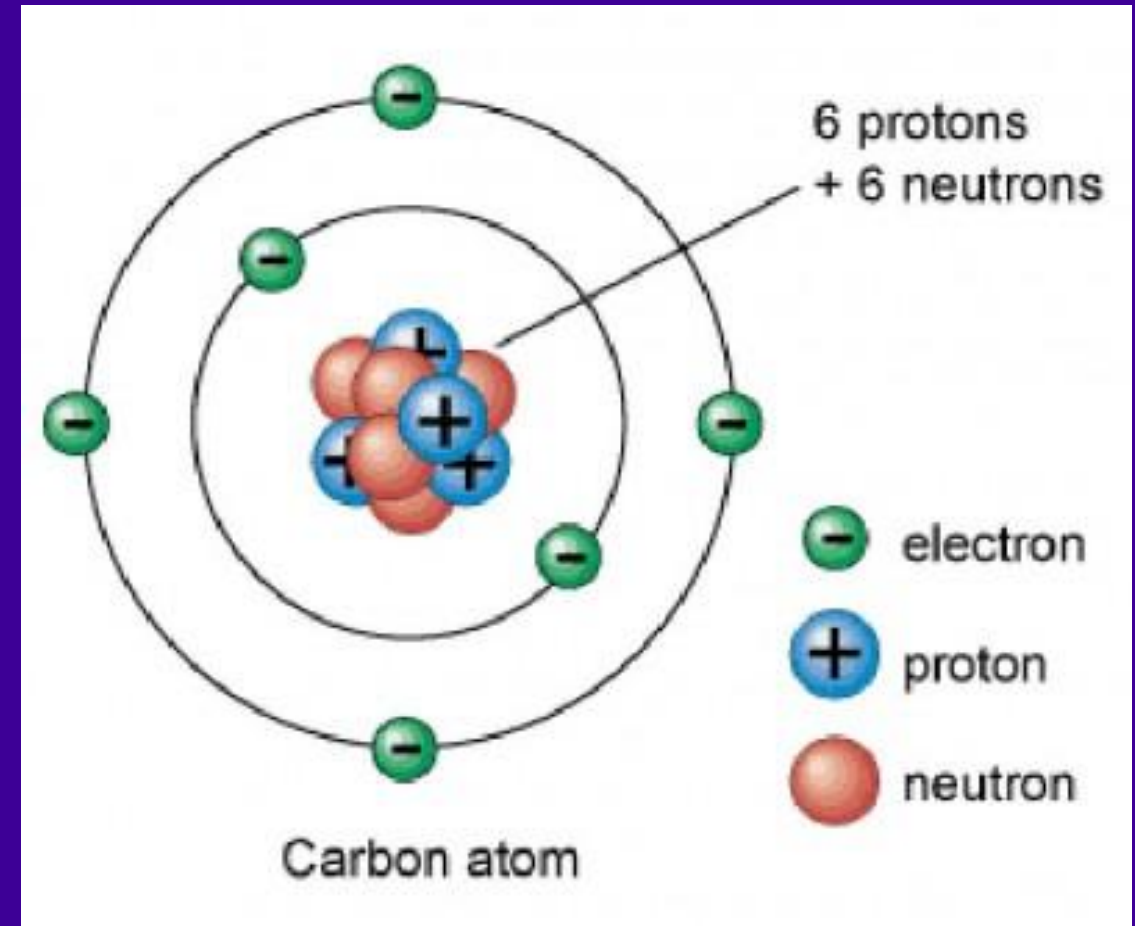
- I.e., can you have impaired ability to recall past events, with intact ability to learn new information?
 - Almost never, but is VERY RARELY POSSIBLE due to neurologic cause
 - Most retrograde amnesia without anterograde amnesia is due to psychological causes
 - But very rare cases of isolated retrograde amnesia (without anterograde amnesia) due to neurologic causes
 - Lesion locations
 - R thalamus
 - R ventral frontal cortex/uncinate fasciculus
 - Uncinate fasciculus connects frontal lobe and parahippocampal gyrus

To remember something, you need to:

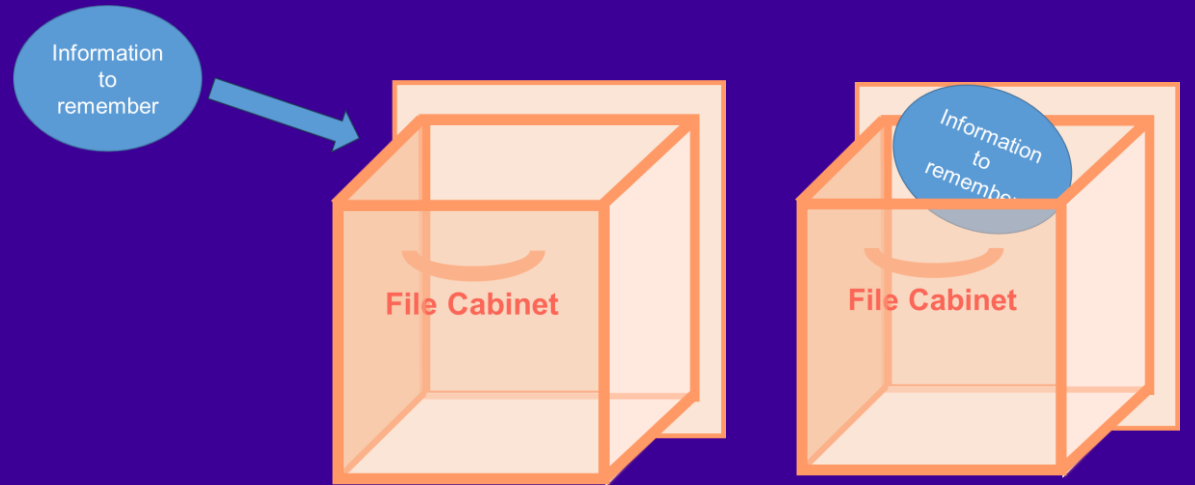
- Encode (learn) it to begin with
 - Store it
 - Retrieve it later
-
- Sometimes referred to as: registration, retention, retrieval
-
- If something goes wrong in one of these steps, you won't remember the piece of information



- We will use a file-cabinet model of memory to explore these concepts
- But memory is NOT a file cabinet!
 - Memories don't just sit there waiting for you—they change with time and new experiences
- Bohr model of the atom
 - Useful to solve problems like how many H atoms can a C atom bond
 - But electrons aren't really like little planets orbiting the nucleus—they're probability waves
- Models can be very useful, but don't mistake them for the real thing

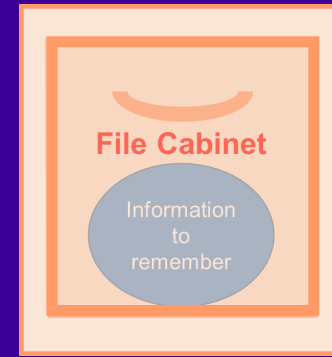


Normally functioning memory



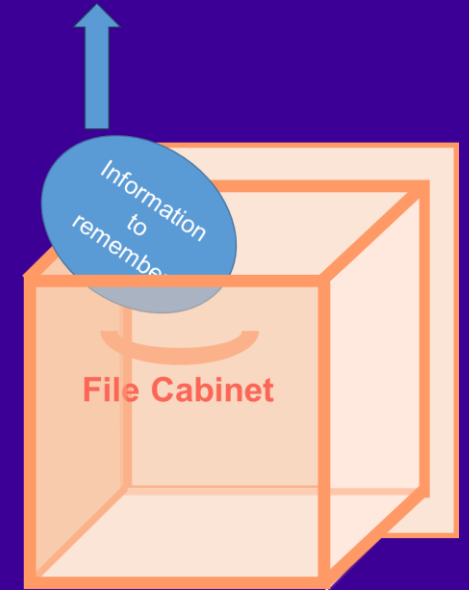
Information goes into memory

- Encoding



Information is stored in memory

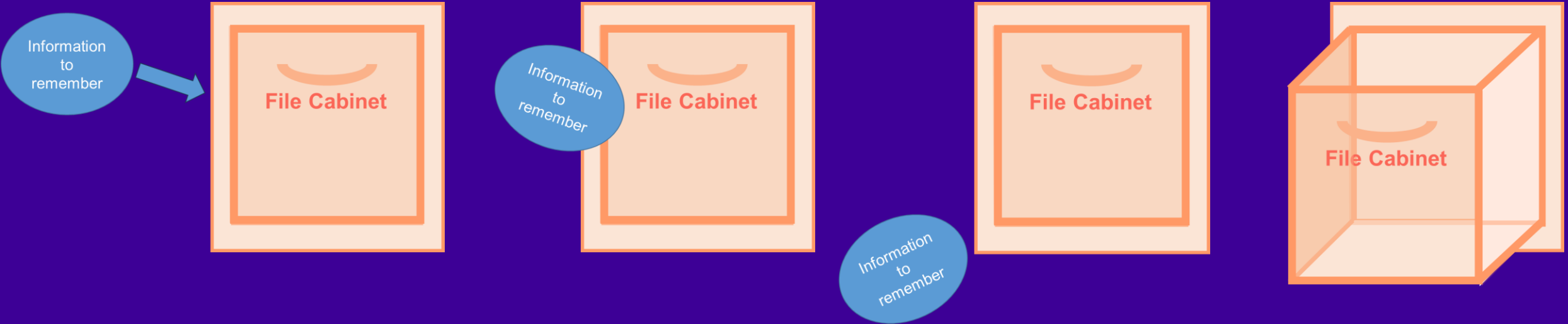
- Storage



Information is retrieved when needed

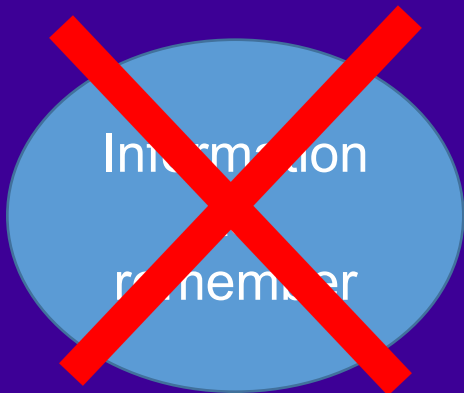
- Retrieval

Impaired encoding

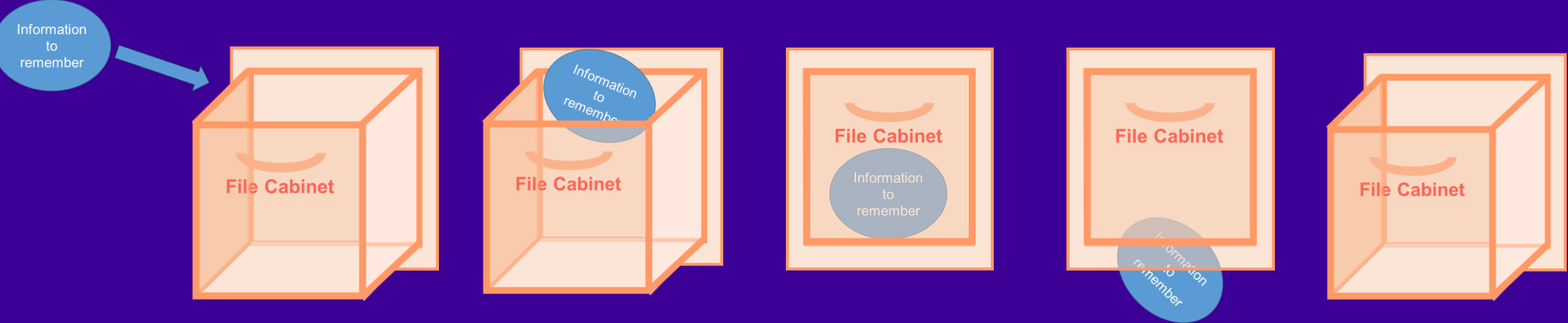


Encoding

- Mediated by prefrontal cortex
- Problems with encoding:
 - Information never got into memory system in the first place
 - Etiologies
 - Sensory loss preventing perception of information
 - Inattention
 - Insufficient effort
 - Damage to PFC

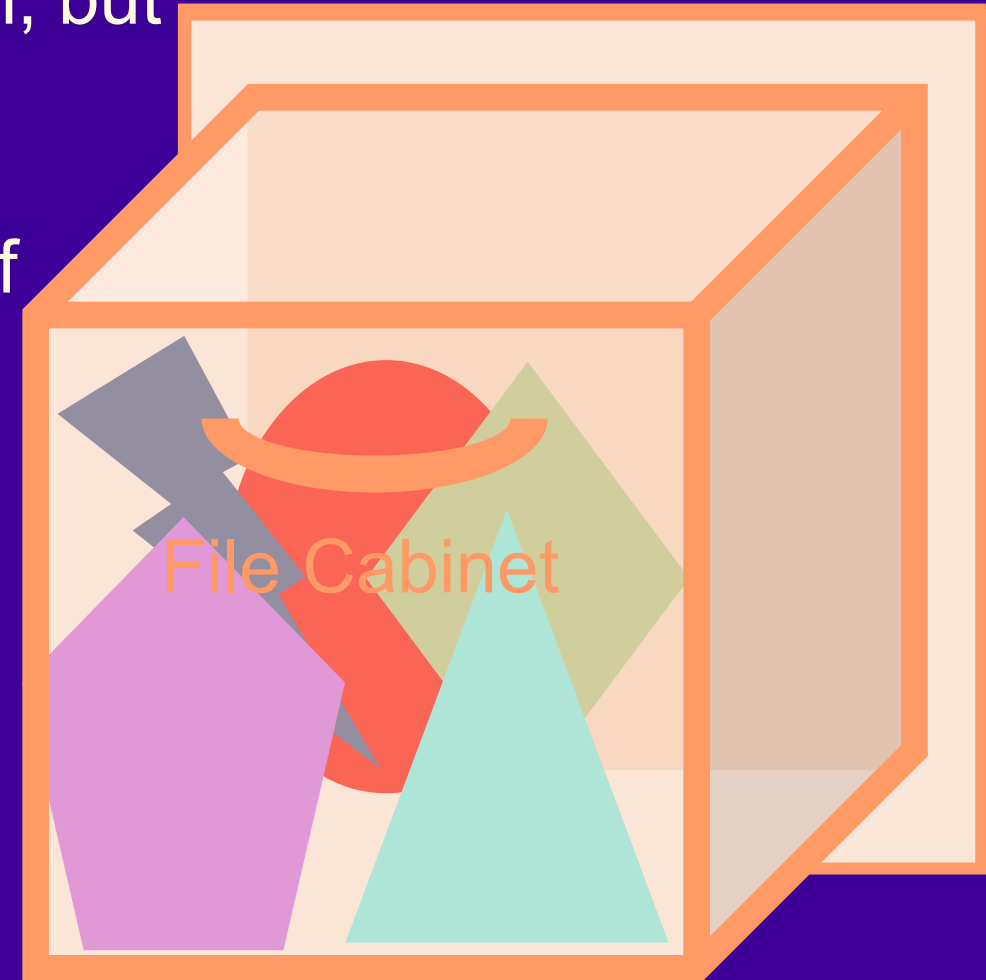
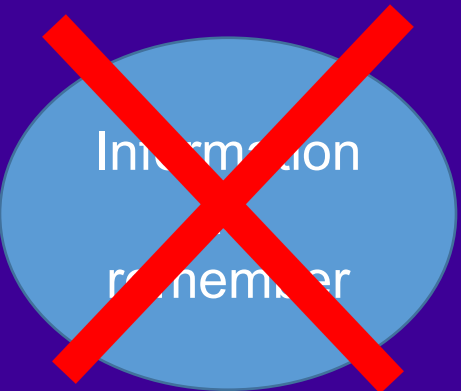


Impaired storage

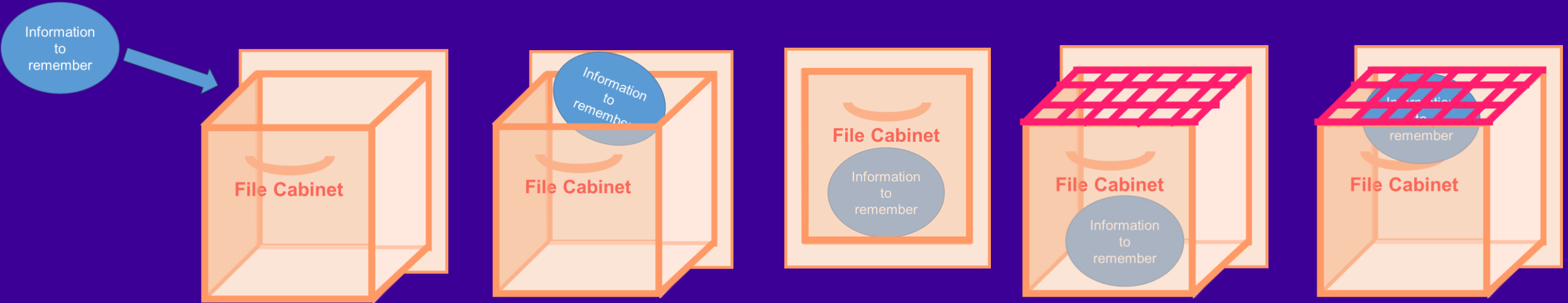


Storage

- Mediated by hippocampus/mesial temporal lobes
- Problems with storage
 - Information gets into memory system, but then gets lost
 - Etiologies
 - Damage to hippocampus/circuit of Papez

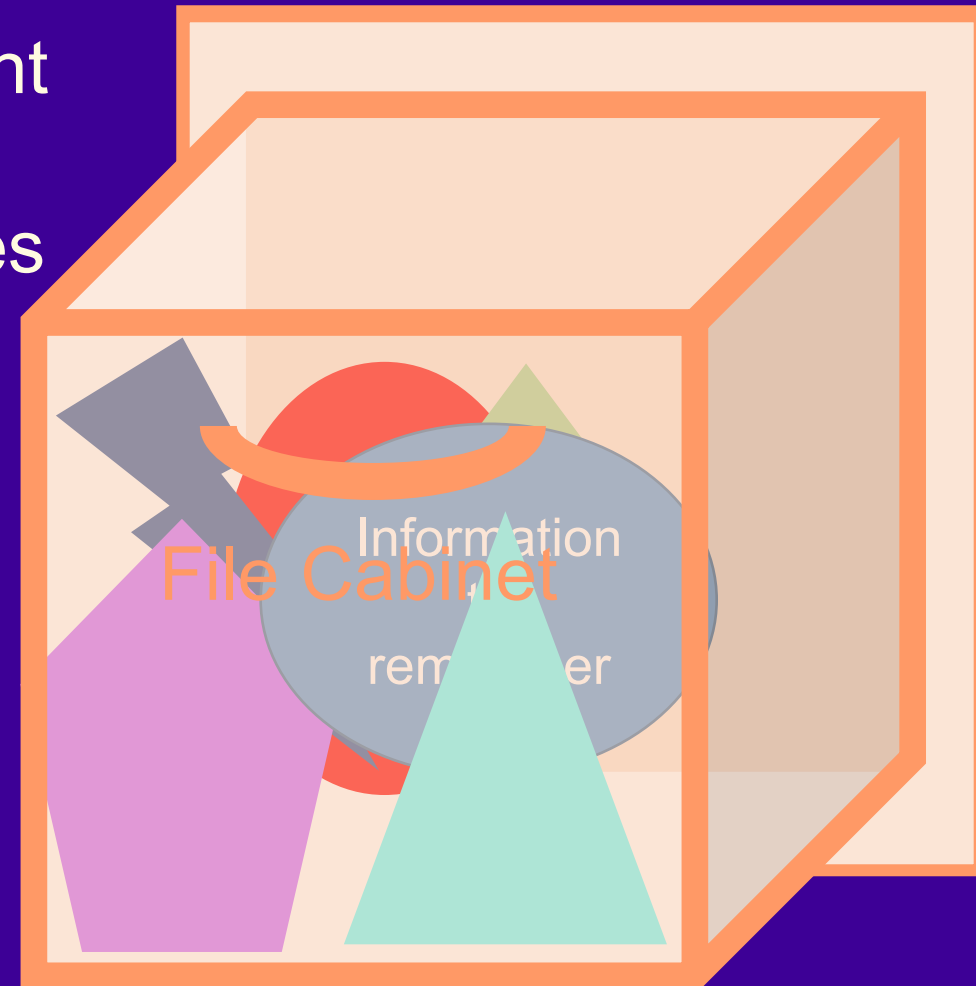


Impaired retrieval



Retrieval

- Mediated by frontal lobes
- Problems with retrieval
 - Information got into memory system and is still in there, but can't get it back out
- Cueing (e.g., “it was a type of fruit”, if patient cannot recall “apple” on the MMSE) can help with retrieval deficits, because provides some structure/context that can “fill in” for the job the frontal lobes should have done
 - Etiologies
 - Damage to frontal lobes
 - Stroke
 - TBI
 - Frontotemporal dementia
 - Cerebrovascular disease



But..

- Memory is not actually like a file cabinet!
- Memories don't sit there undisturbed waiting for you; they interact with the rest of your brain and can undergo changes
- File cabinet is a useful metaphor for understanding the neural basis for memory
 - But it's not reality!



- Displacement
 - New information overwrites old information
- Misattribution
 - Remember something happening, but attribute it to incorrect circumstances/source
- Bias
 - We remember things in a way that fit our expectations
- Suggestibility
 - Implanted memories about things that never occurred
 - Leading questions produce false memories
- State-dependent learning
 - Learn something while drinking, then can only remember while intoxicated



- Explosion of the Challenger Space Shuttle (1986)
 - The day after the event, college students were asked to write down what they were doing and how they felt when they heard the news
 - 3 years later, the students were again asked to write down what they were doing and how they felt when they heard the news
- What percent of the stories had significant changes from immediate post-disaster to 3 years later?
 - >90%
 - 3-years-later memories were significantly less accurate
- How did the students perceive their 3-years-post-disaster accounts (at the time they wrote them)?
 - They were very confident in their accuracy
 - One student, upon seeing her original account, said “I know that’s my handwriting, but I couldn’t possibly have written that.”

Memory assessment

- Observe what patient tells you in conversation
 - Does he/she remember recent events?
 - Is the patient confabulating?
- Formal memory testing
 - To understand nature of memory problem as well as presence/severity, should assess:
 - Encoding
 - Storage
 - Retrieval
 - Ideally test both verbal and visual memory
 - Verbal memory most often tested in practice



HVLT administration

- After delay

ROCF

- After delay



Hopkins Verbal Learning Test

- Read a list of words to the patient while he/she sits quietly and tries to memorize them
- Immediately after reading the list, ask patient to say as many words as can remember
- Repeat for 3 trials
- Wait 20 minutes, do other things in the interim
- Ask patient for any words he/she can remember
- Then read each recognition word and ask patient if was on the list.
 - Note true and false positives.

| | Trial 1 | Trial 2 | Trial 3 | Delayed Recall |
|----------|---------|---------|---------|----------------|
| LION | | | | |
| EMERALD | | | | |
| HORSE | | | | |
| TENT | | | | |
| SAPPHIRE | | | | |
| HOTEL | | | | |
| CAVE | | | | |
| OPAL | | | | |
| TIGER | | | | |
| PEARL | | | | |
| COW | | | | |
| HUT | | | | |

| Recognition | | | | | |
|-------------|----------|----------|---------|------------|----------|
| HORSE | ruby* | CAVE | balloon | coffee | LION |
| house* | OPAL | TIGER | boat | scarf | PEARL |
| HUT | EMERALD | SAPPHIRE | dog* | apartment* | penny |
| TENT | mountain | cat* | HOTEL | COW | diamond* |

HVLT:

- Total learned:

 / 36

≥ 18 is WNL

- Delayed recall:

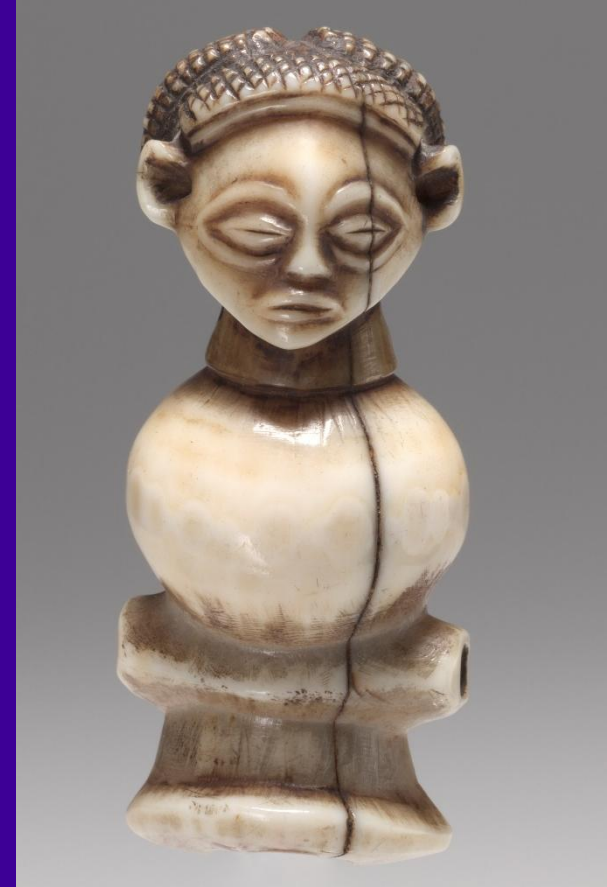
recalled spontaneously / # recalled on best trial

≥ 75% is WNL

- Recognition:

TRUE POSITIVES – (related false positives* + unrelated false positives)

≥ 11 is WNL



- Encoding (learning)?
 - Poor
- Storage?
 - Intact for what was encoded (can only recall things which got encoded in the first place, and patient did do this)
- Retrieval?
 - Intact for what was encoded and stored
- Primary problem?
 - Encoding

| | Trial 1 | Trial 2 | Trial 3 | Delayed Recall | |
|-------------|----------|----------|---------|----------------|----------|
| LION | | ✓ | ✓ | ✓ | |
| EMERALD | | | | | |
| HORSE | | | | | |
| TENT | | | | | |
| SAPPHIRE | | | | | |
| HOTEL | | ✓ | ✓ | ✓ | |
| CAVE | | | | | |
| OPAL | | | | | |
| TIGER | | | | | |
| PEARL | | | | | |
| COW | ✓ | ✓ | ✓ | ✓ | |
| HUT | | | | | |
| Recognition | | | | | |
| HORSE | ruby* | CAVE | balloon | coffee | LION |
| house* | OPAL | TIGER | boat | scarf | PEARL |
| HUT | EMERALD | SAPPHIRE | dog* | apartment* | penny |
| TENT | mountain | cat* | HOTEL | COW | diamond* |

- Encoding (learning?)
 - Intact
- Spontaneous recall?
 - Poor
- Is this a problem with storage or retrieval?
 - Look at recognition:
 - 5 true positives
 - 3 false positives

 Discrimination index: 2
- Did cueing help?
 - No! Just guessing at random on recognition (i.e., words not in memory bank)
- Primary problem?
 - Storage

| | Trial 1 | Trial 2 | Trial 3 | Delayed Recall |
|----------|---------|---------|---------|----------------|
| LION | ✓ | ✓ | ✓ | ✓ |
| EMERALD | ✓ | ✓ | ✓ | |
| HORSE | ✓ | ✓ | ✓ | |
| TENT | | | | |
| SAPPHIRE | ✓ | ✓ | ✓ | |
| HOTEL | | ✓ | ✓ | |
| CAVE | | | | |
| OPAL | | ✓ | ✓ | |
| TIGER | | | ✓ | |
| PEARL | | | | |
| COW | ✓ | ✓ | ✓ | |
| HUT | | ✓ | ✓ | ✓ |

| Recognition | | | | | |
|-------------|----------|----------|---------|------------|----------|
| HORSE | ruby* | CAVE | balloon | coffee | LION |
| house* | OPAL | TIGER | boat | scarf | PEARL |
| HUT | EMERALD | SAPPHIRE | dog* | apartment* | penny |
| TENT | mountain | cat* | HOTEL | COW | diamond* |

- Encoding (learning?)
 - Intact
- Spontaneous recall?
 - Poor
- Is this a problem with storage or retrieval?
 - Look at recognition:
 - 12 true positives
 - 0 false positives

 Discrimination index: 12
- Did cueing help?
 - Yes! Correctly recognized all words actually on the list; not fooled by words not on the list (so list in memory bank somewhere)
- Primary problem?
 - Retrieval

| | Trial 1 | Trial 2 | Trial 3 | Delayed Recall |
|----------|---------|---------|---------|----------------|
| LION | ✓ | ✓ | ✓ | ✓ |
| EMERALD | ✓ | ✓ | ✓ | |
| HORSE | ✓ | ✓ | ✓ | |
| TENT | | | | |
| SAPPHIRE | ✓ | ✓ | ✓ | |
| HOTEL | | ✓ | ✓ | |
| CAVE | | | | |
| OPAL | | ✓ | ✓ | |
| TIGER | | | ✓ | |
| PEARL | | | | |
| COW | ✓ | ✓ | ✓ | |
| HUT | | ✓ | ✓ | ✓ |

| Recognition | | | | | |
|-------------|----------|----------|---------|------------|----------|
| HORSE | ruby* | CAVE | balloon | coffee | LION |
| house* | OPAL | TIGER | boat | scarf | PEARL |
| HUT | EMERALD | SAPPHIRE | dog* | apartment* | penny |
| TENT | mountain | cat* | HOTEL | COW | diamond* |

ROCF: Recognition

