

# Limbic system – outline

---

① *Introduction*

- history
- definition

② *Review of anatomy*

- amygdaloid complex
- septal complex

③ *Theories of hippocampal function*

- declarative memory
- episodic memory
- cognitive map
- relational memory

④ *The amygdala and emotion*

- theories of emotion
- fear and fear conditioning

⑤ *The hippocampus beyond memory*

- exploratory behavior and anxiety
- species typical behaviors
- home cage behavior

# Theories of hippocampal function - history

---

1888	S. Brown H. Schäfer	early report of forgetfulness in a monkey with large bilateral temporal lobe lesions
until the 1930s		prevailing view of hippocampus as part of the olfactory system
1937	J.W. Papez	component of Papez circuit of emotion
1938	R. Jung A. Kornmüller	discovery of hippocampal EEG theta rhythm in rabbits, temporally linked to desynchronization of cortical EEG
1957	W. Scoville B. Milner	bilateral surgical lesions of medial temporal lobe associated with global amnesia in several patients including H.M.
1960s	R. Isaacson D. Kimble	lesion studies fail to model amnesia in monkey or rats, but show deficits of exploration and behavioral disinhibition.
1971	T. Hirano O. Vinogradowa	first implantations of microelectrodes to record single unit activity in the hippocampus of freely moving animals
1978	J. O'Keefe L. Nadel	the hippocampus as a cognitive map
1982	J. Gray	septo-hippocampal theory of anxiety, updated 2000
1992	S. Tonegawa E.R. Kandel	first papers using genetically modified mice to investigate cellular mechanisms of cognitive function

# Theories of hippocampal function - memory

---

## Declarative memory theory

Hippocampus is part of a medial temporal lobe memory system that selectively mediates declarative memory in a time-limited manner.

- founded on global amnesia syndrome in human patients
- primate models of amnesia: DMTS and DNMTS tasks
- rodent models: object recognition / discrimination

## Episodic memory theory

The hippocampus is a structure that mediates episodic memory, the recall of discrete events via mental time travel. Episodic-like memory in animals is the memory of "what", "when" and "where".

- founded on global amnesia syndrome in human patients
- bird model: what-where-when, rodent model: order of events

## Cognitive map theory

The hippocampus harbors the locale system, a memory system that represents stimuli as a cognitive map with respect to an allocentric spatial framework and permits navigation in space.

- founded on single unit recordings in freely moving animals
- rodent models: radial maze, water maze, Barnes maze

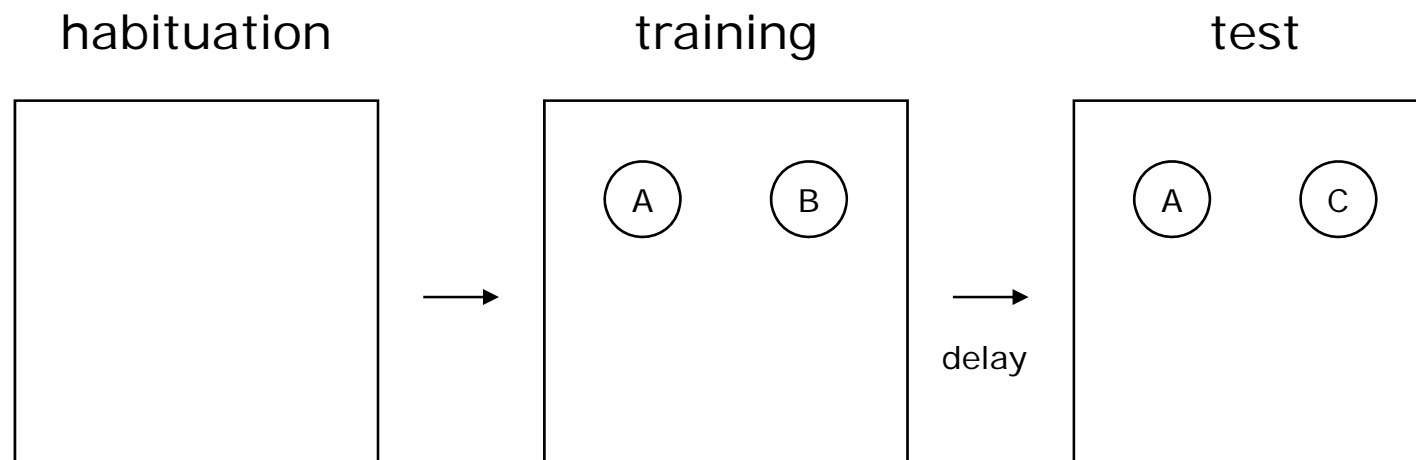
## Configural, relational, contextual theories

The hippocampus is a learning system that deals flexibly with overlapping sets of stimuli in which the meaning of each stimulus may depend on temporal sequence or presence of other stimuli.

- roots in instrumental and classical conditioning
- rodent: contextual conditioning, transitive inference, paired associate

# Object recognition / discrimination

---



Measures of recognition memory:

- time exploring object
- exploration of A test < training
- exploration during test A < C

Control measures:

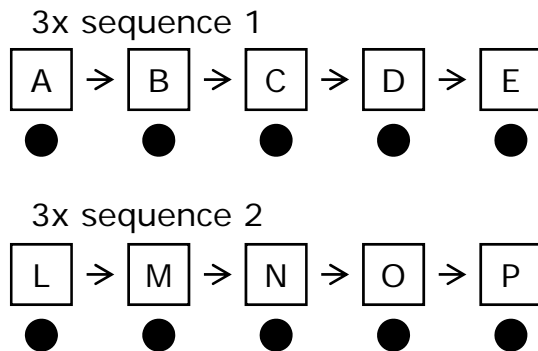
- activity during habituation
- total exploration time
- exploration A = B during training

Variants: more objects, multiple training trials, object displacement

# Odor sequence task

---

## Training

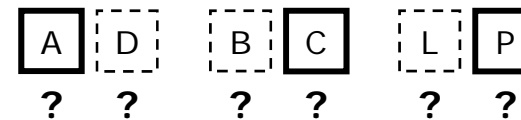


- repeated day 1-5
- delay within sequence 3s
- delay between sequences 3h

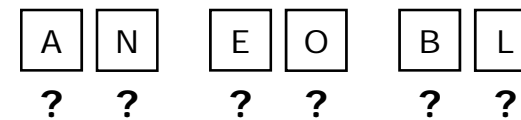
- Dig in cup with scented sand
- training: one cup with reward
  - test: 2 cups without reward

## Choice tests

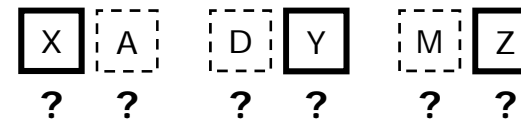
Within sequence: order  
(requires hippocampus)



Between sequence: relative recency  
(no discrimination)



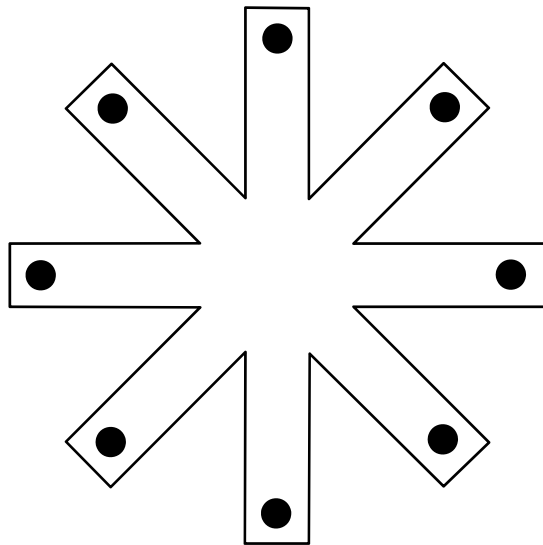
odor novelty:  
(hippocampus not required)



# Radial-maze tasks

---

spatial working memory

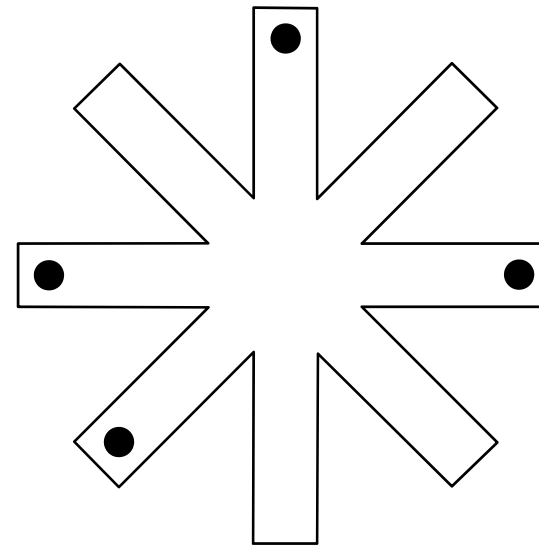


● bait

Errors:

- working memory = reentry after bait collect
- procedural (bait or arm neglect)

spatial working and reference memory

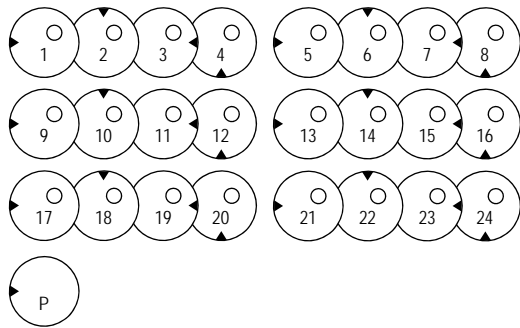


Errors:

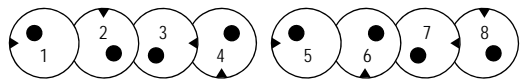
- working memory = reentry after bait collect
- reference memory: entry to unbaited arm
- procedural (bait or arm neglect)

# Water-maze tasks

Place navigation task  
with massed training



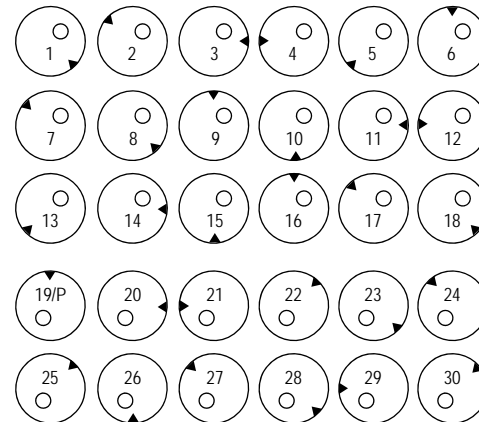
Cue navigation task  
with massed training



control task for sensory  
motor performance

- hidden platform
- visible platform
- ▶ release point

Place navigation task  
with spaced training and reversal



Training parameters:

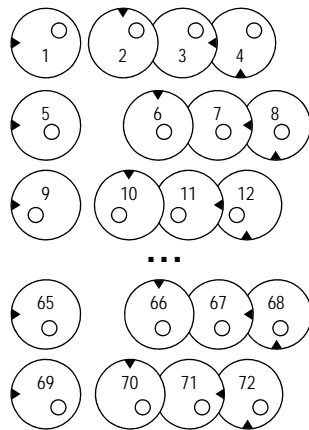
- escape latency
- swim path
- cumulative search error
- Whishaw's error

Probe trial parameters:

- quadrant time
- annulus crossings
- zone time
- proximity

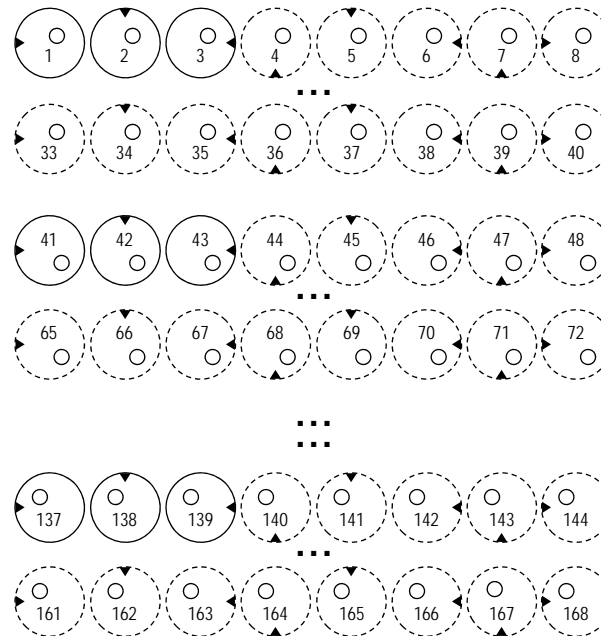
# Water-maze tasks

Matching to place task with varying delays



- hidden platform
- visible platform
- ▶ release point
- trials given until criterion met

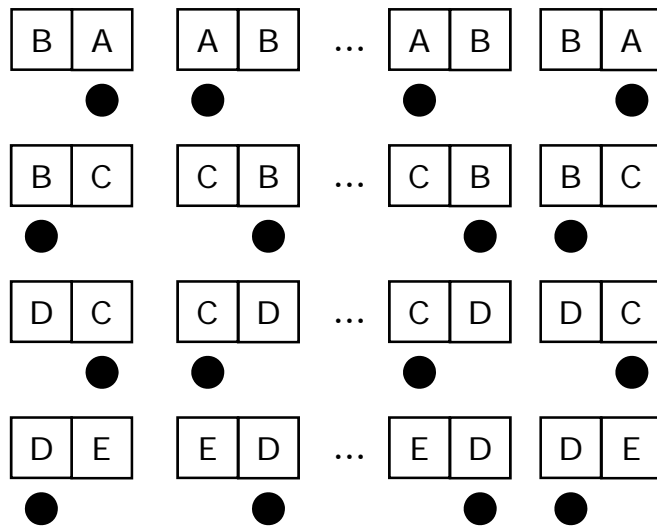
Serial reversal task with training to criterion



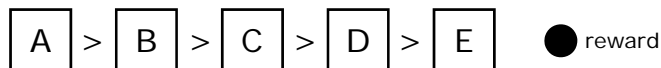


# Transitive inference task

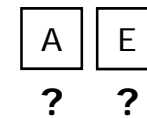
Odor discrimination training



ordered mental representation of relations

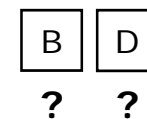


Choice test of non-transitive novel pairing



solved by rat with hippocampal lesion, based on single associations

Choice test of transitivity

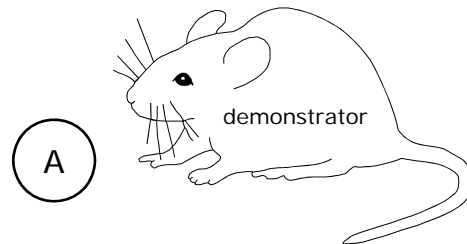


not solved by rat with hippocampal lesion, single associations are all ambiguous

# Social transmission of food preferences

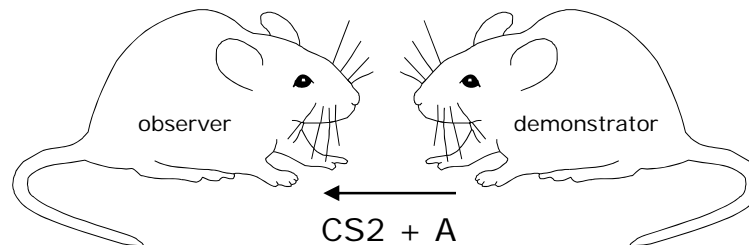
---

Phase I



Odor guided  
paired associate learning  
in mice and rats

Phase II

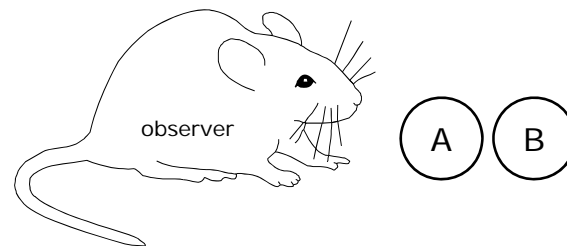


Memory measure:  
- amount food eaten  
A > B in phase III

delay



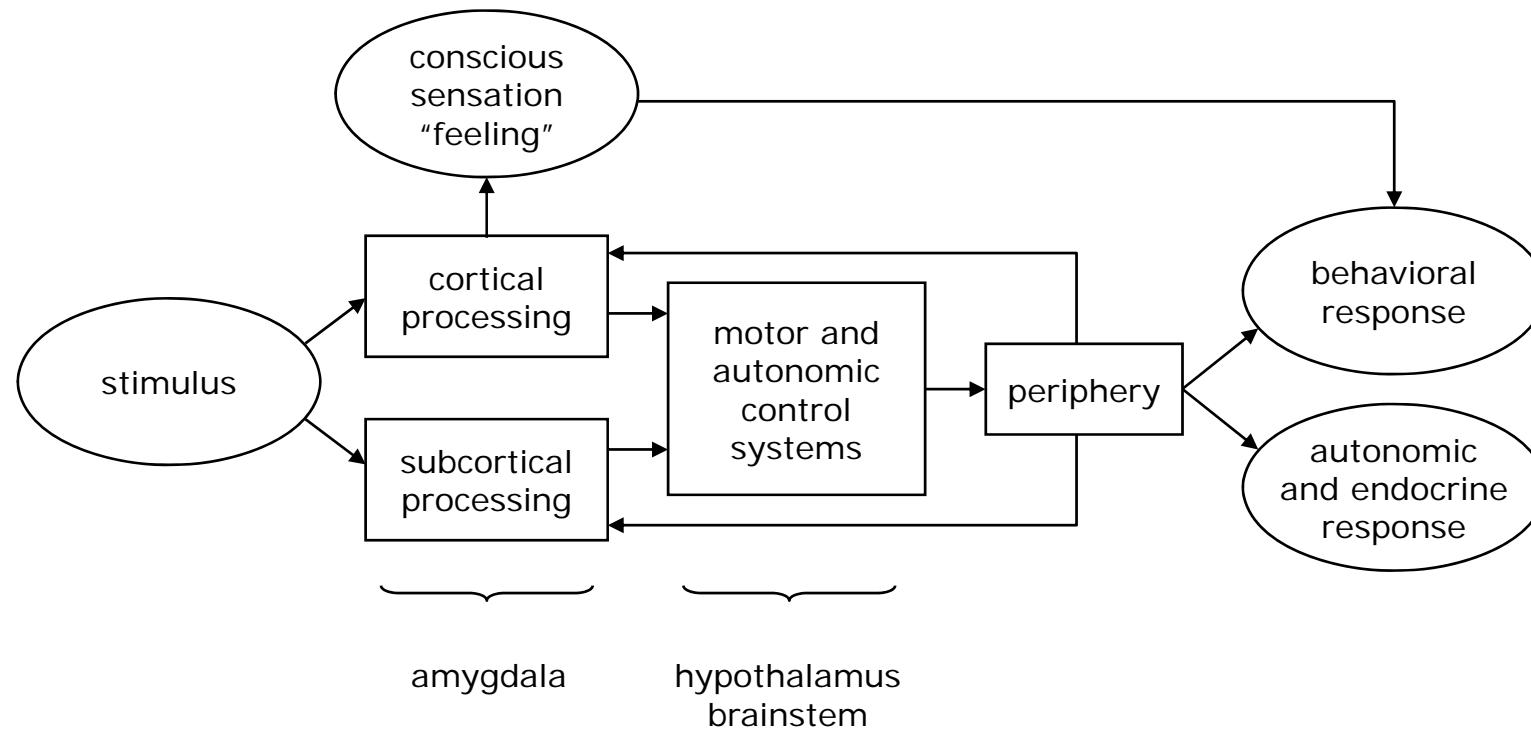
Phase III



Control measures:  
- amount food eaten  
in phase I  
- amount food eaten  
A+B in phase III  
- interaction time  
phase II

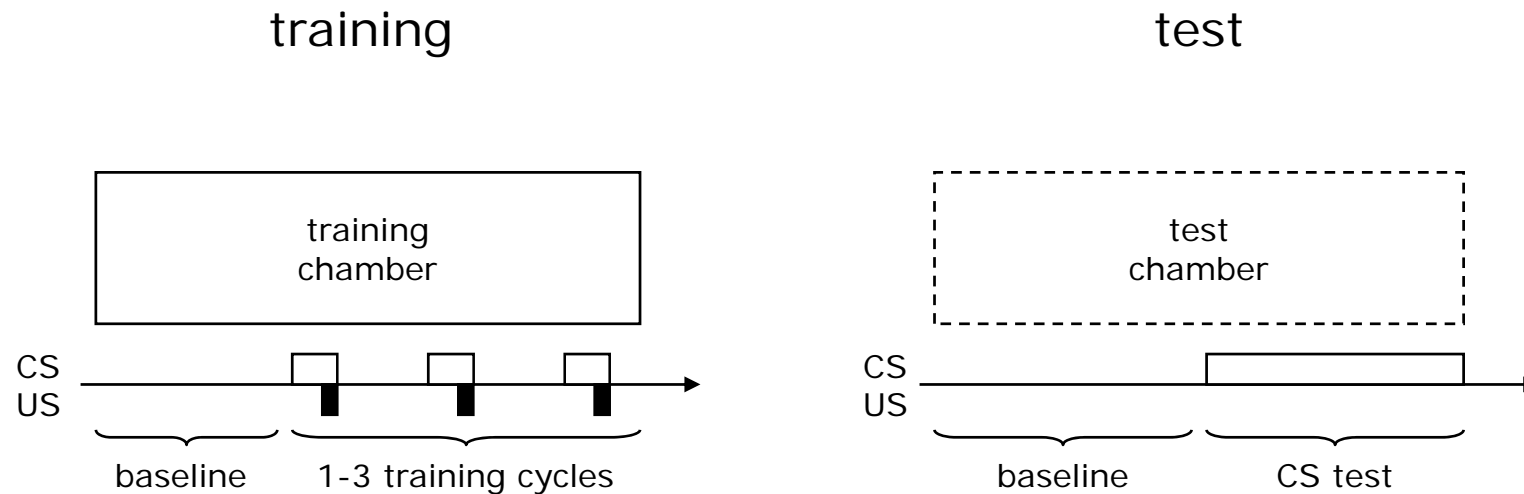
# Emotions

---



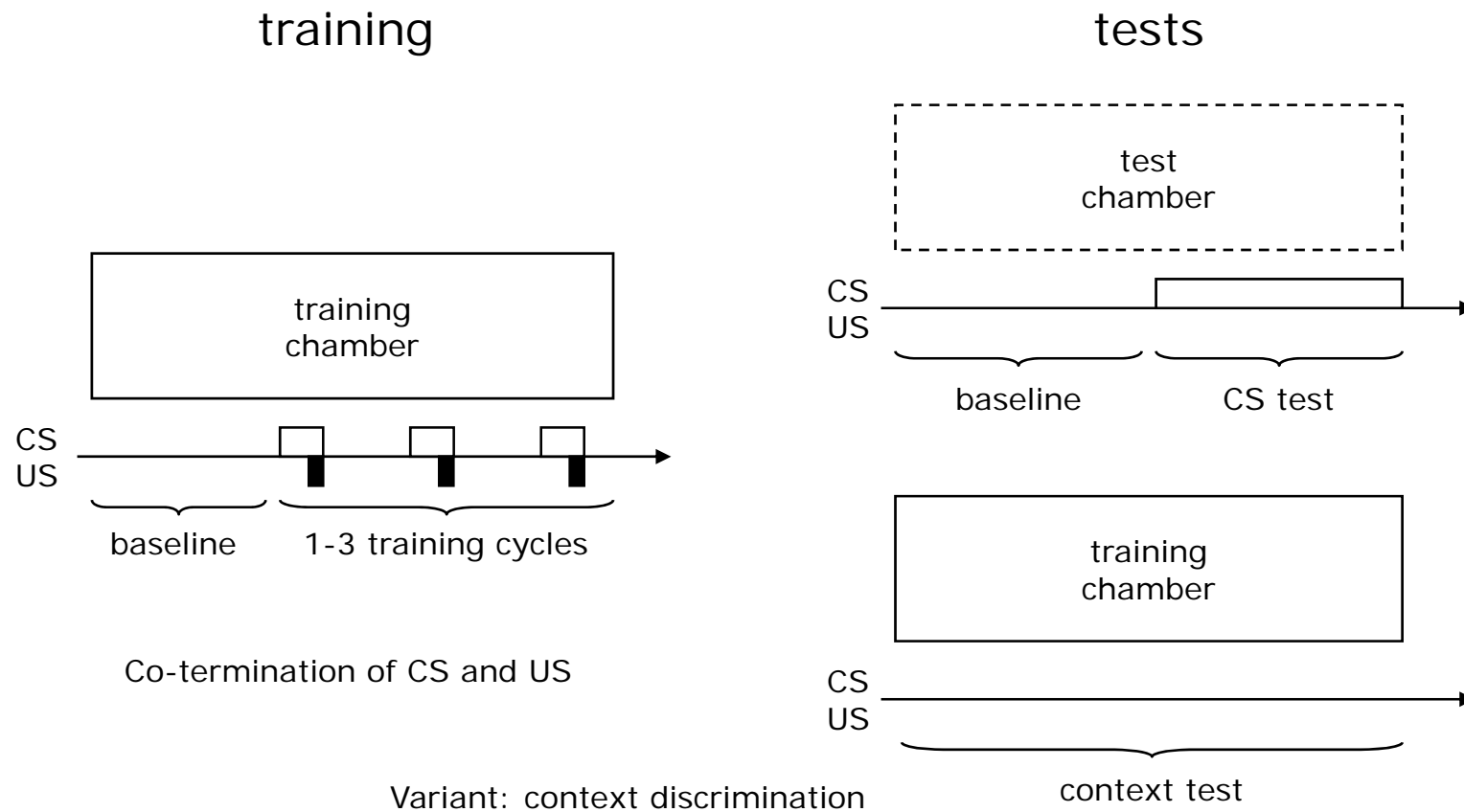
# Pavlovian (cued) fear conditioning

---



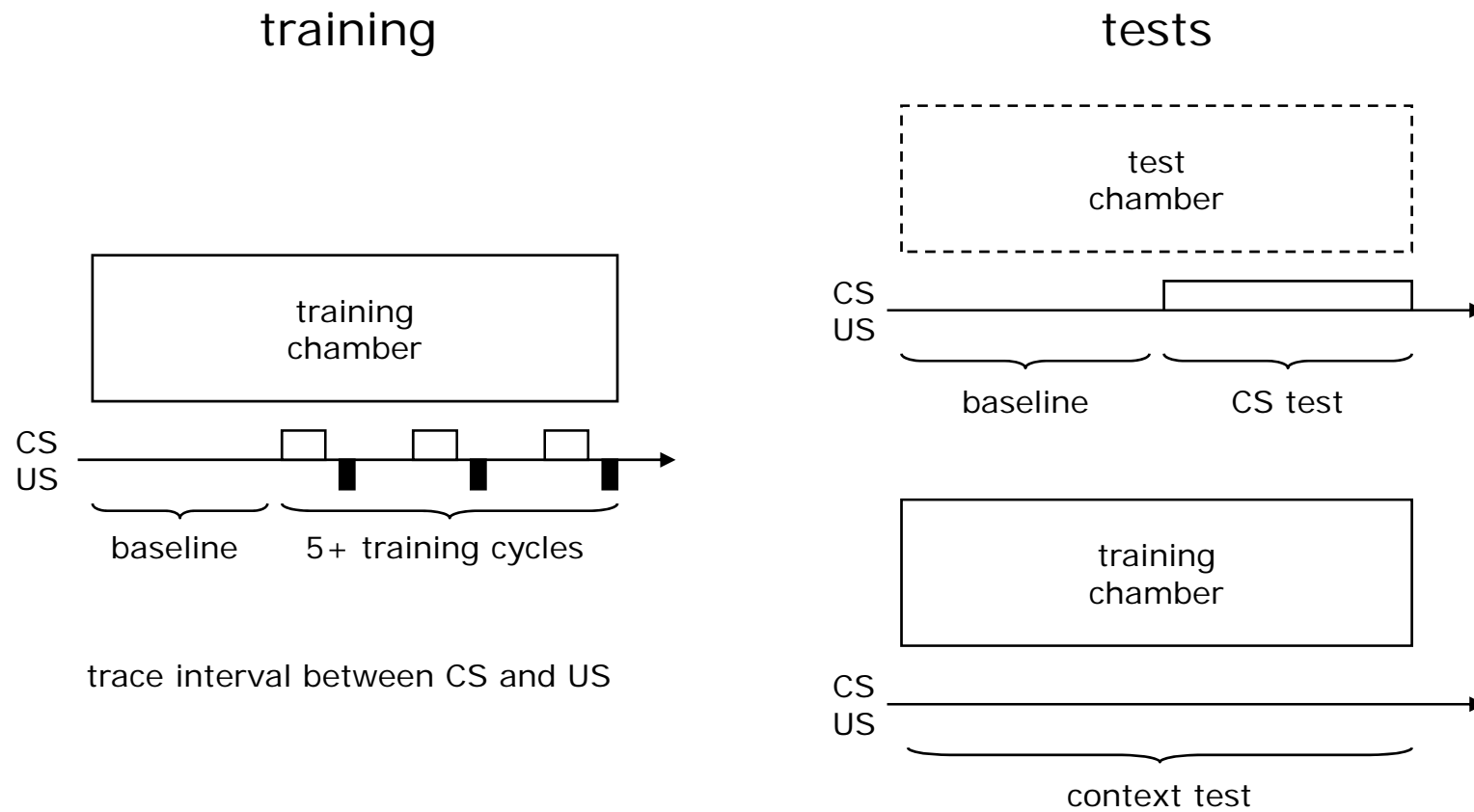
- measured response
- defensive behavior (freezing, vocalization, flight)
  - reflex potentiation (startle)
  - hypoalgesia
  - autonomic arousal (blood pressure, heart rate)
  - HPA axis stimulation

# Cued and contextual fear conditioning

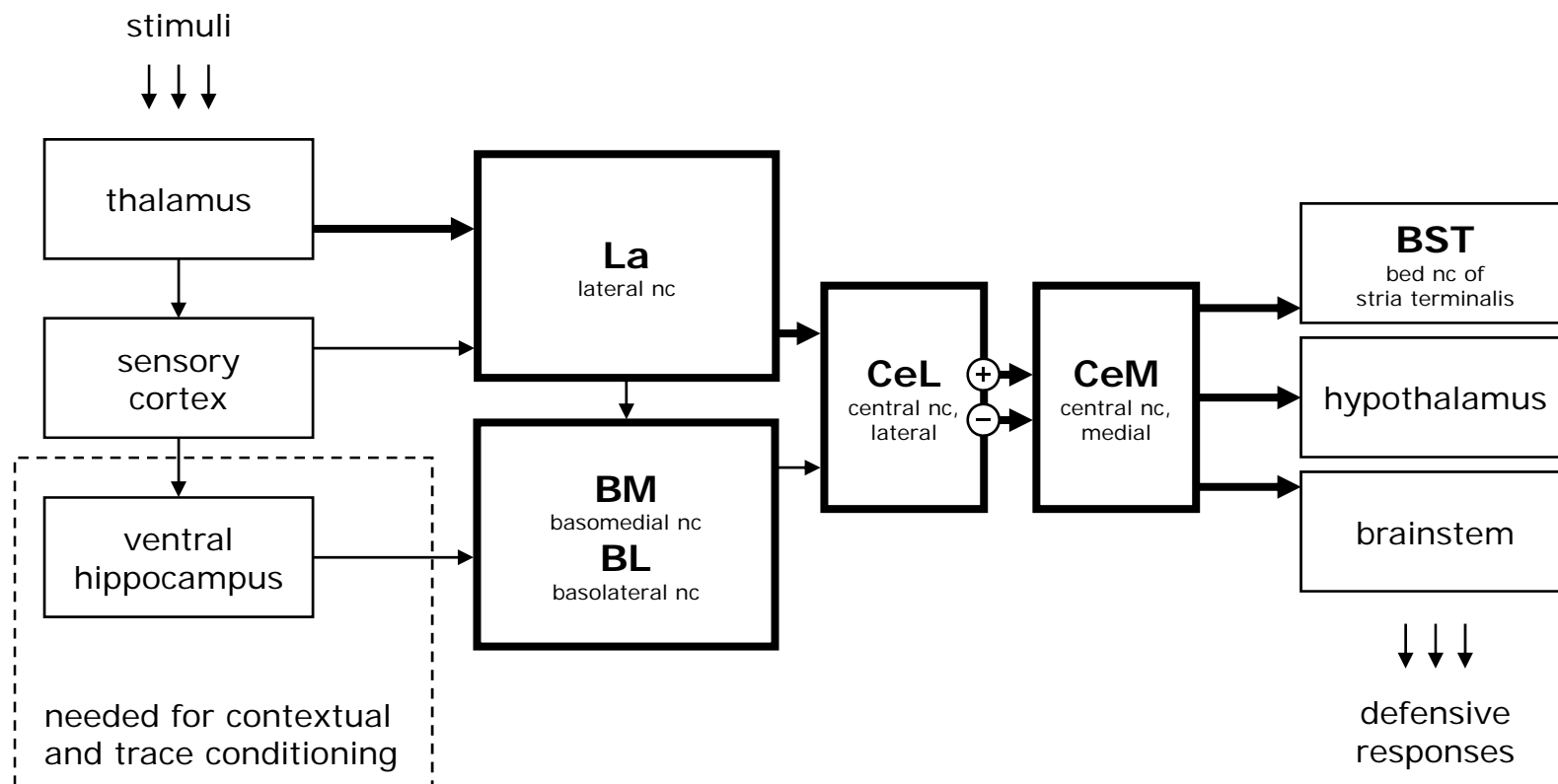


# Trace fear conditioning

---



# Fear conditioning circuitry



# The hippocampus beyond memory

---

Lesions of the hippocampus or other experimental manipulations that affect hippocampal function in rodents have also effects that are unrelated to memory function:

Exploration Novelty	<ul style="list-style-type: none"><li>- hyperlocomotion in novel or aversive environment</li><li>- delayed exploration, delayed or no habituation</li><li>- increased exploratory activity toward new objects</li></ul>
Shuttlebox	<ul style="list-style-type: none"><li>- facilitated active avoidance learning</li></ul>
Anxiety	<ul style="list-style-type: none"><li>- reduced anxiety-related parameters in anxiety tests</li><li>- increased center time in open field test</li><li>- increased open arm entries in plus maze test</li><li>- reduced dark time in light-dark transition test</li></ul>
Perseverance	<ul style="list-style-type: none"><li>- inability to suppress inadequate spontaneous or learned responses</li><li>- tendency to develop stereotypical behavior</li><li>- reduced spontaneous alternation on T-maze</li></ul>
Nesting	<ul style="list-style-type: none"><li>- reduced nest quality, more unused nesting material</li></ul>
Burrowing	<ul style="list-style-type: none"><li>- reduced burrowing activity in burrowing test</li></ul>