

ANIMAL MODELS OF AMNESIA (PART II)

Norbert Fortin, PhD



Bio Sci 38: Mind, Memory, and the Brain

OVERVIEW

- Field research
- Lab research: classic approaches
 - Mazes (and cheese)
 - Skinner or operant boxes
- Lab research: modern approaches
 - Newer “mazes”
 - Context memory
 - Item and list memory
 - Spontaneous preference tasks

FIELD RESEARCH

HIGH EXTERNAL VALIDITY, BUT DIFFICULT AND LESS FLEXIBLE

Examples:

- Memory for caching locations



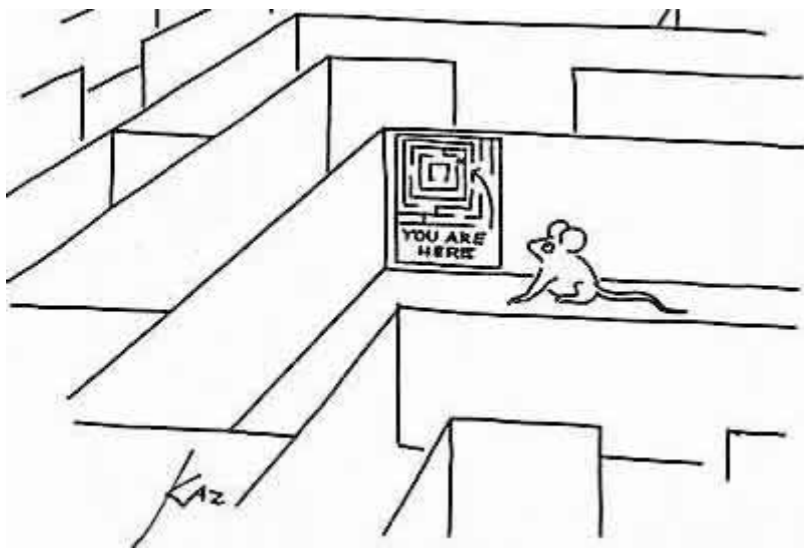
- Social behavior in the wild



LAB RESEARCH: CLASSIC APPROACHES

MAZES (AND CHEESE)

Very common in popular culture (but not in lab)



LAB RESEARCH: CLASSIC APPROACHES

WHERE DO MAZES COME FROM?

- The first maze used to test learning and memory in rats (Small, 1901)

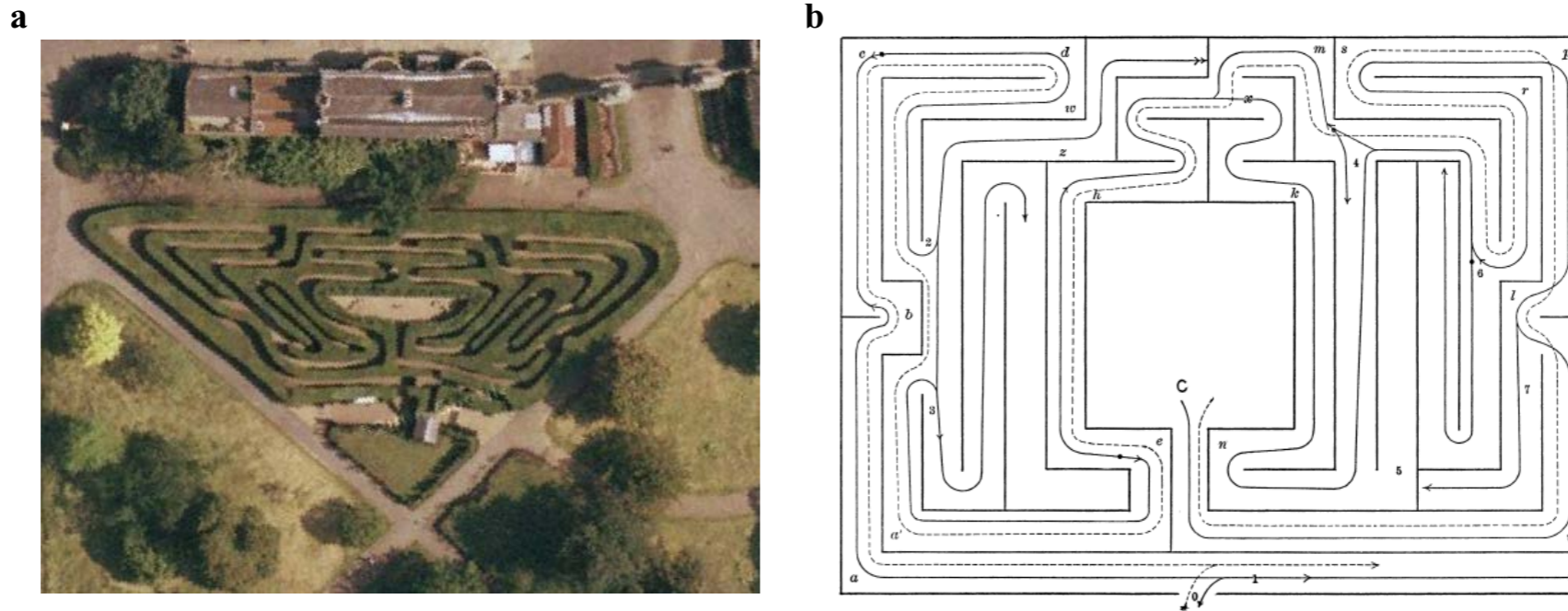


Figure 2. Complex maze learning (Small, 1901). **a**, picture of the Hampton Court Palace maze outside London, which served as inspiration (from Google Maps). **b**, Diagram of one of the maze used by Small (1901).

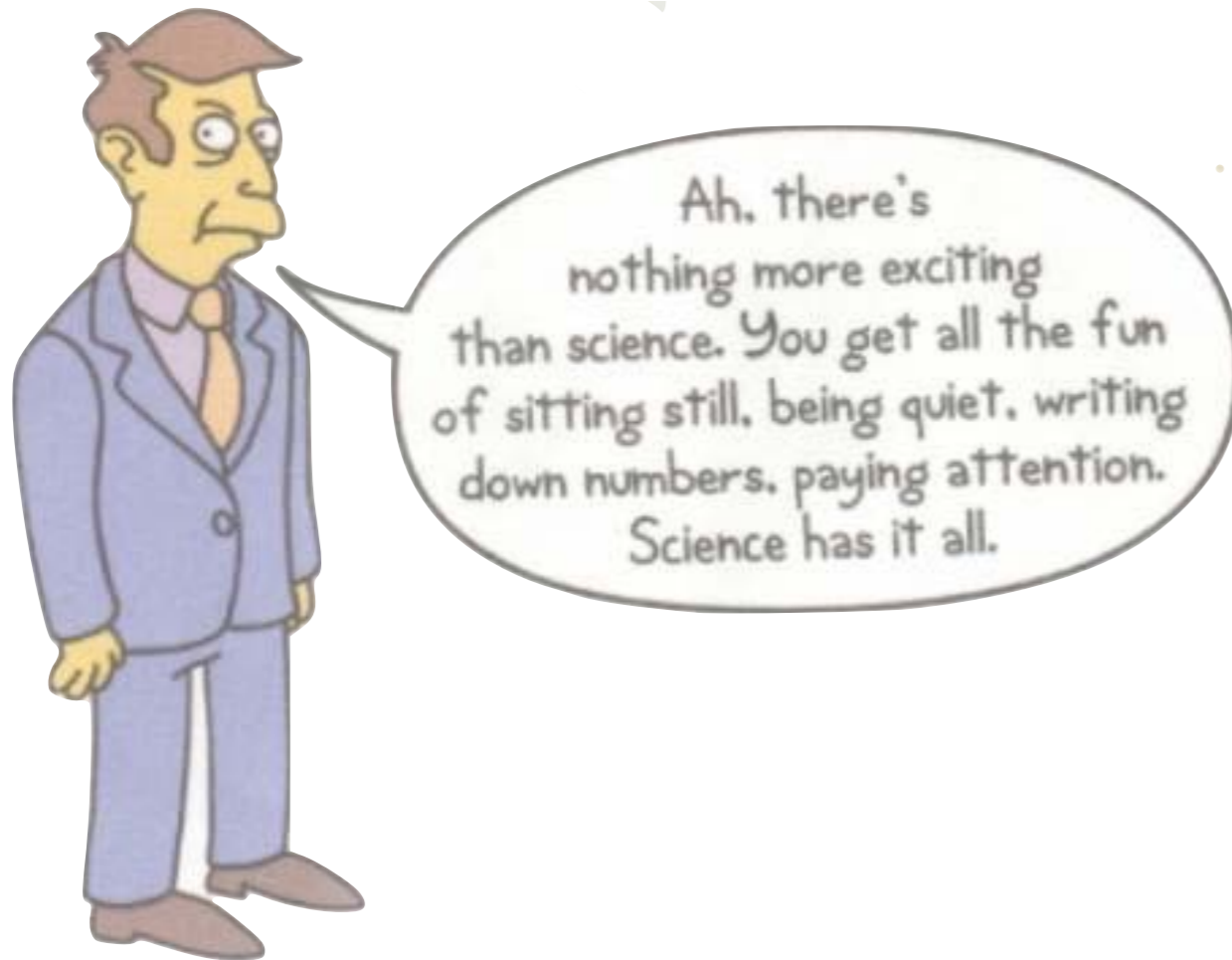
Fortin, 2008

- The goal was to use a naturalistic (externally valid) task that allows precise measurement of behavior
- But this approach has problems...

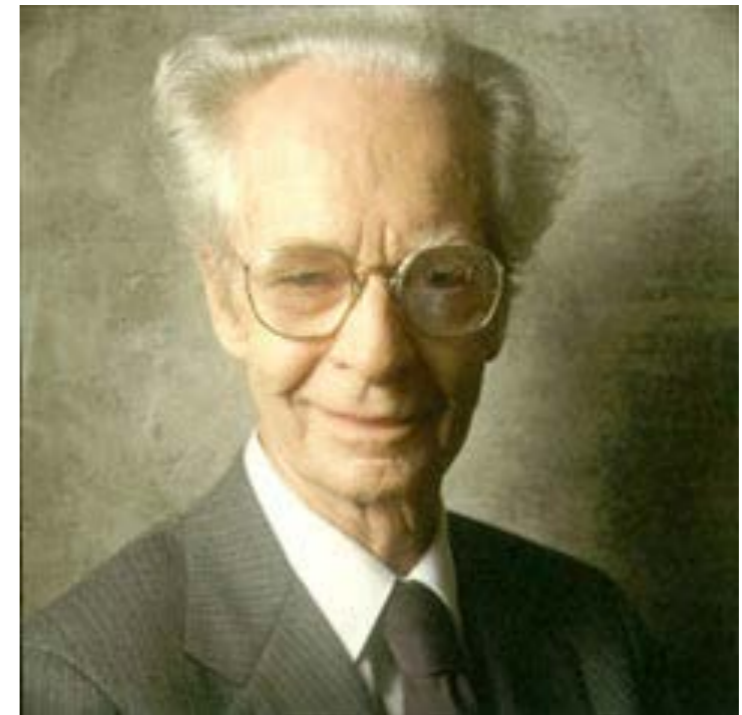
LAB RESEARCH: CLASSIC APPROACHES

SKINNER OR OPERANT BOXES

Not this Skinner...



... this one!



Burrhus Frederic "B. F." Skinner
Harvard University

LAB RESEARCH: CLASSIC APPROACHES

SKINNER OR OPERANT BOXES

- Also common in popular culture, but not so much in lab anymore

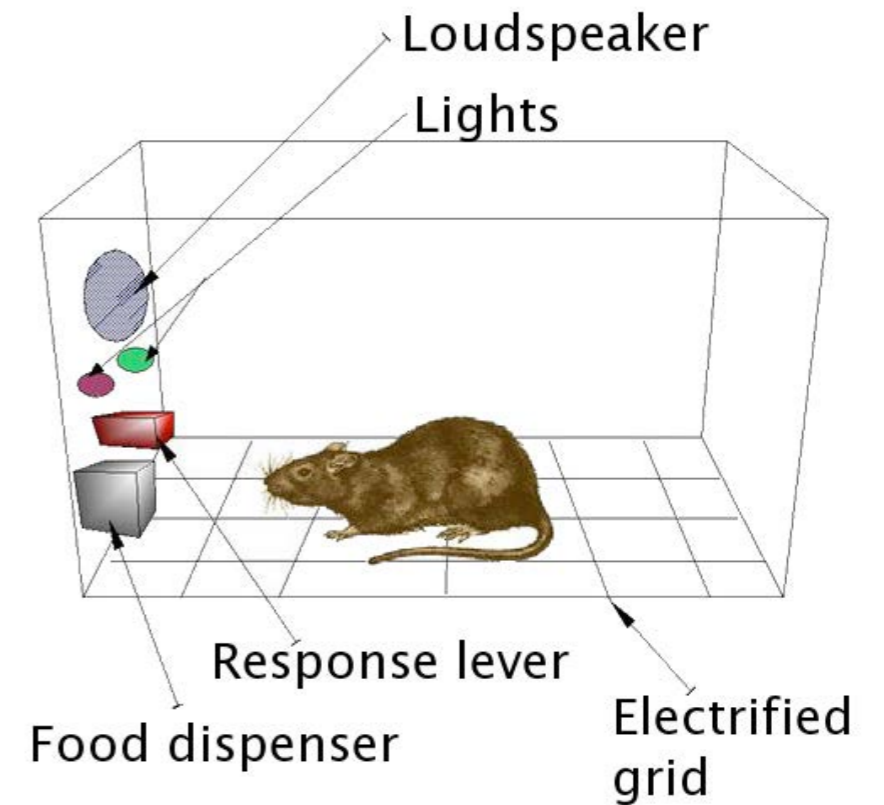
"B. F." Skinner and his box



CRAIG SWANSON © WWW.PERSPECTIVITY.COM



Typical box



http://en.wikipedia.org/wiki/Operant_conditioning_chamber

- Very precise measurements (bar presses) and control over stimuli
- Limited flexibility and external validity

LAB RESEARCH: CLASSIC APPROACHES

ARE THEY GOOD ANIMAL MODELS OF AMNESIA?

- These approaches are not good animal models of human amnesia.
 - They do not specifically depend on the medial temporal lobe (MTL)
 - They can be solved using different strategies and different brain systems.

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Not good models
of human amnesia

- Lab research: modern approaches
 - Newer “mazes”
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LAB RESEARCH: MODERN APPROACHES

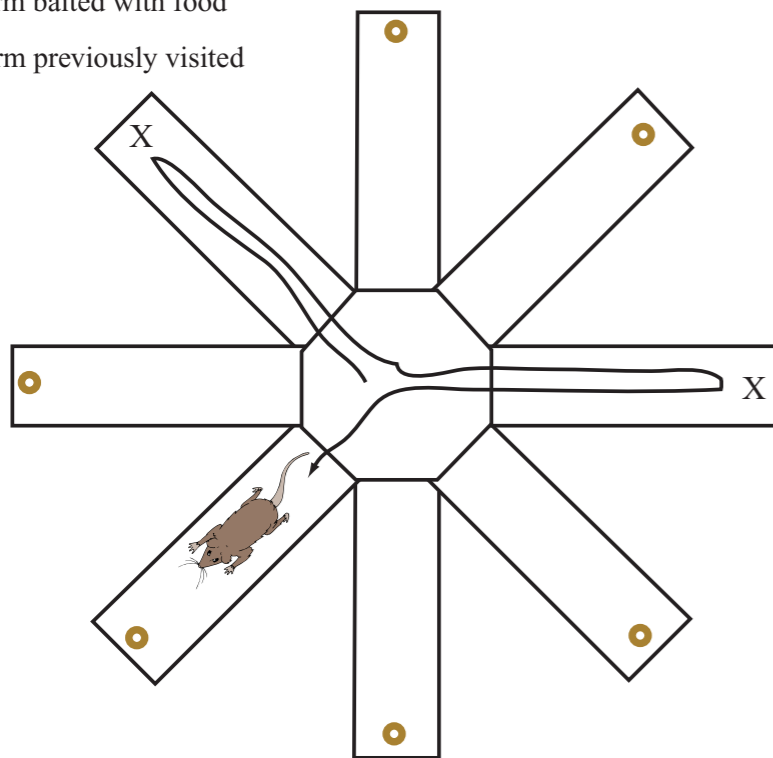
NEWER MAZES

- The radial-arm maze (Olton & Samuelson, 1976)

a

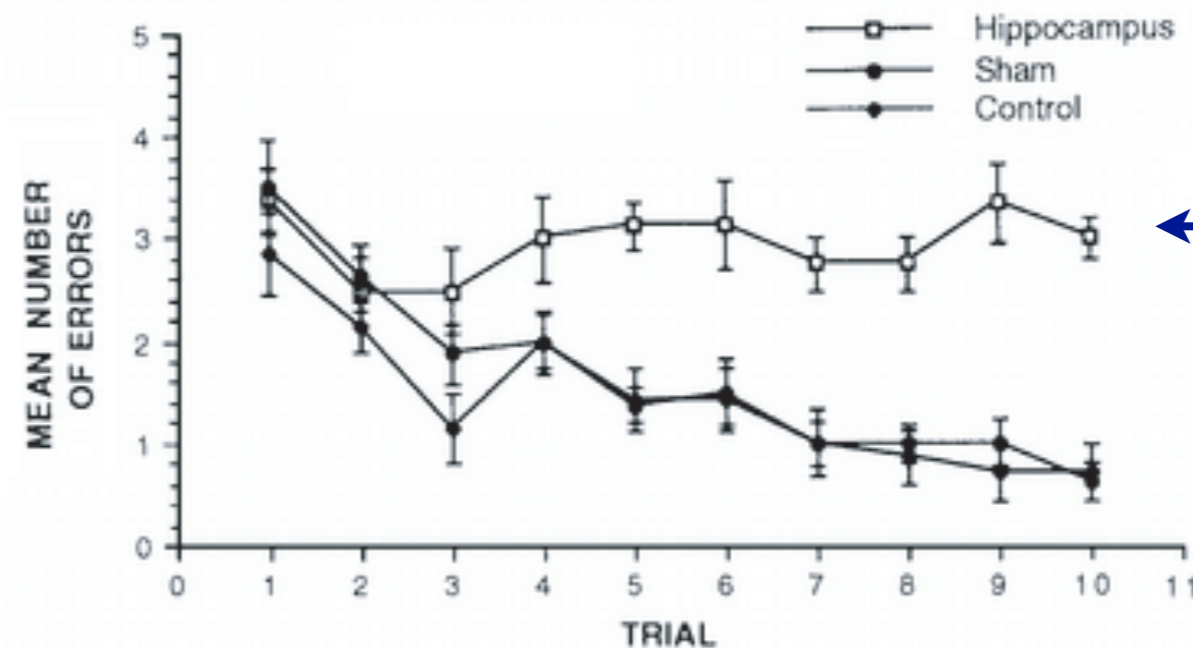
● Arm baited with food

X Arm previously visited



b

Radial-arm maze performance



Damage to the hippocampus impairs performance

Figure 4. Radial-arm maze task. **a**, The maze consists of 8 arms radially extending from a central platform. Before each session, all arms were baited with a food reward and optimal foraging performance would consist of running down the end of each arm only once (Olton and Samuelson, 1976). **b**, Animals with hippocampal damage were severely impaired in learning the task compared to control groups (McDonald and White, 1993).

LAB RESEARCH: MODERN APPROACHES

NEWER MAZES

- Performance of a control animal in the radial-arm maze

**MOUSE #145
IL-16 WILD TYPE
7 DAYS AFTER MAZE
LEARNING**

LAB RESEARCH: MODERN APPROACHES

NEWER MAZES

- Performance of a transgenic animal in the radial-arm maze

MOUSE #166
IL-16 KNOCK-OUT
7 DAYS AFTER MAZE
LEARNING

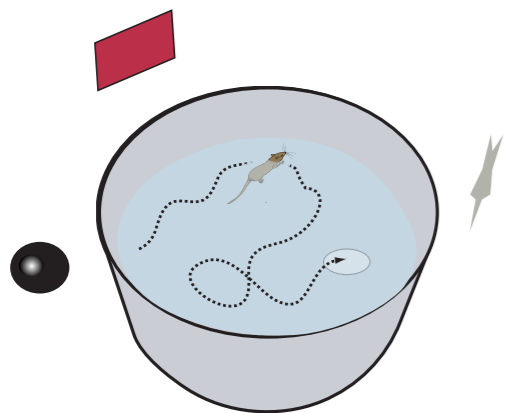
Animal with hippocampal damage would perform similarly

LAB RESEARCH: MODERN APPROACHES

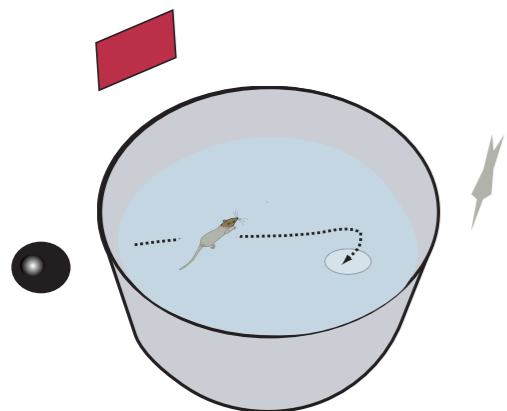
NEWER MAZES

- The Watermaze (Morris, 1981)
- The most widely used test of memory in rodents

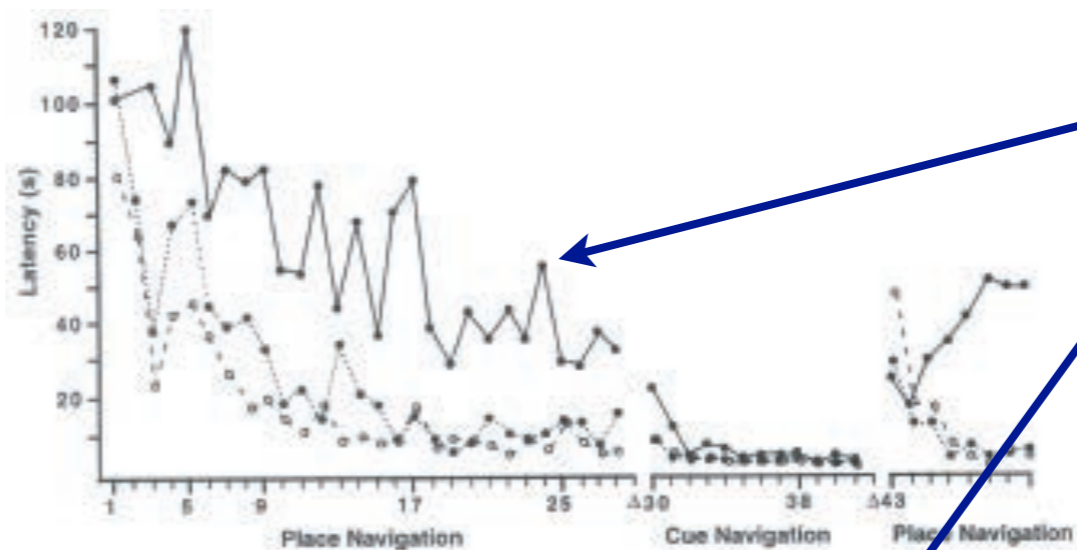
Early in training (e.g., Trial 1)



Late in training (e.g., Trial 25)

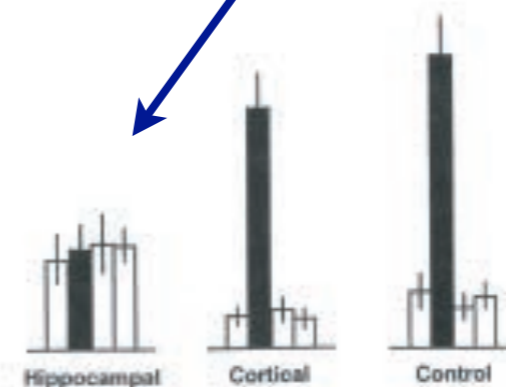


Latency to find platform over trials



Damage to the hippocampus impairs performance

Probe trial (no platform)



LAB RESEARCH: MODERN APPROACHES

NEWER MAZES

- A mouse learning the watermaze

**Morris
Water Maze**

**Mouse # 109
Day 1, Trial 1**

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Not good models
of human amnesia

All impaired by
MTL damage

LAB RESEARCH: MODERN APPROACHES

CONTEXT MEMORY

Remembering in which context a specific event occurred



- Contextual fear conditioning:

- In which testing box did you get shocked?
- Measure: Percent time spent “freezing” in “scary” box

Model of PTSD and anxiety disorders

- Conditioned place preference:

- In which context (or location) did you receive something rewarding (e.g., food, cocaine,...)
- Measure: Percent time spent in “preferred” context/location

Model of addiction

More on this later in the quarter...

LAB RESEARCH: MODERN APPROACHES

ITEM AND LIST MEMORY

Remembering which items (objects, odors) were presented on specific trials

- One item per trial:
 - Delayed non-match to sample task (DNMS; last lecture)

A → Delay → A B

- Many items per trial
 - Similar procedure as DNMS, but for lists of items

A, B, C, D → Delay → B X

Model of “every day memory” impairments for research on Alzheimer’s disease or on normal aging

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ITEM AND LIST MEMORY

- Video of a list learning experiment:

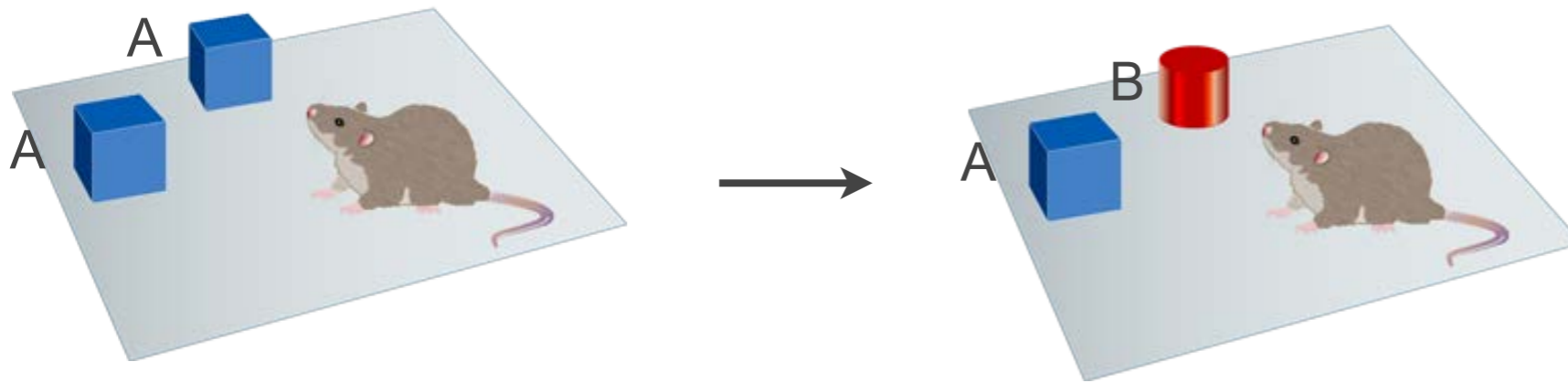
Odor Sequence

A, B, C, D, E

LAB RESEARCH: MODERN APPROACHES

SPONTANEOUS PREFERENCE TESTS

- Take advantage of the natural tendency of animals (including humans) to preferentially investigate novel (or less familiar) stimuli



Which object will he prefer to investigate?

- Originally used to test memory in infants



- Now widely used in human and animal research to test memory for faces, objects, odors, locations, etc.

What are the advantages/disadvantages of this approach?

LAB RESEARCH: MODERN APPROACHES

SPONTANEOUS PREFERENCE TESTS

- Video of spontaneous preference test using odors

Odor Recognition Task

Feinberg LM, Allen TA, Ly D & Fortin NJ

University of California Irvine

LAB RESEARCH: MODERN APPROACHES

SPONTANEOUS PREFERENCE TESTS

- Can also be used to determine if people (with or without amnesia) notice something is missing (by tracking their eye movements)



There was something in that location last time the picture was shown



Same picture as presented before (no info missing in the box)

- Now also used in rodents - they preferentially investigate locations where items are missing, or items that were moved

SUMMARY

- Classical approaches to study learning and memory in animals are not useful models of human amnesia.
 - They can be solved by different strategies and brain systems (i.e., not just the MTL)
- Modern approaches have proved more successful (specifically depend on MTL)
 - Therefore, there are now many tasks that can be used to model human amnesia in animals.