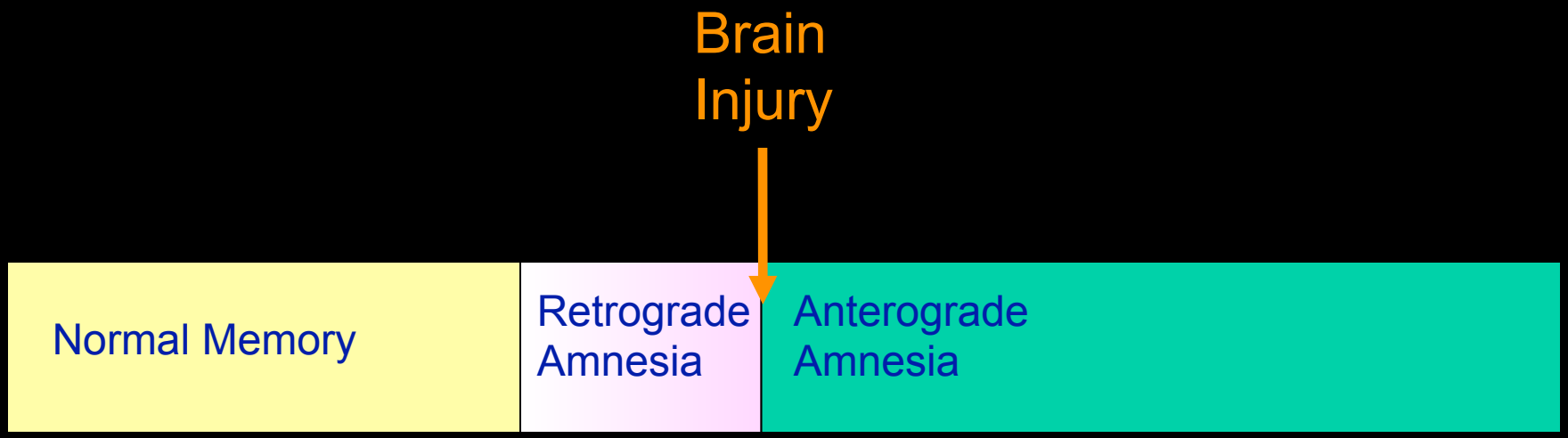
Outline

- Amnesia (anterograde and retrograde)
- Medial Temporal Lobe and Episodic Memory
  - MTL Anatomy and Connectivity
  - Relational Memory Theory
- Consolidation

Definition of Amnesia



Anterograde Amnesia – the inability to remember new events

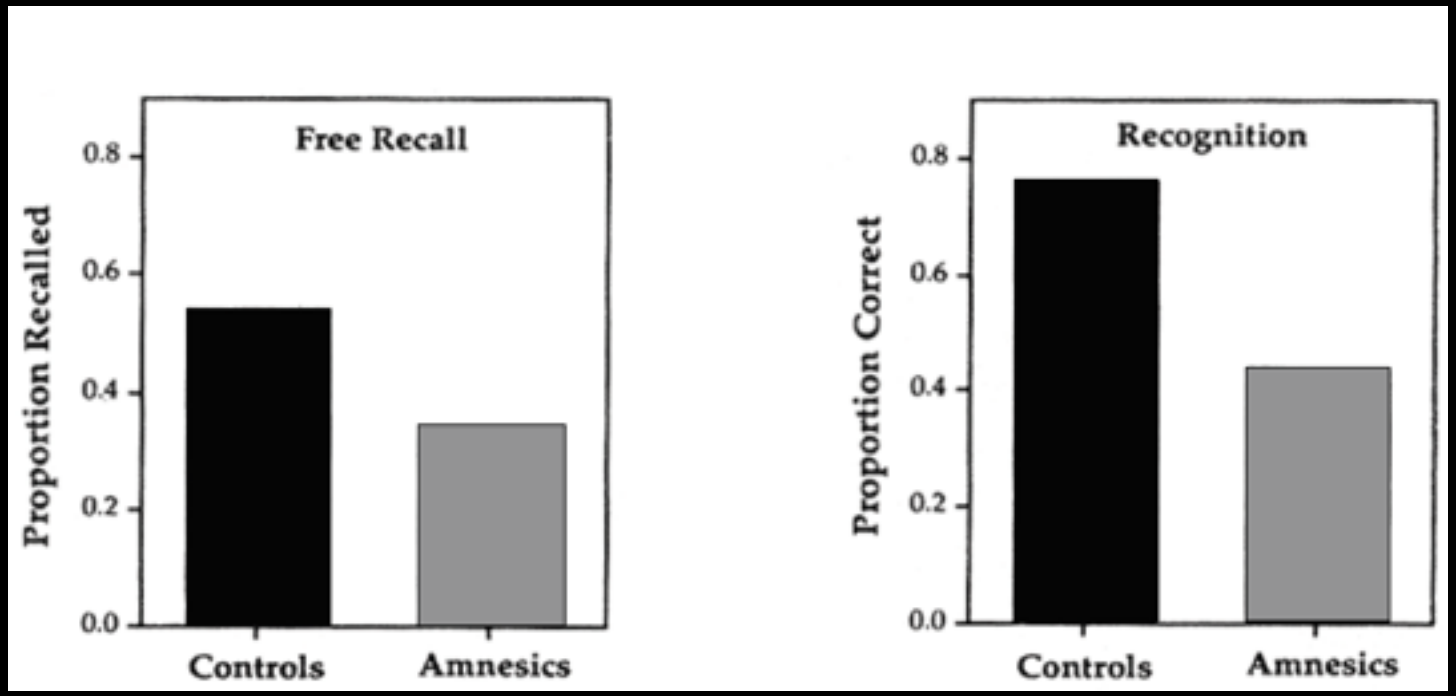
Retrograde Amnesia – the inability to recollect memories acquired before the brain injury

Alan Alda, in *Scientific American Frontiers — Don't Forget (2004)*

Patient EP
(extensive MTL damage)

Impairments following MTL Damage

- Impaired ability to remember new events (episodic memories)



Warrington and Weiskrantz (1970)

GLOBAL Memory Impairment in Medial Temporal Lobe Amnesia

Assessment Test	*Materials and Events*	*Modalities*
Free recall	Words, digits, paragraphs	Vision
Cued recall	Nonsense syllables	Audition
Yes/no recognition	Faces, shapes	Somesthesis
Multiple choice Recognition	Clicks, tones, sounds	Olfaction
Learning to criterion	Mazes	Gustation
	Public events, Personal events	

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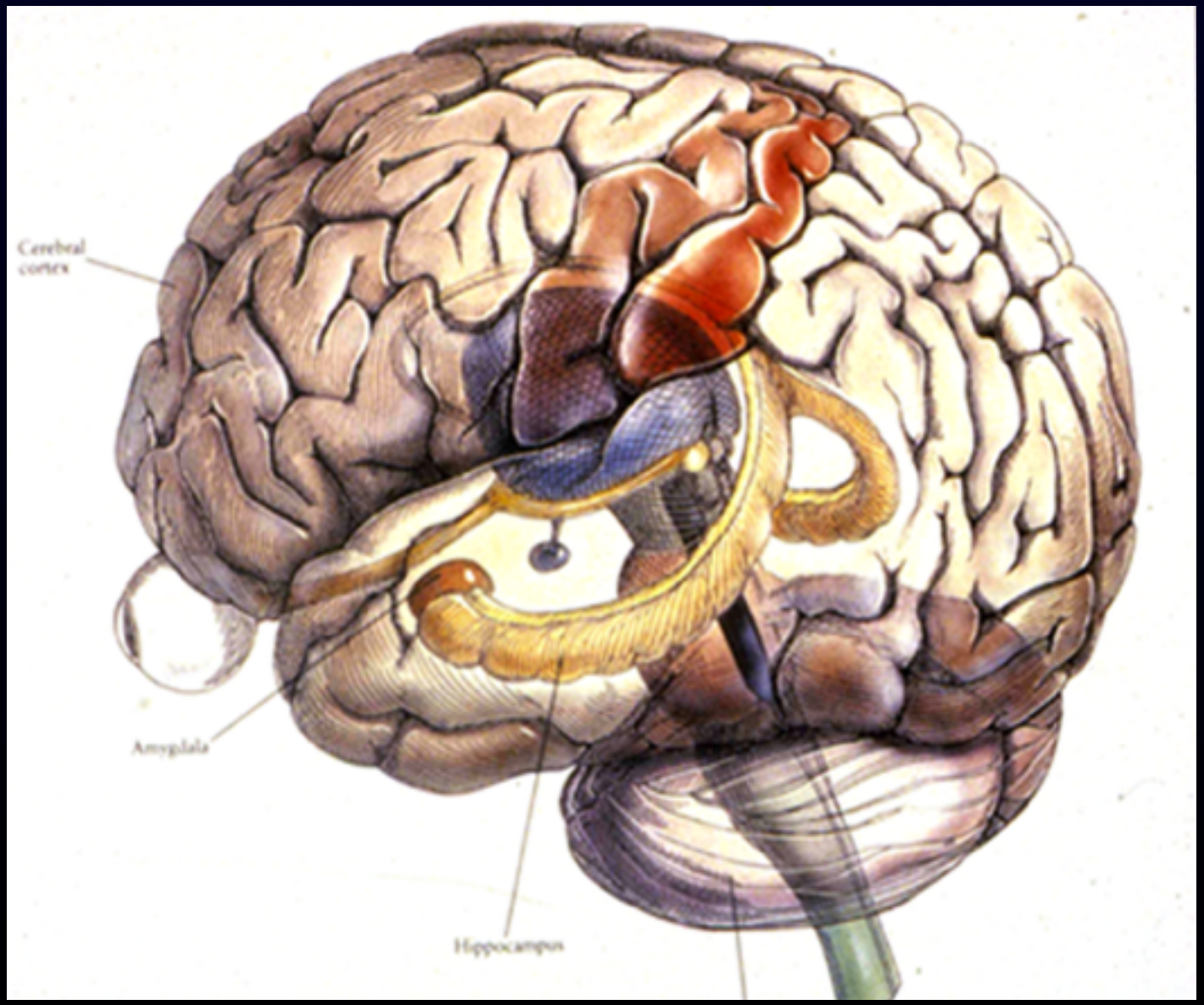
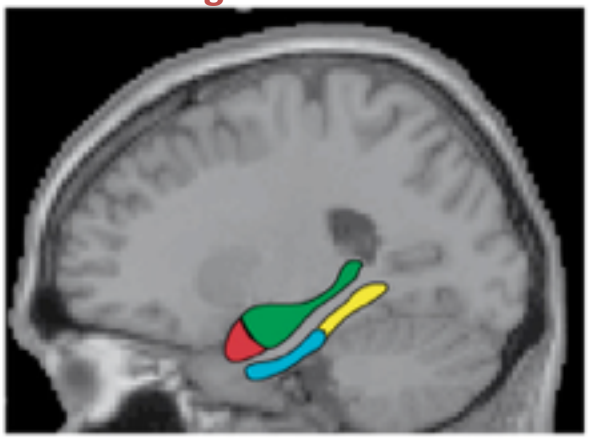
Human Hippocampus



Medial Temporal Lobe

Sagittal slice

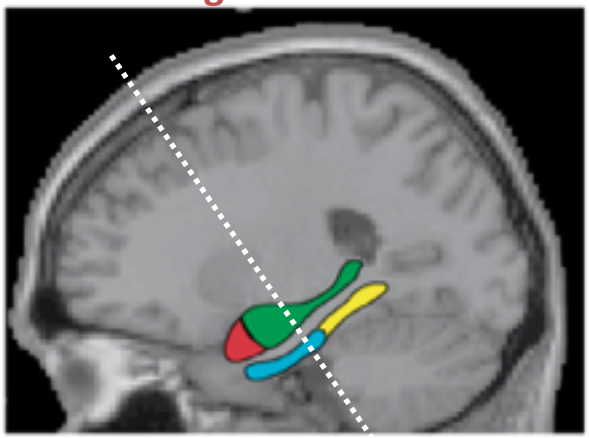


Medial temporal lobe

- Hippocampus
- Amygdala
- Parahippocampal cortex
- Entorhinal and perirhinal cortex

Medial Temporal Lobe

Sagittal slice

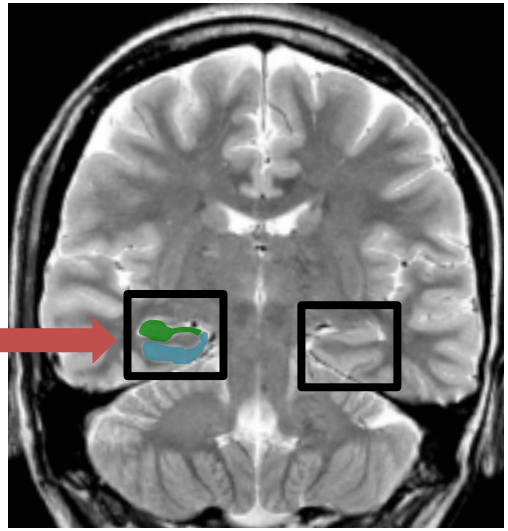


Medial temporal lobe

- Hippocampus
- Amygdala
- Parahippocampal cortex
- Entorhinal and perirhinal cortex

Coronal slice

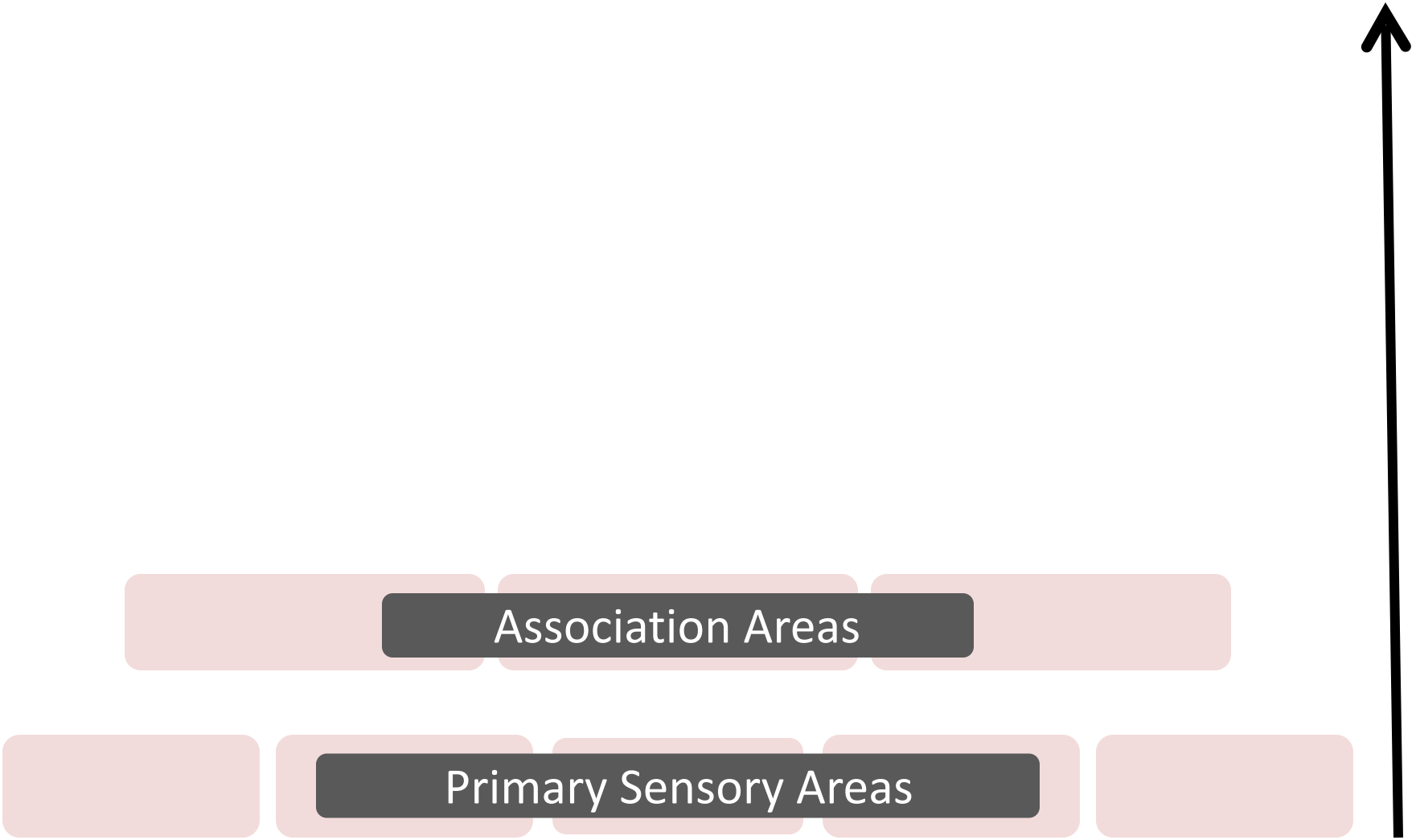
Medial temporal lobe



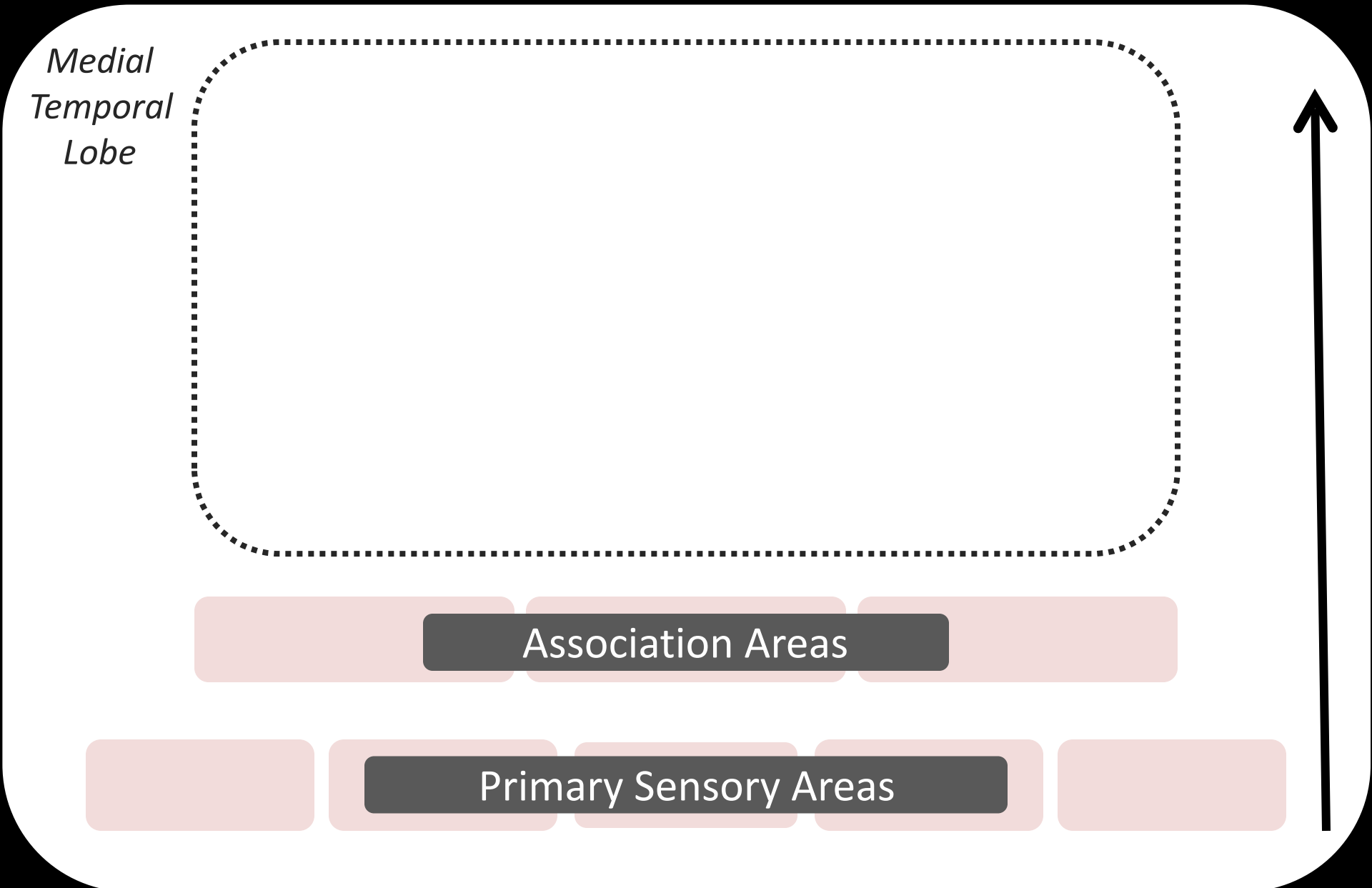
Hierarchy of Information Flow

Primary Sensory Areas

Hierarchy of Information Flow



Hierarchy of Information Flow



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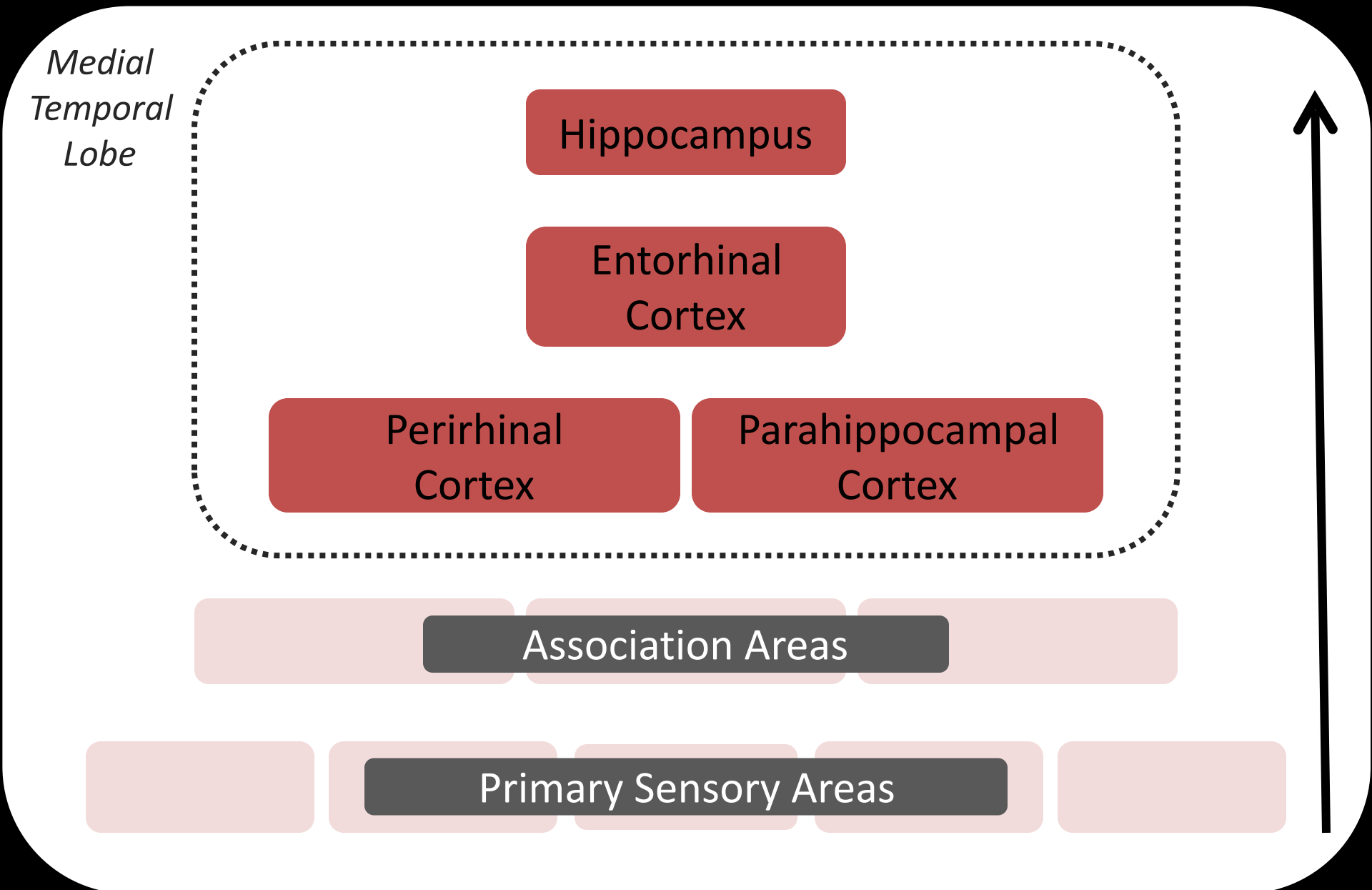
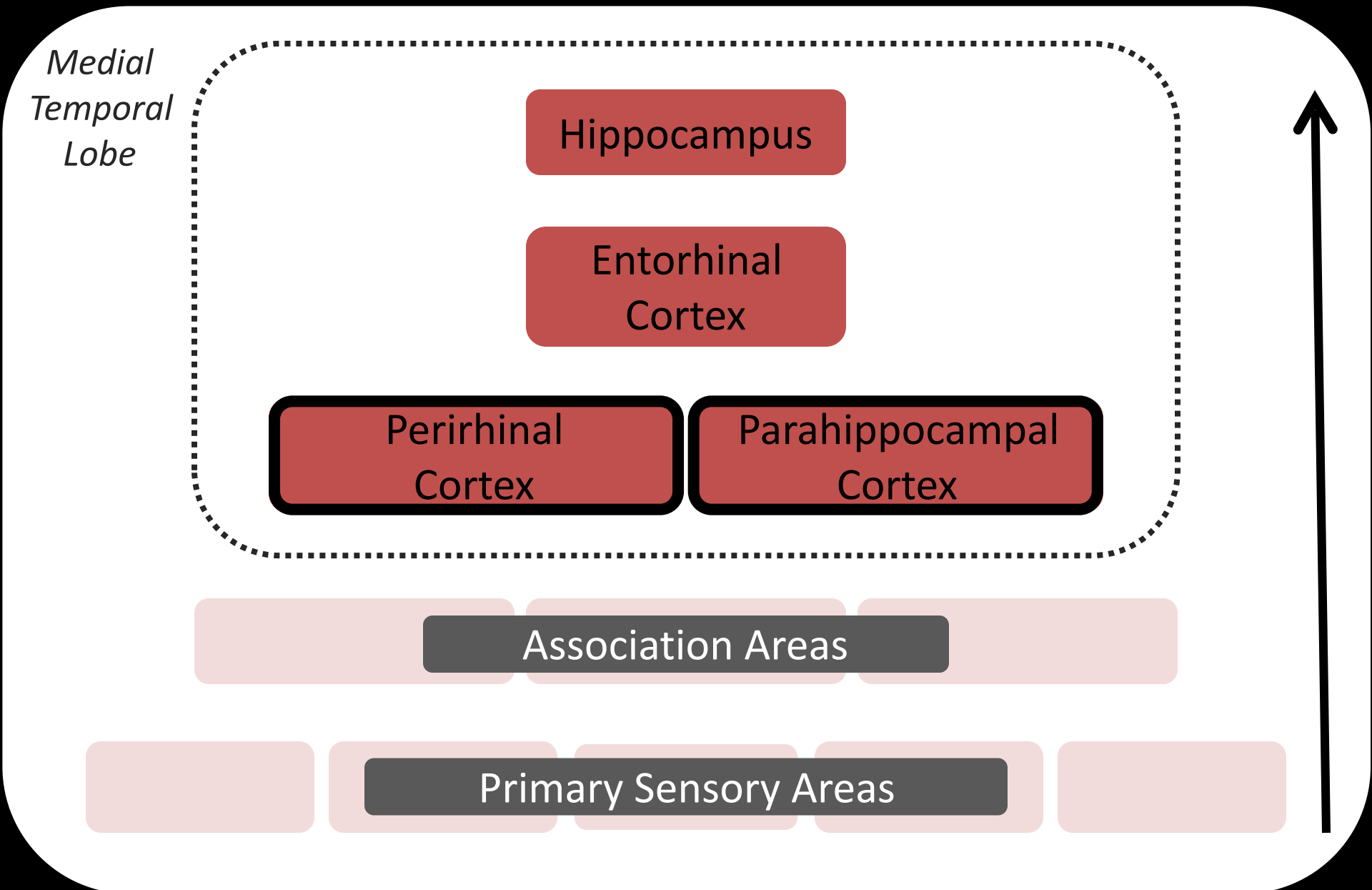
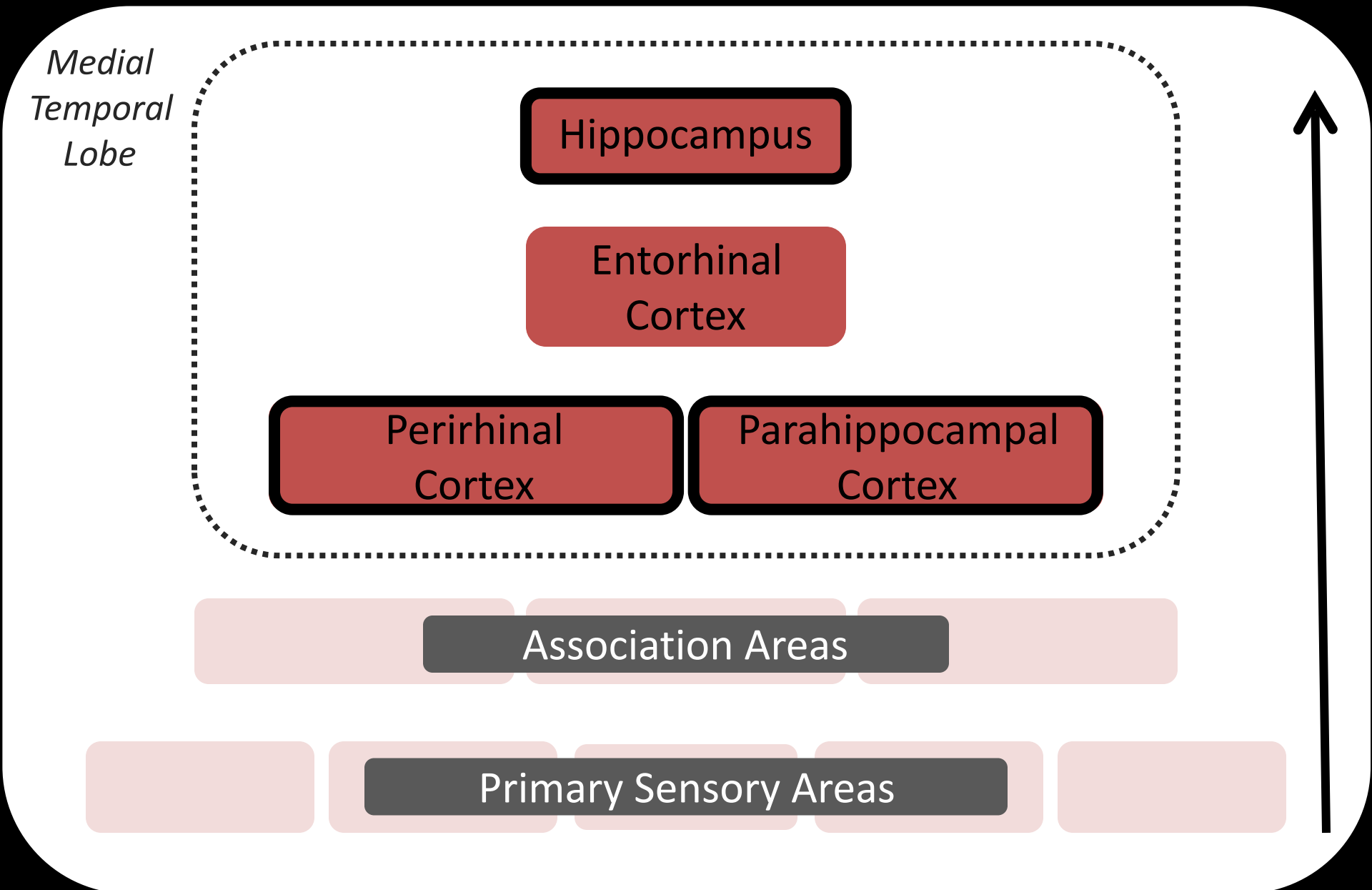


Hierarchy of Information Flow

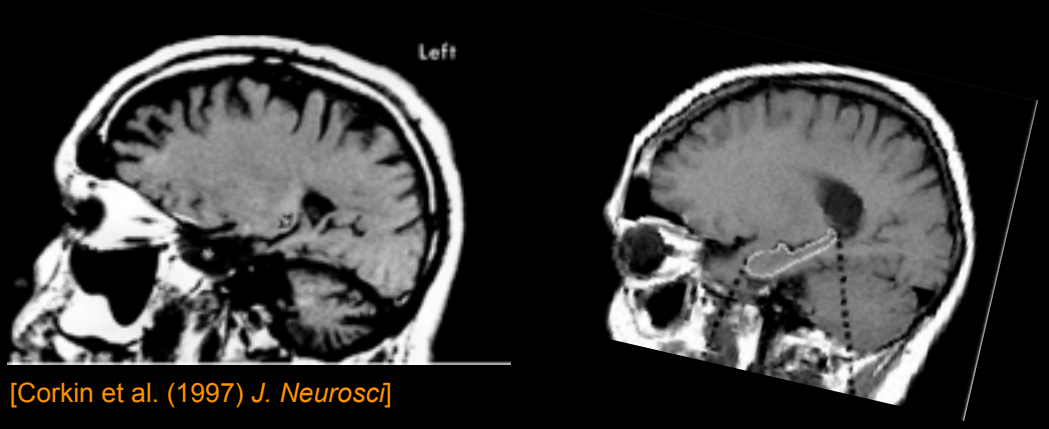


Hierarchy of Information Flow



MTL Structures and Episodic Memory

H.M. & E.P. had an almost complete bilateral MTL damage



[Corkin et al. (1997) *J. Neurosci*]

- Do you have to have this much damage to have amnesia?

MTL Structures and Episodic Memory

Patient R.B. had damage to only one region (CA1) of the hippocampus

- damage limited to the hippocampus can cause amnesia (Zola-Morgan et al., 1986).

As extent of MTL damage increases, the amnesic syndrome becomes more severe

Outline

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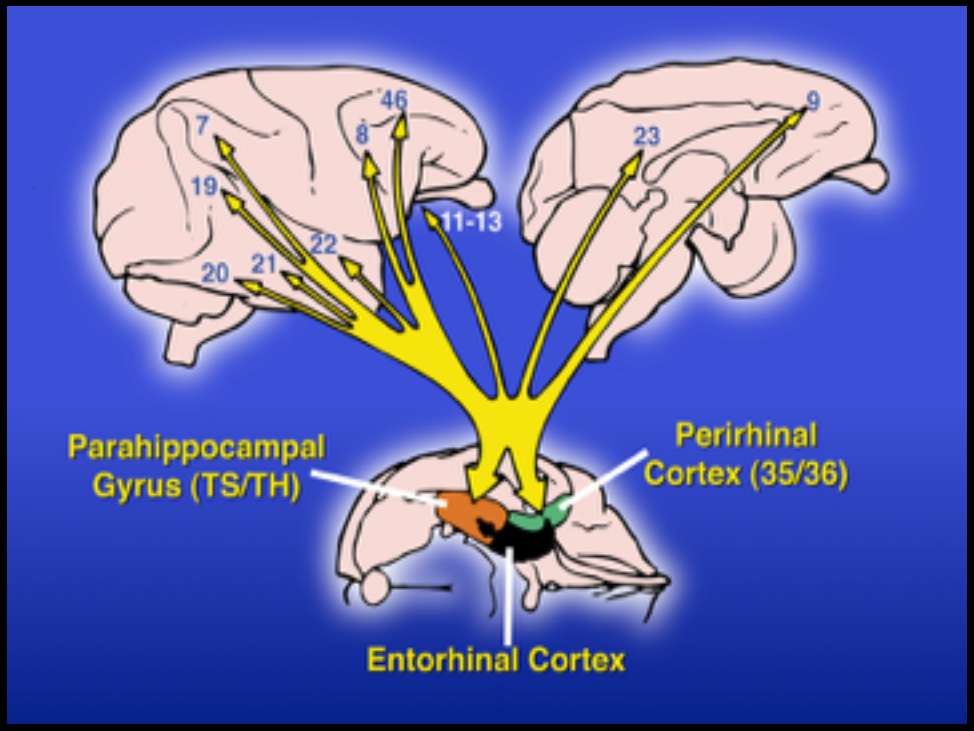
RELATIONAL MEMORY THEORY

The MTL, in interaction with neocortical storage sites, supports ***conjunctive memory binding & activation***



…representing the ***relations*** *among perceptually distinct items of scenes or events, and mediating their retrieval*

[Adapted from Neal Cohen]

RELATIONAL MEMORY THEORY

1. Hippocampus, in interaction with MTL cortex, supports *declarative memory* → memory for facts & events
2. Declarative memory is a fundamentally *relational* system
3. Hippocampus contributes the critical processes of *conjunctive memory binding & reactivation of conjunctions*
4. It represents & retrieves *all manner of relations* among the elements of experiences, events, or scenes
5. It *rapidly acquires* (1-trial learning) these representations
6. Representations are *flexibly addressable*
7. MTL cortex contributes to memory for *individual items / features*

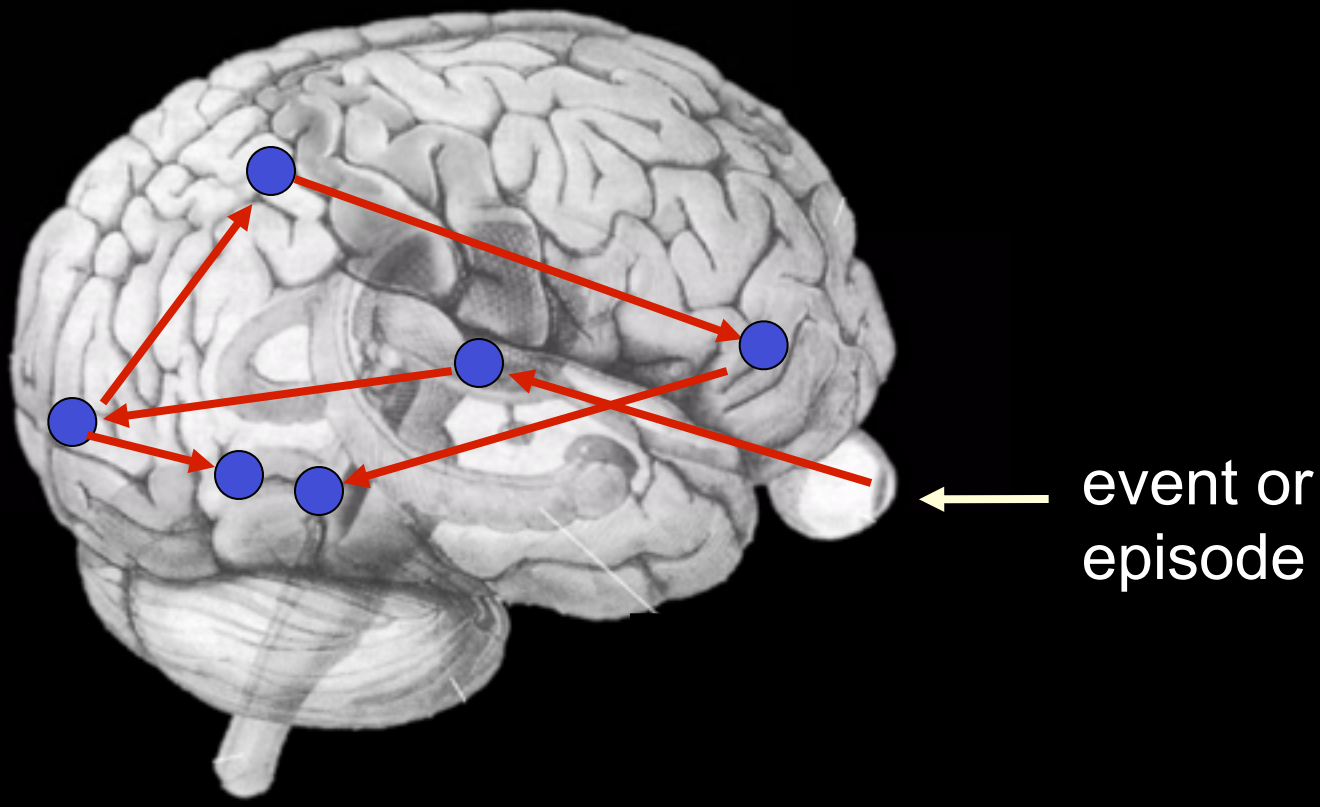
[adapted from Neal Cohen]

MTL & Conjunctive Memory Formation

event or episode

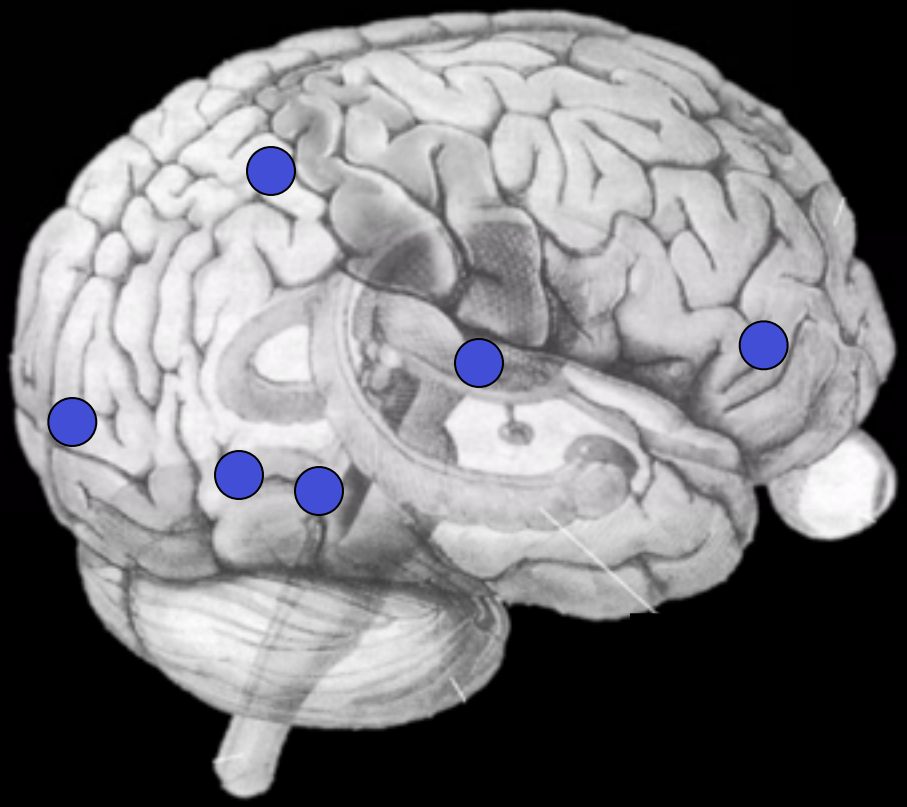
ENCODING

MTL & Conjunctive Memory Formation



ENCODING

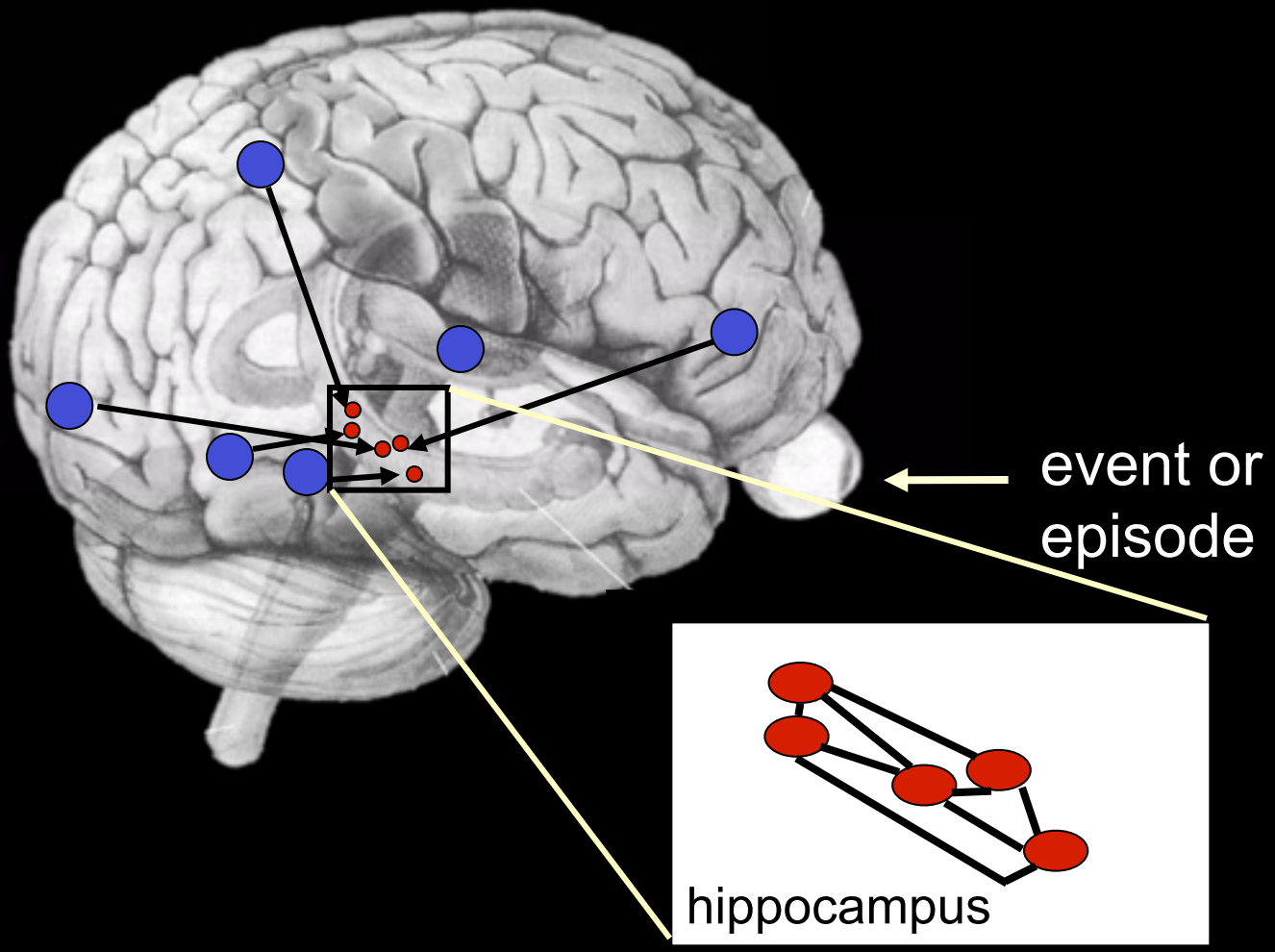
MTL & Conjunctive Memory Formation



event or episode

ENCODING

MTL & Conjunctive Memory Formation



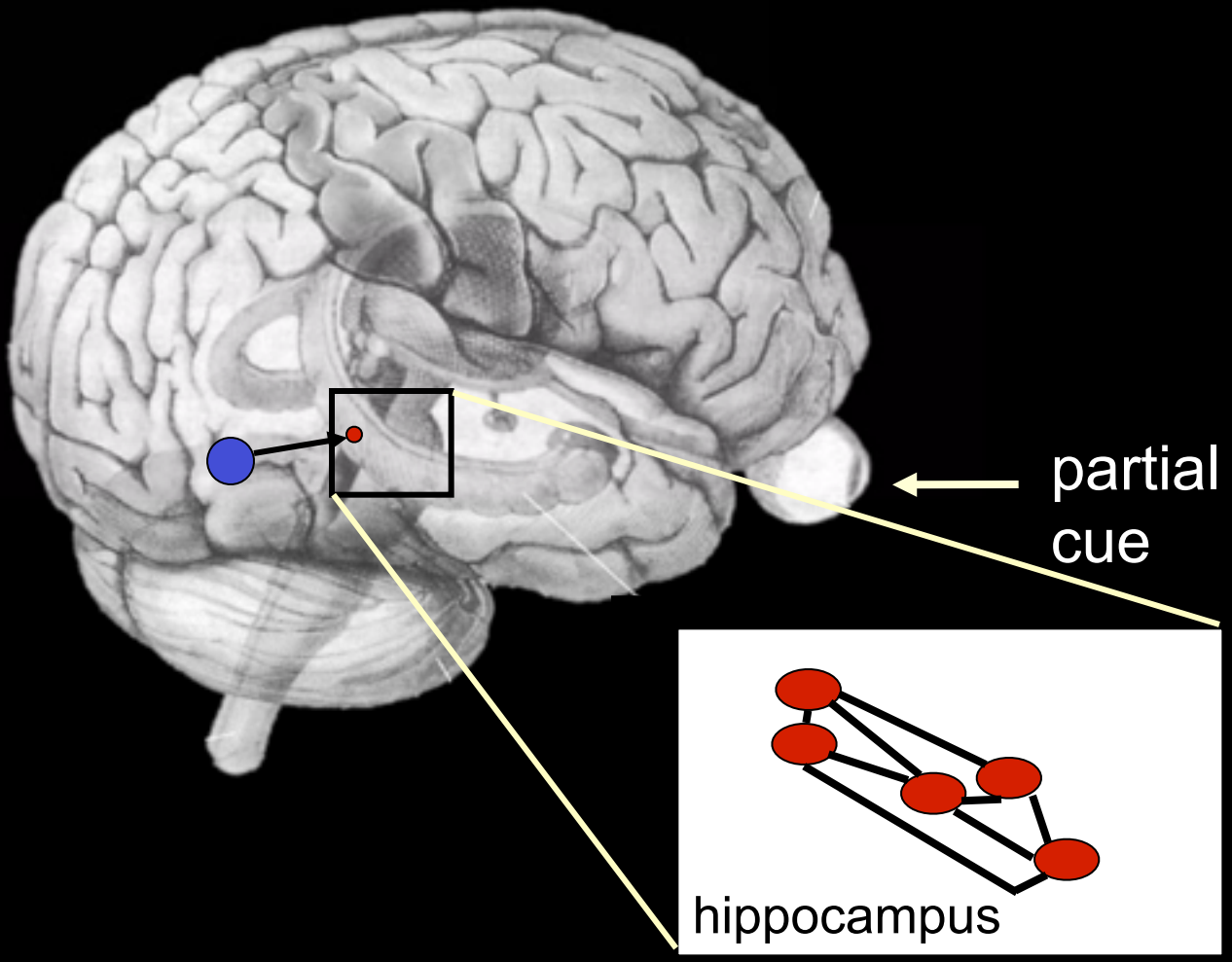
ENCODING

MTL & Pattern Completion

partial cue

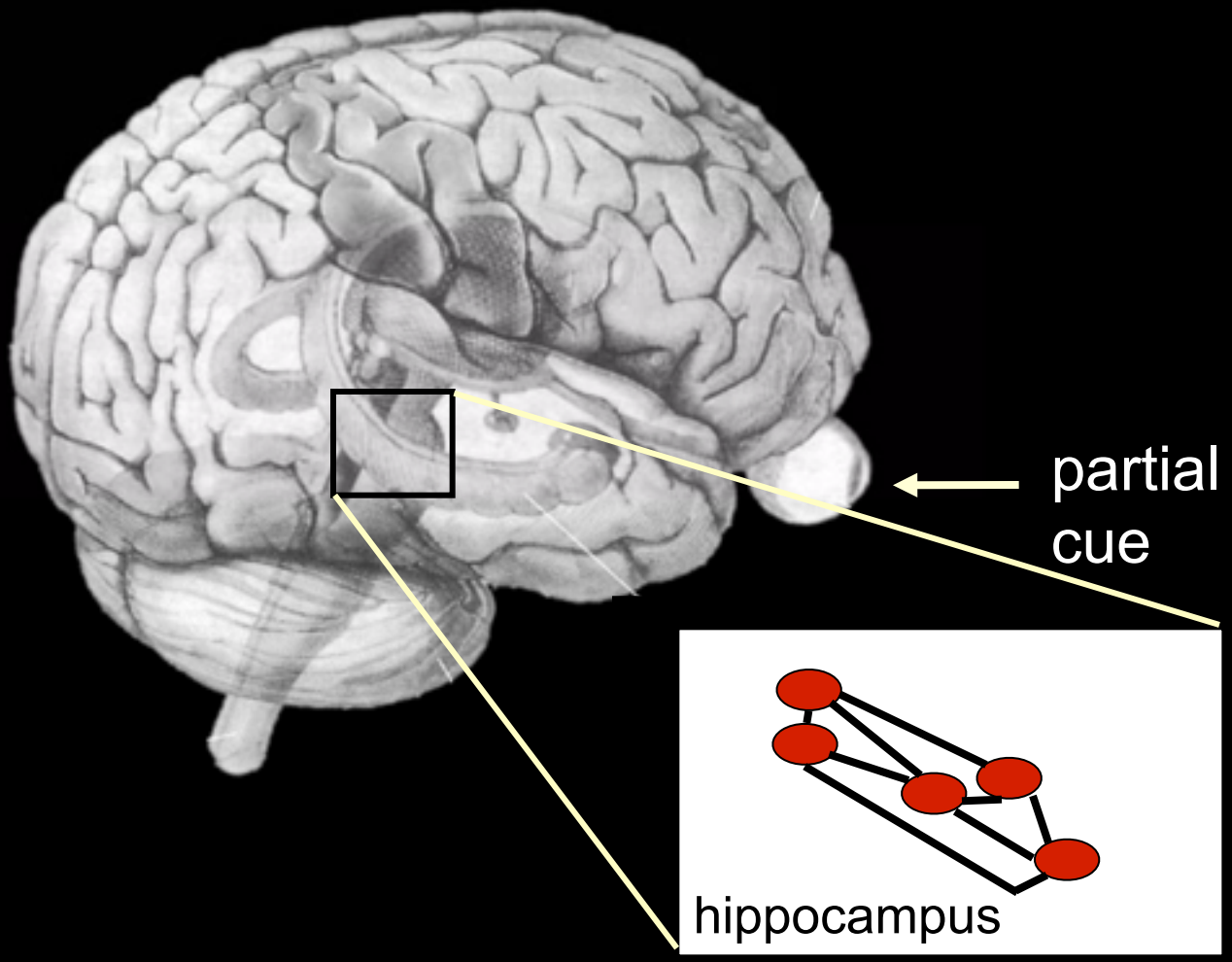
RETRIEVAL

MTL & Pattern Completion



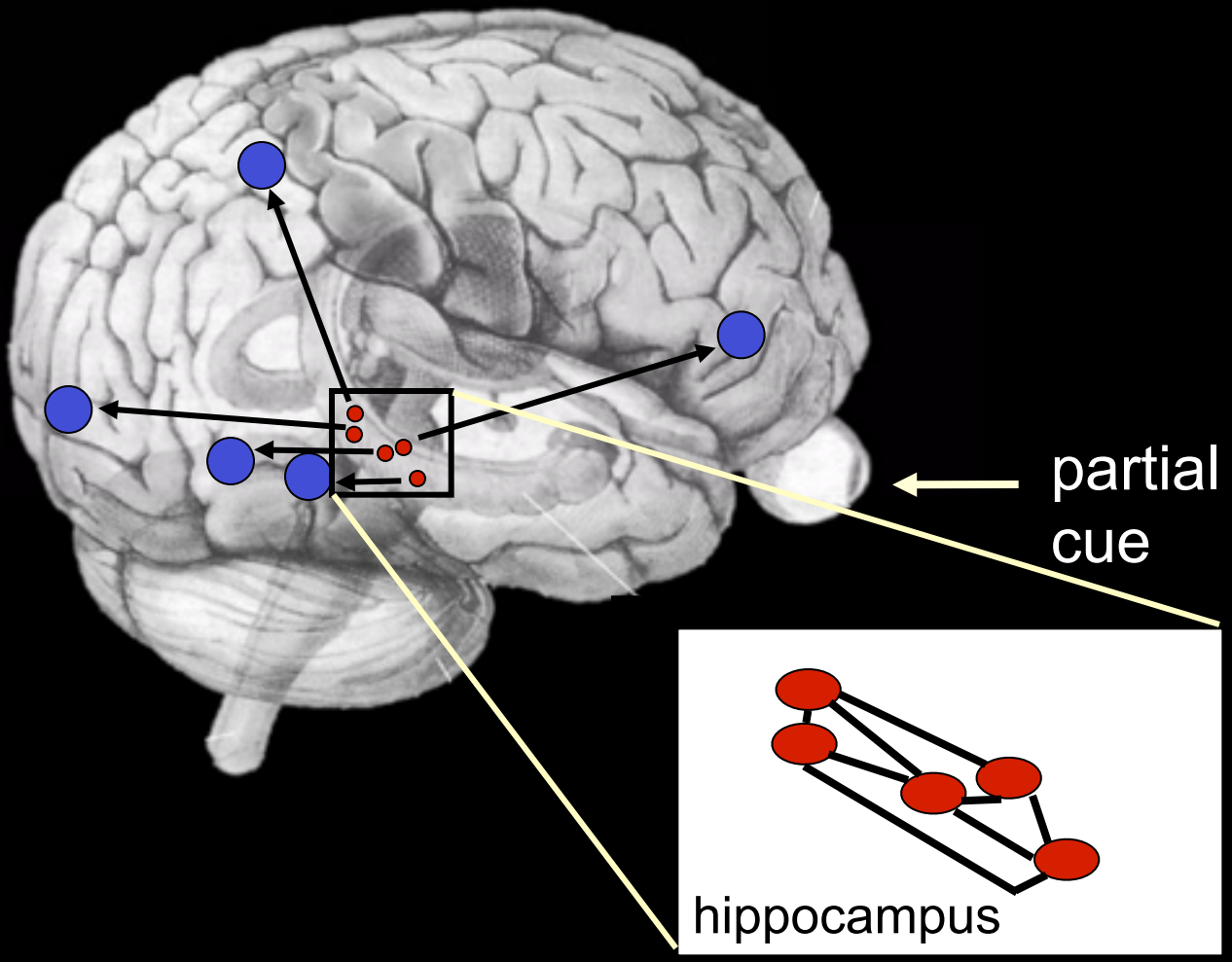
RETRIEVAL

MTL & Pattern Completion



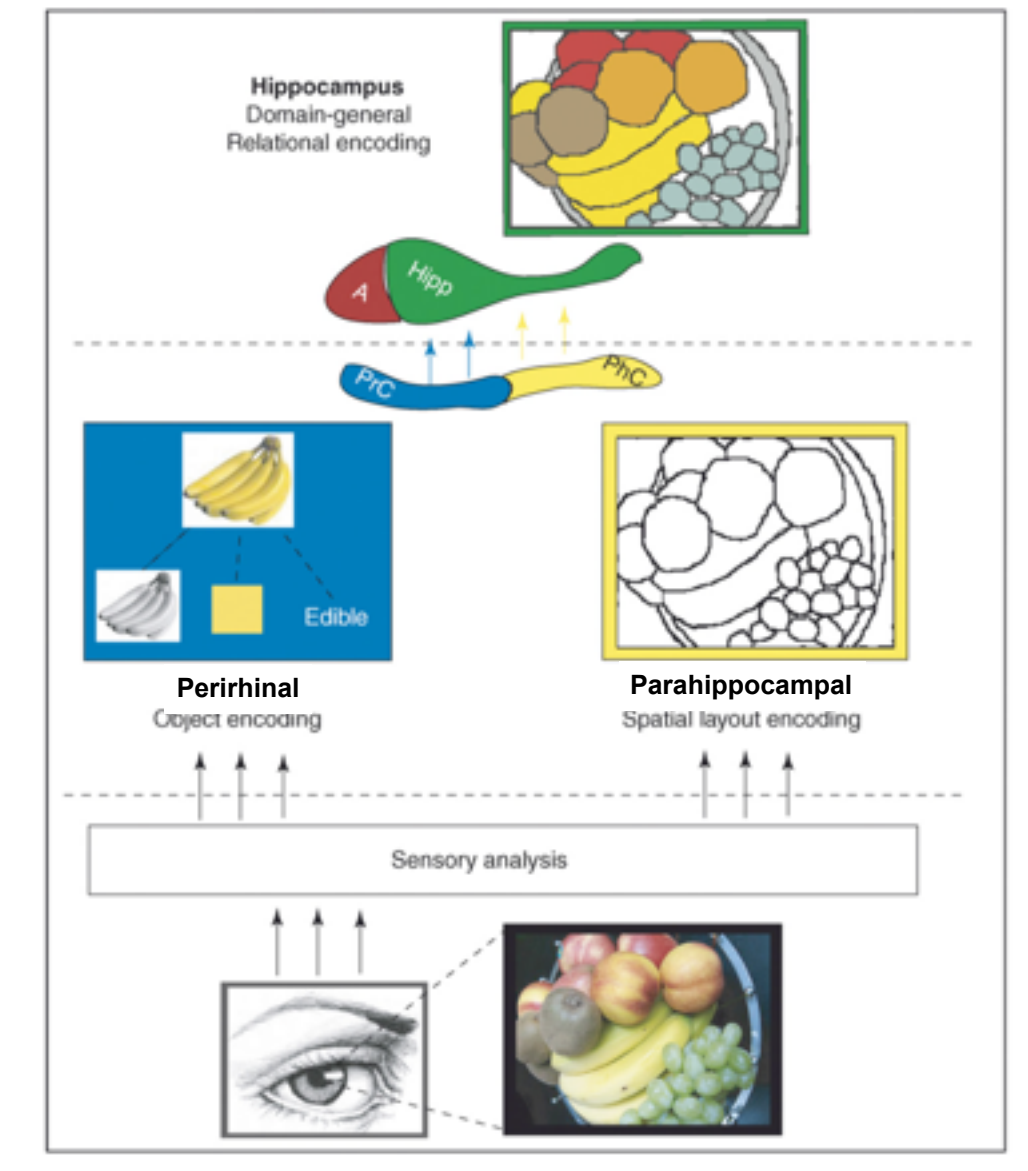
RETRIEVAL

MTL & Pattern Completion



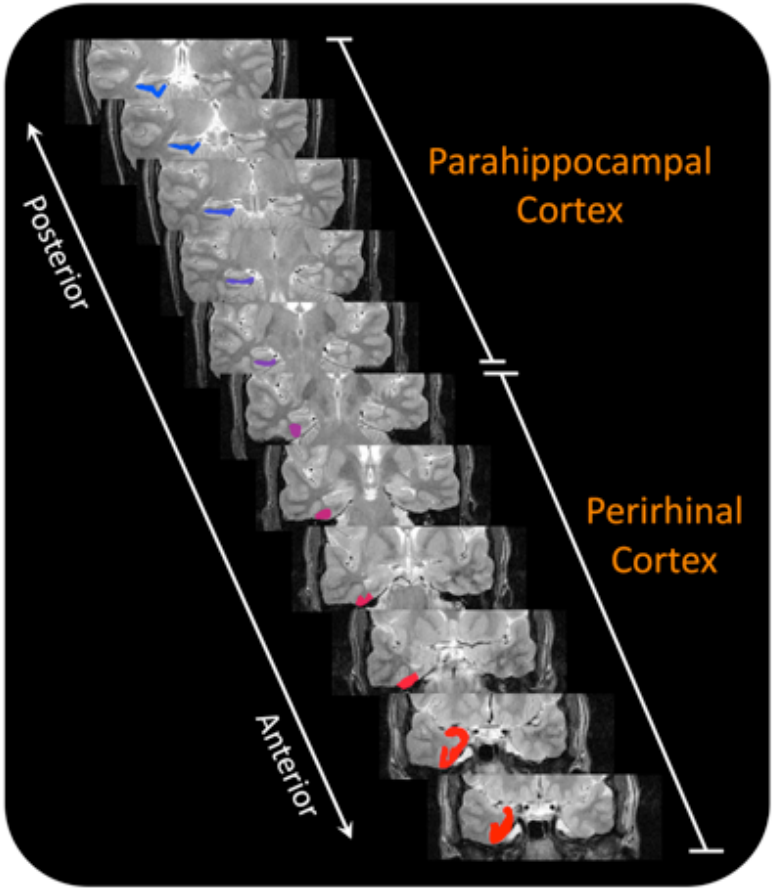
RETRIEVAL

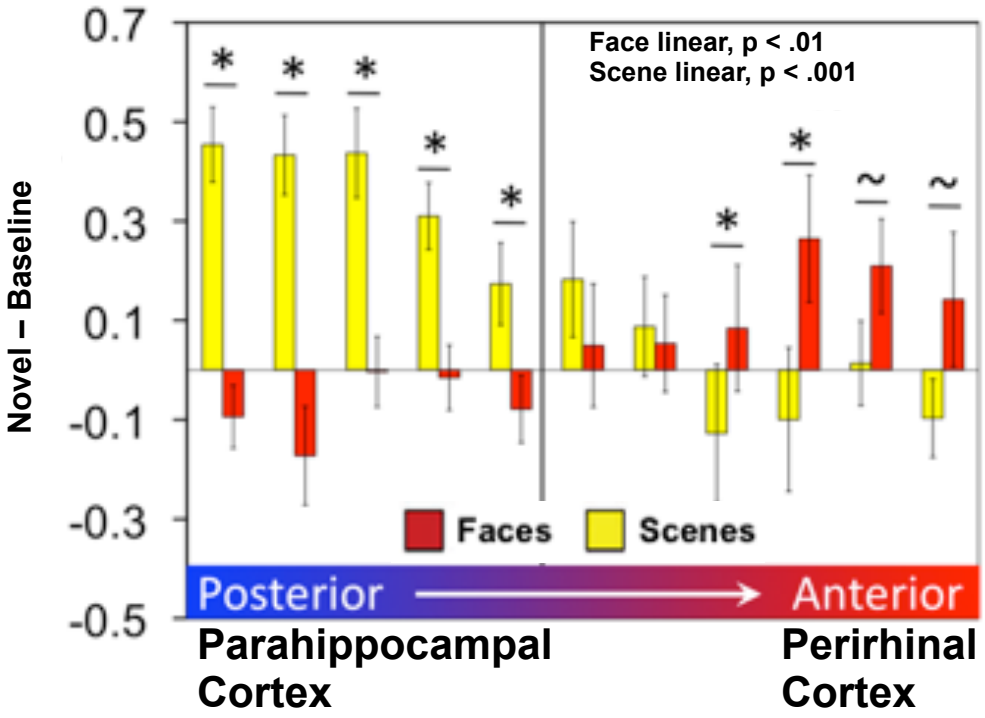
Functional Distinctions within the MTL



[Davachi, 2006]

Functional Distinctions within the MTL: MTL Cortex Represents Specific Types of Event Content





[Liang et al., 2013]

Functional Distinctions within the MTL: Encoding Item-Context Conjunctions vs. Item Recognition

STUDY:

WORD1 - Context 1 (visual imagery task)
WORD2 - Context 2 (phonological task)

TEST:

Studied Word

Item Memory

"old" (Hit)

"new" (**Forgotten**)

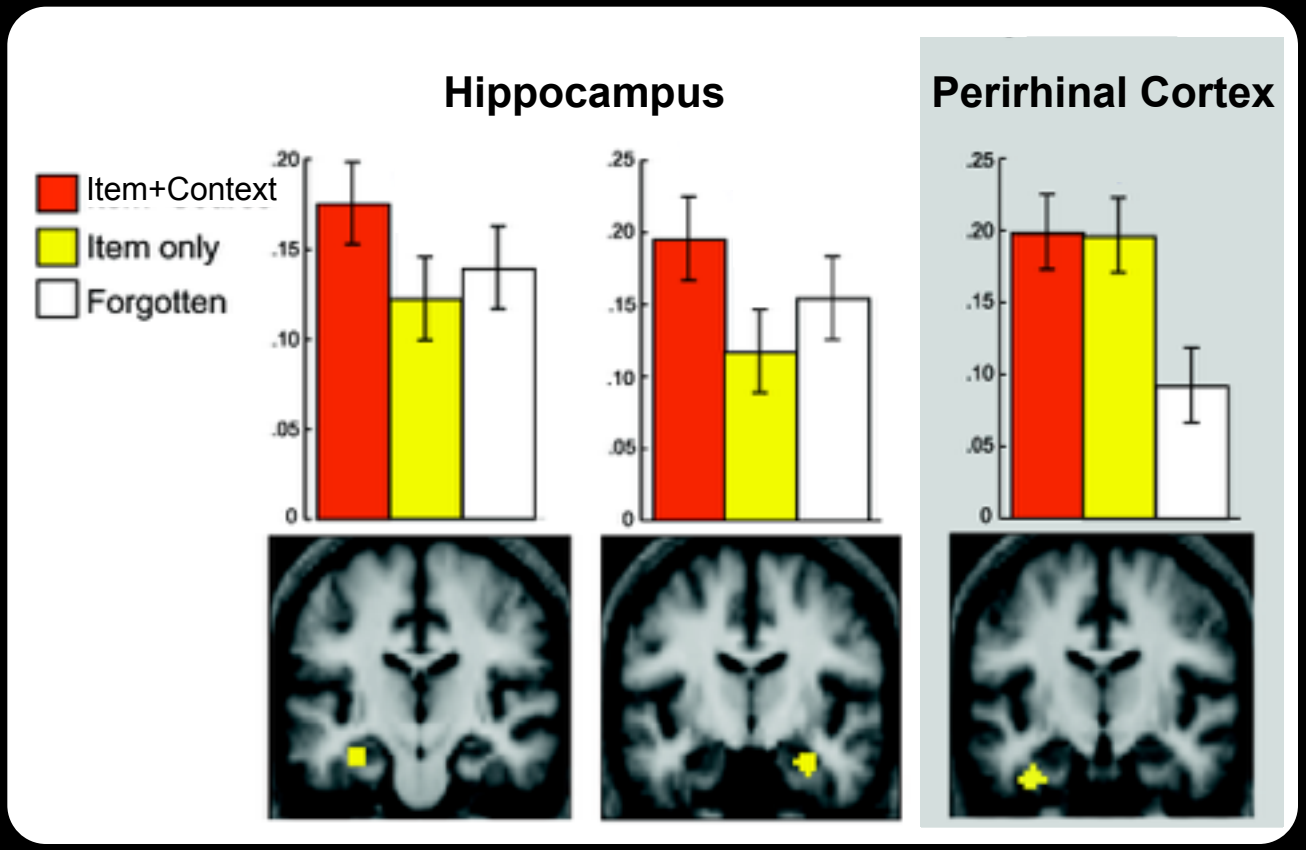
Conjunctive Memory

Context Correct (**Item+Context**)

Context Incorrect (**Item only**)

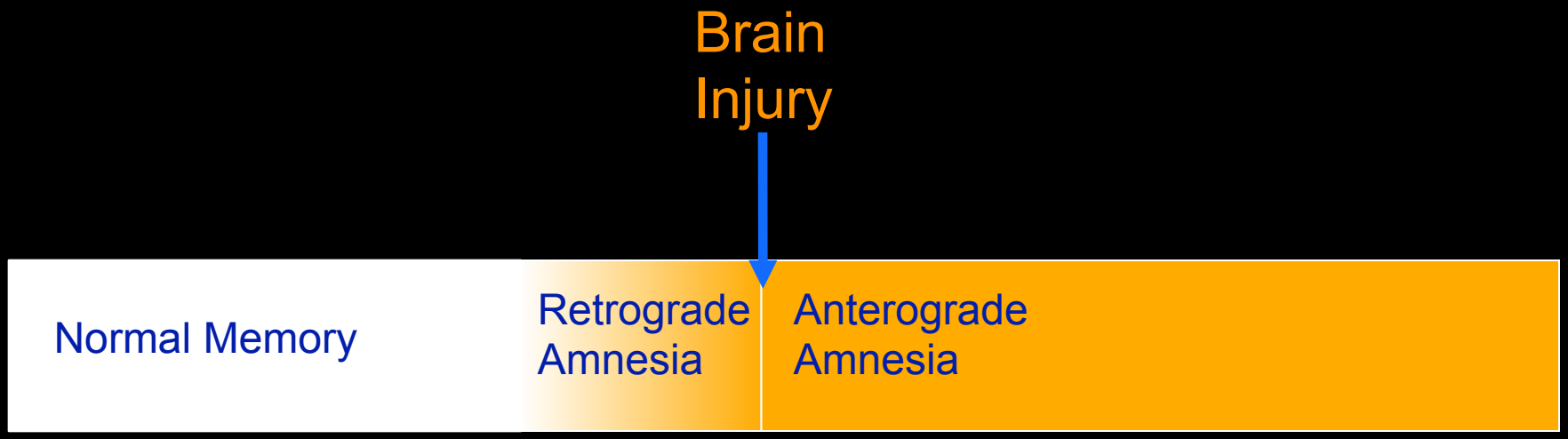
[Davachi, Mitchell, & Wagner (2003) *PNAS*]

Functional Distinctions within the MTL: Encoding Item-Context Conjunctions vs. Item Recognition



[Davachi, Mitchell, & Wagner (2003) *PNAS*]

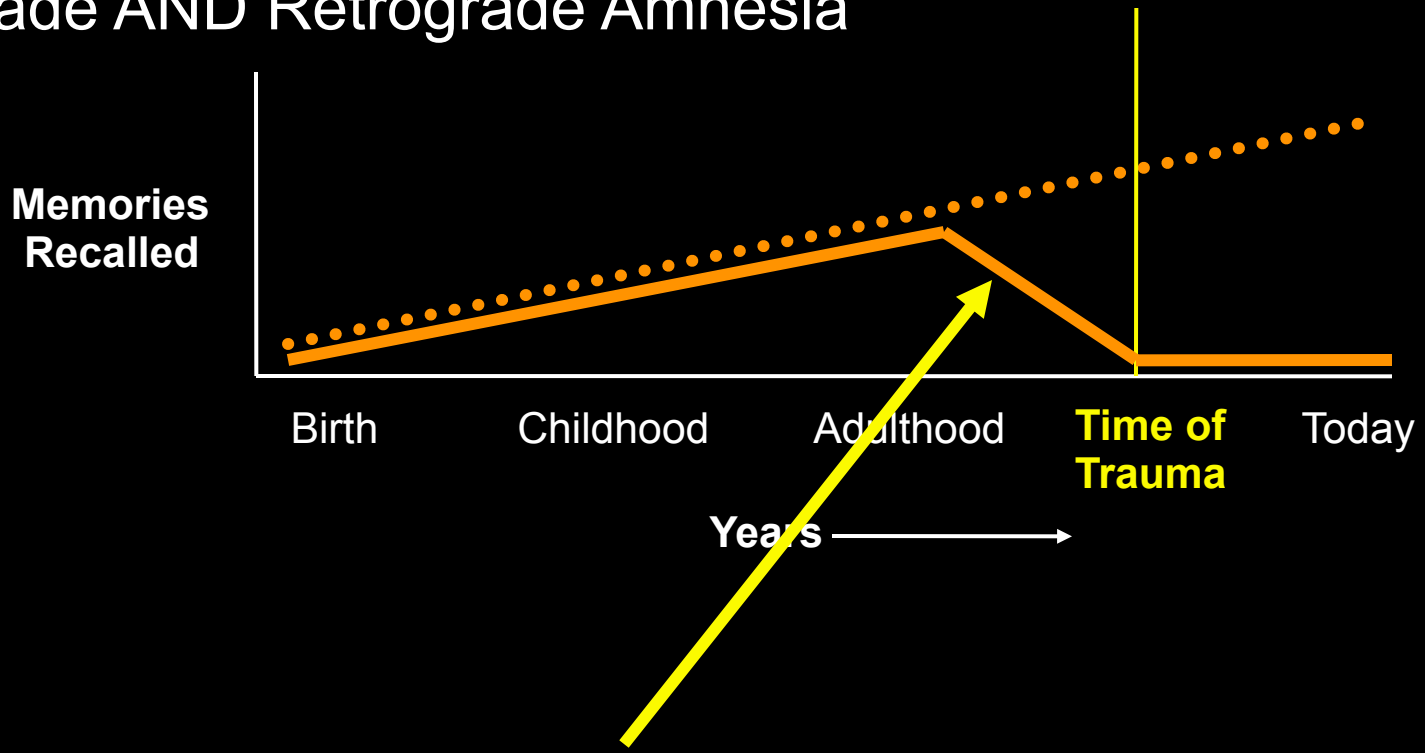
MTL and Retrograde Amnesia



MTL damage impairs not only new learning, but also disrupts memories acquired before the injury (Retrograde Amnesia)

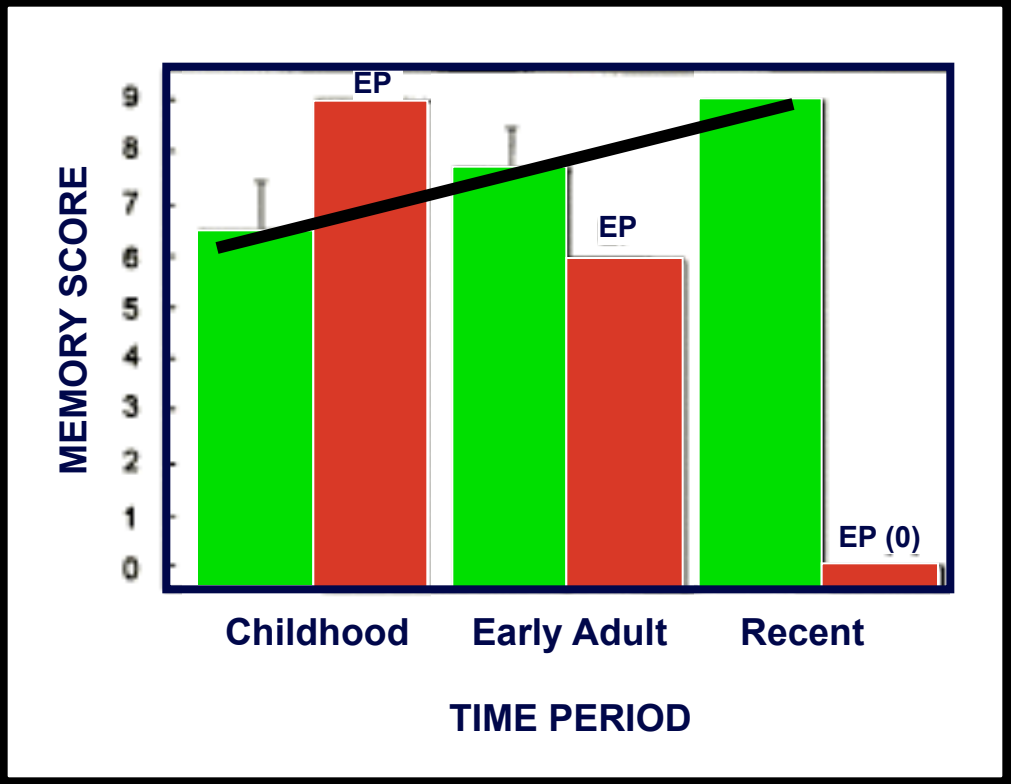
Typical Amnesic Pattern

Anterograde AND Retrograde Amnesia

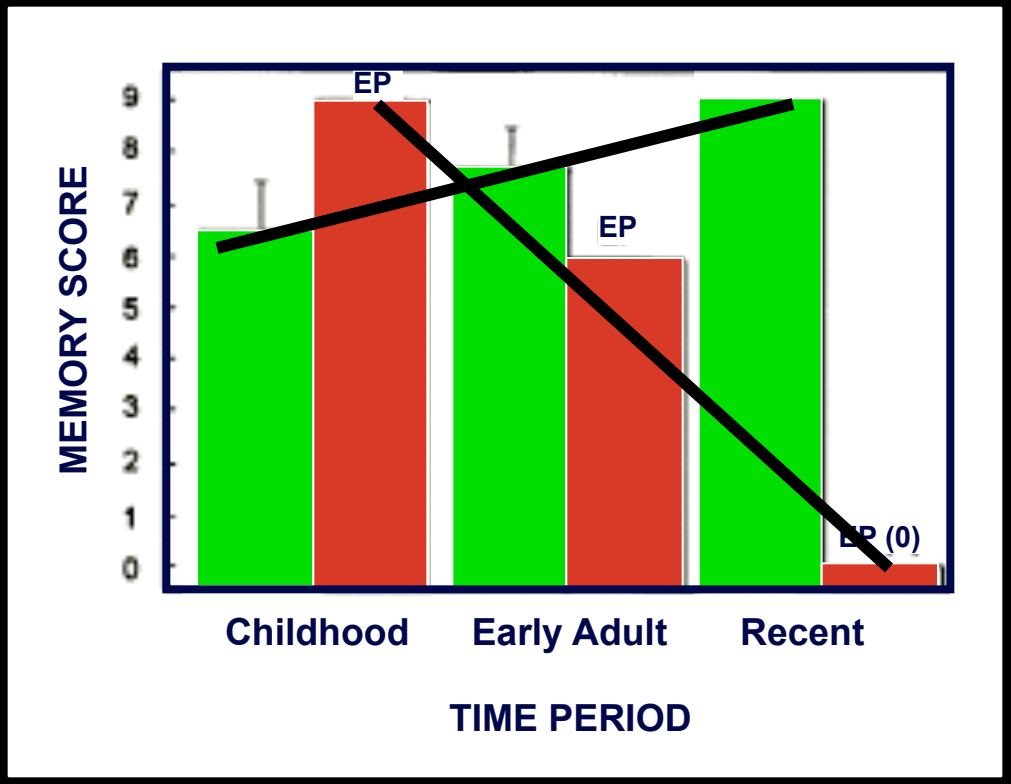


Temporally-Graded RA

E.P.'s Temporally-Graded Retrograde Amnesia



E.P.'s Temporally-Graded Retrograde Amnesia



Retrograde Amnesia – Consolidation

Temporally-graded loss of pre-morbid memories

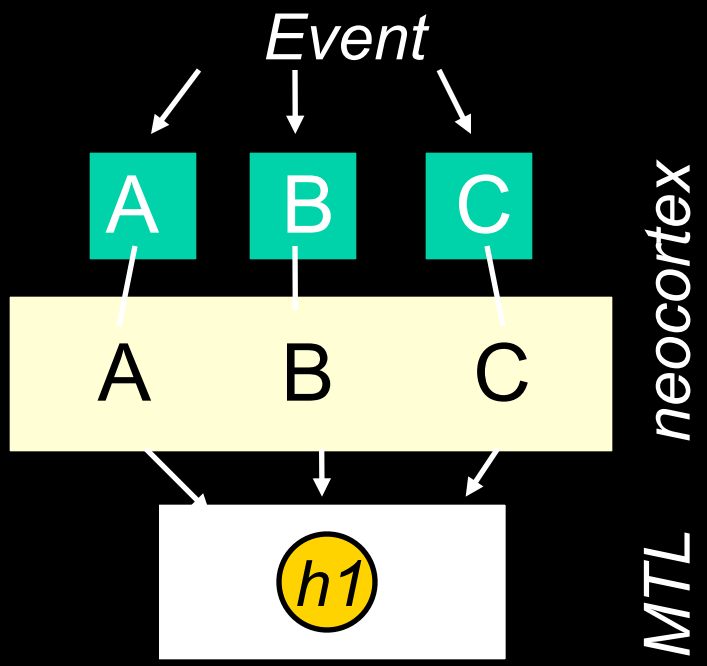
- Ribot's law (1881)

"This law, which I shall designate as the *law of regression or reversion* seems to me to be a natural conclusion from the observed facts… This loss of memory is, as the mathematicians say, inversely as the time that has elapsed between any given incident and the fall [injury]…the new perishes before the old, the complex before the simple."

Standard Consolidation Theory

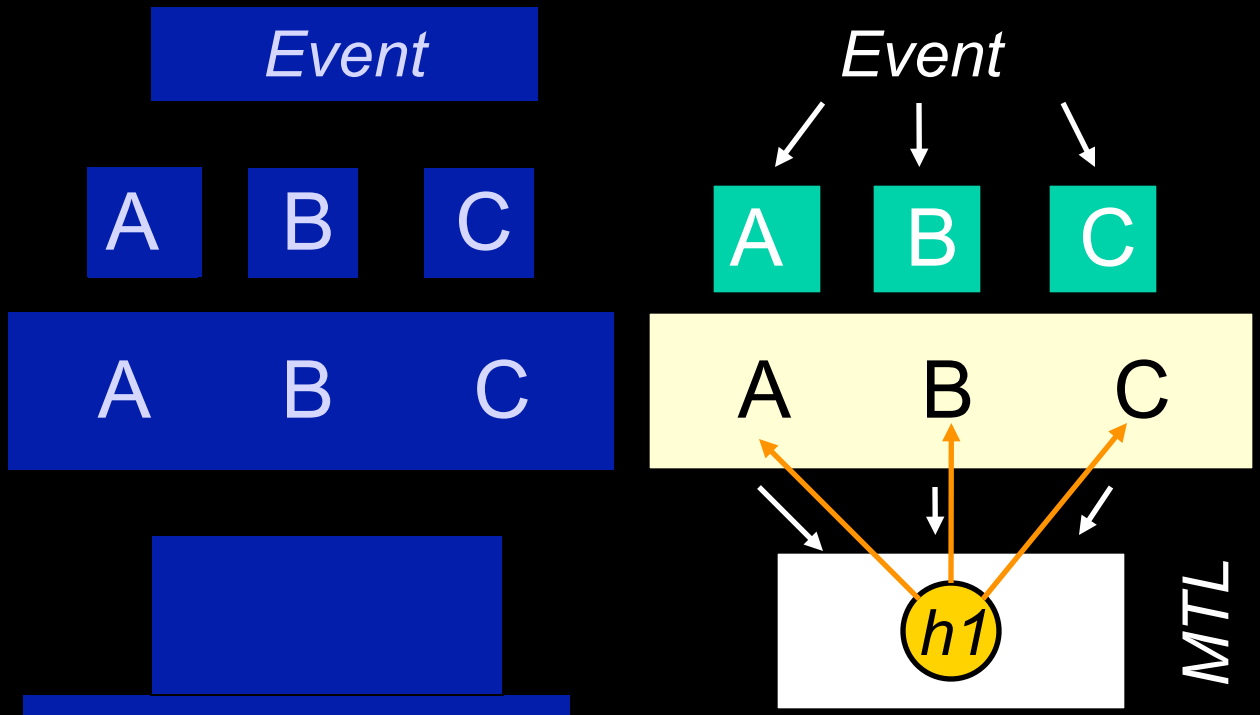
- Consolidation: process that transforms a memory trace into a durable representation that is **independent** of the MTL
- The cortex learns more slowly than the hippocampus, but it is also capable of storing conjunctive/associative memories
  - Repeatedly remembering your high school graduation will reactivate cortical areas relating to what you saw, heard, etc that day
  - Repeated co-activation of cortical areas that represent individual event features allows cortex to gradually bind features together into a conjunctive memory
- Temporally-graded retrograde amnesia occurs because more recently acquired memories have not yet been consolidated

Standard Consolidation Theory



Hippocampus rapidly encodes a conjunctive representation

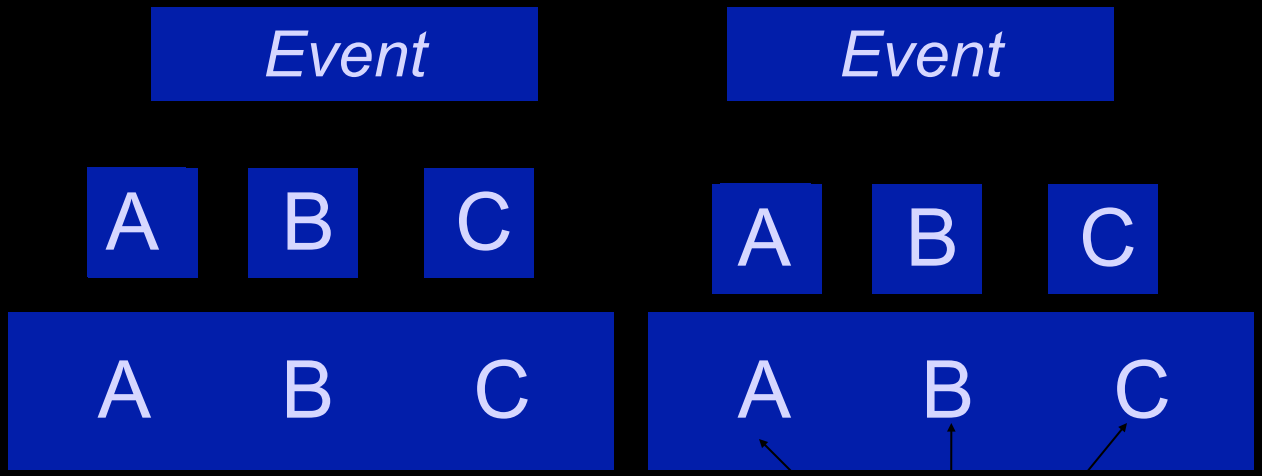
Standard Consolidation Theory



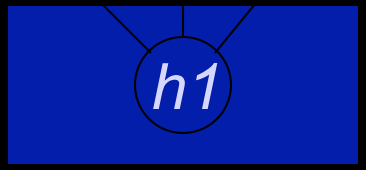
Hippocampus rapidly encodes a conjunctive representation

Encode in a distributed ensemble of hippocampal neurons that act as a pointer to neocortical neurons representing the attended information.

Standard Consolidation Theory



Hippocampus rapidly encodes a conjunctive representation



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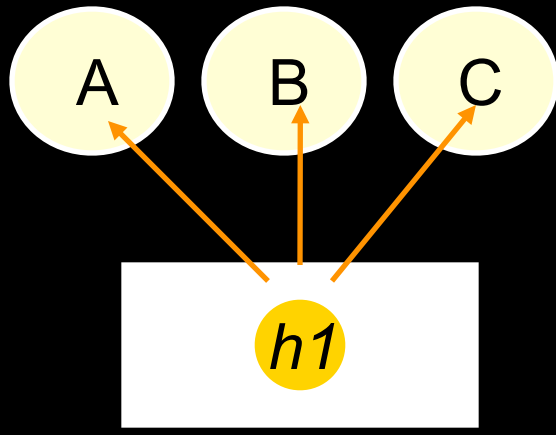
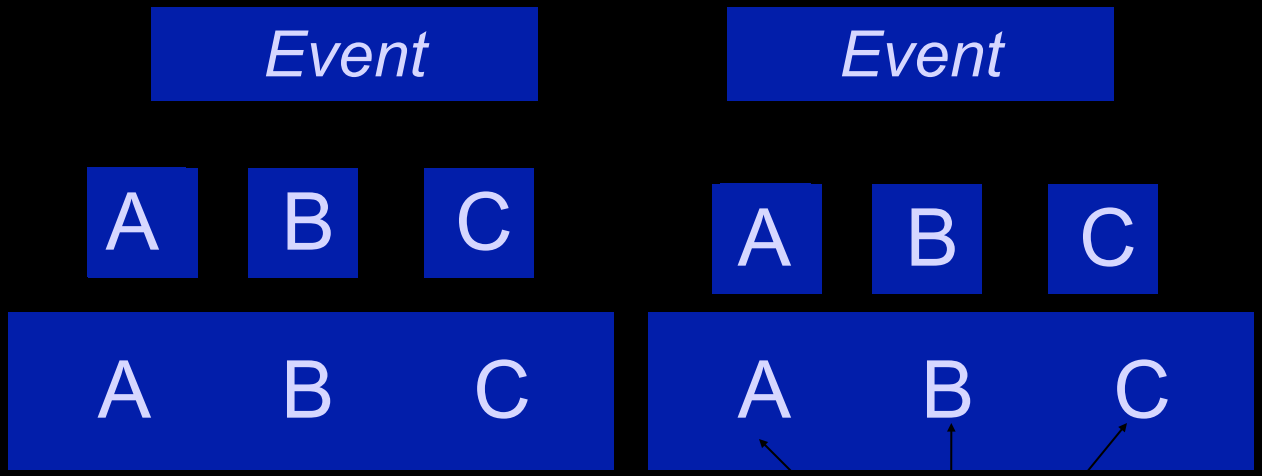
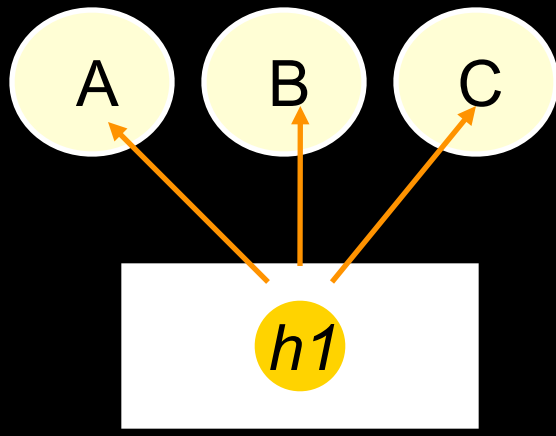


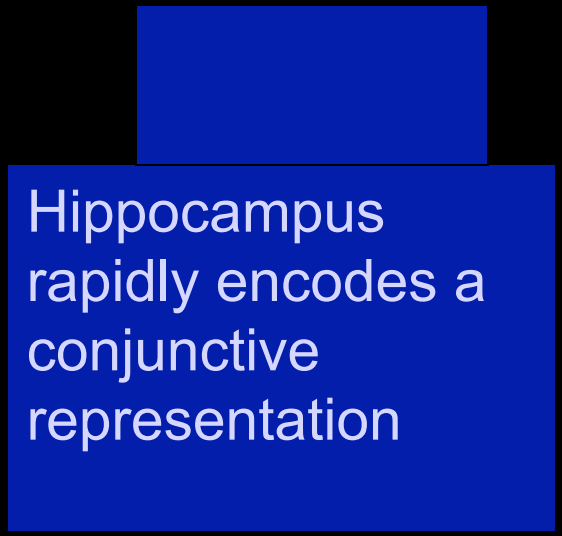
HIPP "pointer" and neocortical feature traces constitute the memory

Standard Consolidation Theory

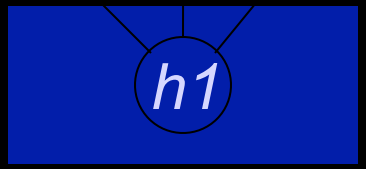


Replaying feature information to neocortex allows it to gradually bind information together





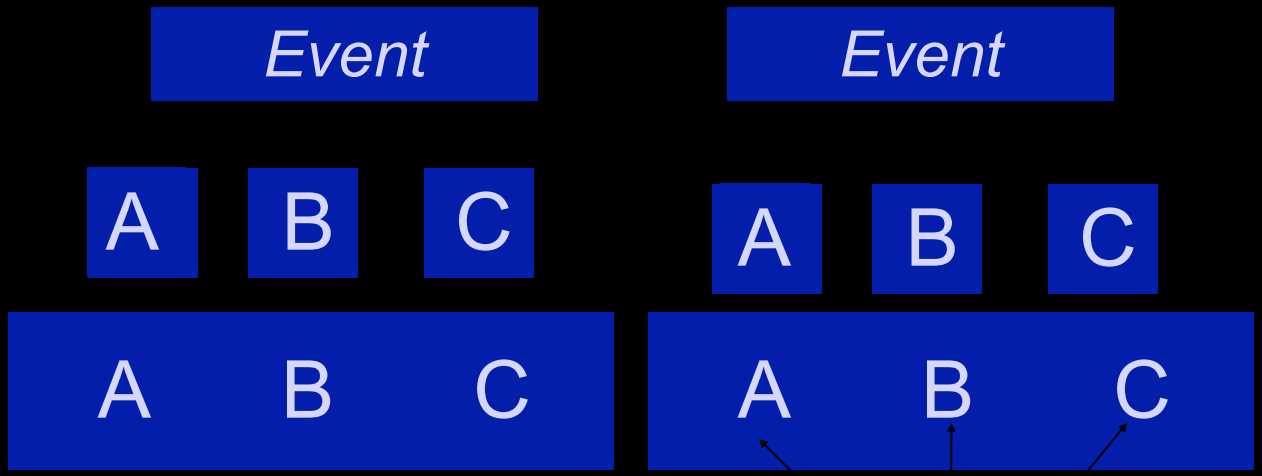
Hippocampus rapidly encodes a conjunctive representation



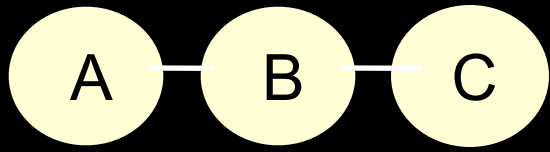
Encode in a distributed ensemble of hippocampal neurons that act as a pointer to neocortical neurons representing the attended information.

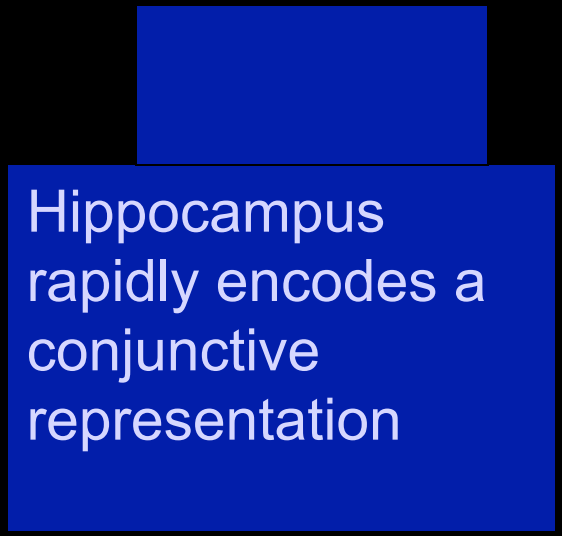
HIPP "pointer" and neocortical feature traces constitute the memory

Standard Consolidation Theory

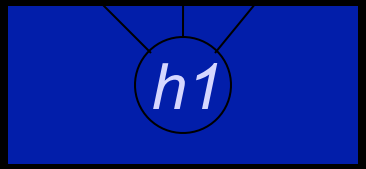


Feature information in neocortex is bound together





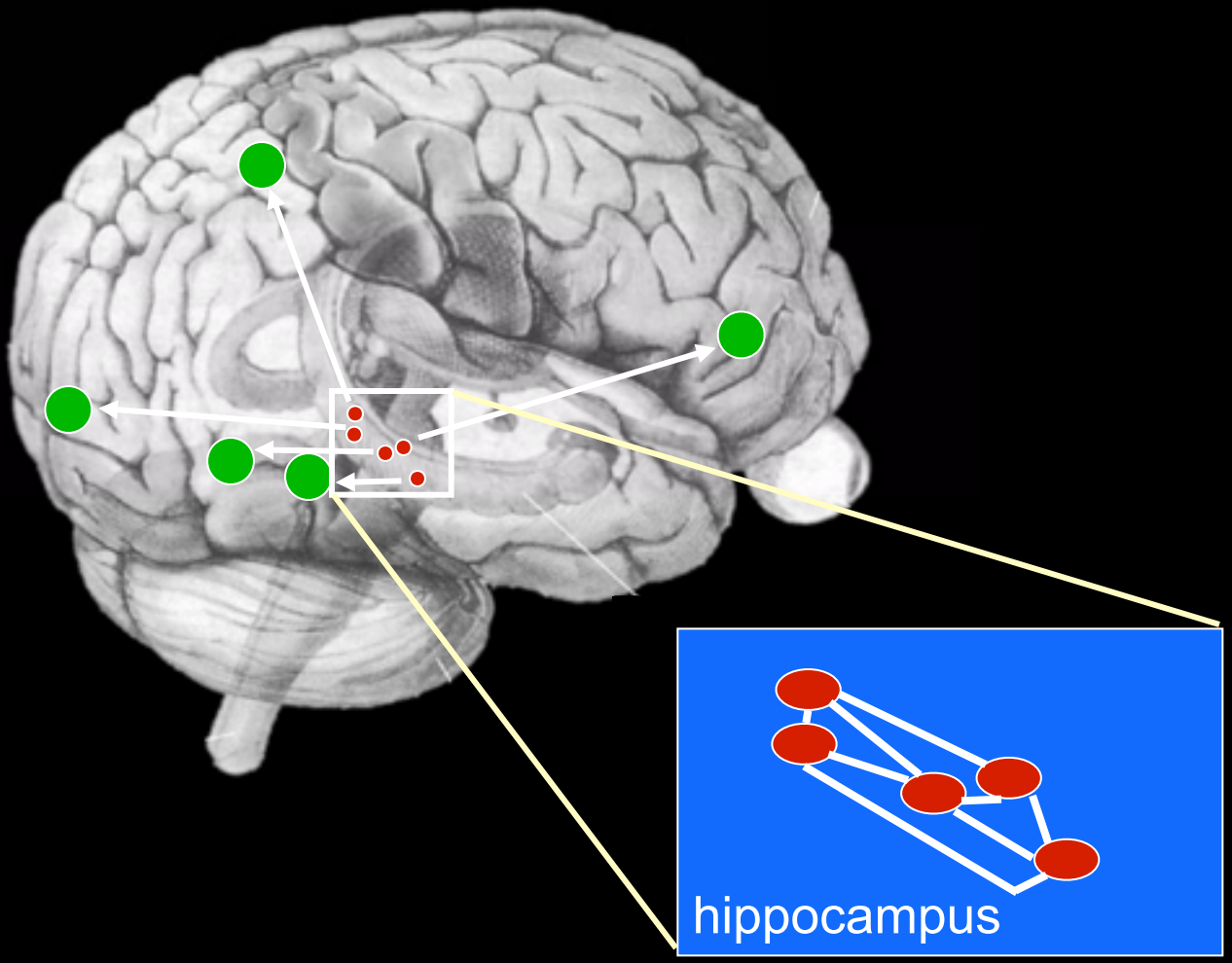
Hippocampus rapidly encodes a conjunctive representation



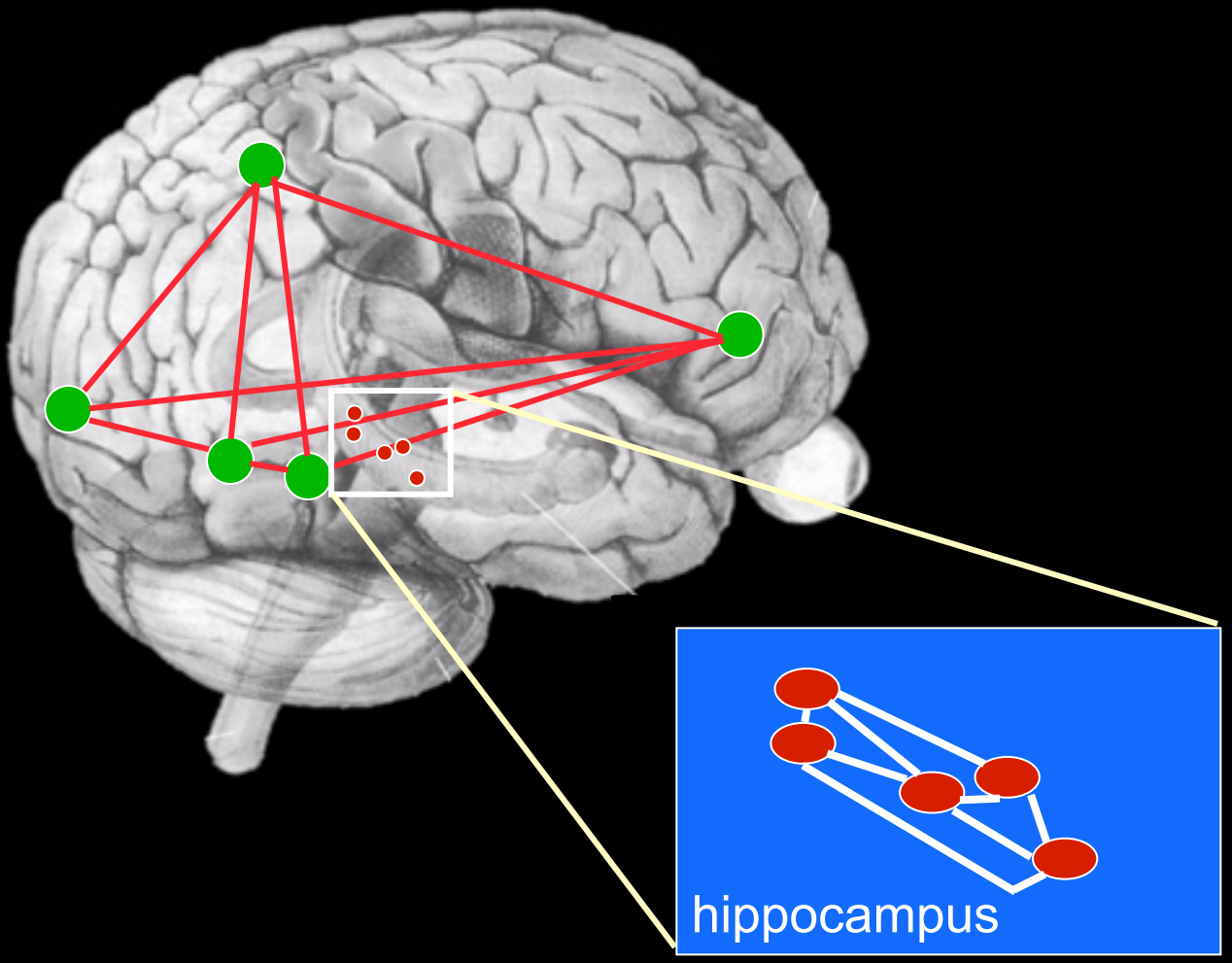
Encode in a distributed ensemble of hippocampal neurons that act as a pointer to neocortical neurons representing the attended information.

The neocortex is eventually capable of representing the memory without the aid of HIPP (consolidated memory)

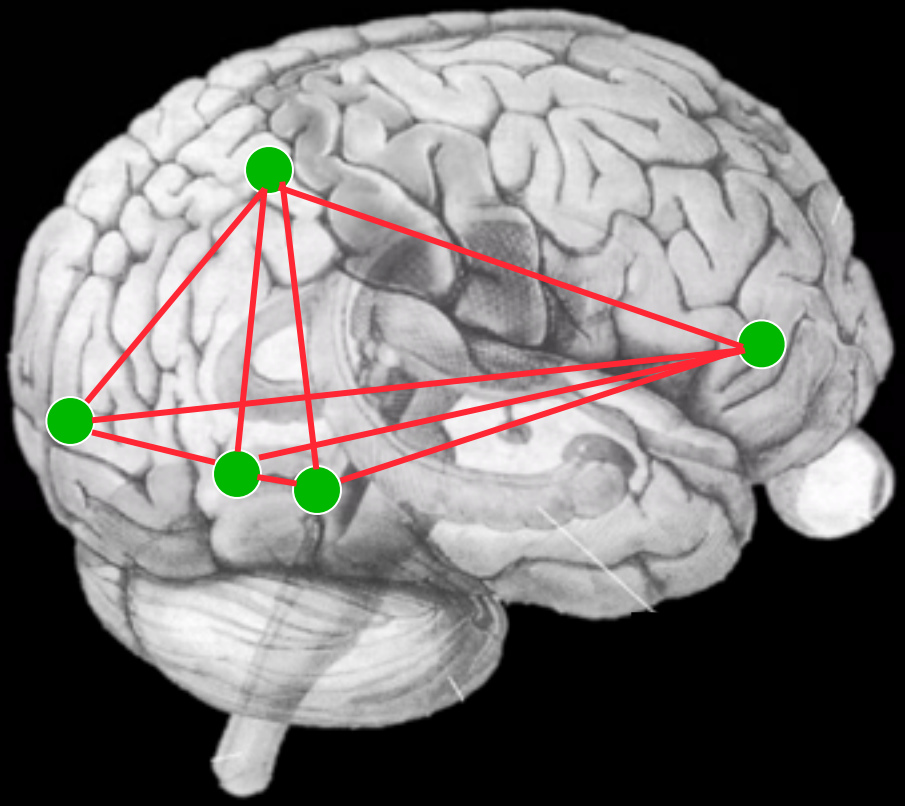
Hippocampus & Memory Consolidation: Transferring Memories to Neocortex



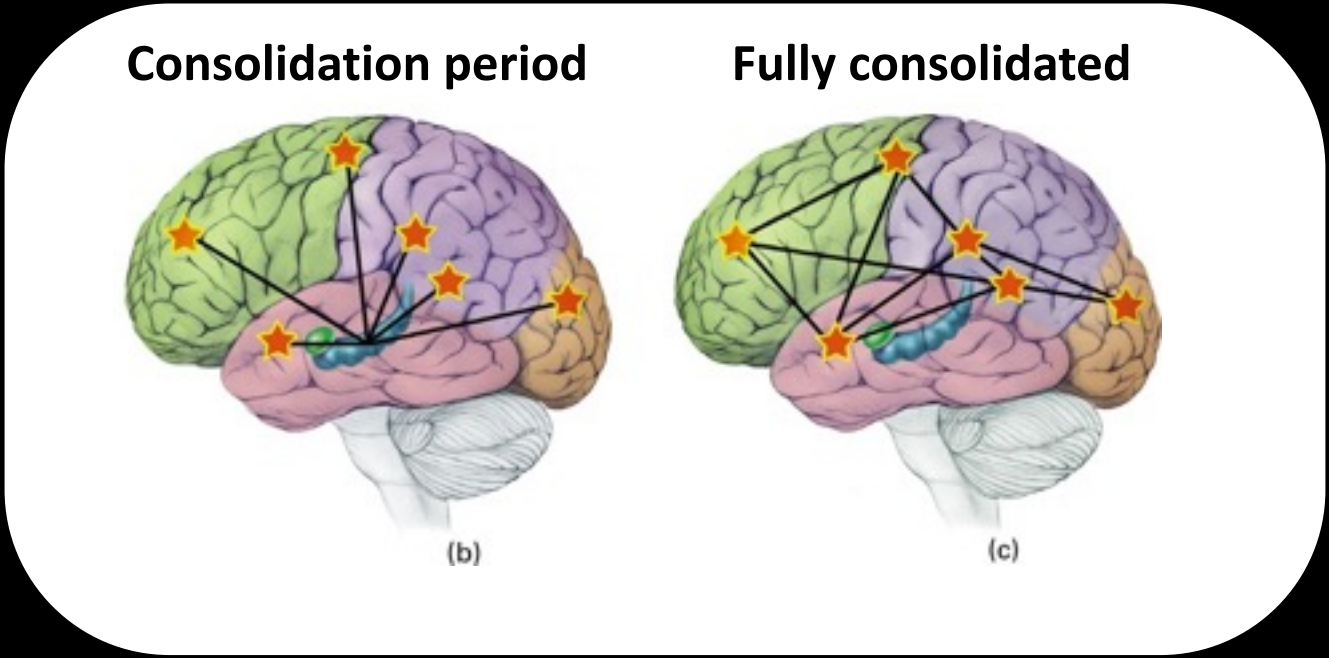
Hippocampus & Memory Consolidation: Transferring Memories to Neocortex



Hippocampus & Memory Consolidation: Transferring Memories to Neocortex



Temporal Gradient of Retrograde Amnesia



MTL damage impairs recent memories still undergoing consolidation, but memories that are already fully consolidated (in the cortex) remain intact

Participation Prompt #2

- Try to remember some experience from this past weekend, bringing as many details to mind
- Do you think what you've remembered contains all of the event information that you had encoded into episodic memory during the experience?
- Do you think what you've remembered is a highly accurate memory of the event, with no distortions or errors?
- If the answer to either of the above is 'no', what are the implications for how the event memory is being consolidated in cortex?