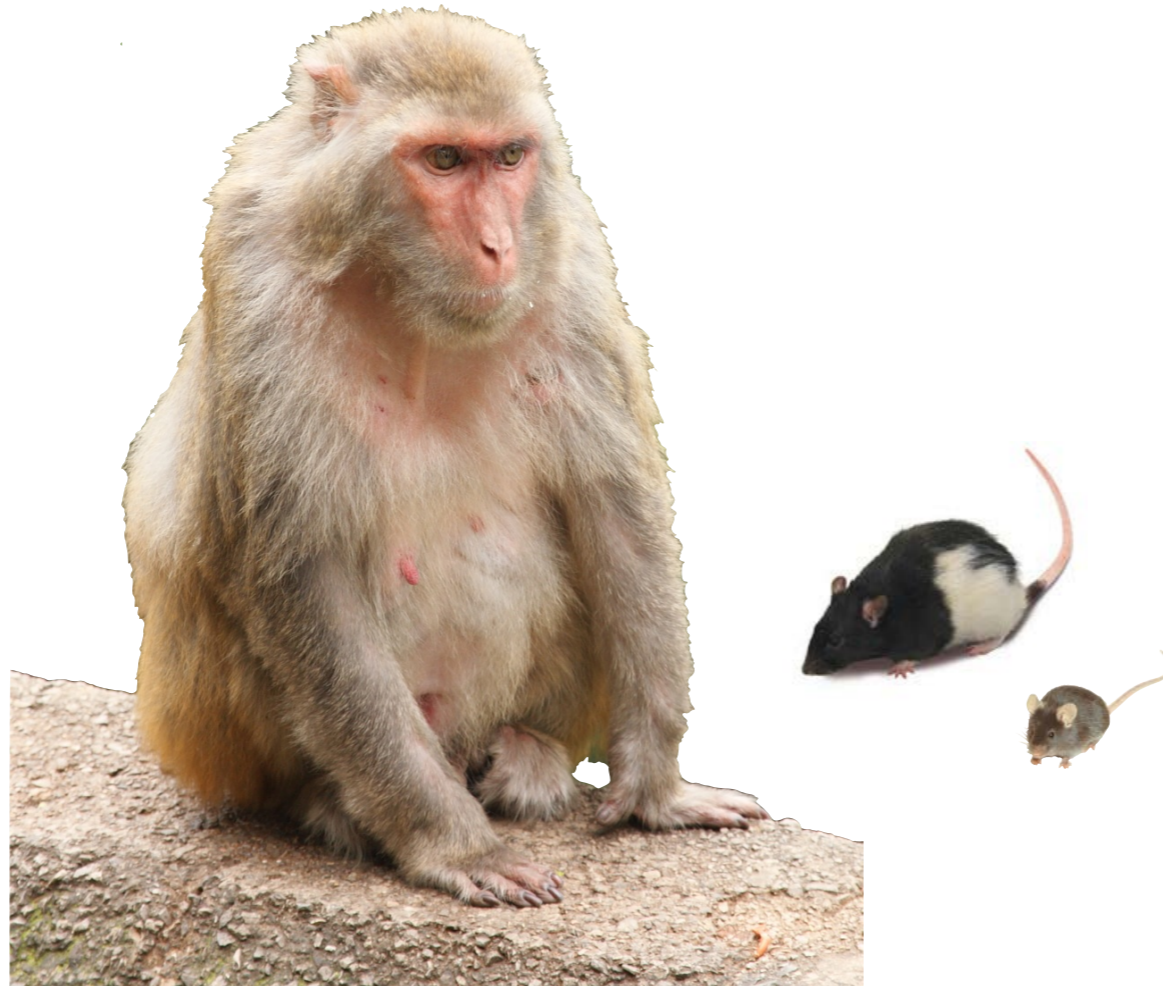


# ANIMAL MODELS OF AMNESIA (PART I)

Norbert Fortin, PhD



*Bio Sci 38: Mind, Memory, and the Brain*

# OVERVIEW

- Need for an animal model of human amnesia
- Comparing the brain across mammals
- Properties of a valid animal model of amnesia
- The first model to “work”:
  - The delayed non-match to sample task

# ANIMAL MODELS IN BIOMEDICAL RESEARCH

- Animal models are critical to medical research
  - Knowledge of organ function and diseases
  - Development of treatments and medicines
- Same principle applies to brain research
  - We cannot treat cognitive disorders (e.g., Alzheimer's disease) unless we understand how the normal brain works

# WHY DO WE NEED ANIMAL MODELS OF AMNESIA?

- Limitations of memory experiments performed in humans
  - Variability in extent of neurological damage
  - Variability in subjects' learning history
  - Low spatial and temporal resolution of techniques
- Advantages of animal models
  - Control extent and timing of brain damage
  - Control information learned before and after brain damage
  - Can use high-precision techniques that are not available in humans



# OVERVIEW

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## YOU'RE PROBABLY THINKING....

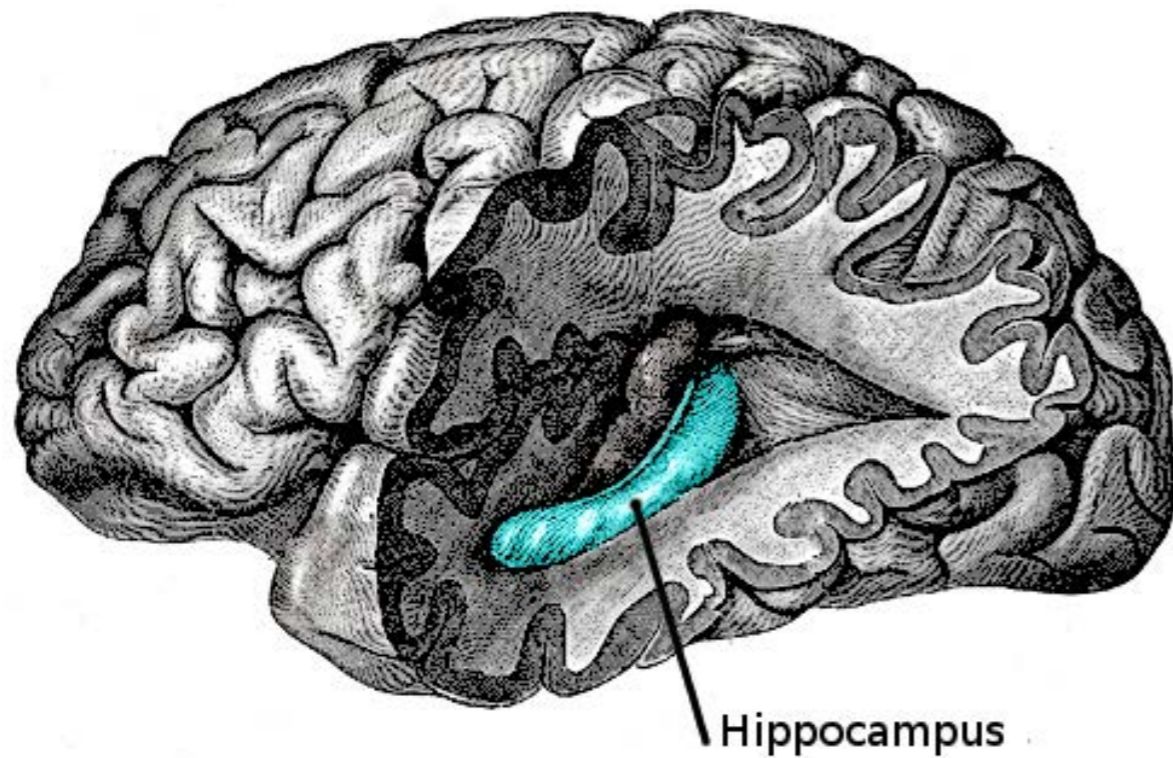
*“OK. I can understand that the heart, kidneys, liver, and spinal cord may be very similar across mammals. But the brain? Really?”*



# COMPARING THE BRAIN ACROSS MAMMALS

## BASIC ANATOMY OF THE HIPPOCAMPUS

Where is it in the human brain?



<http://en.wikipedia.org/wiki/File:Gray739-emphasizing-hippocampus.png>

Where does the name come from?

The sea creature



[http://en.wikipedia.org/wiki/File:Hippocampus\\_and\\_seahorse\\_cropped.JPG](http://en.wikipedia.org/wiki/File:Hippocampus_and_seahorse_cropped.JPG)

The brain structure



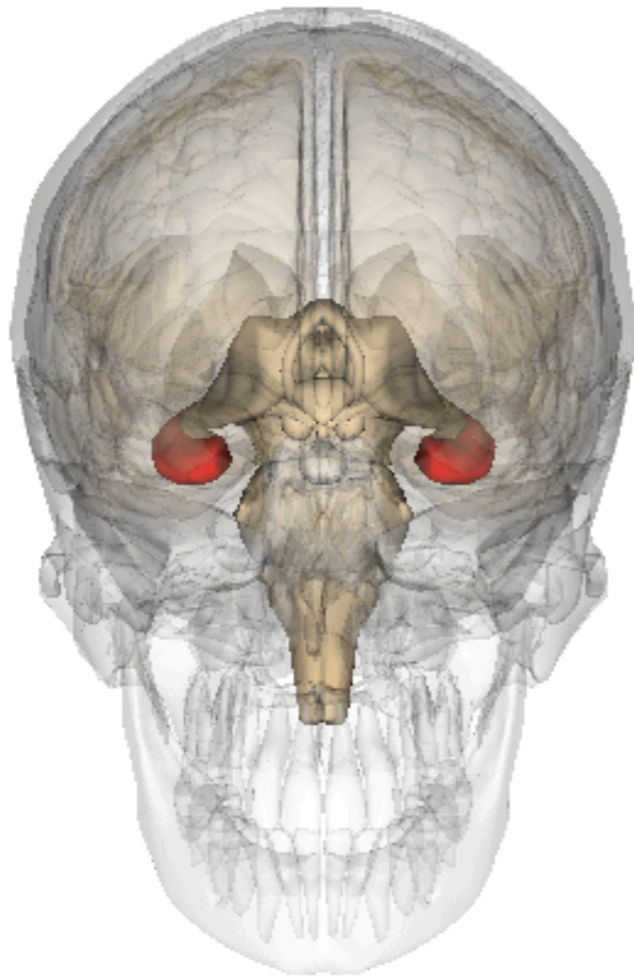


# COMPARING THE BRAIN ACROSS MAMMALS

## BASIC ANATOMY OF THE HIPPOCAMPUS

It has a distinctive 3-D shape

Human



Rat

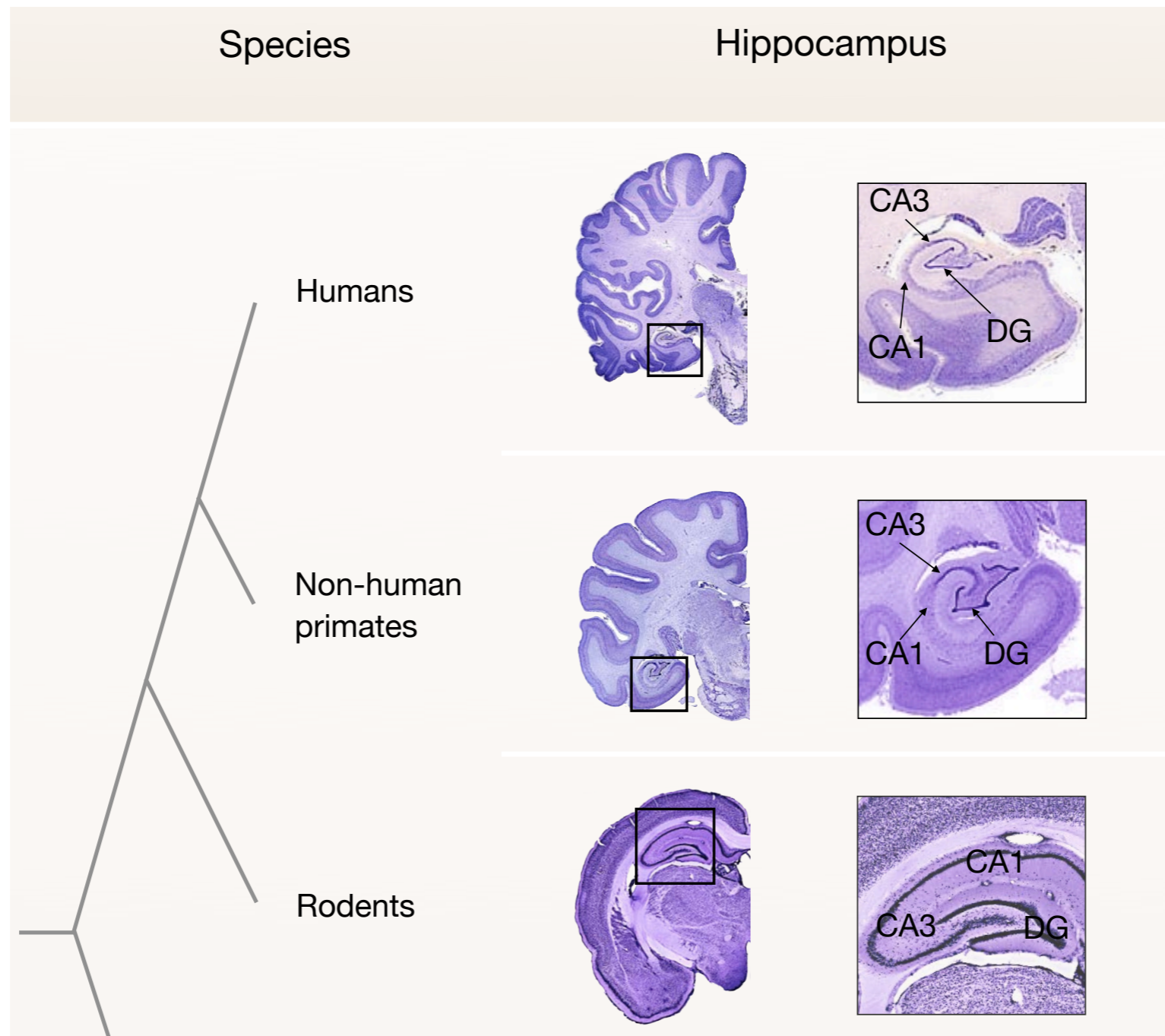




# COMPARING THE BRAIN ACROSS MAMMALS

## THE HIPPOCAMPUS IS VERY SIMILAR ACROSS SPECIES

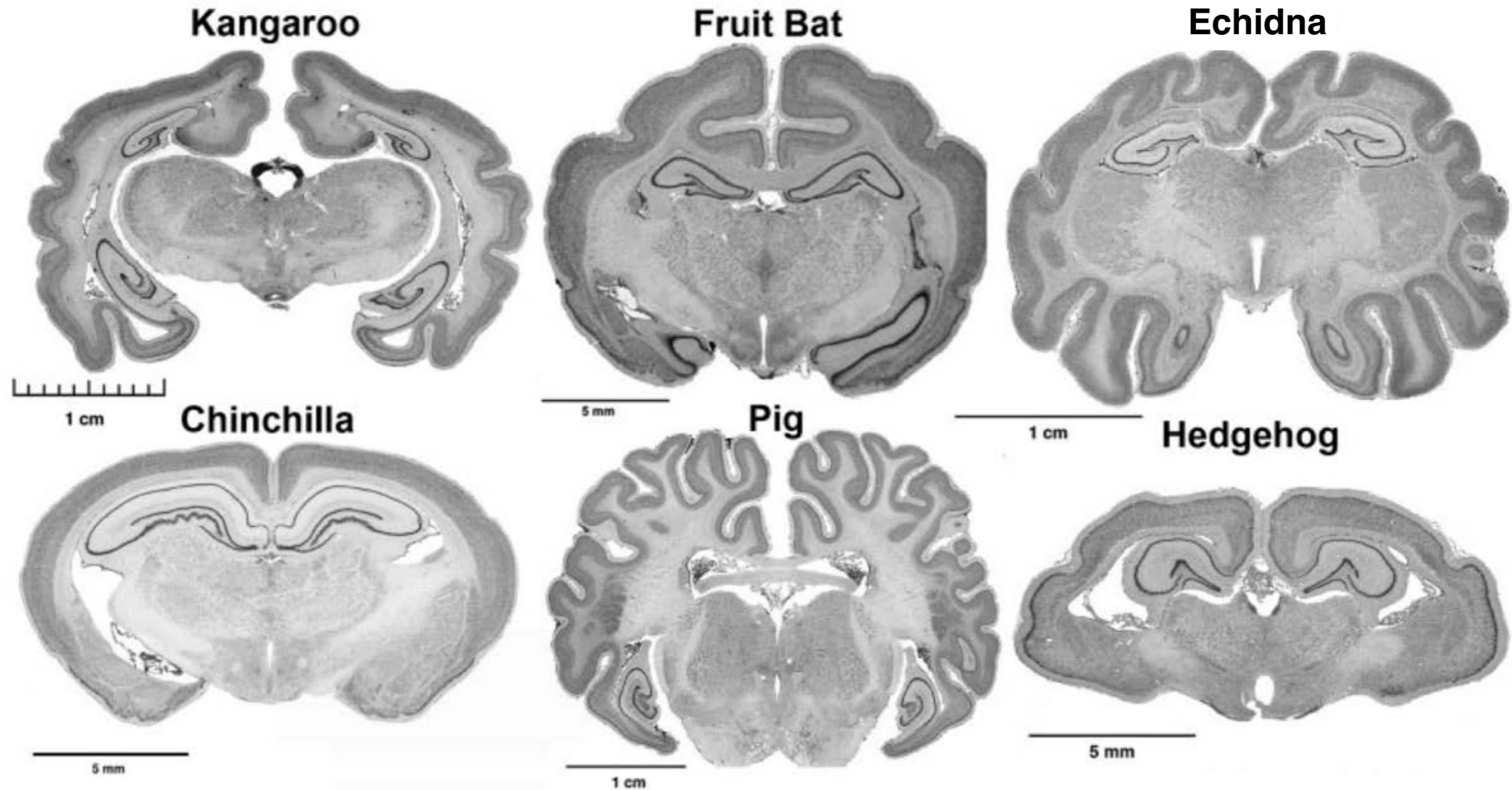
Species typically used in memory research



# COMPARING THE BRAIN ACROSS MAMMALS

## THE HIPPOCAMPUS IS VERY SIMILAR ACROSS SPECIES

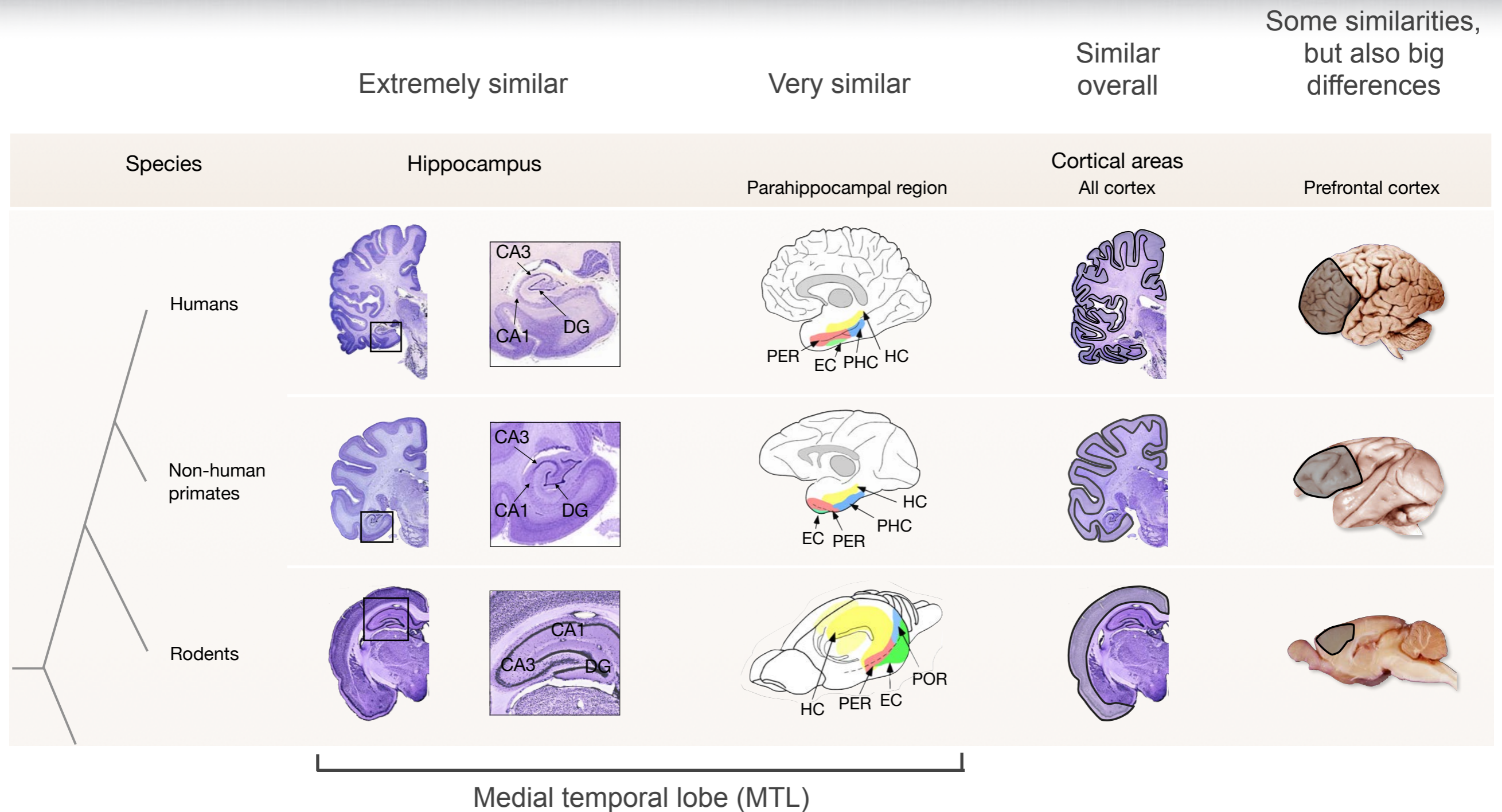
### Other mammals





# COMPARING THE BRAIN ACROSS MAMMALS

## THE HIPPOCAMPUS AND CORTEX



*Allen & Fortin (2013) PNAS*

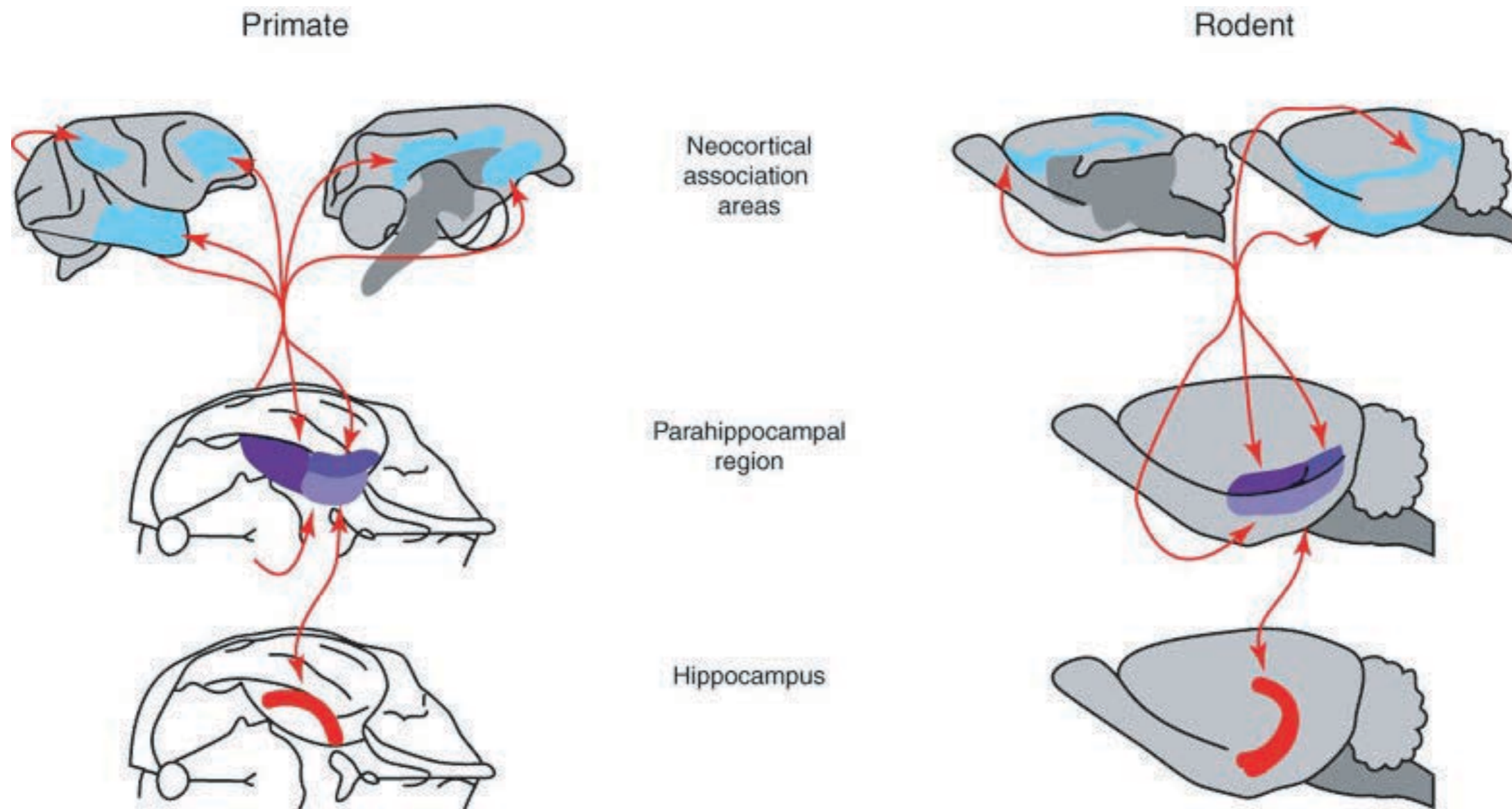
Abbreviations: Entorhinal cortex (EC), Hippocampus (HC), Perirhinal cortex (PER), Parahippocampal cortex (PHC) (PHC is called postrhinal in rodents, or POR)



# COMPARING THE BRAIN ACROSS MAMMALS

## HIPPOCAMPAL-CORTICAL CONNECTIONS

Similar pattern of connections between brain structures



# OVERVIEW

- Need for an animal model of human amnesia
- Comparing the brain across mammals
- Properties of a valid animal model of amnesia
- The first model to “work”:
  - The delayed non-match to sample task

# PROPERTIES FOR VALID ANIMAL MODEL OF HUMAN AMNESIA (e.g., patients H.M. or E.P.)

- Property #1: Sensory, motor, motivational and cognitive processes are intact
- Property #2: Short-term memory (STM) is intact
- Property #3: Beyond STM, memory declines rapidly
  - “Faster forgetting”
- Property #4: Memory deficit is global
  - Not limited to one modality or type of stimulus
- Property #5: Graded retrograde impairment
  - Recent memories are more impaired than remote memories



## YOU'RE PROBABLY THINKING...

*“Dr. Stark showed us some videos. I saw the memory tests they give to patients. How can you do that in animals?”*

# OVERVIEW

- Need for an animal model of human amnesia
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# DELAYED NON-MATCH TO SAMPLE TASK (DNMS) IN PRIMATES

- After many *failures*, this is the first model to work  
(Gaffan, 1974; Mishkin and Delacour, 1975)

*i.e., scientists were damaging the MTL but it wasn't producing amnesia*

- Task procedures

Sample phase → Delay → Test phase



Move sample object to get a reward



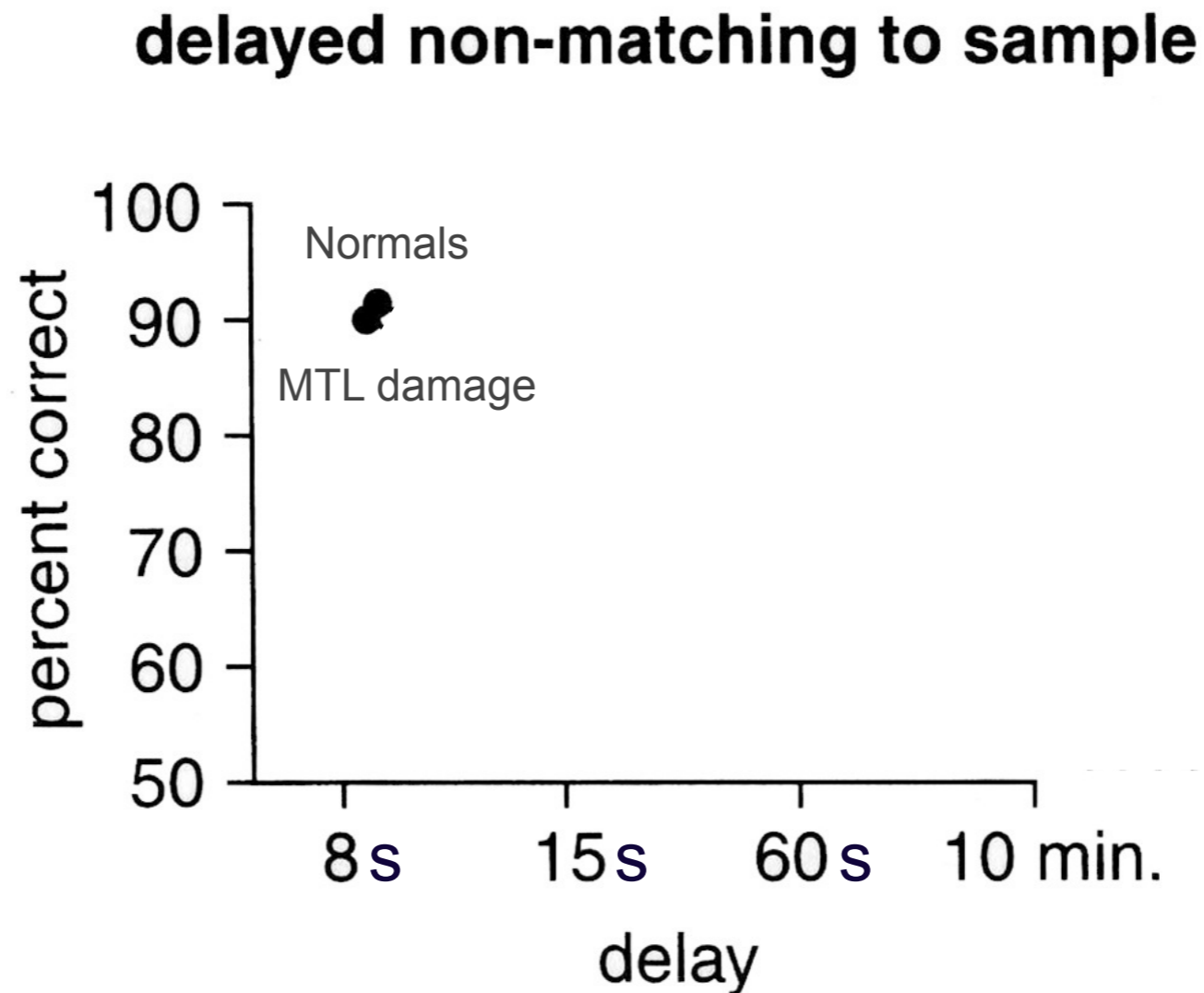
Move the "new" object to get a reward

\*\*\* Breakthrough is the use of trial-unique stimuli, and the non-match strategy \*\*\*



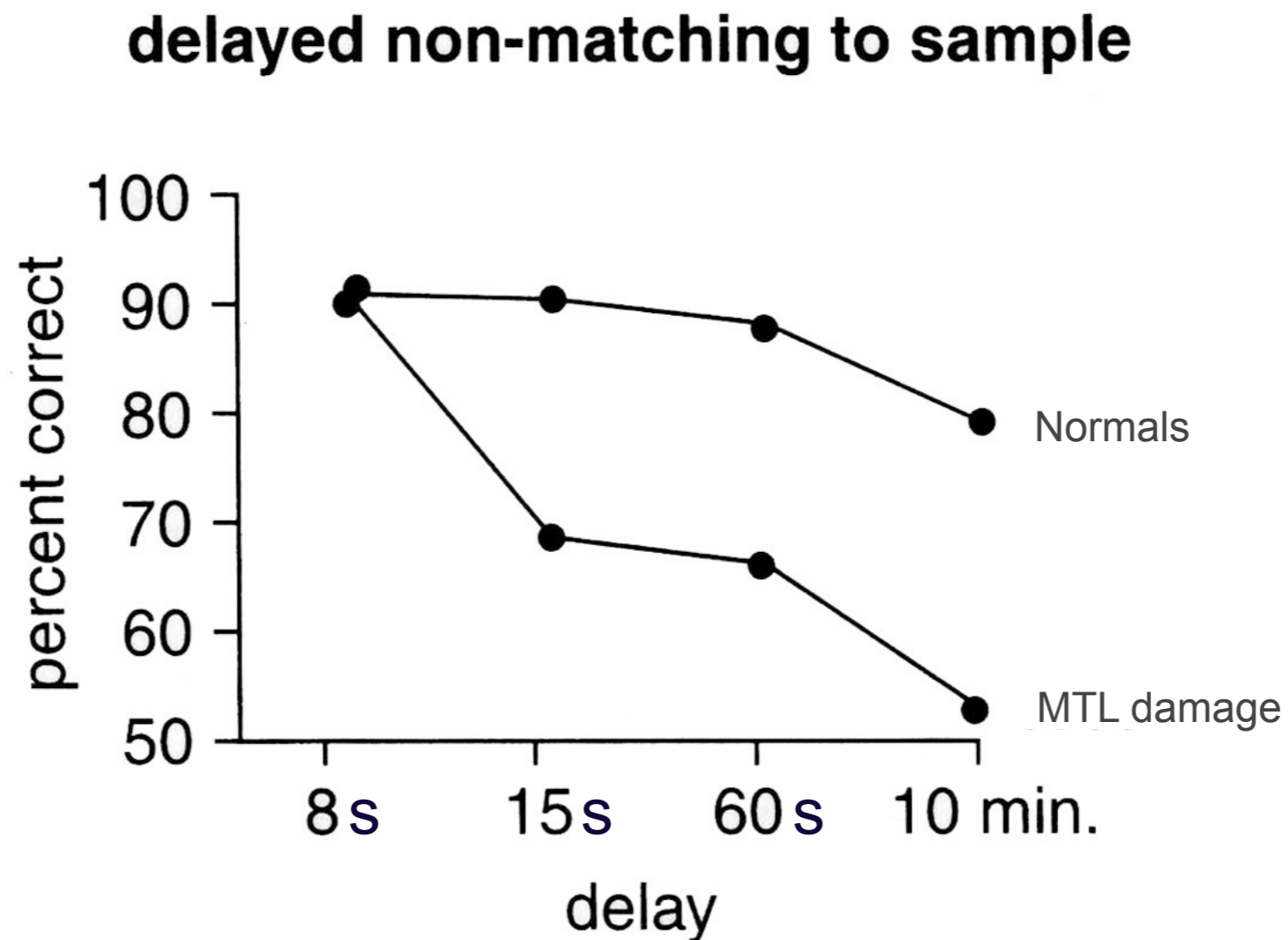
# DELAYED NON-MATCH TO SAMPLE TASK (DNMS) IN PRIMATES

- Property #1: Sensory, motor, motivational and cognitive processes are intact
- Property #2: Short-term memory (STM) is intact



# DELAYED NON-MATCH TO SAMPLE TASK (DNMS) IN PRIMATES

- Property #3: Beyond STM, memory declines rapidly
  - “Faster forgetting”



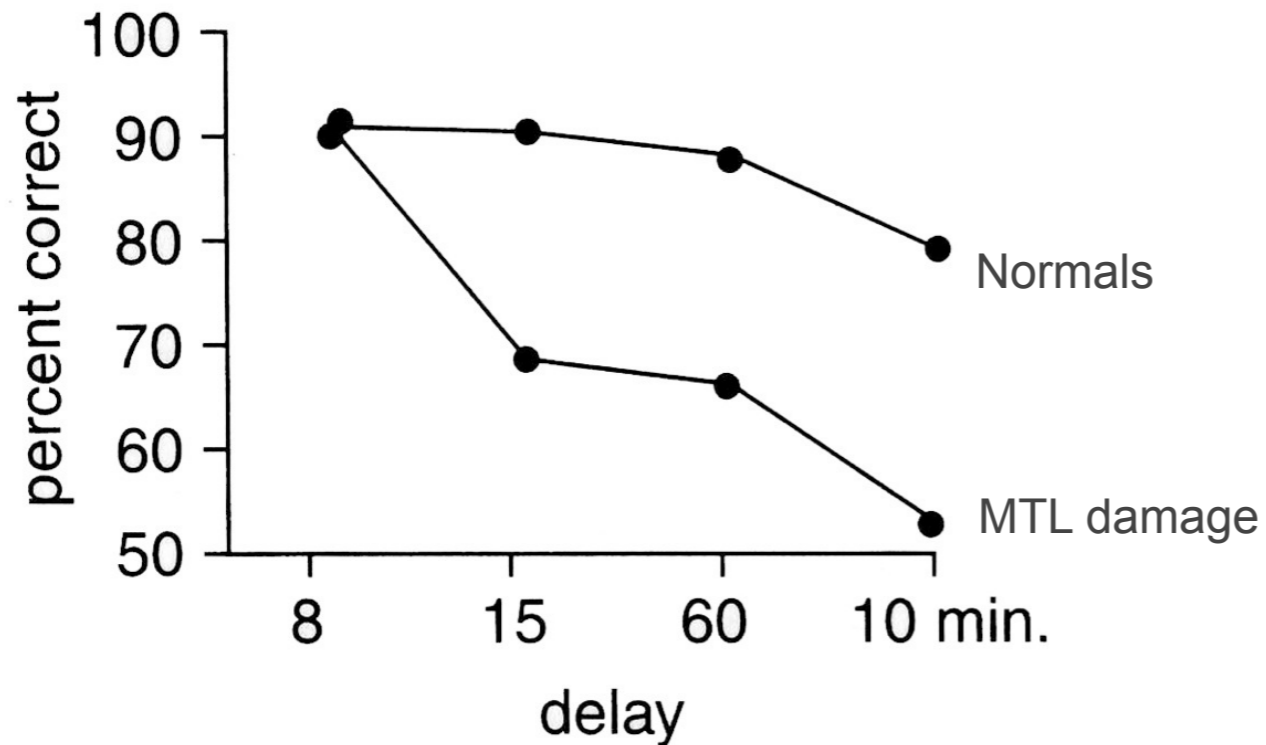


# DELAYED NON-MATCH TO SAMPLE TASK (DNMS) IN PRIMATES

- Property #4: Memory deficit is global
  - Not limited to one modality or type of stimulus

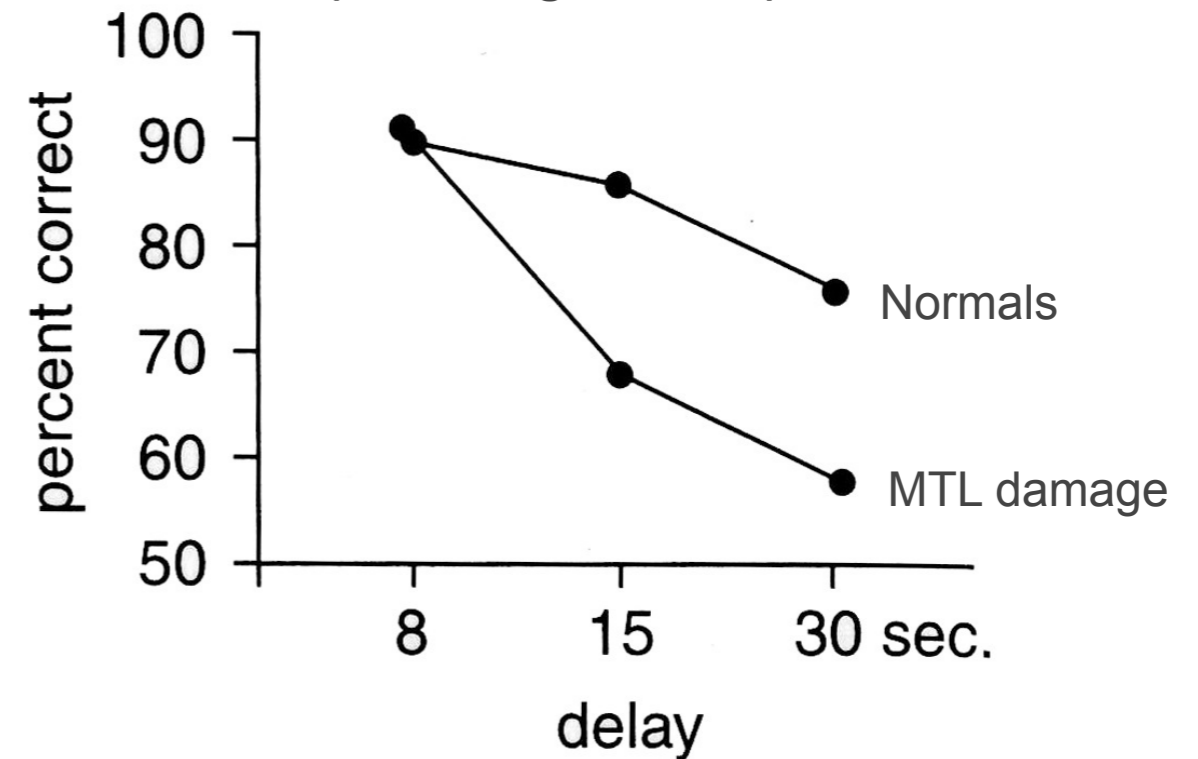
## delayed non-matching to sample

(Object A or B?)



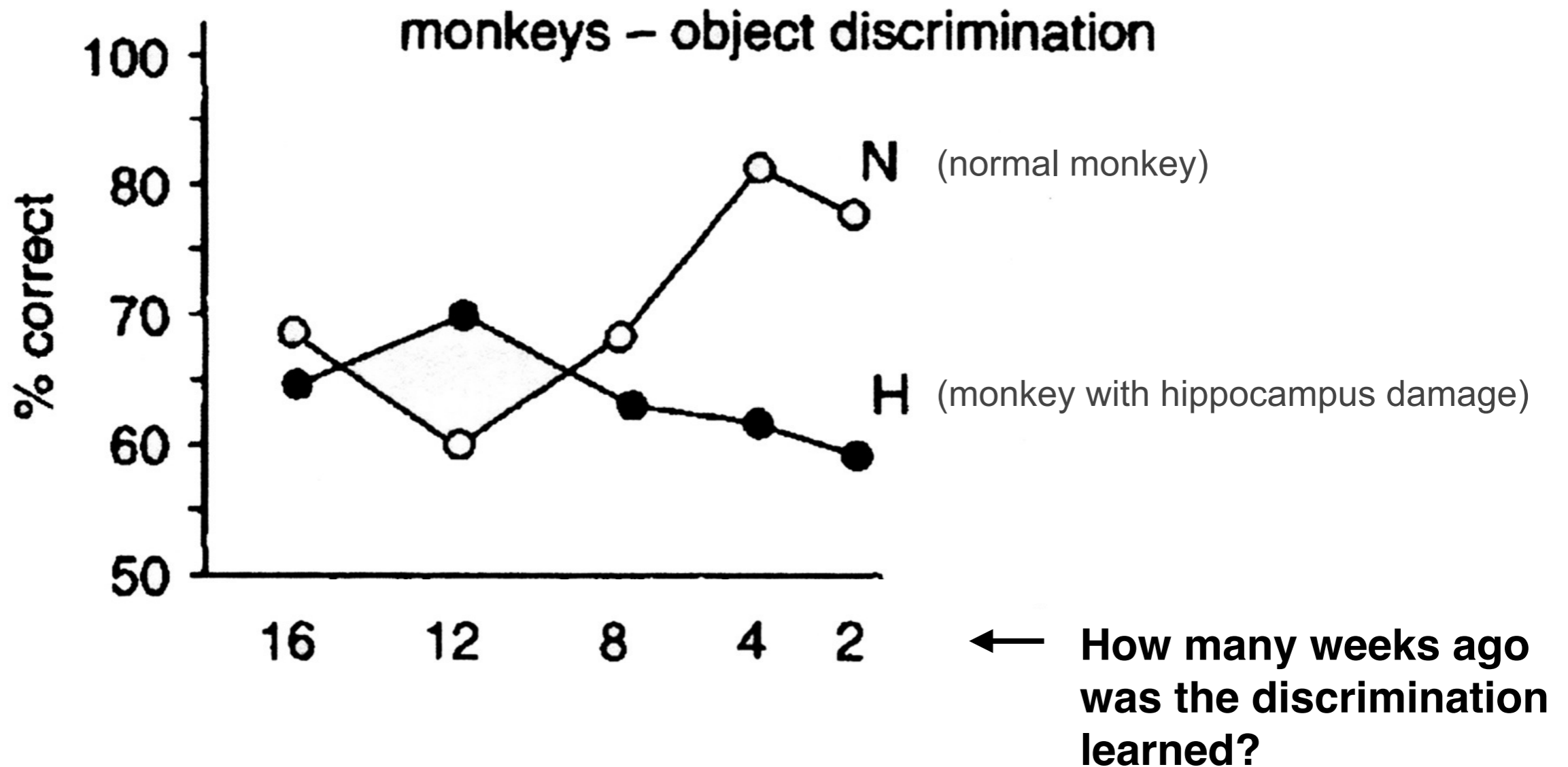
## delayed response

(Left or right lever?)



# DELAYED NON-MATCH TO SAMPLE TASK (DNMS) IN PRIMATES

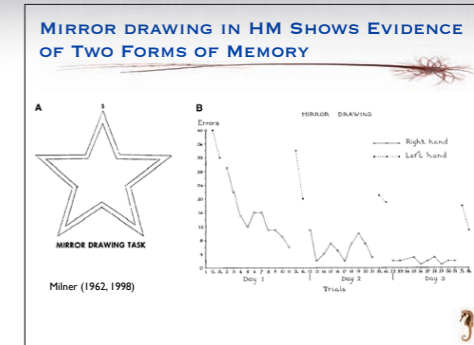
- Property #5: Graded retrograde impairment
  - Recent memories are more impaired than remote memories



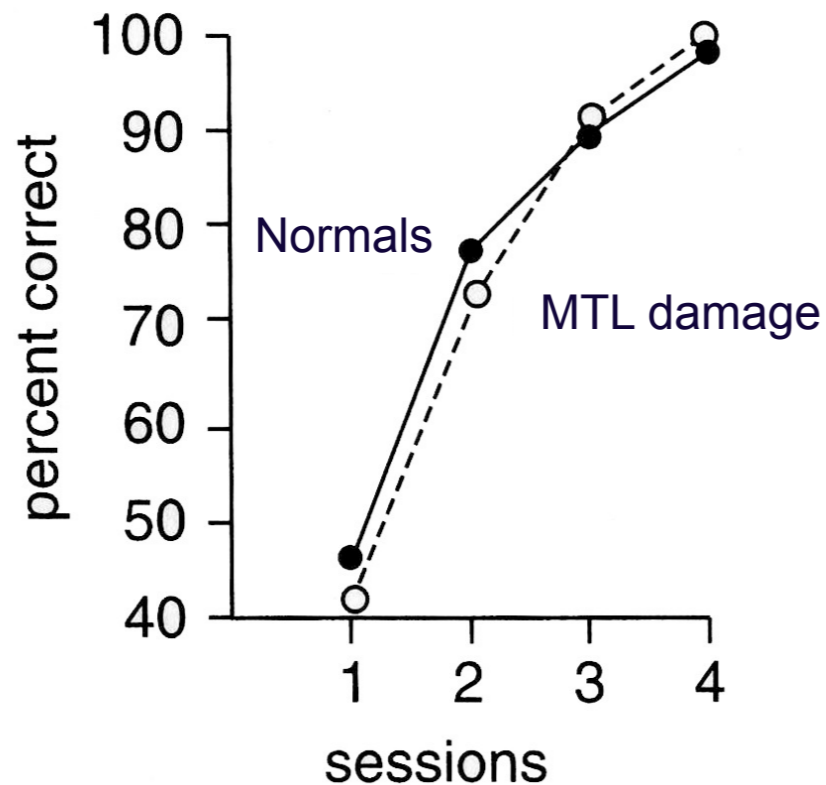


# OTHER MEMORY SYSTEMS ARE INTACT

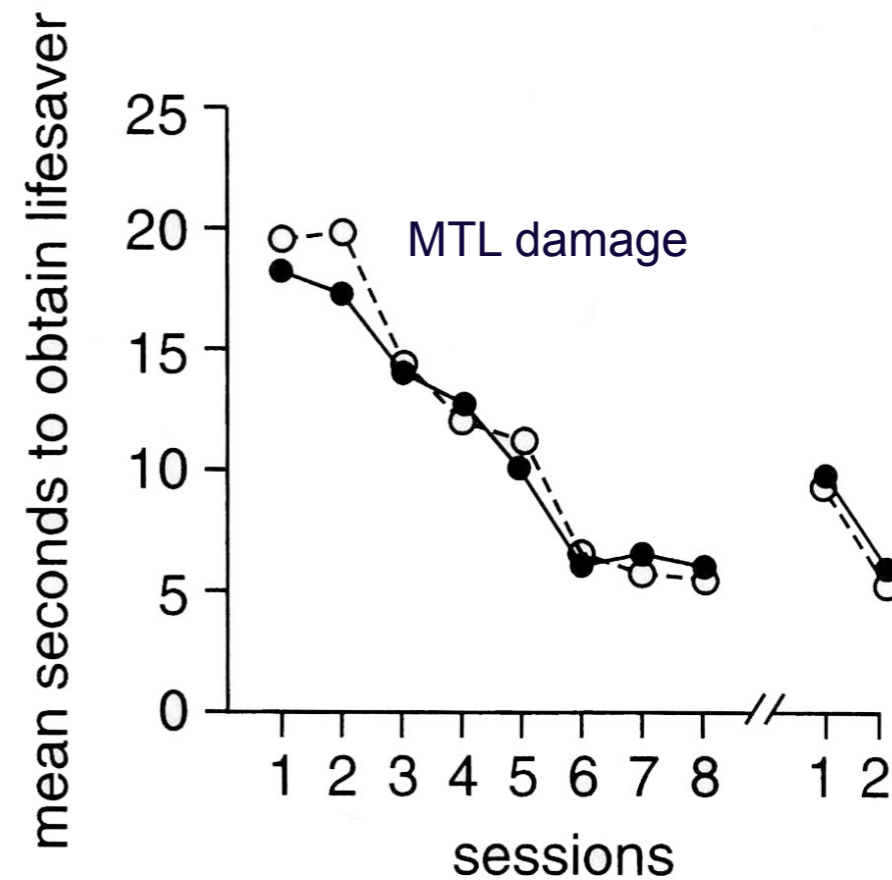
- Just like amnesic patients can do the “mirror drawing task”, these monkeys can still learn motor skills.



**barrier motor-skill task**



**lifesaver motor-skill task**



# SUMMARY

- Animal models of human amnesia are crucial to our understanding of memory
- Overall, the brain is very similar across mammals, especially with regard to the hippocampus and the medial temporal lobe (MTL). The rest of the cortex has many similarities, but also a number of species-specific differences.
- The delayed non-match to sample task, developed in primates, has all the important properties of a valid animal model of amnesia.