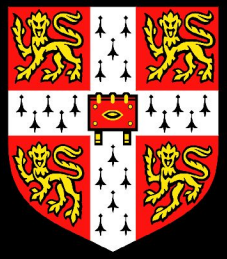
NST II Psychology
NST II Neuroscience (Module 5)

Brain Mechanisms of Memory and Cognition – 5

Neural basis of memory (2): multiple memory systems

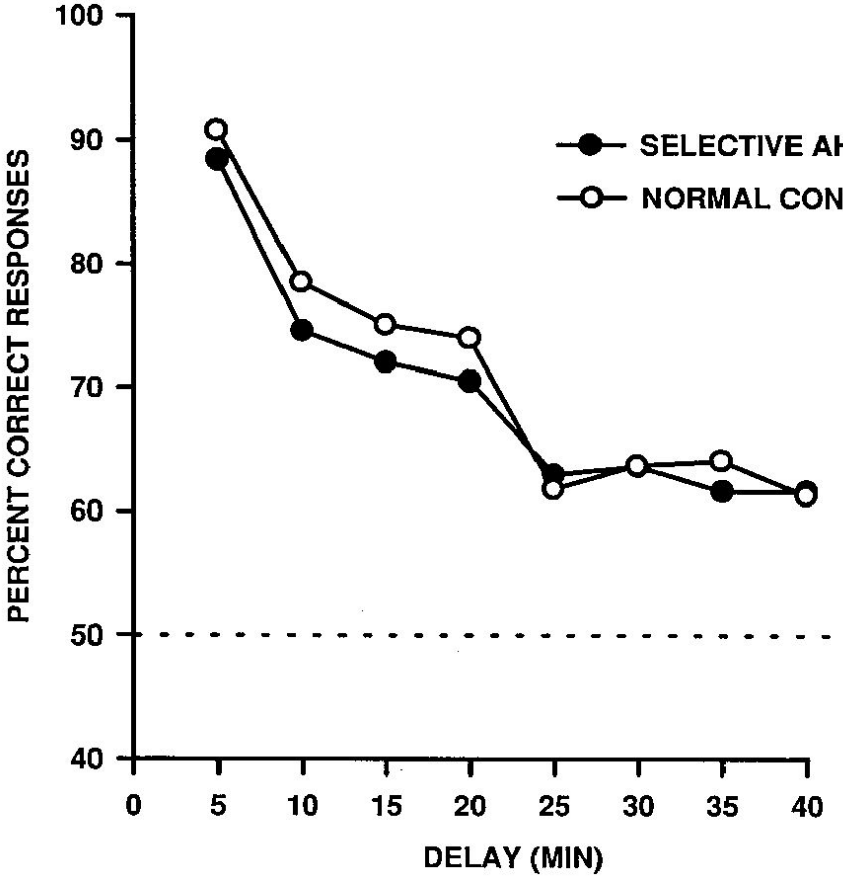
Rudolf Cardinal
Department of Experimental Psychology

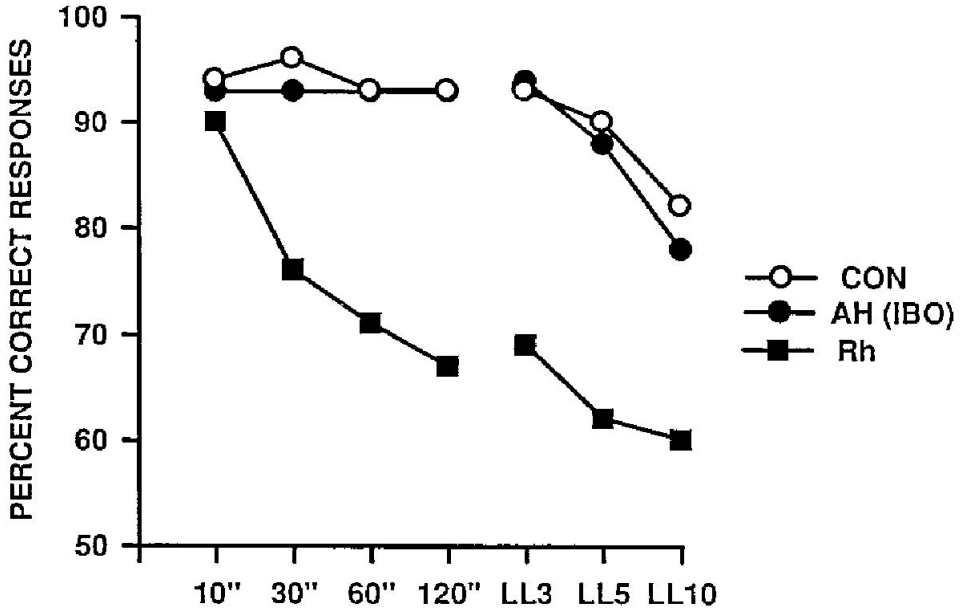


Monday 13, 20, 27 Jan; 3, 10, 24 Feb 2003; 10 am
Physiology Main Lecture Theatre

Rhinal cortex

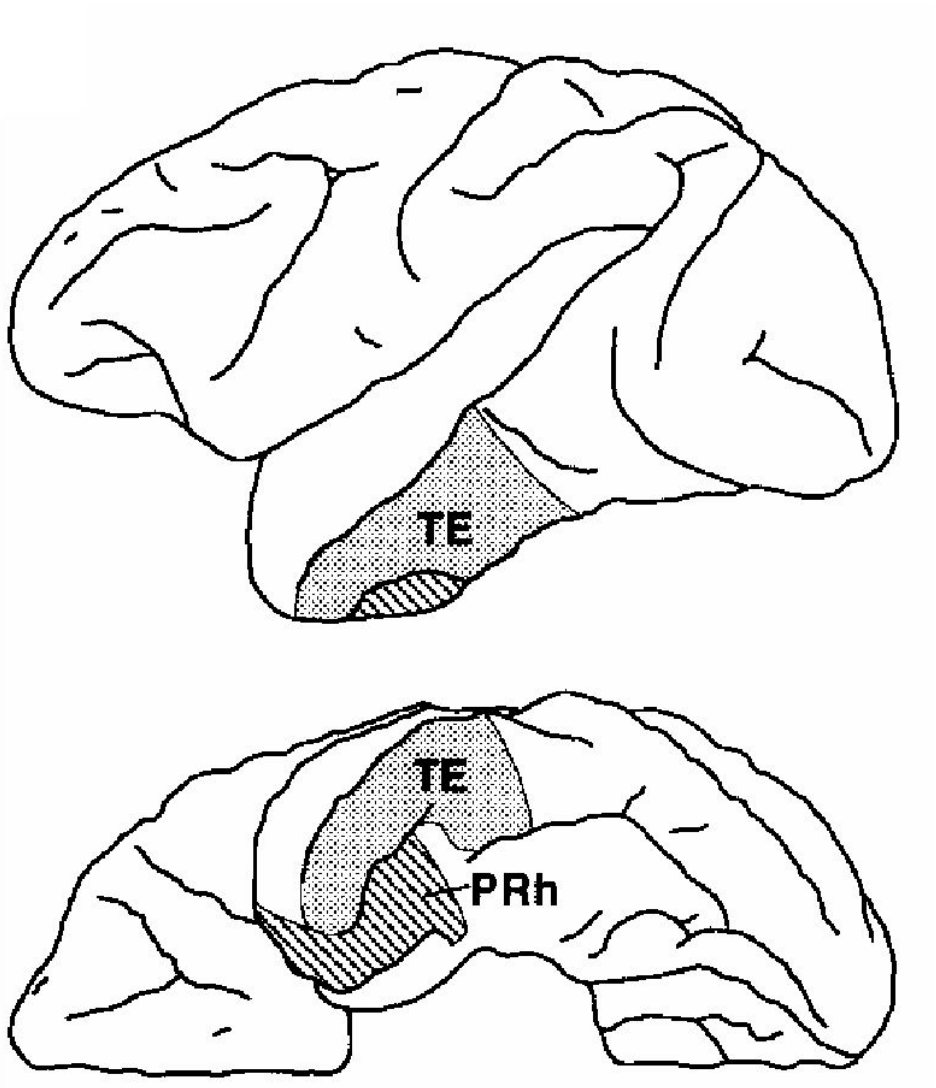
Medial temporal lobe lesions and DNMTS





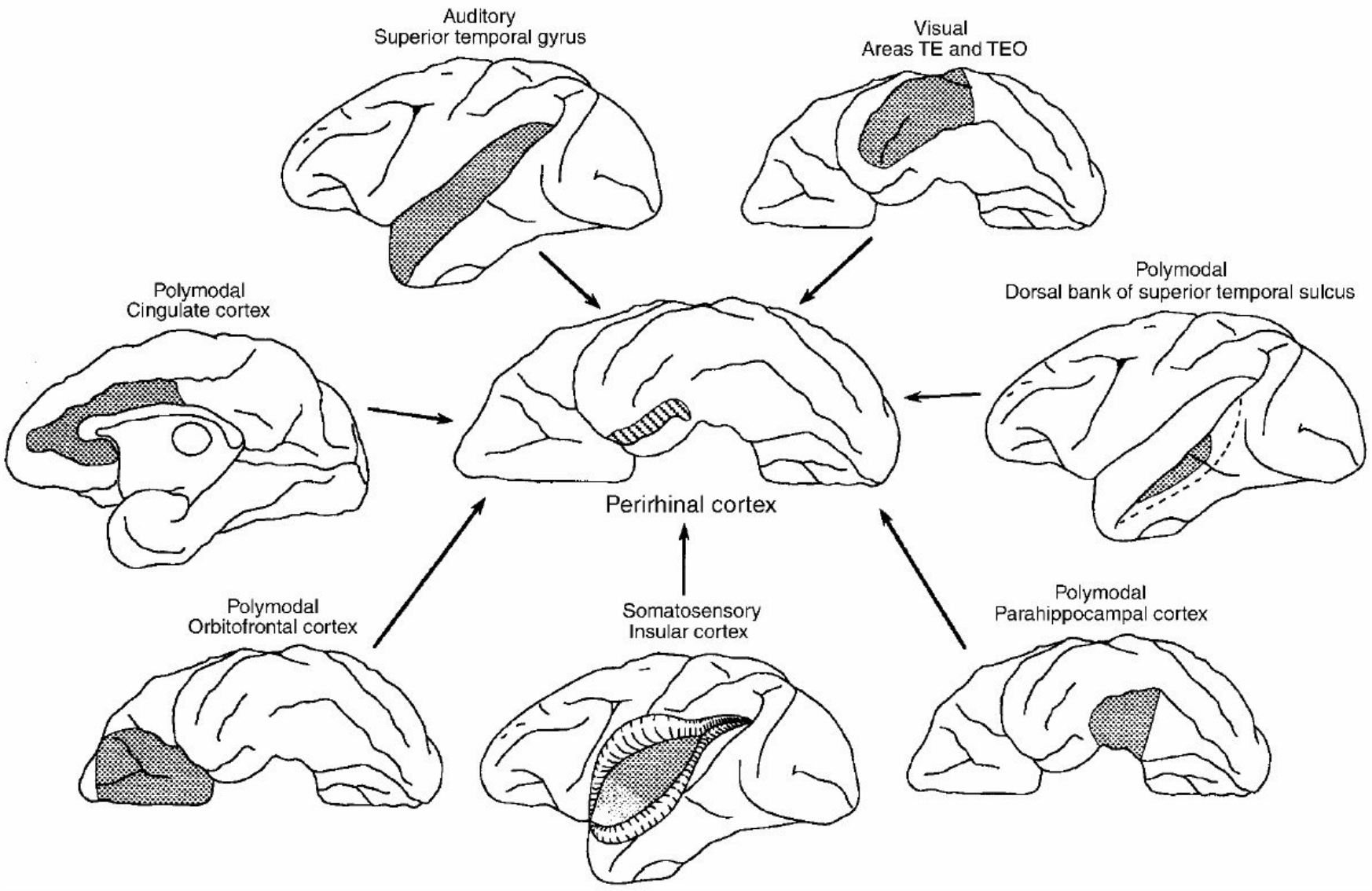
Murray & Mishkin (1998)

TE (part of inferotemporal cortex) and perirhinal cortex



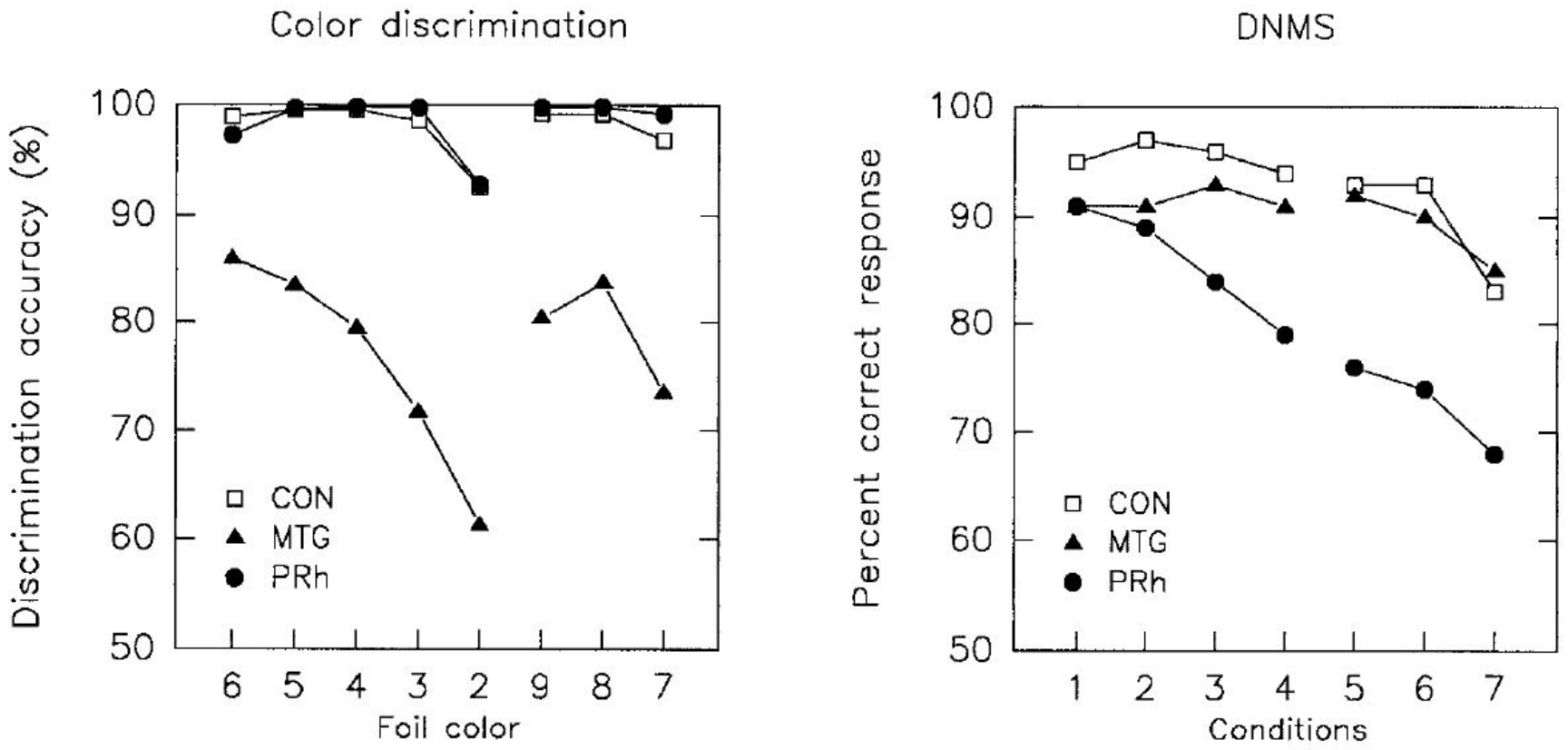
Murray & Bussey (1999)

Perirhinal cortex is the first polymodal ventral stream area



Murray & Bussey (1999)

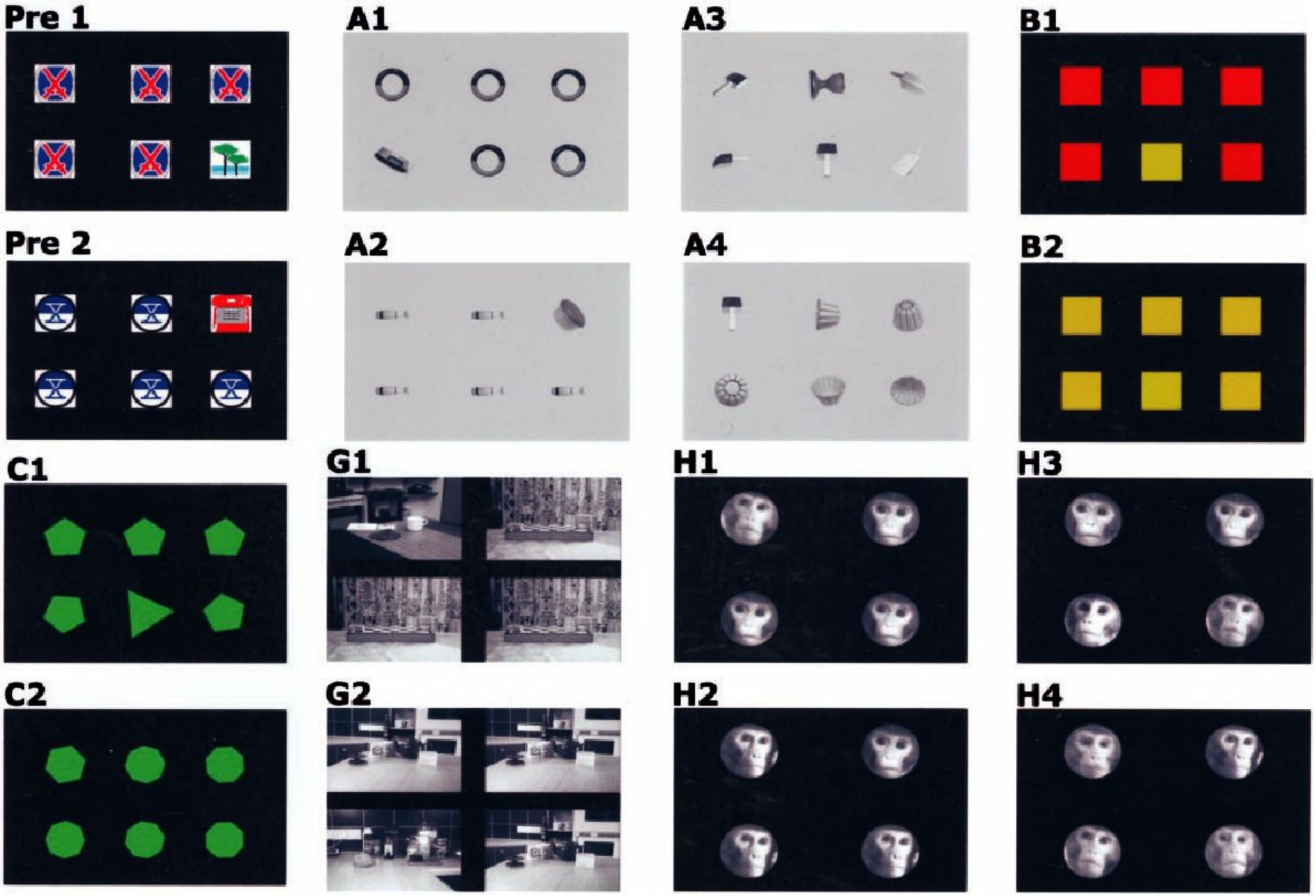
Double dissociation of TE and perirhinal lesions



CON = control
MTG = dorsal TE, in inferotemporal cortex
PRh = perirhinal cortex

Buckley et al. (1997)

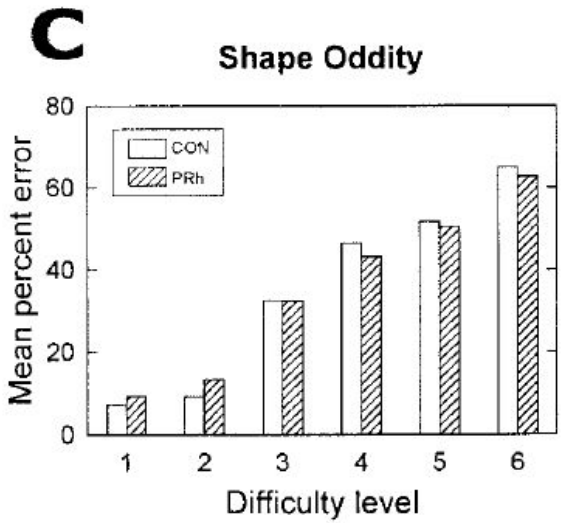
‘Odd one out’: perirhinal cortex and visual discrimination (1)

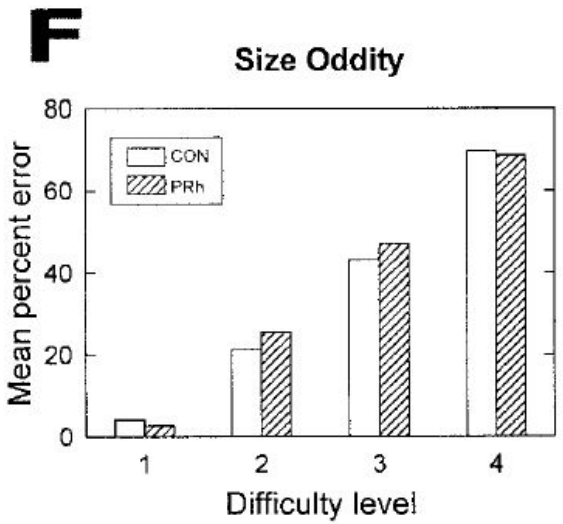


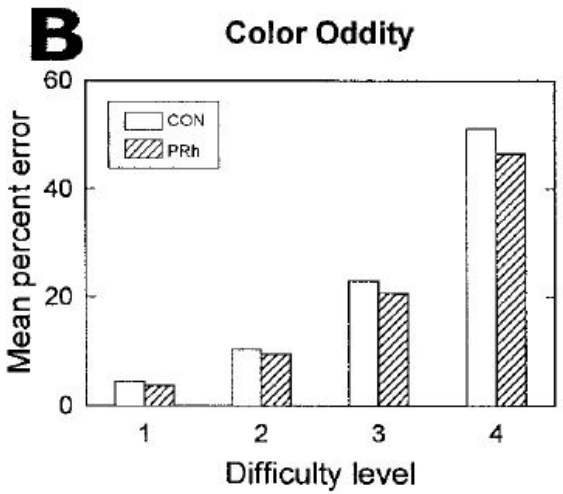
Buckley et al. (2001)

‘Odd one out’: perirhinal cortex and visual discrimination (2)

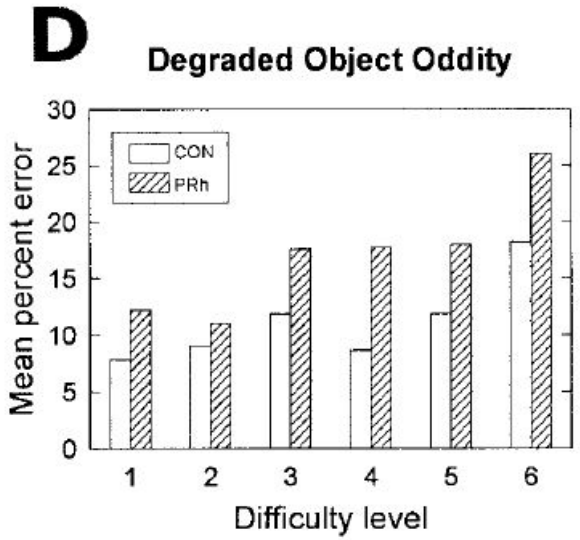
Some tasks: fine (even if tasks are difficult)

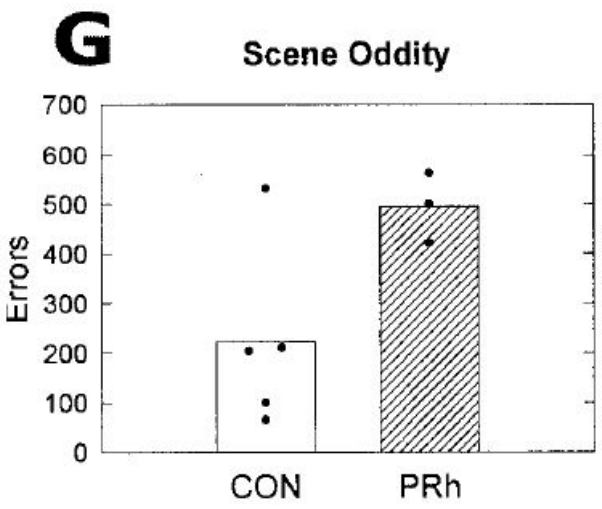


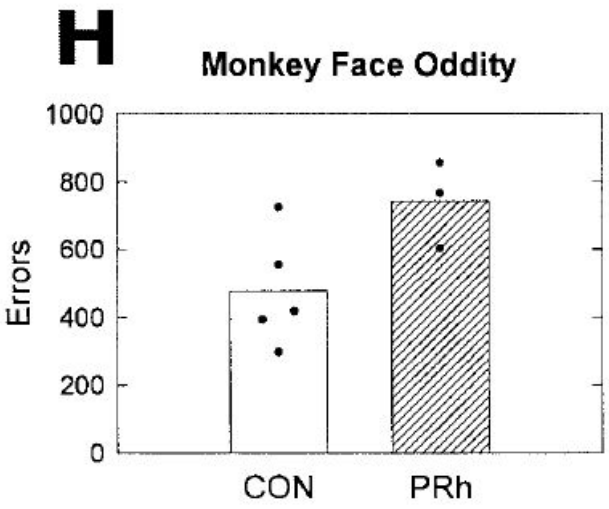




Others: impaired. Why?

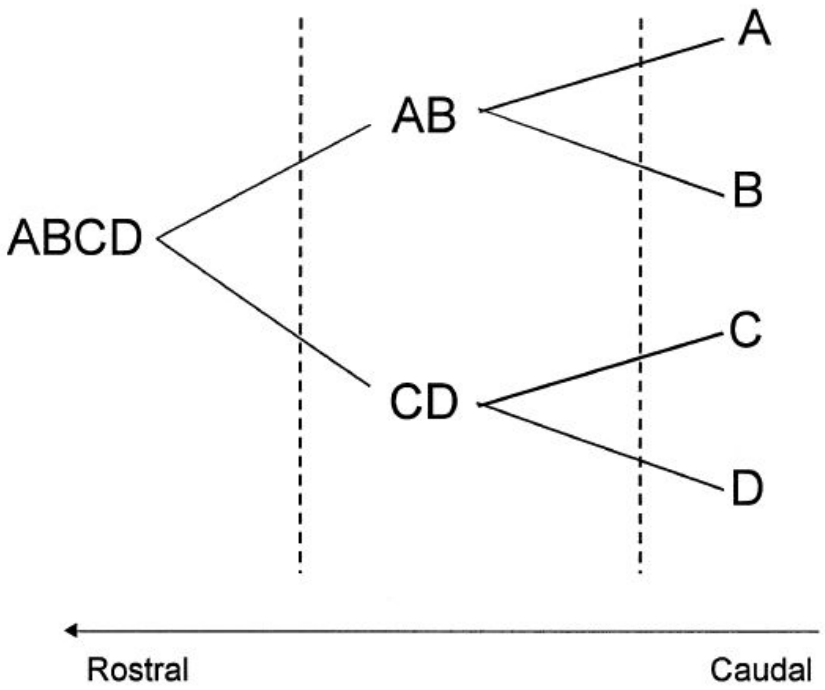


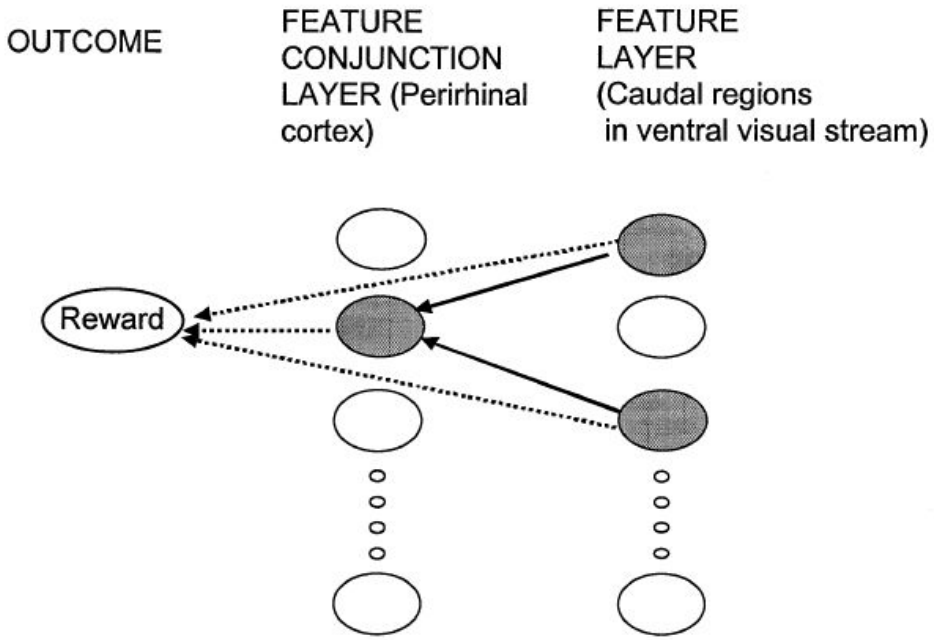




Buckley et al. (2001)

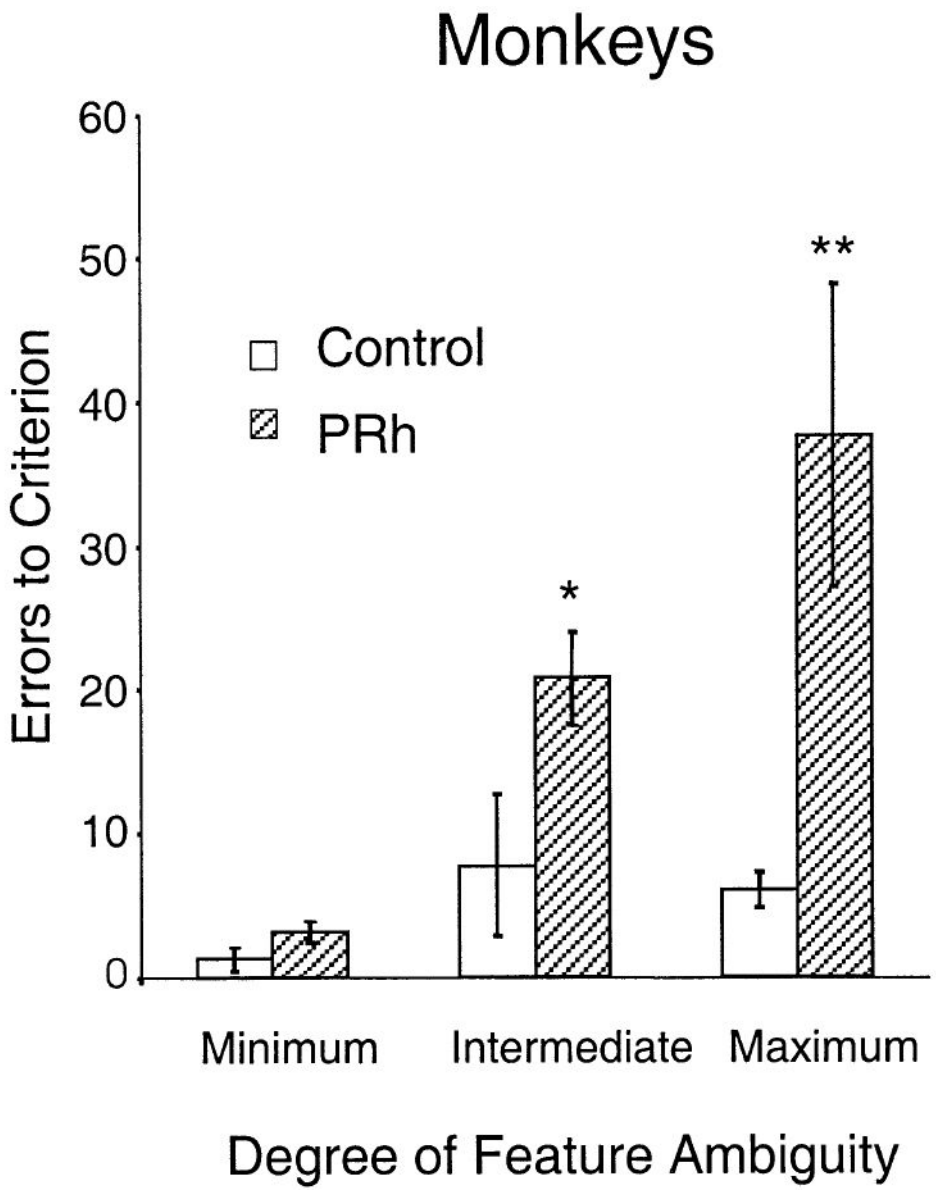
Perirhinal cortex: feature conjunctions (resolving ambiguity) 1





Bussey & Saksida (2002)

Perirhinal cortex: feature conjunctions (resolving ambiguity) 2



Bussey et al. (2002)

Semantic memory

Perinatal hypoxia: impaired episodic, preserved semantic

Table 1 *Results of neuropsychological tests*

	Case 1	Case 2	Case 3	Case 4	Case 5	Mean ± SD	Normal subjects (n = 35)
Age at testing (years)	12.8	11.7	11.6	16.3	12.3	12.9 ± 1.9	13.6 ± 1.3
Digit span							
Forward	6	7	6	8	7	6.8 ± 0.8	6.4 ± 1.2
Backward	5	5	6	6	3	4.7 ± 1.3	4.2 ± 1.5
Literacy (WORD) subtests							
Basic reading (standard score)							
Actual score	85	97	99	102	105	97.6 ± 7.7	100 ± 15†
IQ predicted score	83	86	89	106	92	91.2 ± 8.9	
Spelling (standard score)							
Actual score	77	96	88	84	118	92.6 ± 15.8	100 ± 15†
IQ predicted score	85	88	90	105	93	92.2 ± 7.7	
Reading comprehension (standard score)							
Actual score	84	87	74	97	87	85.8 ± 8.2	100 ± 15†
IQ predicted score	81	85	87	107	91	90.2 ± 10.1	
VIQ subtests							
Information	9	7	8	10	9	8.6 ± 1.1	10 ± 3†
Vocabulary	7	7	8	11	9	8.4 ± 1.7	10 ± 3†
Comprehension	7	8	9	14	8	9.2 ± 2.8	10 ± 3†

normal digit span, vocabulary, verbal information, and verbal comprehension

Table 2 *Results of tests of memory function*

	Case 1	Case 2	Case 3	Case 4	Case 5	Mean ± SD (n = 33)	Normal subjects
Story recall* (%)							
Immediate	25.0	38.9	20.8	27.2	11.3	24.6 ± 10.0	41.4 ± 14.9
Delayed	2.2	2.8	0	3.5	3.4	2.4 ± 1.4	32.3 ± 15.4
Geometric design† (± %)							
Immediate	53.6	32.1	57.1	64.2	35.7	48.5 ± 14.0	82.2 ± 13.5
Delayed	14.3	14.3	0	3.6	10.7	10.7 ± 5.0	77.8 ± 16.9
Children's Auditory Verbal Learning Test‡ (%)							
Immediate memory span	105	82	89	109	74	91.8 ± 14.9	100 ± 15.0§
Delayed	60	60	61	63	60	60.8 ± 1.3	100 ± 15.0§

severe delay-dependent impairment

Gadian et al. (2000)

Semantic dementia: impaired semantic, preserved episodic? 1

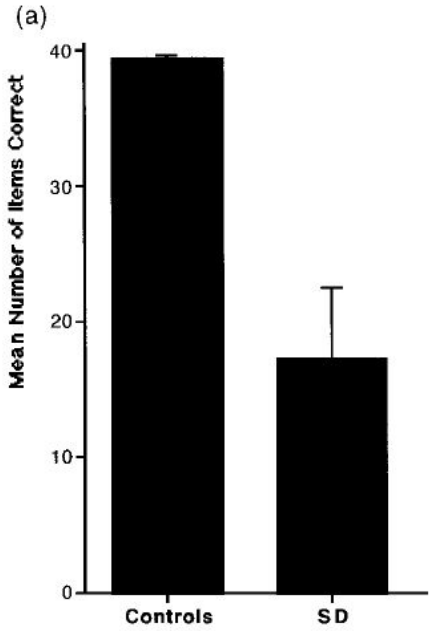
semantic task *— name a familiar object*

episodic task *— recognize an object ('perceptually identical')*

mixed task *— recognize a different example of an object ('perceptually different')*

Graham et al. (2000)

Semantic dementia: impaired semantic, preserved episodic? 2

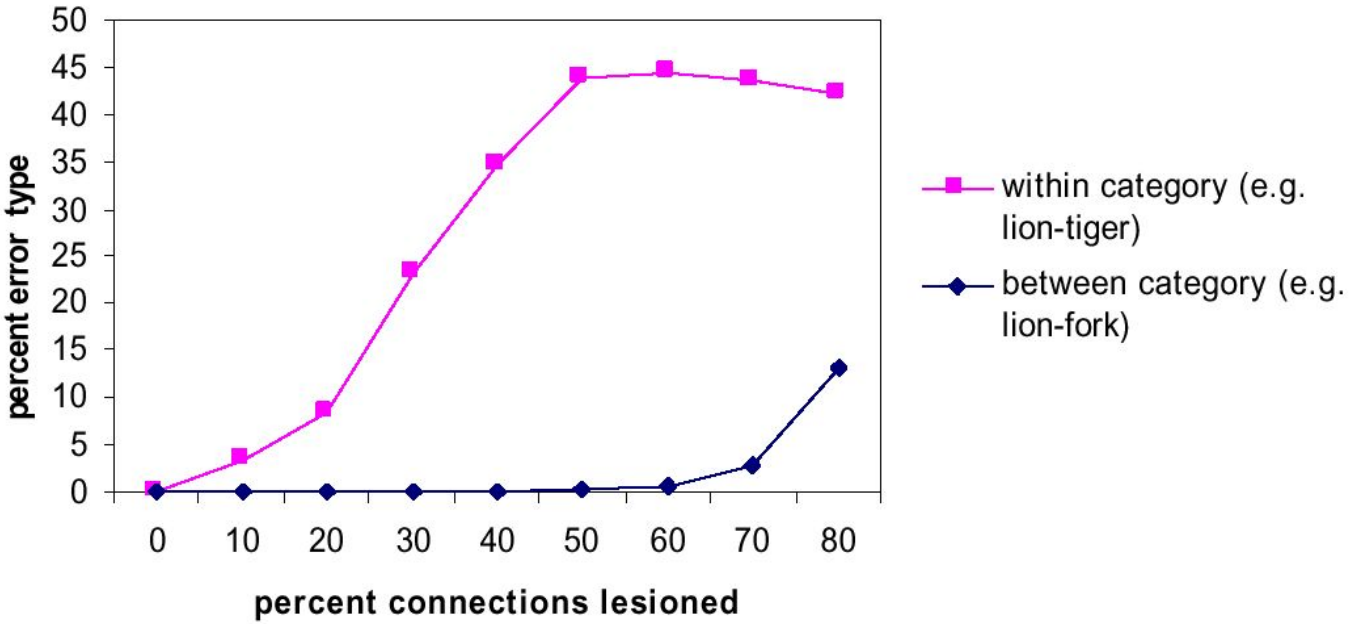


impaired semantic performance

normal object recognition;
failure to recognize a different example of the same kind of object

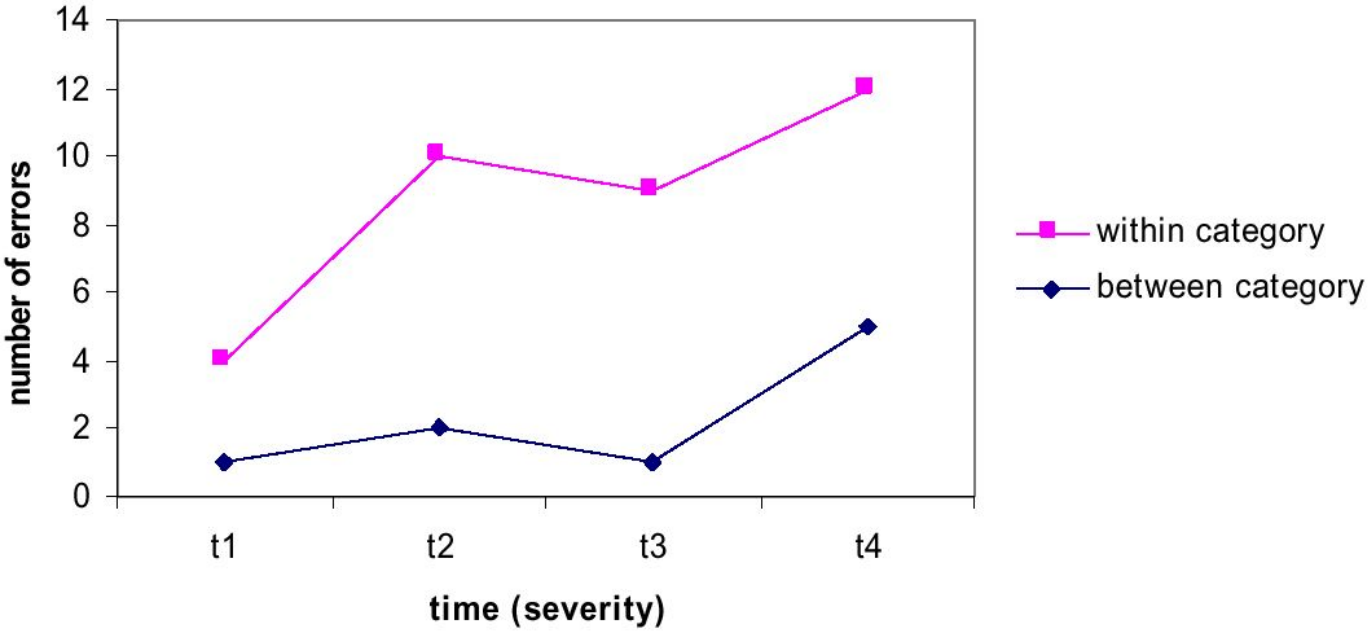
Graham et al. (2000)

Semantic dementia: damage to a simple associative net?



computational model

patient with progressive semantic dementia



Moss et al. (2002)

Consolidation: hippocampal–cortical interactions?

Retrograde amnesia: hippocampus / medial temporal lobe

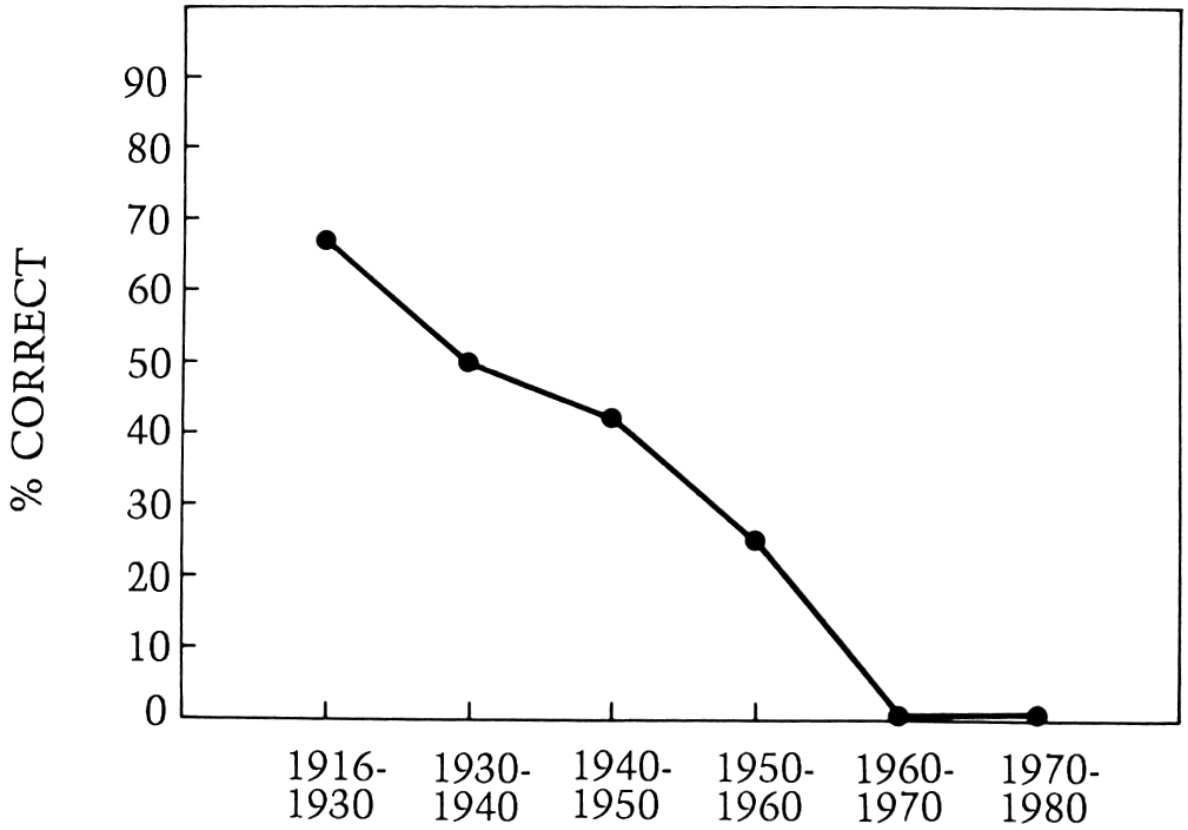


Figure 14.9. Recall of information from the patient's (P.Z.) published autobiography (Butters and Cermak, 1986).

Gradual transfer of memories from hippocampus (or MTL) to cortex elsewhere?

Scoville & Milner (1957); Squire et al. (2001)

Alternative: the 'multiple memory trace' model

- This suggests that the hippocampus is ALWAYS important for certain types of memory, especially autobiographical memory.
- Memories are 'laid down' in both hippocampus and neocortex elsewhere.
- Repeated/rehearsed memories have **multiple traces.**
- For some kinds of memory (e.g. semantic), older memories have more cortical traces that can be used for retrieval. For these memories, hippocampal lesions can lead to temporally-graded retrograde amnesia (older memories survive better).
- However, autobiographical and other 'context'-dependent memories always require the hippocampal system ('contextual index') for retrieval.

Nadel & Moscovitch (1997)

Patient VC: seizures (associated with a tachyarrhythmia), subsequently amnesic. MRI: hippocampal atrophy, sparing of adjacent cortex. **Flat** retrograde amnesia.

Cipolotti et al. (2001)

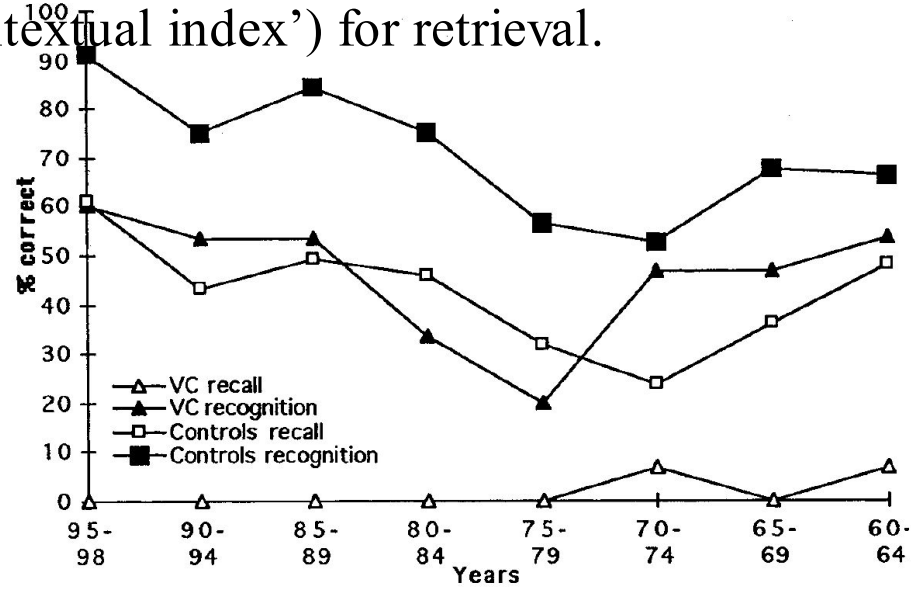
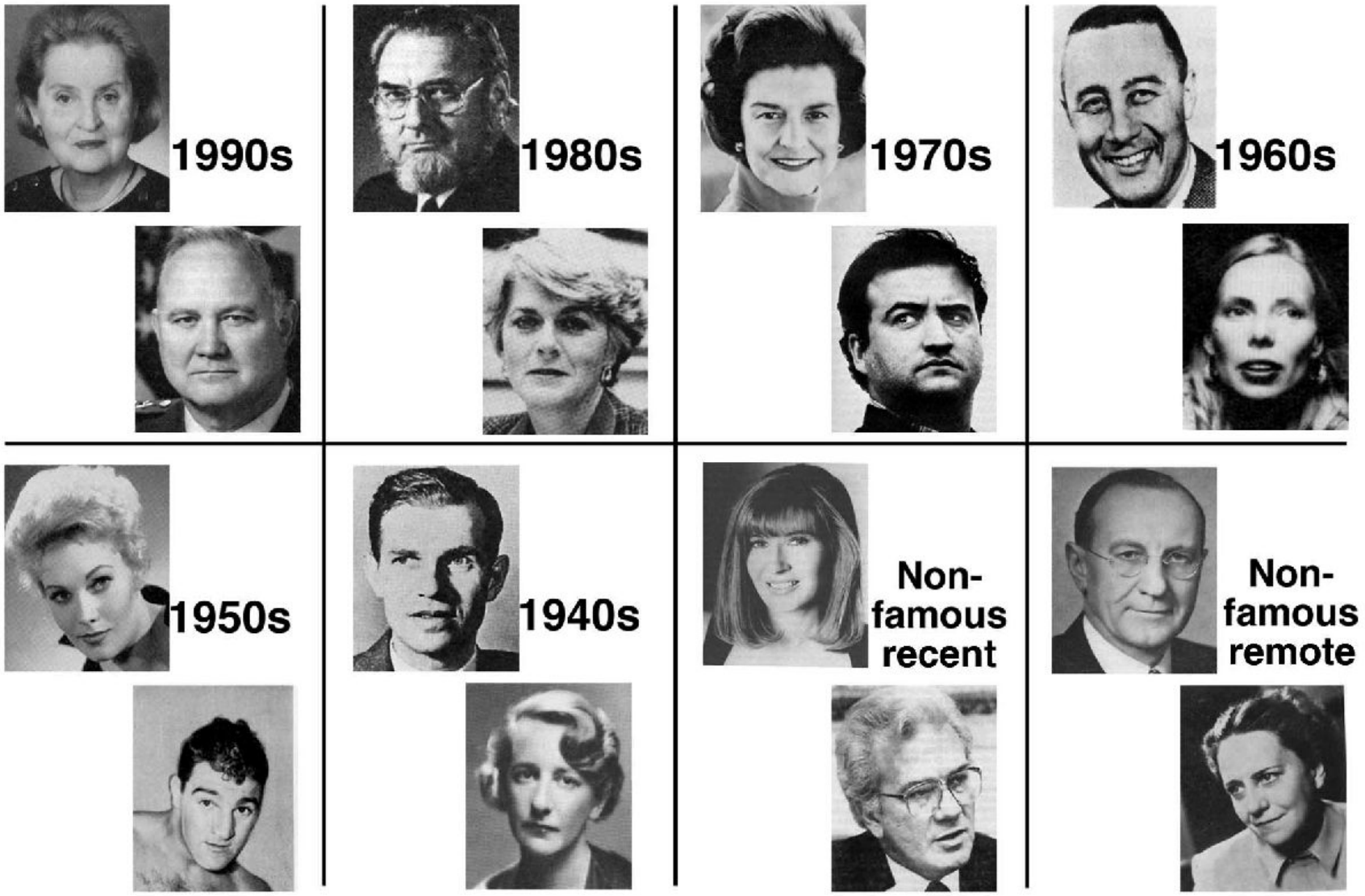


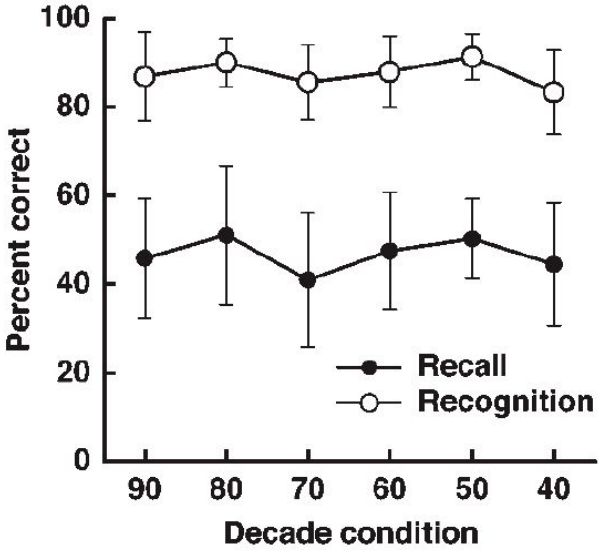
Fig. 6. Results on the famous public events questionnaire test.

Temporally-graded activation (1)



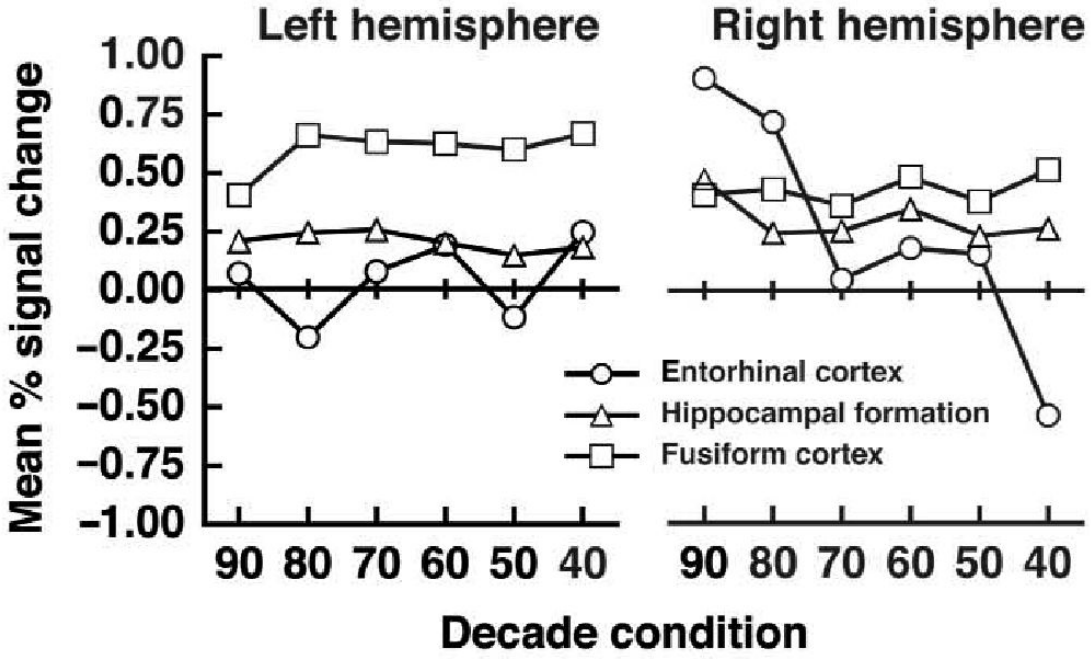
Haist et al. (2001)

Temporally-graded activation (2)



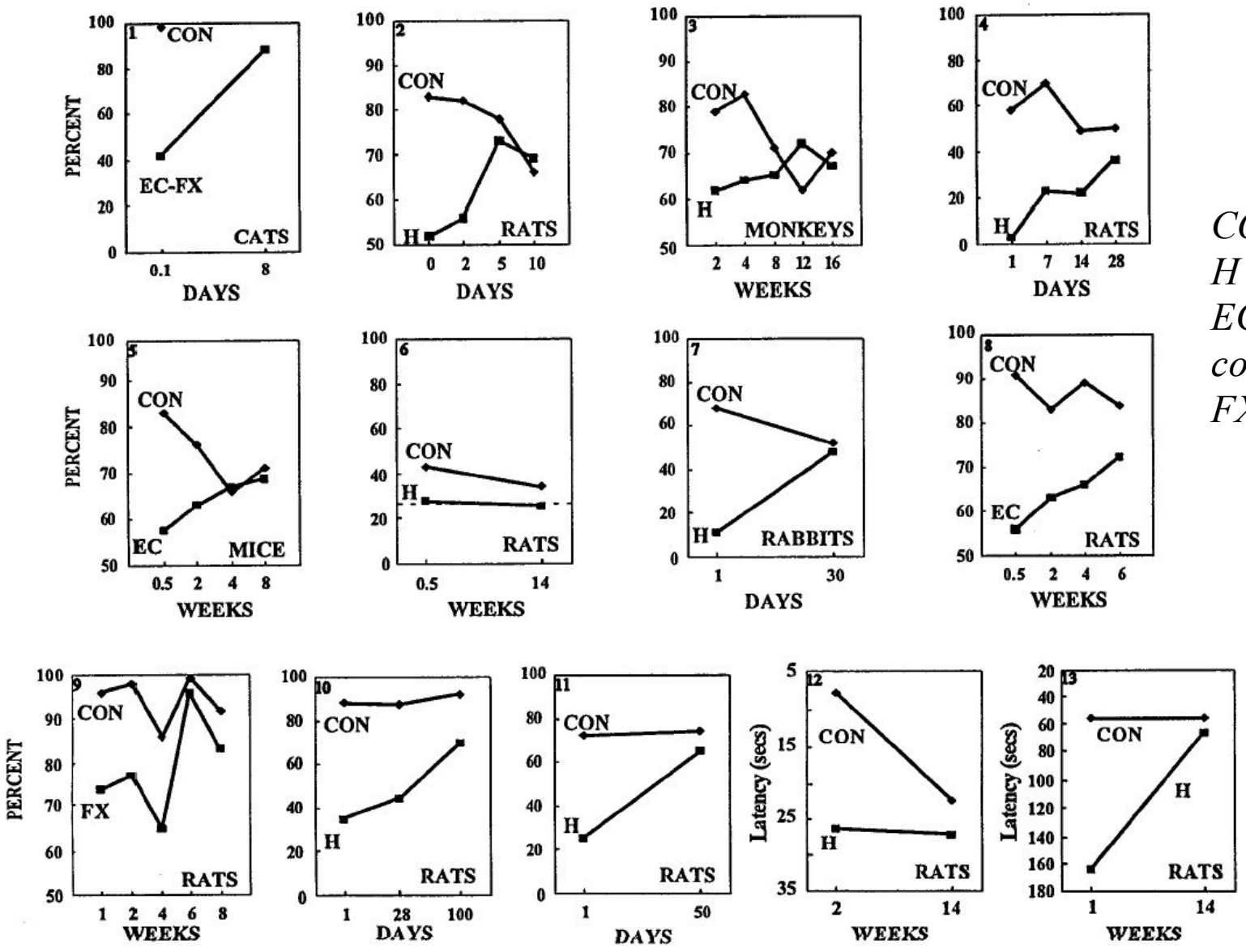
behavioural

neural (fMRI)



Haist et al. (2001)

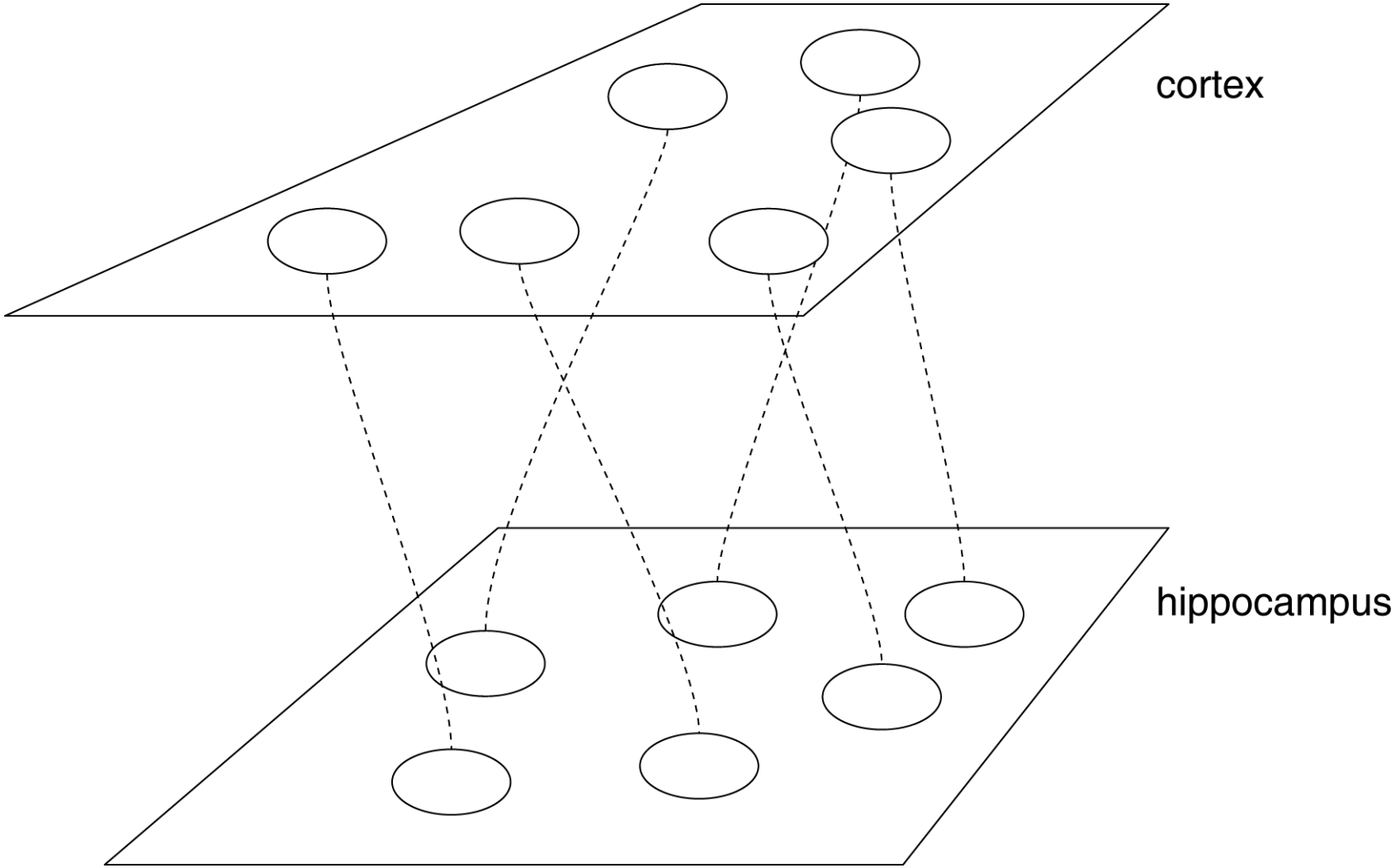
Prospective animal studies of retrograde amnesia



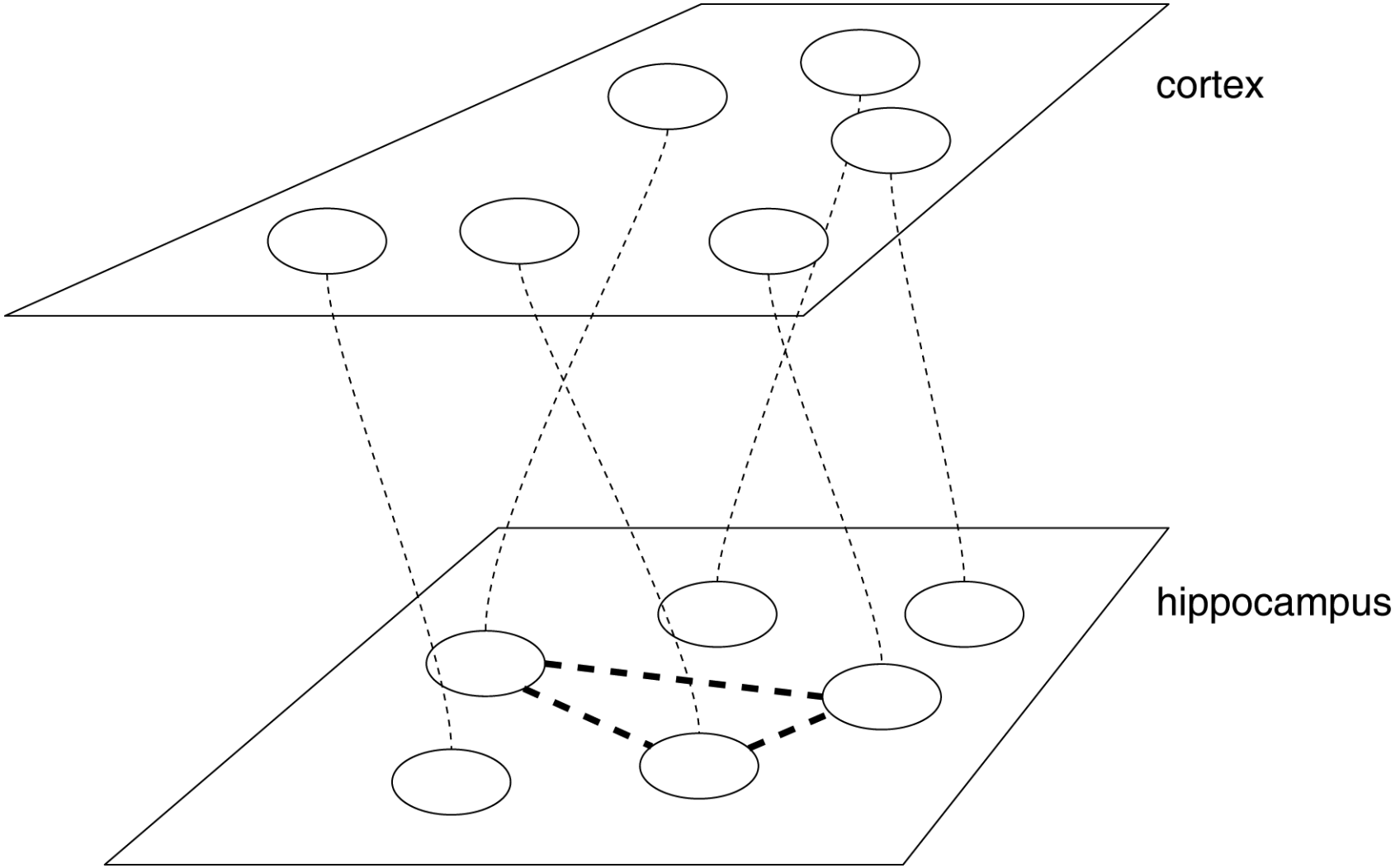
CON = control
H = hippocampus
EC = entorhinal cortex
FX = fornix

from Squire et al. (2001)

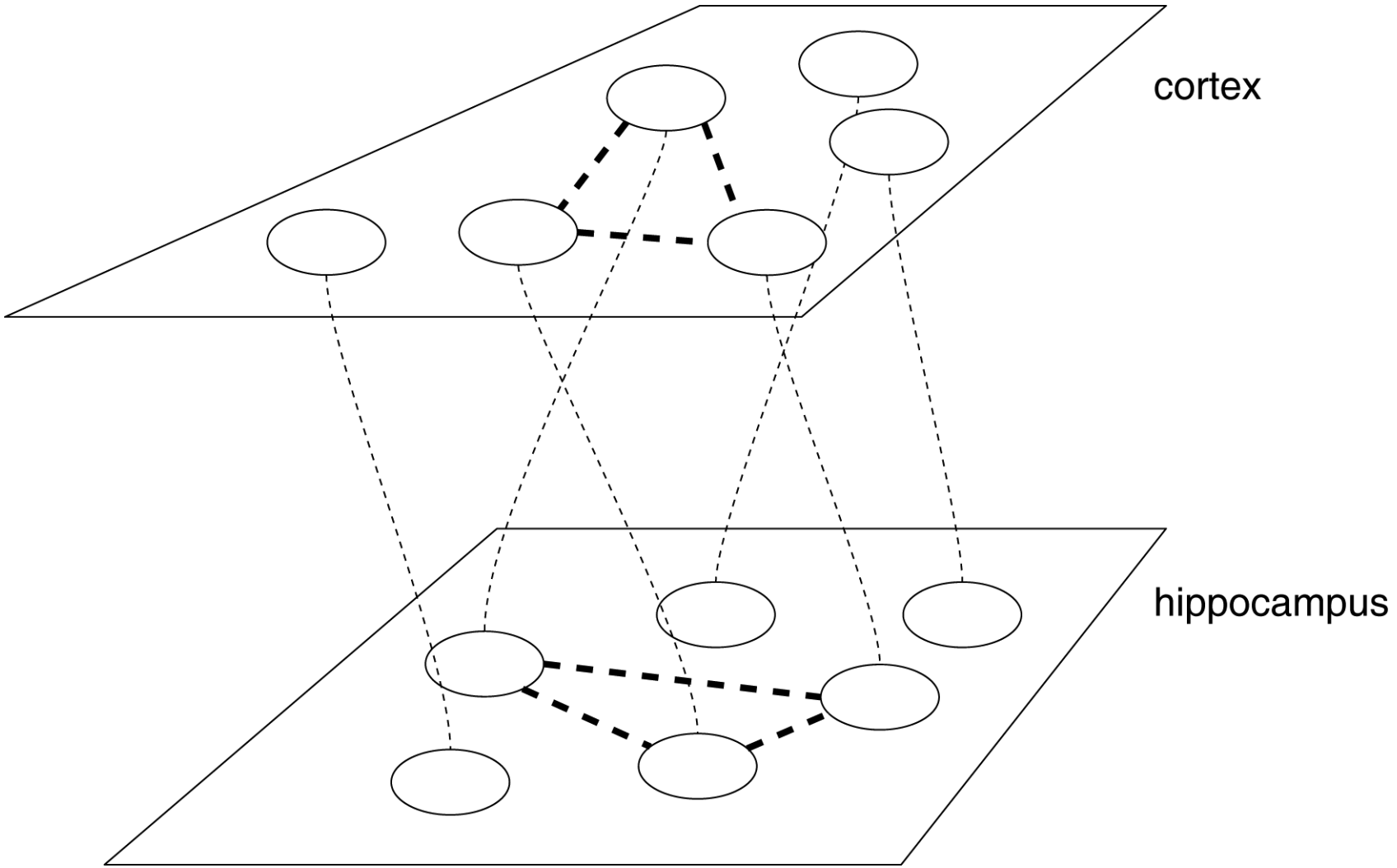
Hippocampal-cortical consolidation (1)



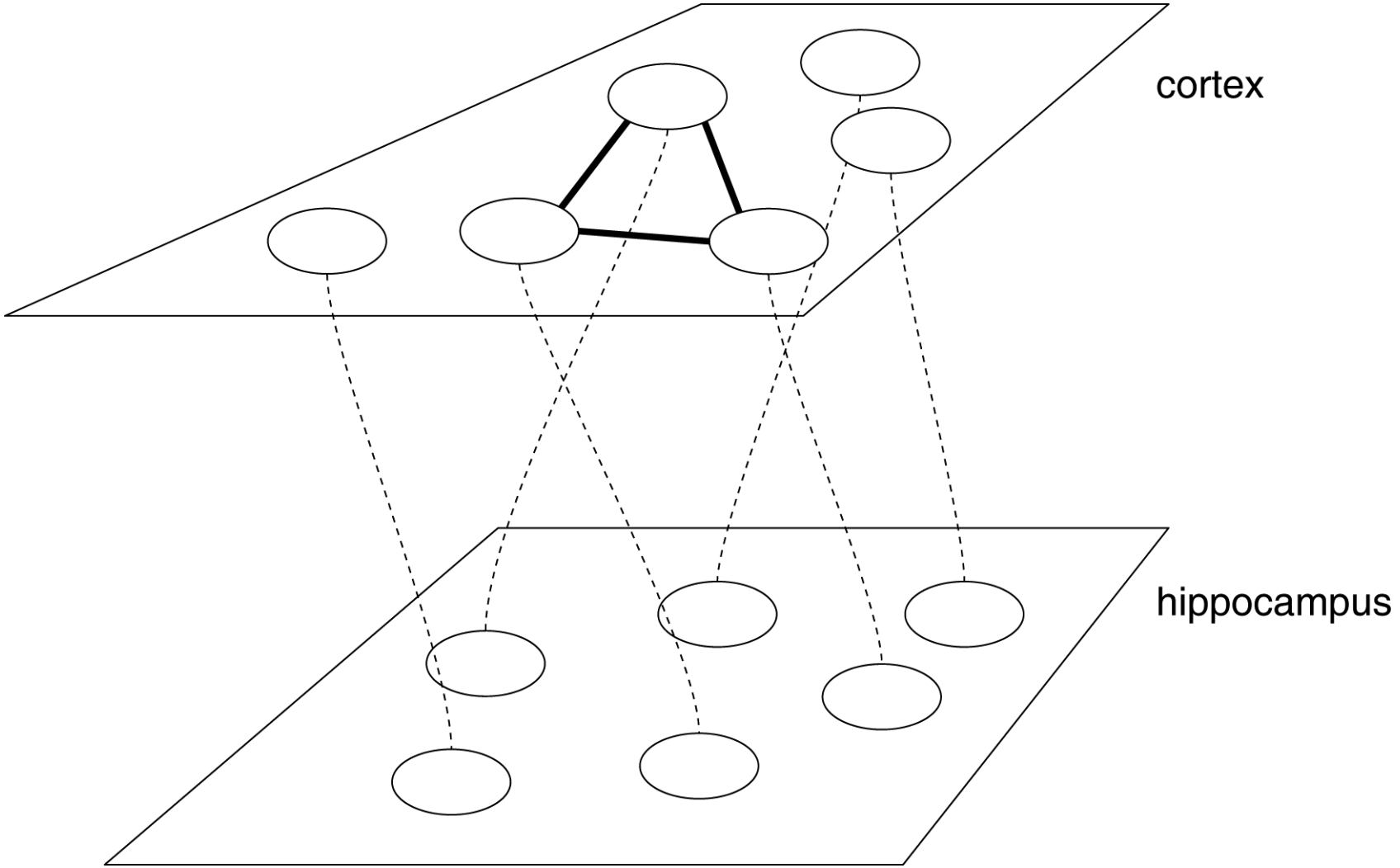
Hippocampal-cortical consolidation (2)



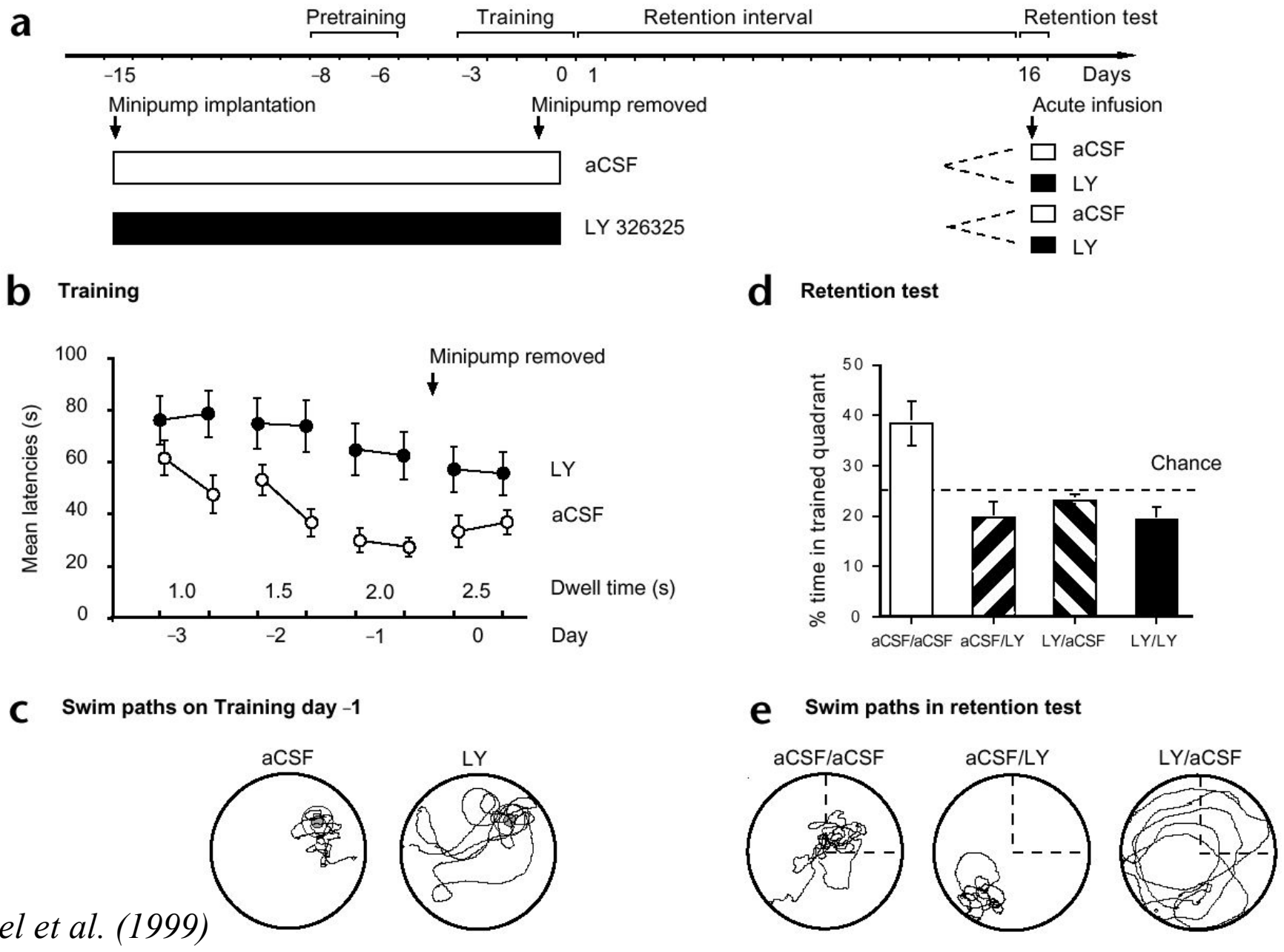
Hippocampal-cortical consolidation (3)



Hippocampal-cortical consolidation (4)

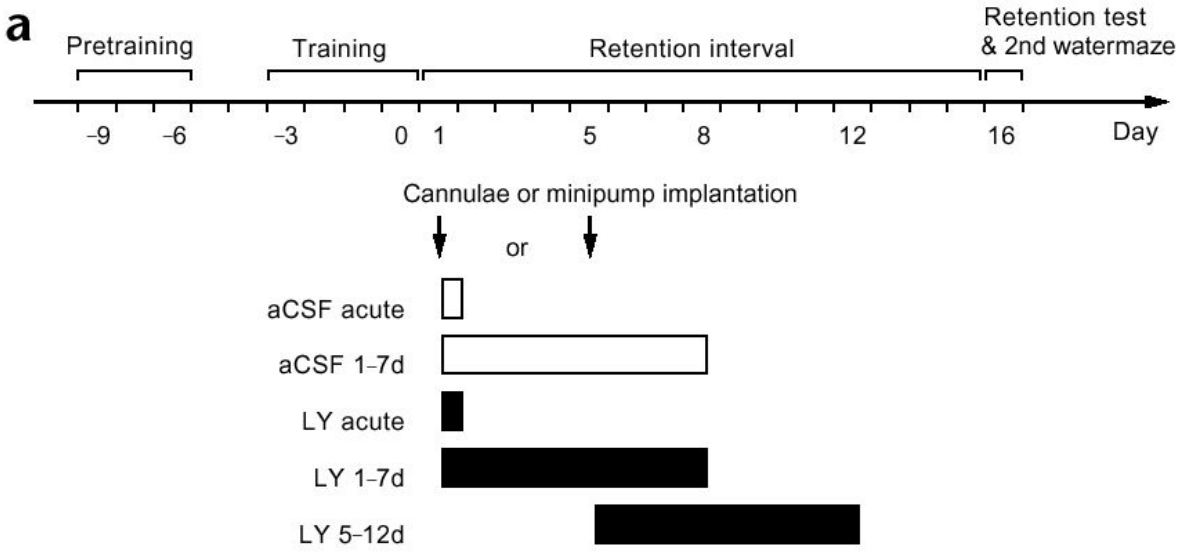


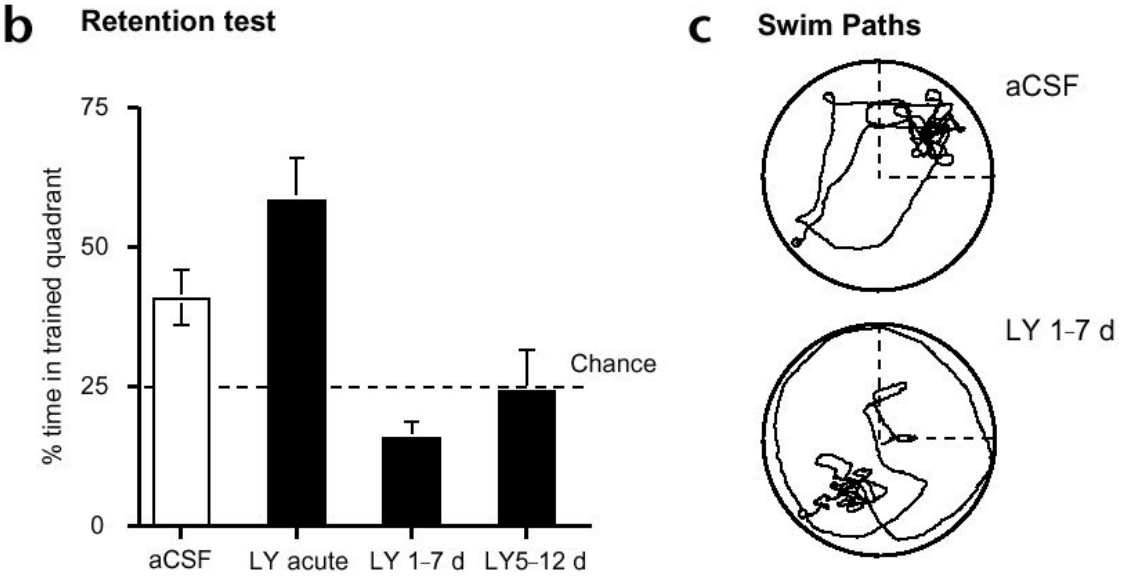
The hippocampus encodes, retrieves, ?consolidates (1)



Riedel et al. (1999)

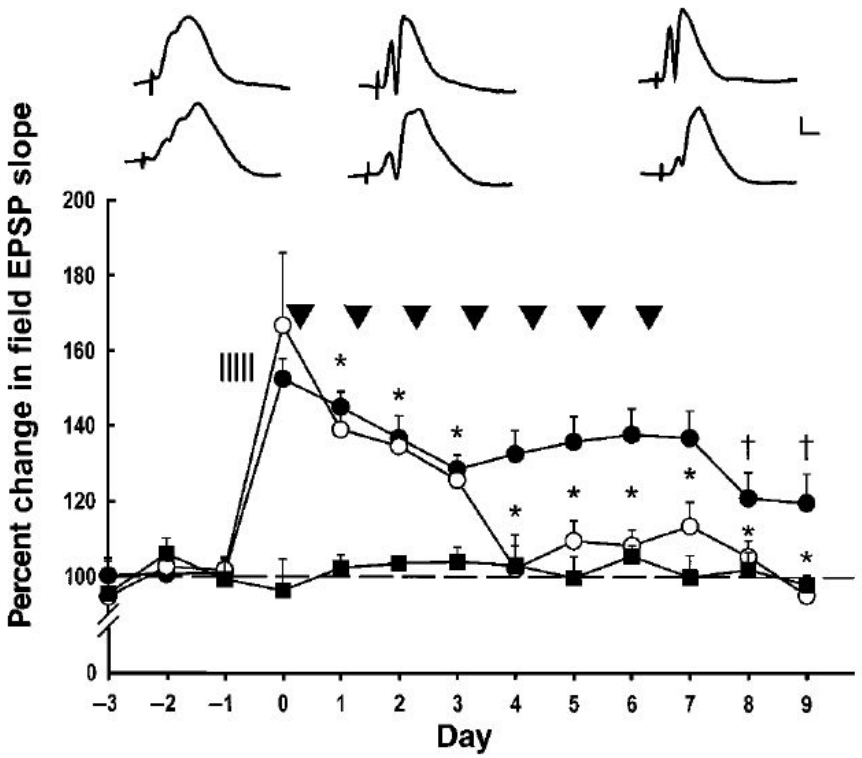
The hippocampus encodes, retrieves, ?consolidates (2)



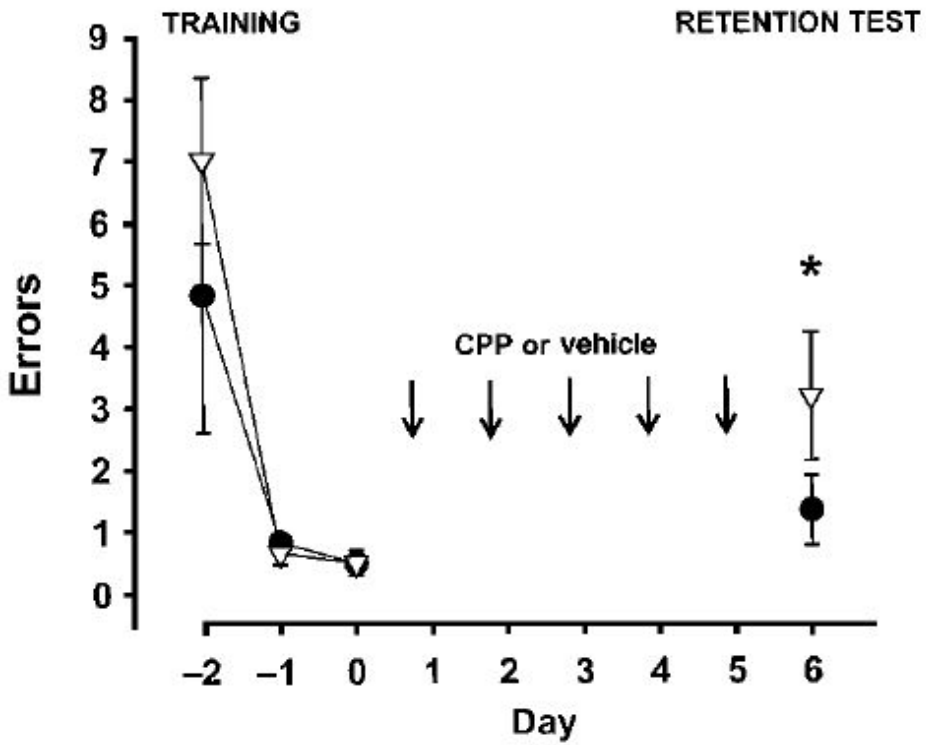


Riedel et al. (1999)

Does blockade of NMDA receptors prevent forgetting?



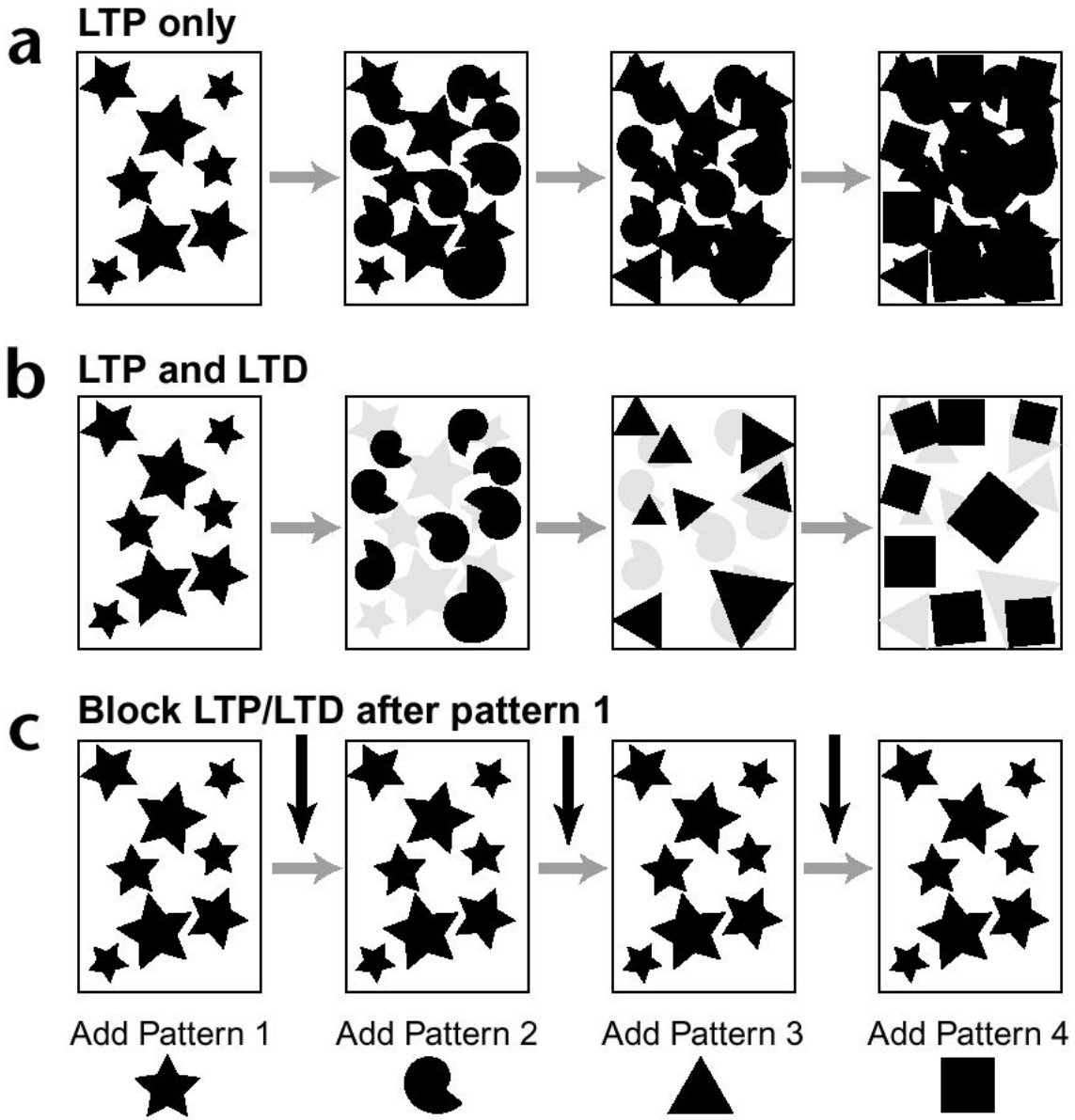
Systemic CPP (black circles) blocks decay of hippocampal LTP, compared to vehicle (white circles).



Systemic CPP (black circles) blocks decay of a memory for 8-arm radial maze performance, a task that is hippocampus-dependent, compared to vehicle (white triangles).

Villarreal et al. (2001)

The stability–plasticity dilemma: catastrophic interference



Rosenzweig et al. (2002), after an idea by Grossberg (1982)

Sleep and consolidation

‘Replay’ of hippocampal activity during sleep

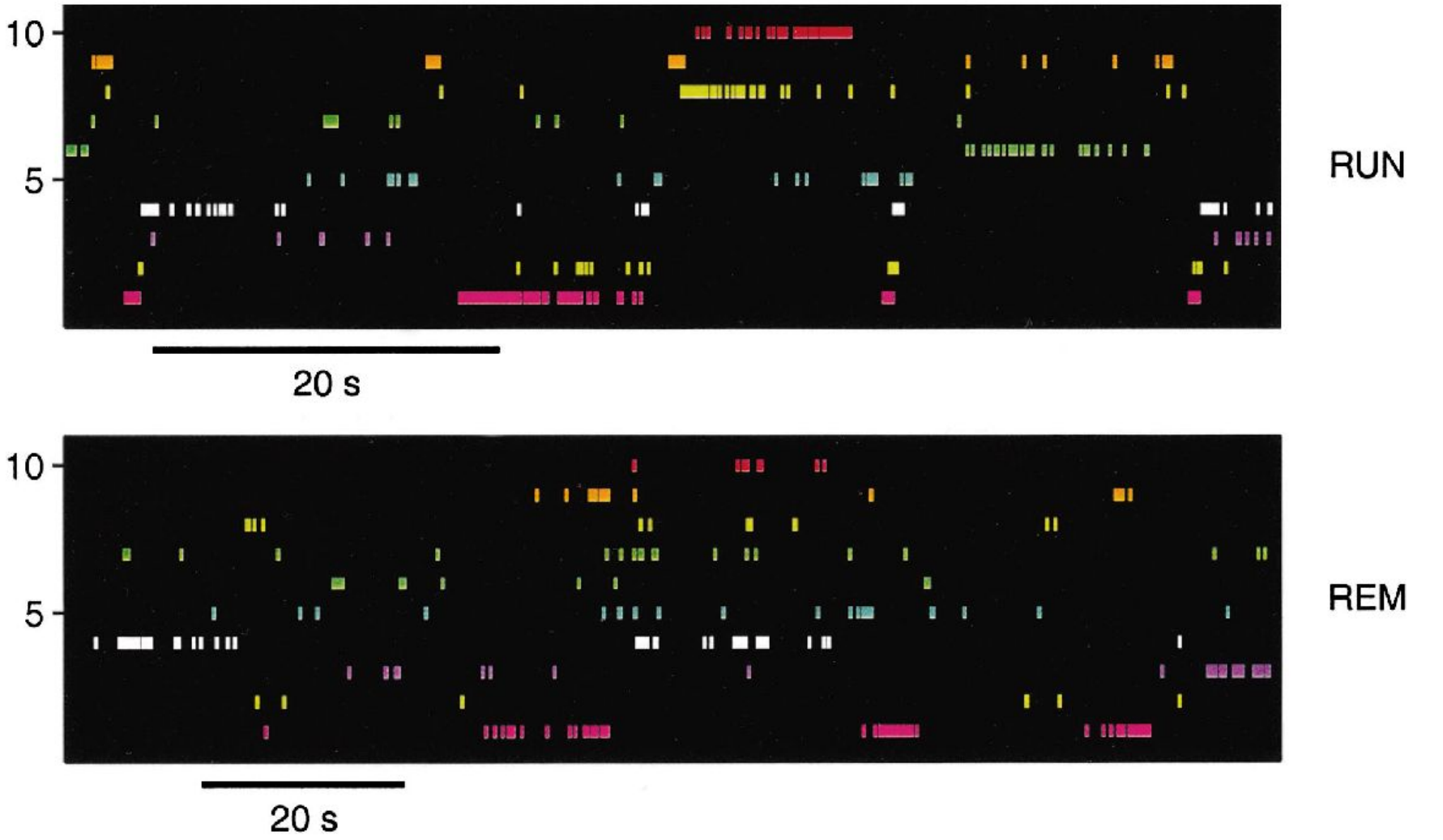
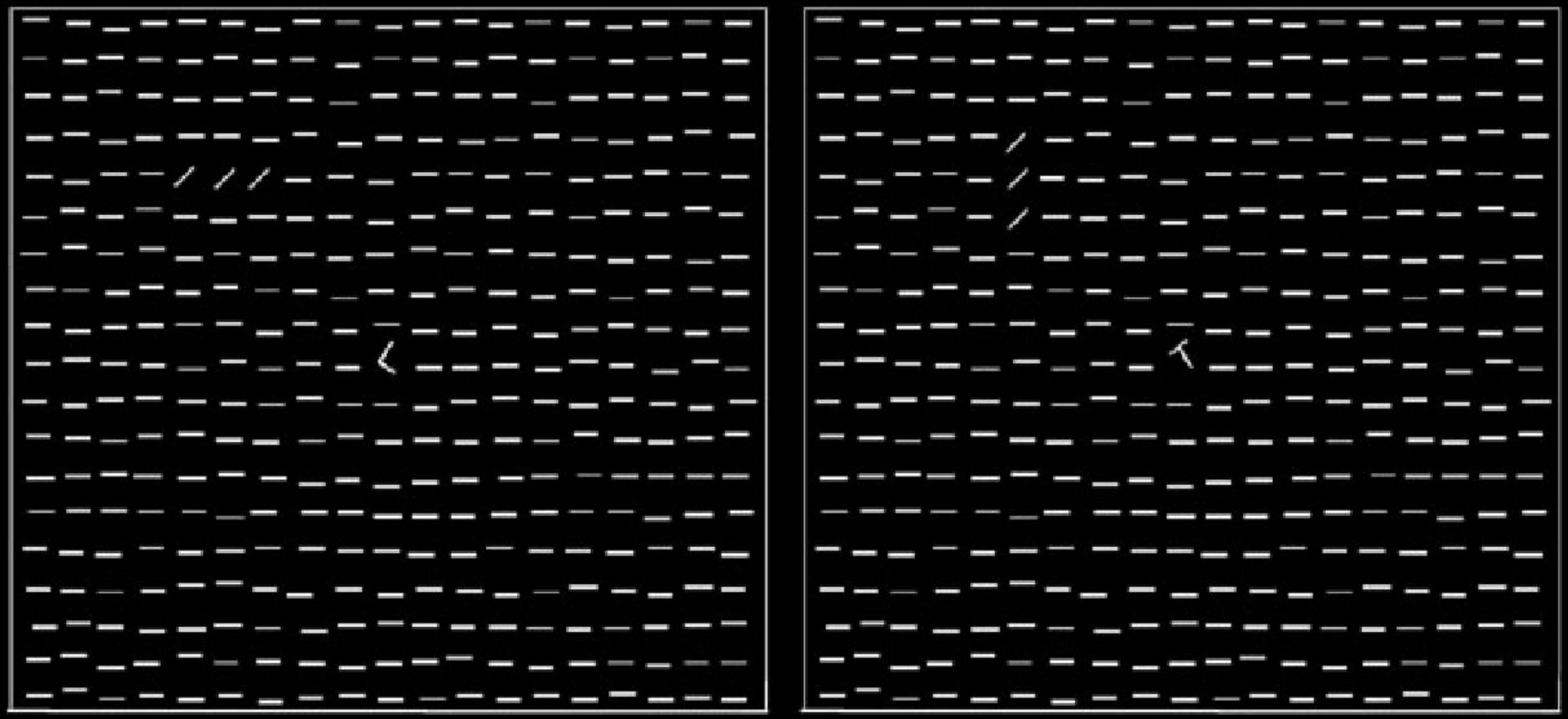


Figure 3. Example Correspondence between a REM Template and RUN Activity

(Top) Rasters of 10 pyramidal cells during a 75 s window from RUN. The RUN time axis is scaled to maximize raster alignment with REM (SF = 1.6). (Bottom) Rasters of the same cells over the duration of a 120 s REM template.

Louie & Wilson (2001)

‘Procedural’ memory consolidation and sleep (1)

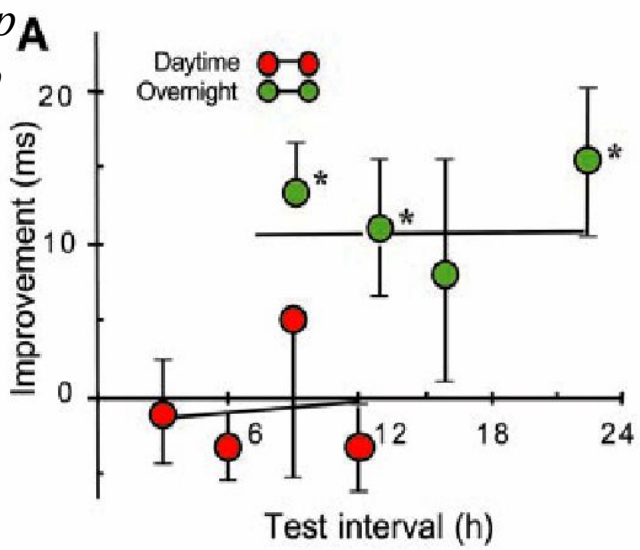


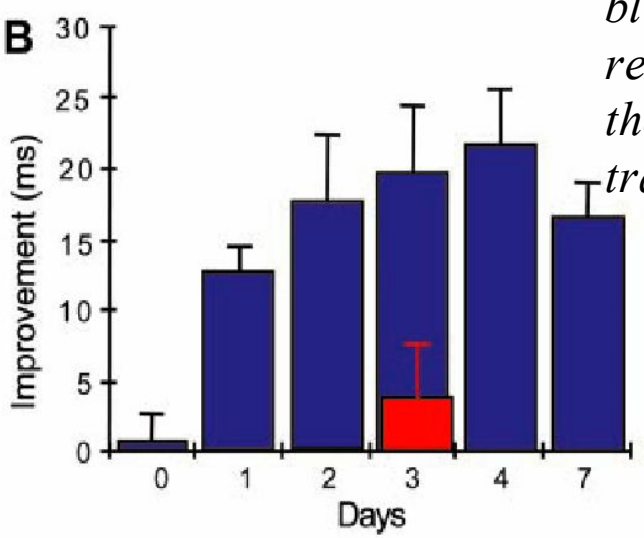
- *Subject must fixate centre and detect orientation of the /// pattern.*
- *Performance doesn’t improve until several hours **after** practice.*
- *Improvements are specific to the trained quadrant (and eye), and last for years, suggesting alterations in early visual processing.*

Karni & Sagi (1991); Stickgold et al. (2002)

‘Procedural’ memory consolidation and sleep (2)

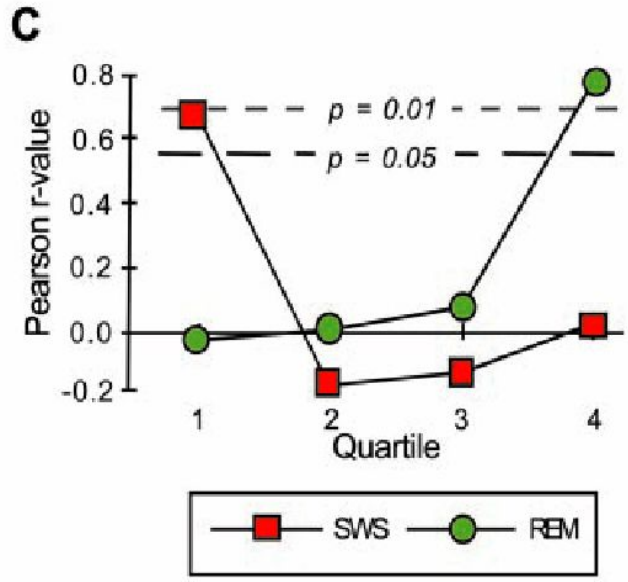
red = no sleep
green = sleep

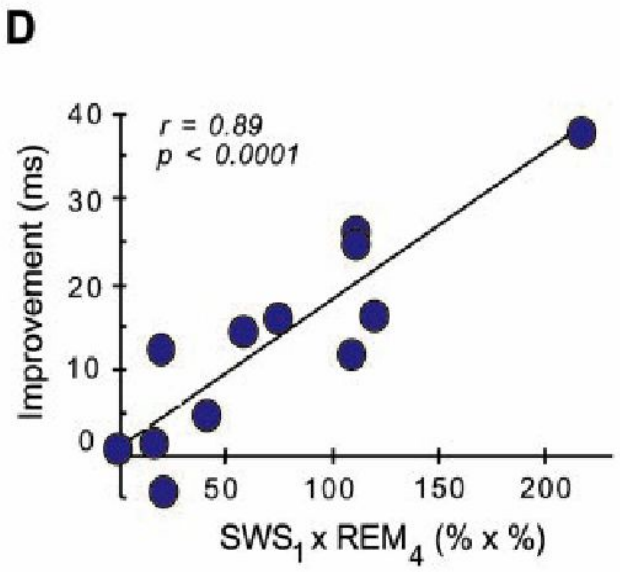




blue = sleep
red = no sleep
the night after training

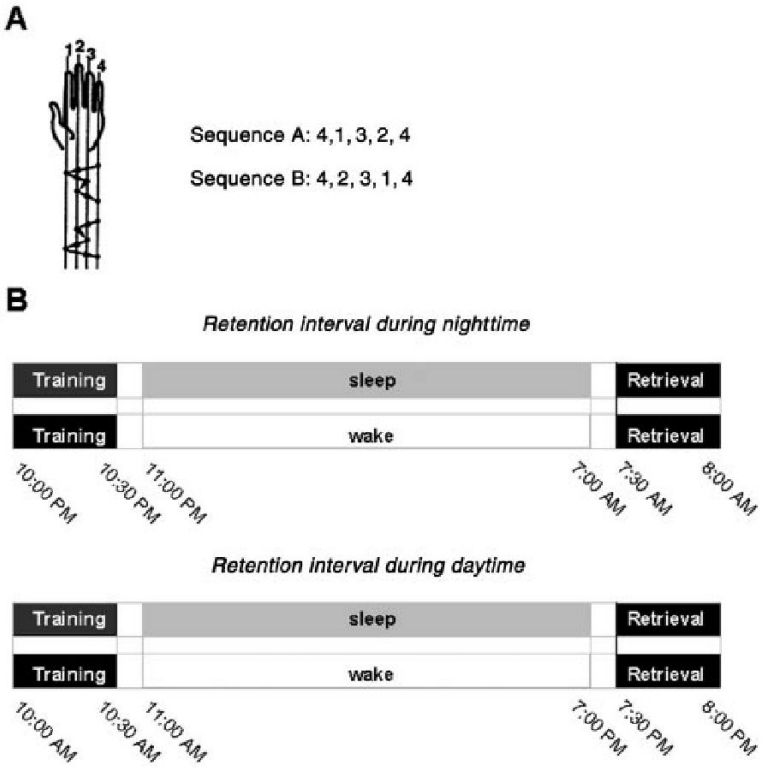
improvement correlated with sleep type

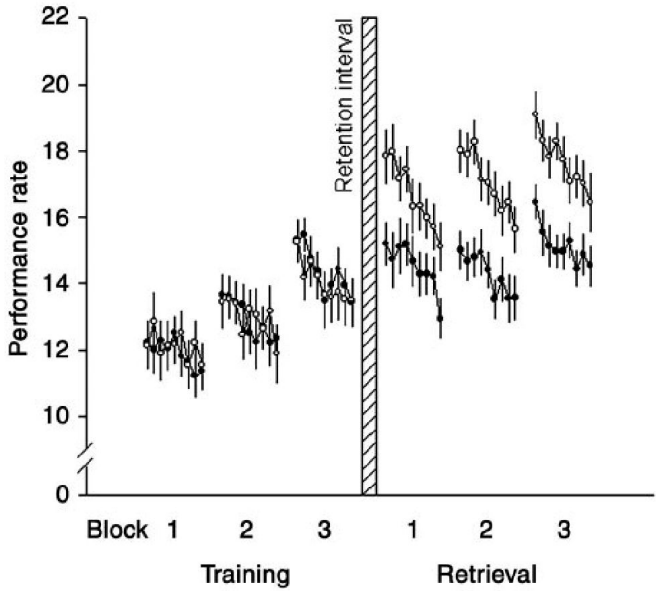


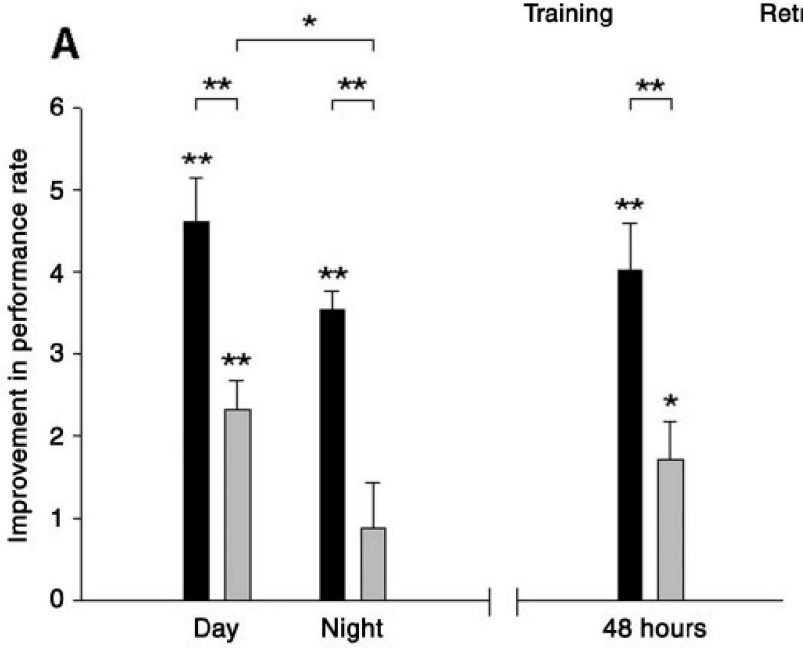


Stickgold et al. (2002). Between-subjects design (subjects were tested only once).

‘Procedural’ memory consolidation and sleep (3)







Fischer et al. (2002). “Sleep forms memory for finger skills.” Retention interval

REM sleep across species

High REM Sleep
≥ 3 hours of REM sleep/day

Platypus
Ornithorhynchus anatinus

8 REM, 14 Total

Thick-tailed Opossum
Lutreolina crassicaudata

6.6 REM, 18 Total

Ferret
Mustela nigripes

6 REM, 14.5 Total

Big Brown Bat
Eptesicus fuscus

3.9 REM, 19.7 Total

European Hedgehog
Erinaceus europaeus

3.5 REM, 10.1 Total

Armadillo
Dasypus novemcinctus

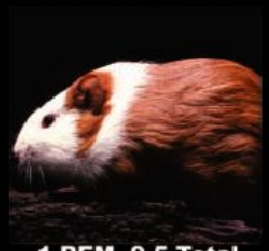
3 REM, 17 Total

Human
Homo sapiens

2 REM, 8 Total

Low REM Sleep
≤ 1 hour of REM sleep/day

Guinea Pig
Cavia porcellus



1 REM, 9.5 Total

Guinea Baboon
Papio papio

1 REM, 9.5 Total

Sheep
Ovis aries

0.6 REM, 5.9 Total

Horse
Equus caballus

0.5 REM, 3 Total

Giraffe
Giraffa camelopardalis

0.5 REM, 4.5 Total

Bottlenose Dolphin
Tursiops truncatus

<0.2 REM, 10 Total

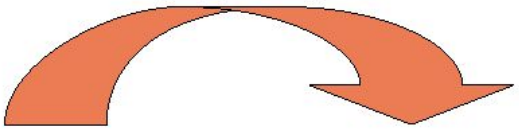
Siegel (2001)

Reconsolidation

‘Reconsolidation’

consolidation

(a)



Short-term memory (STM)

- Lasts for seconds to hours
- ‘Labile’ (sensitive to disruption)
- Does not require new RNA or protein synthesis

Long-term memory (LTM)

- Lasts for days to weeks
- Consolidated (insensitive to disruption)
- Does require new RNA or protein synthesis

reconsolidation

(b)

Active state (AS)

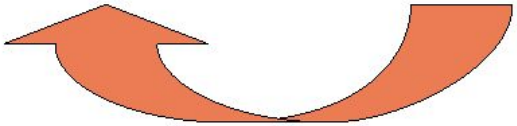
- Lasts for seconds to hours
- ‘Labile’ (sensitive to disruption)

(Does not require new RNA or protein synthesis)

Inactive state (IS)

- Lasts for days to weeks
- Inactive (insensitive to disruption)

(Does require new RNA or protein synthesis)



Nader (2003)

Reconsolidation in the amygdala (1)

Conditioned freezing requires the basolateral amygdala (BLA) — the BLA is a key site of association.

- *Train CS(tone)→US(shock)*
- *Present CS; infuse anisomycin (protein synthesis inhibitor) or vehicle into BLA*
- *Test conditioned freezing to the CS*

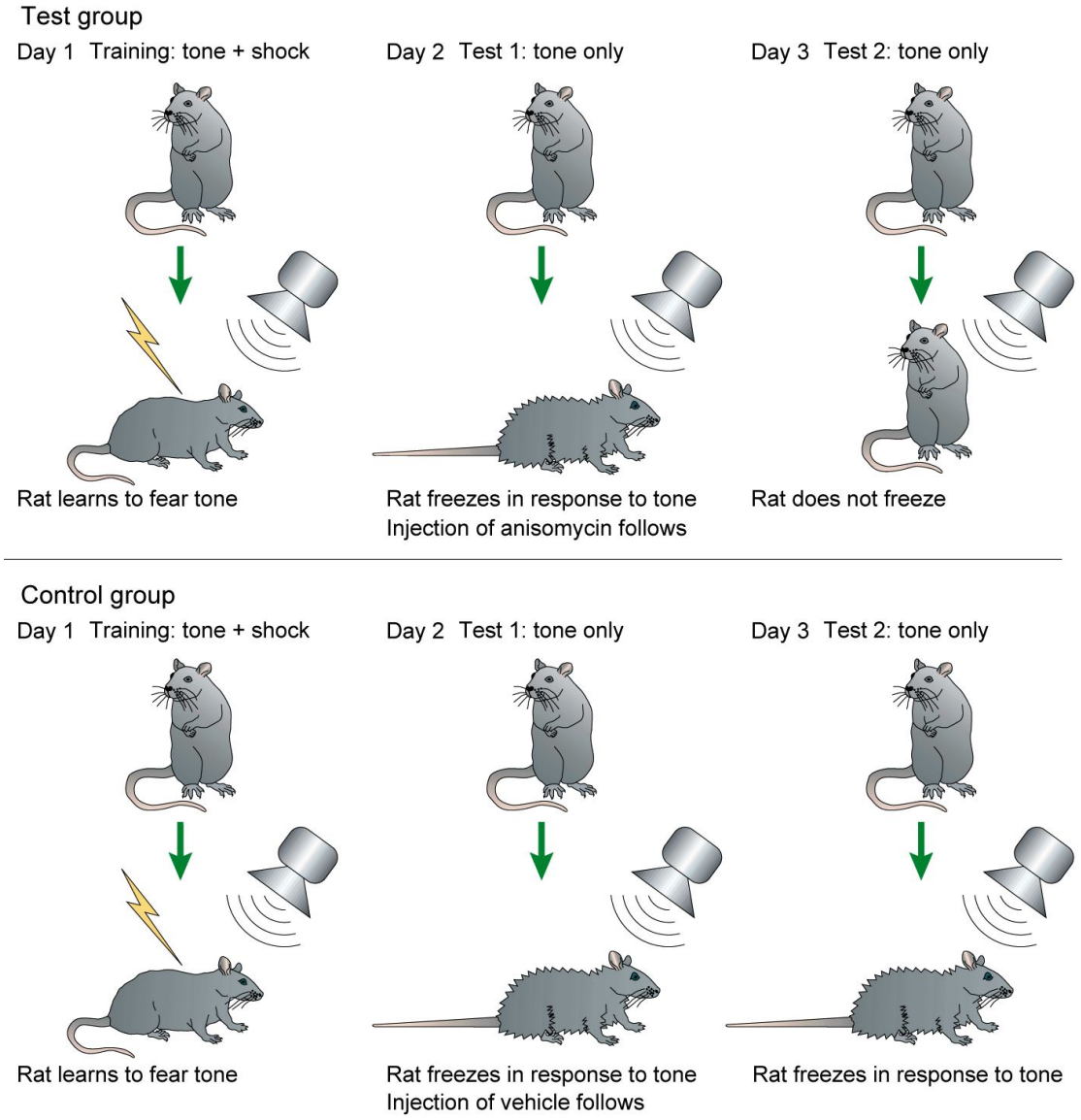
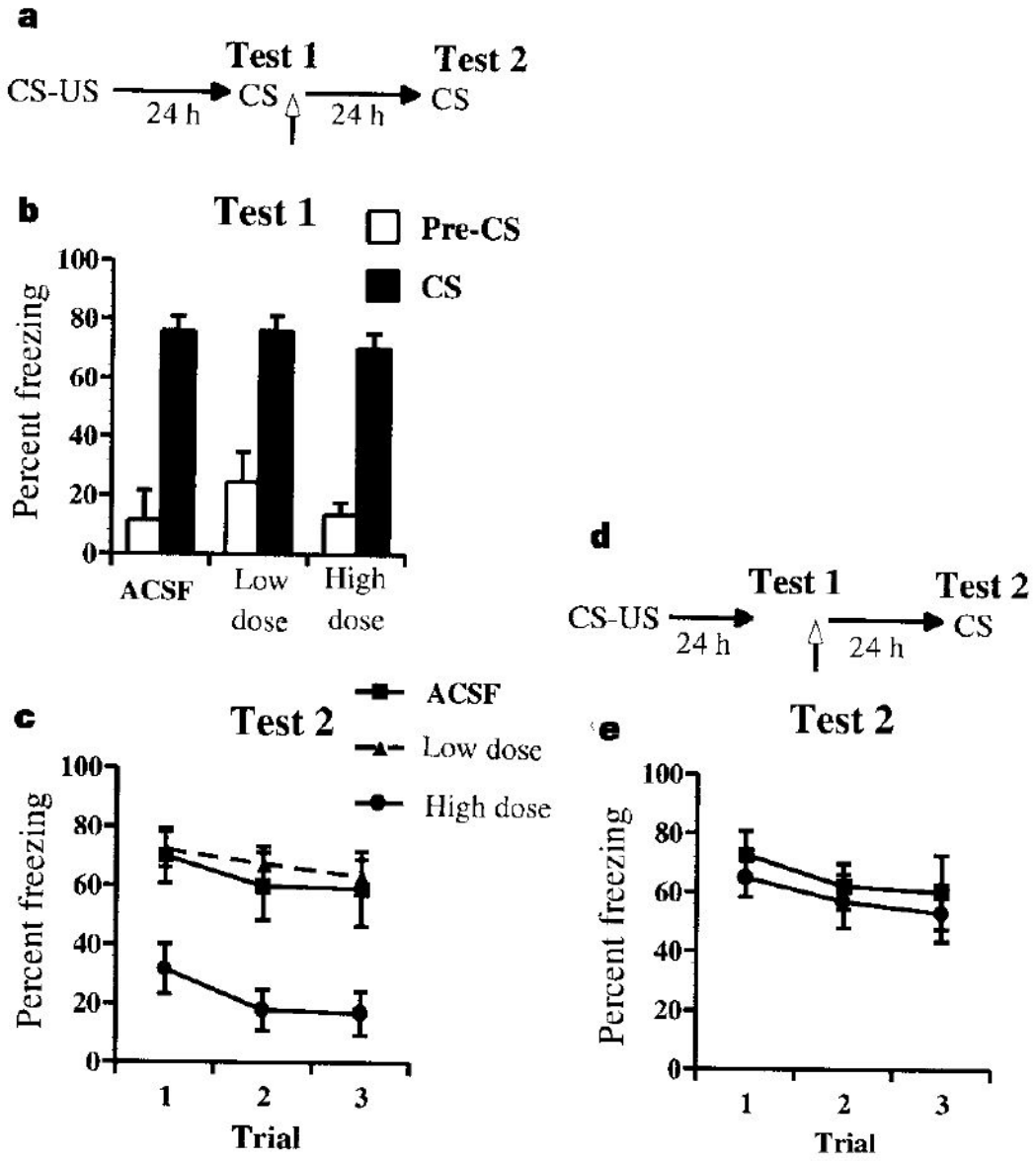


Figure 1 | Manipulations used to show reconsolidation. Memory for fear is disrupted in the test group if the tone is presented before the injection of anisomycin. In the control group, fear conditioning persists after the initial retrieval event (day 3).

Nader et al. (2000)

Reconsolidation in the amygdala (2)



Nader et al. (2000)

Reconsolidation in the amygdala (3)

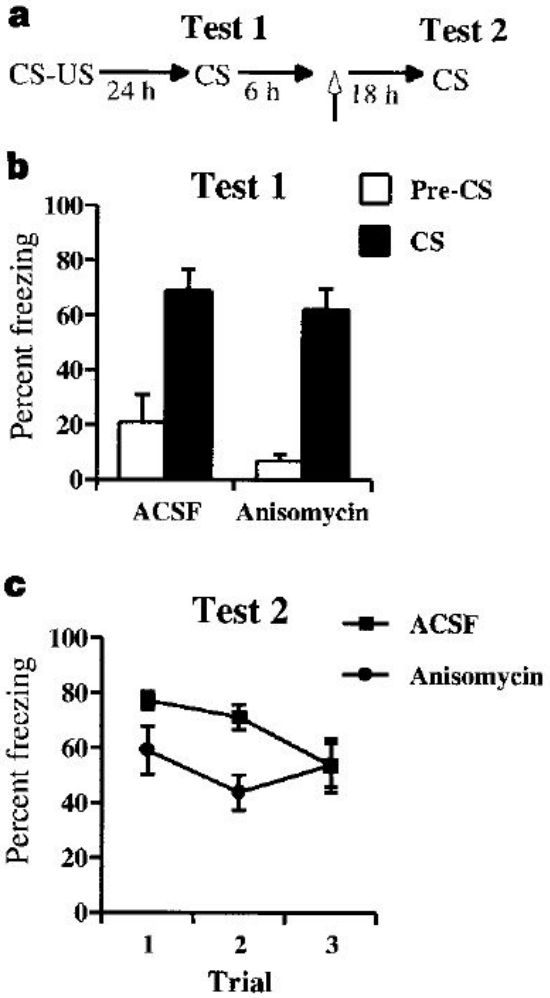


Figure 3 Intact memory if anisomycin infusions are delayed by 6 h. **a**, The behavioural procedure used for experiment 2. Vertical open-headed arrows represent infusions. **b**, Freezing on test 1 was specific to the CS and comparable across groups. **c**, Percent freezing during test 2. The groups are not significantly different. All data points represent group means ± s.e.m.

Nader et al. (2000)

Reconsolidation in the amygdala (4)

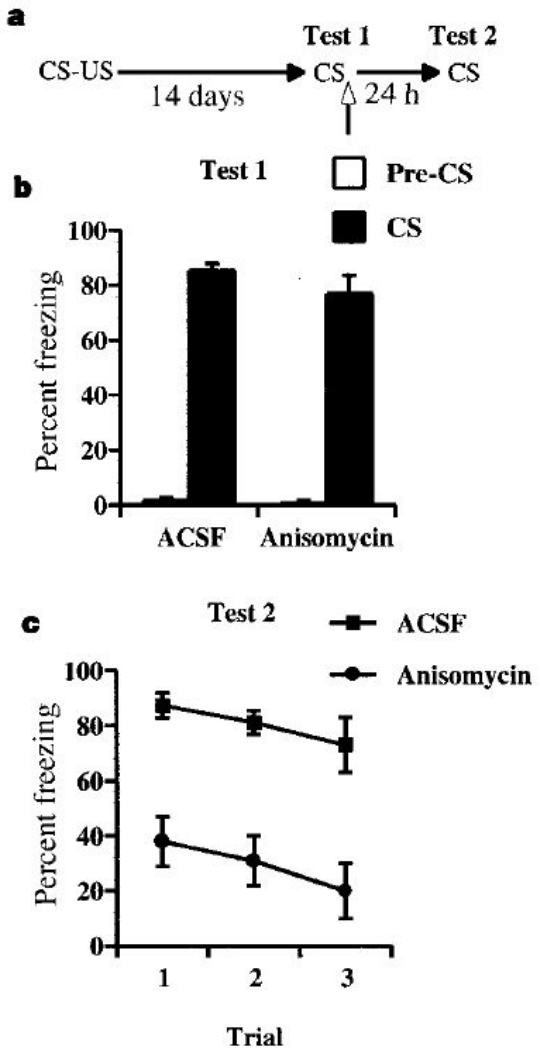
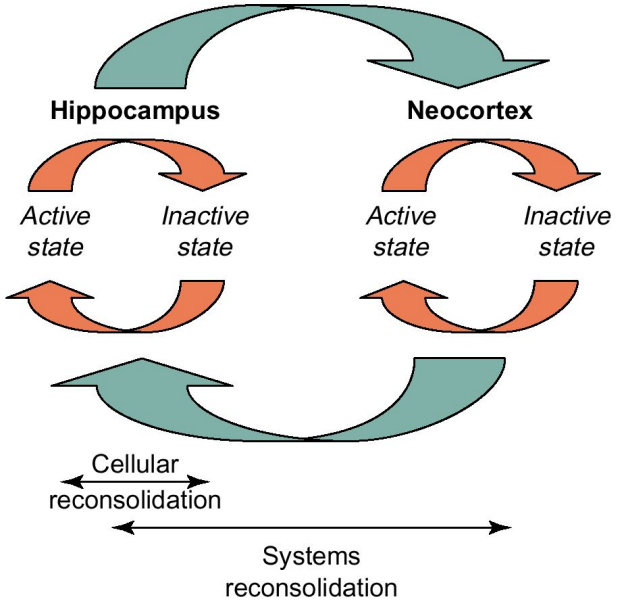


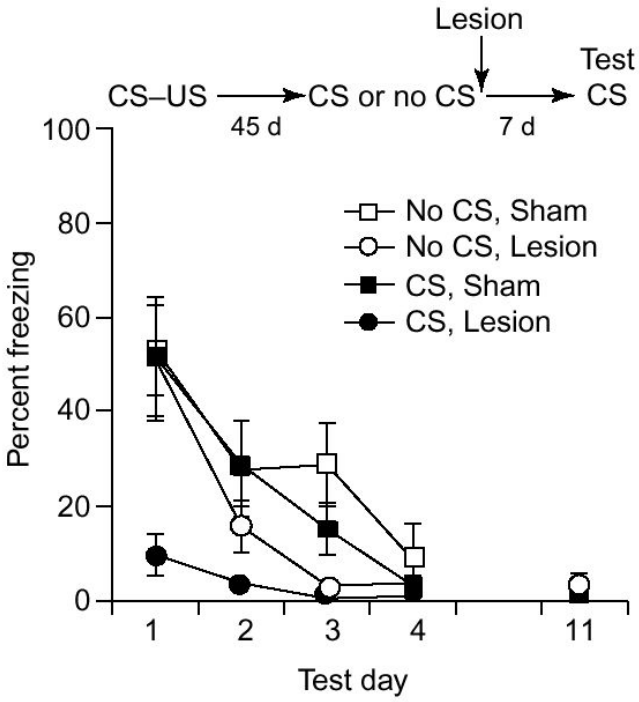
Figure 4 Fourteen days after training, anisomycin infusions after reactivation of the memory still produce amnesia. **a**, The behavioural procedure used for experiment 3. Vertical open-headed arrows represent infusions. **b**, Freezing during test 1 was specific to the CS and was comparable across groups. **c**, Percent freezing on test 2. All data points represent group means ± s.e.m.

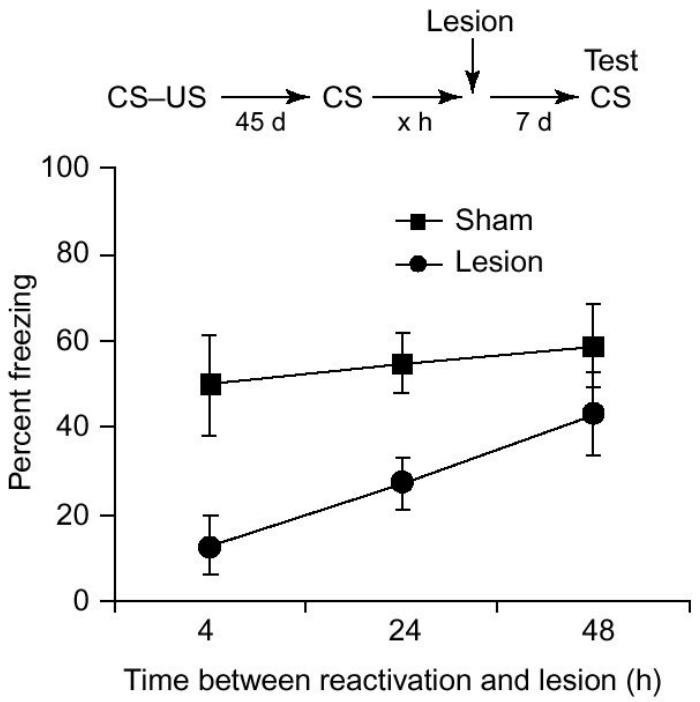
Nader et al. (2000)

‘Cellular’ and ‘systems’ reconsolidation in the hippocampus



- *Train CS(context)→US(shock)*
- *Present CS (or not); lesion hippocampus (or not).*
- *Test conditioned freezing to the CS*





Debiec et al. (2002)

1969: ECT for obsessive–compulsive disorder

Patients with OCD or hallucinations were given ECT after being prompted to act out their desires or after their hallucination had begun. All 28 patients... improved dramatically for periods ranging from 3 months to the time of publication of the manuscript, 10 years later. One relapsed, but was treated once using the same approach and recovered.

Many of the subjects had previously received between 5 and 28 ECT sessions, while anaesthetized, with little benefit.

Case study. 30-year-old woman with OCD received 22 ECT treatments in 1 year while anaesthetized, but became worse. She was made to act out her compulsion of killing her mother with a butcher's knife and was then administered a single session of ECT while still awake. 'The next day, greatly improved, she went home and spoke kindly to her mother for the first time in years. She asked her mother "Do you love me?" and then kissed her. When the author asked if she still felt like stabbing her mother, she laughed and said, "Oh, she doesn't deserve anything like that"'. She returned home and to work, and remained free of symptoms for

Ruben et al. (1969), Ruben (1976), see Nadeu (2003)

Cautionary note…

- There's a long history of research into the effects of protein synthesis inhibitors on memory (Flexner *et al.*, 1963).

- Protein synthesis inhibitors have side-effects. Might these be responsible for effects on consolidation — or interfere with *retrieval* of the memory?

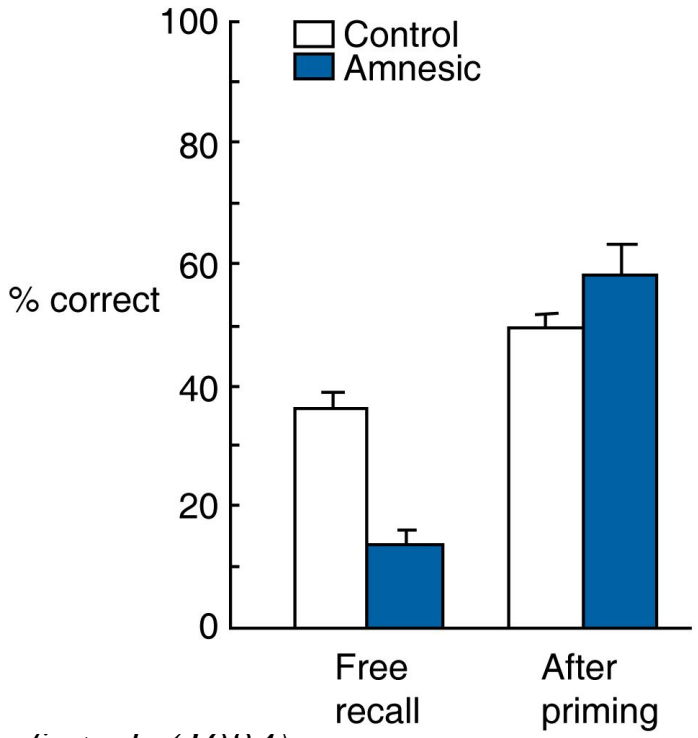
- The original work foundered because the amnesic effects of puromycin (a protein synthesis inhibitor) were not duplicated by another protein synthesis inhibitor; it turned out that a metabolite of puromycin was responsible for its effects (by an unknown mechanism) (Flexner *et al.* 1967).

Those who cannot remember the past are condemned to repeat it.

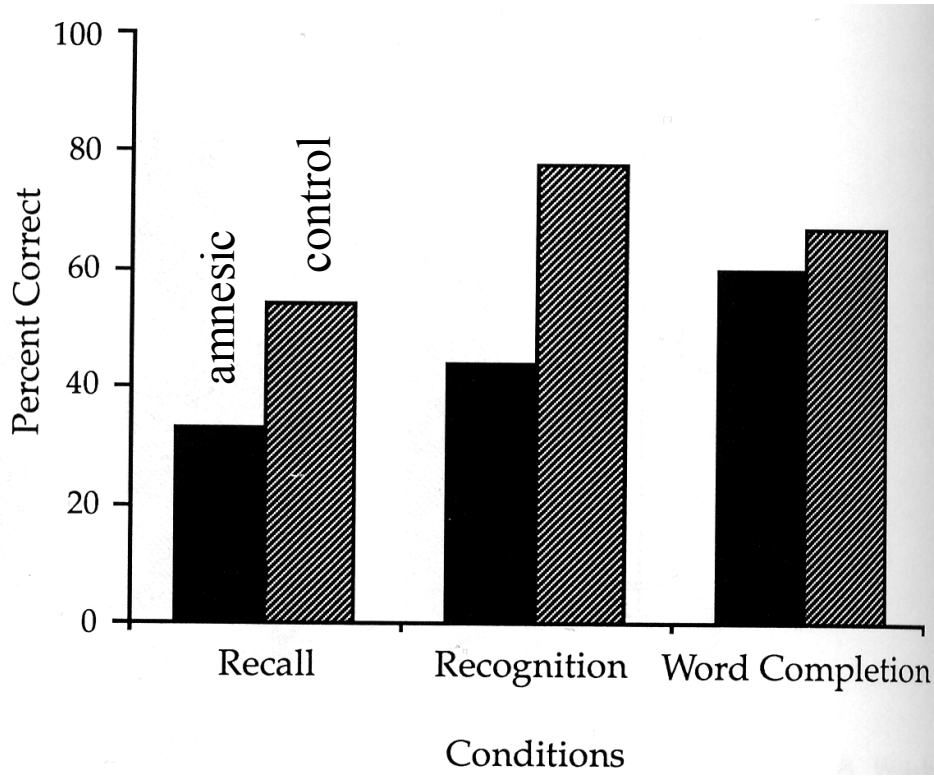
George Santayana, 1863–1952

Amnesia… a problem with *retrieval?*

ABSENT	ABS_____
INCOME	INC_____
FILLY	FIL_____
DISCUSS	DIS_____
CHEESE	CHE_____
ELEMENT	ELE_____



Graf et al. (1984)



Warrington & Weiskrantz (1970)

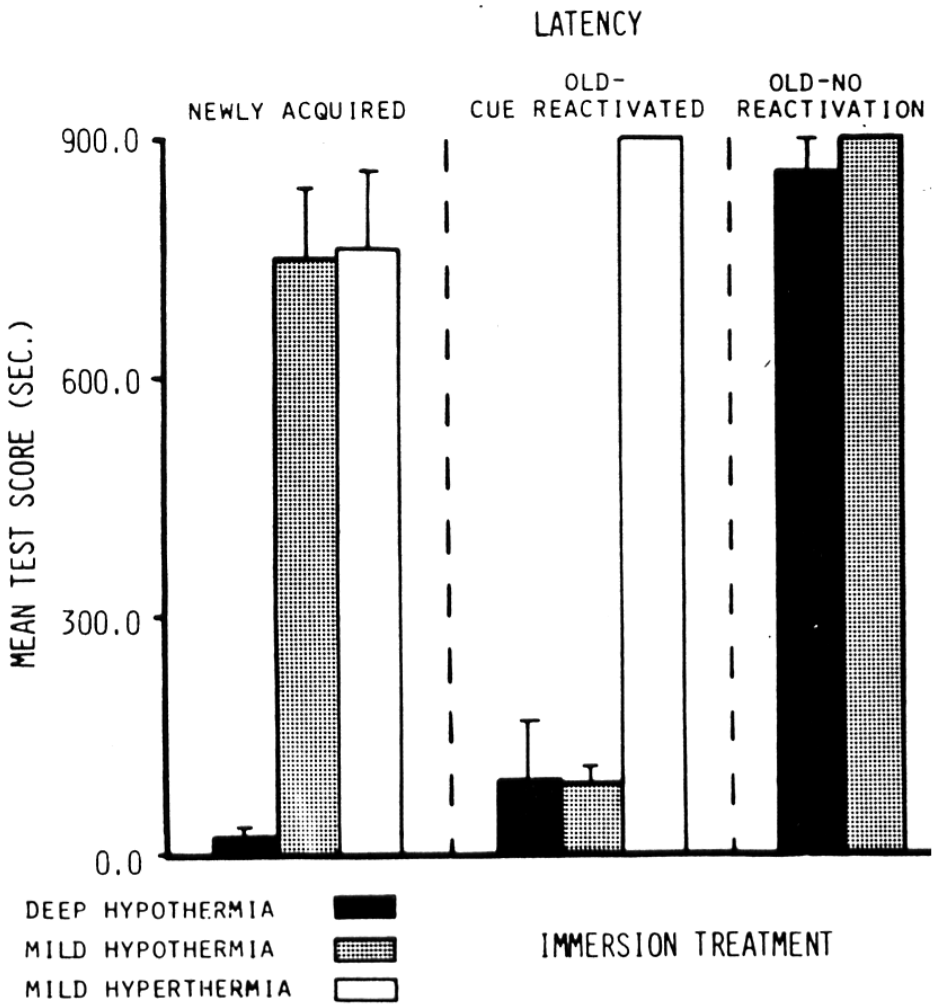
‘Loss’ of new or reactivated memories following hypothermia

- *Passive avoidance task (black chamber → shock; measure latency to re-enter black chamber). So* ***high latency = good memory.***
- ***Hypothermia*** *(21°C) to induce amnesia.*
- *‘Cue reminder’ = putting the animals back in the black chamber briefly (no shock).*

‘Newly acquired’: *training → hypothermia*

‘Old, cue reactivated’: *training → cue reminder → hypothermia*

‘Old, no reactivation’: *training → ... → hypothermia*



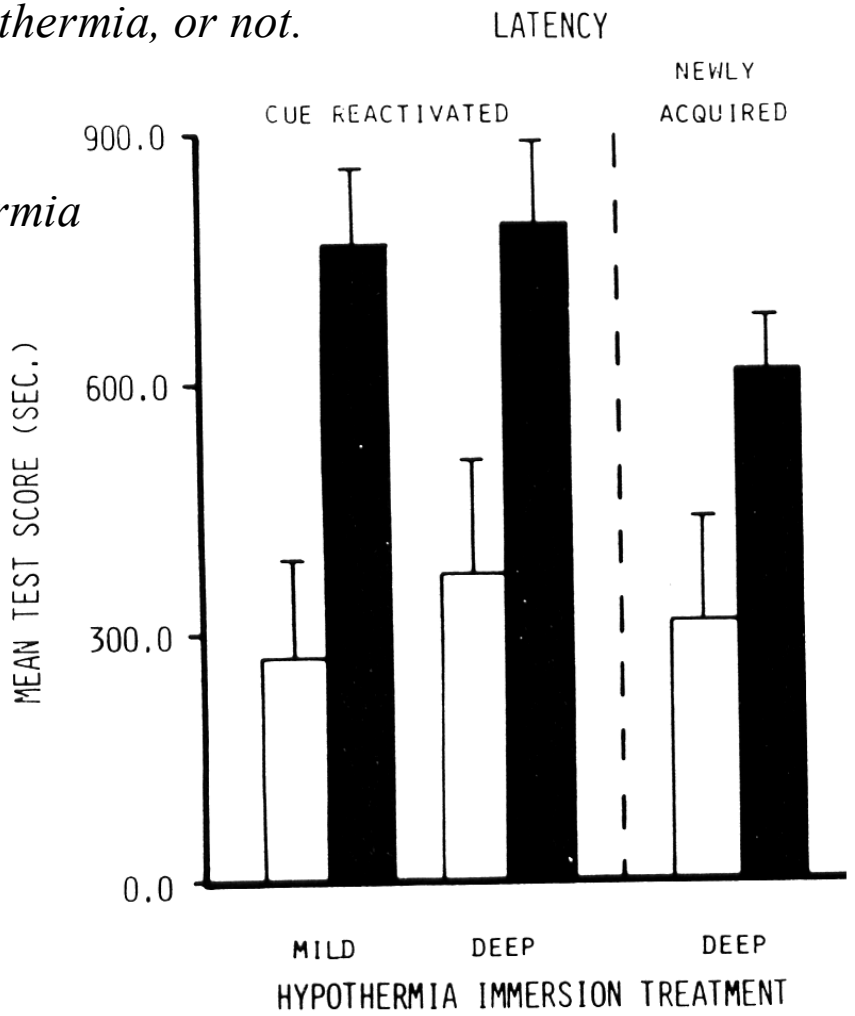
Mactutus et al. (1982), experiment 1

Interfering with reconsolidation… or a problem with *retrieval?*

- *Remember,* ***high latency = good memory.***

'Newly acquired' group: training → hypothermia.
'Cue reactivated' group: training → … → cue reminder → hypothermia.
All groups then receive additional 'reminder' hypothermia, or not.

black = reminder hypothermia
white = no reminder



Mactutus et al. (1982), experiment 6

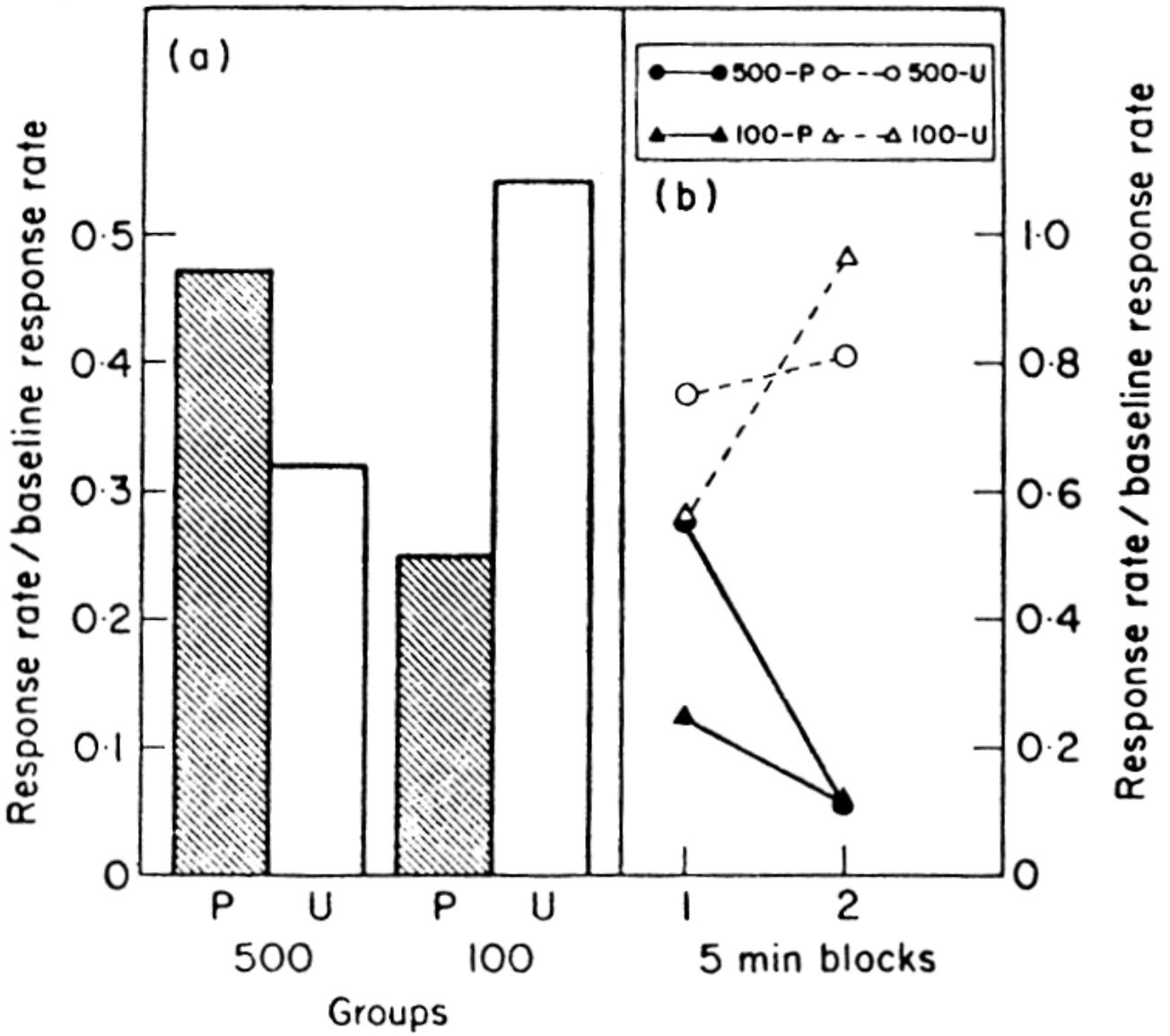
Amnesia and interference with reconsolidation…

"Common to the amnesias for both new and old learning is a striking persistence of the original information."

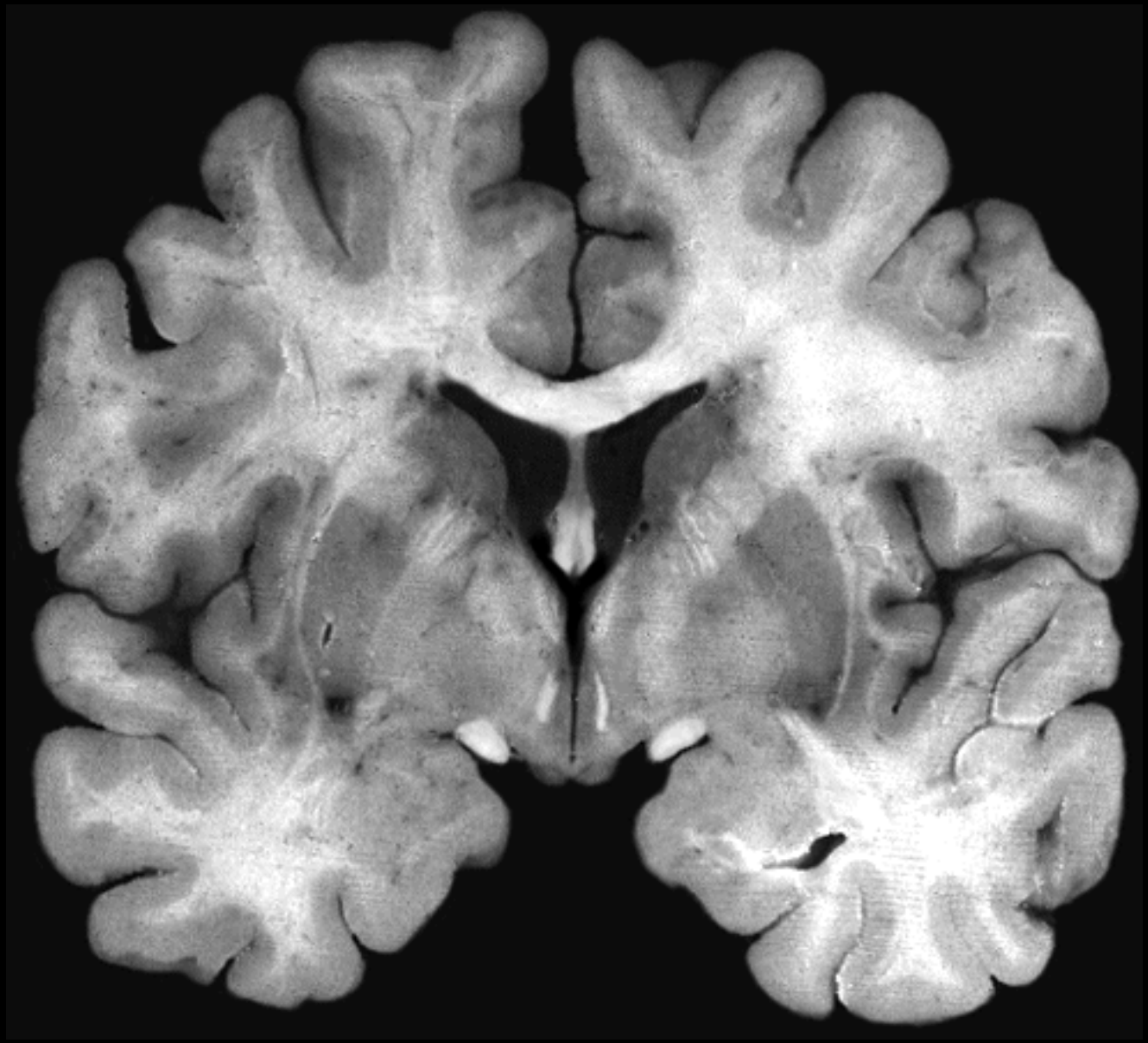
Mactutus et al. (1982)

Habit learning

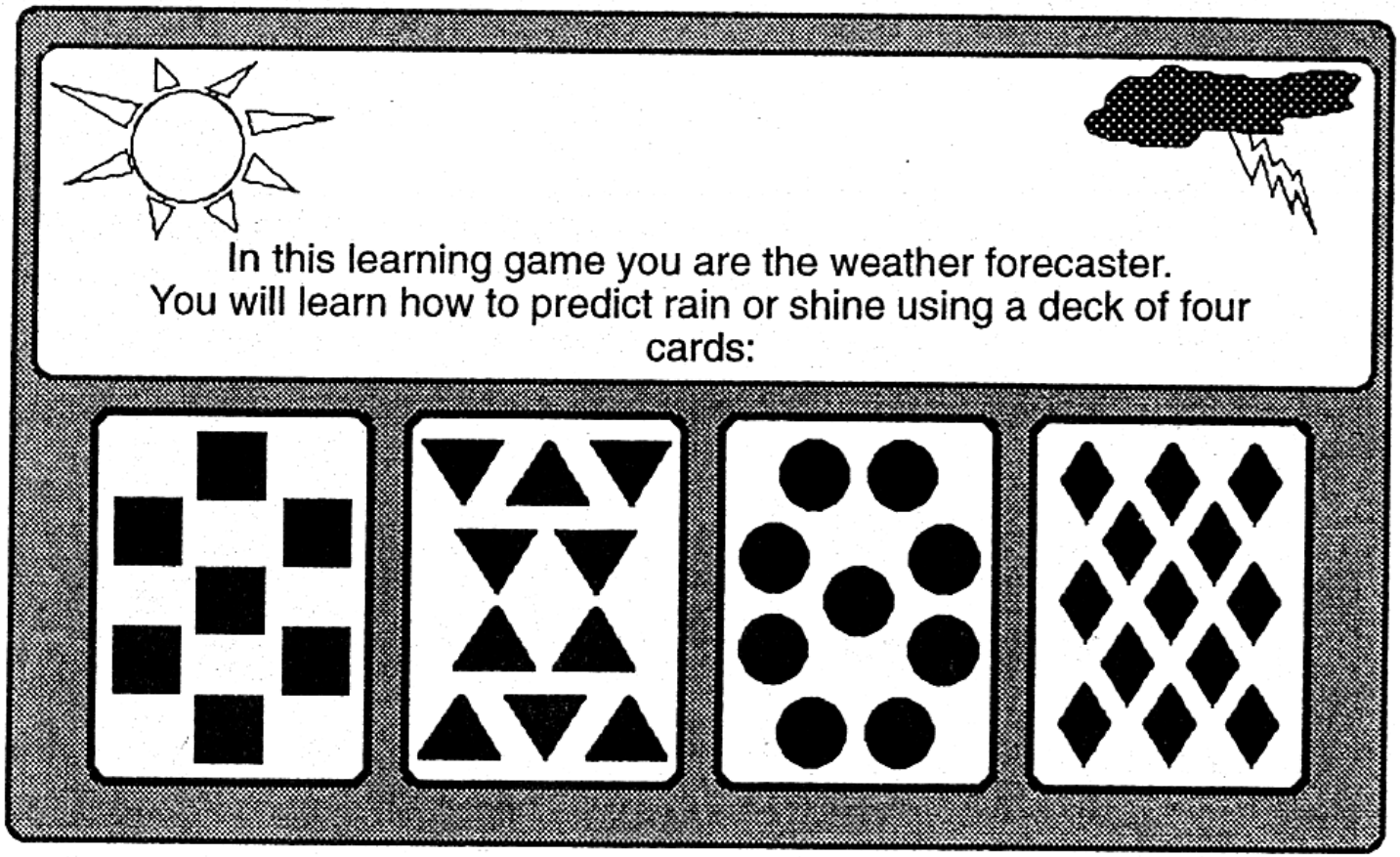
Habits and learning theory



Adams (1982)



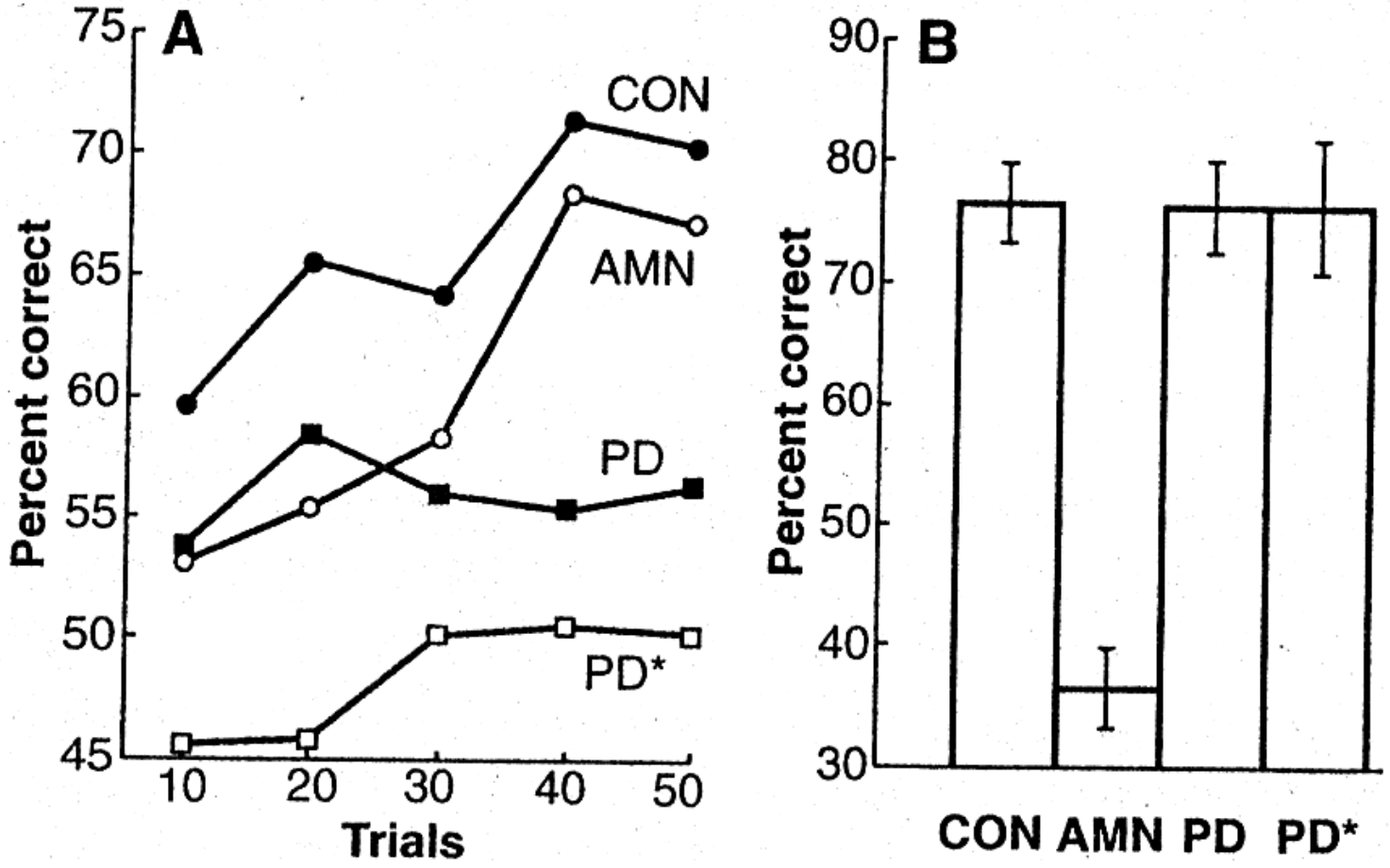
A double dissociation between PD and amnesiacs (1)



- ***Task 1 (probabilistic classification):*** *one to three cards are shown. The subject must predict sunshine or rain. Feedback is provided (correct/incorrect). One cue is associated with sunshine on 25% of occasions; one on 43% of occasions; one 57%; one 75%.*
- ***Task 2 (declarative):*** *memory for features of the game (screen layout, cues, etc.) is tested with four-way multiple-choice questions.*

Knowlton et al. (1996)

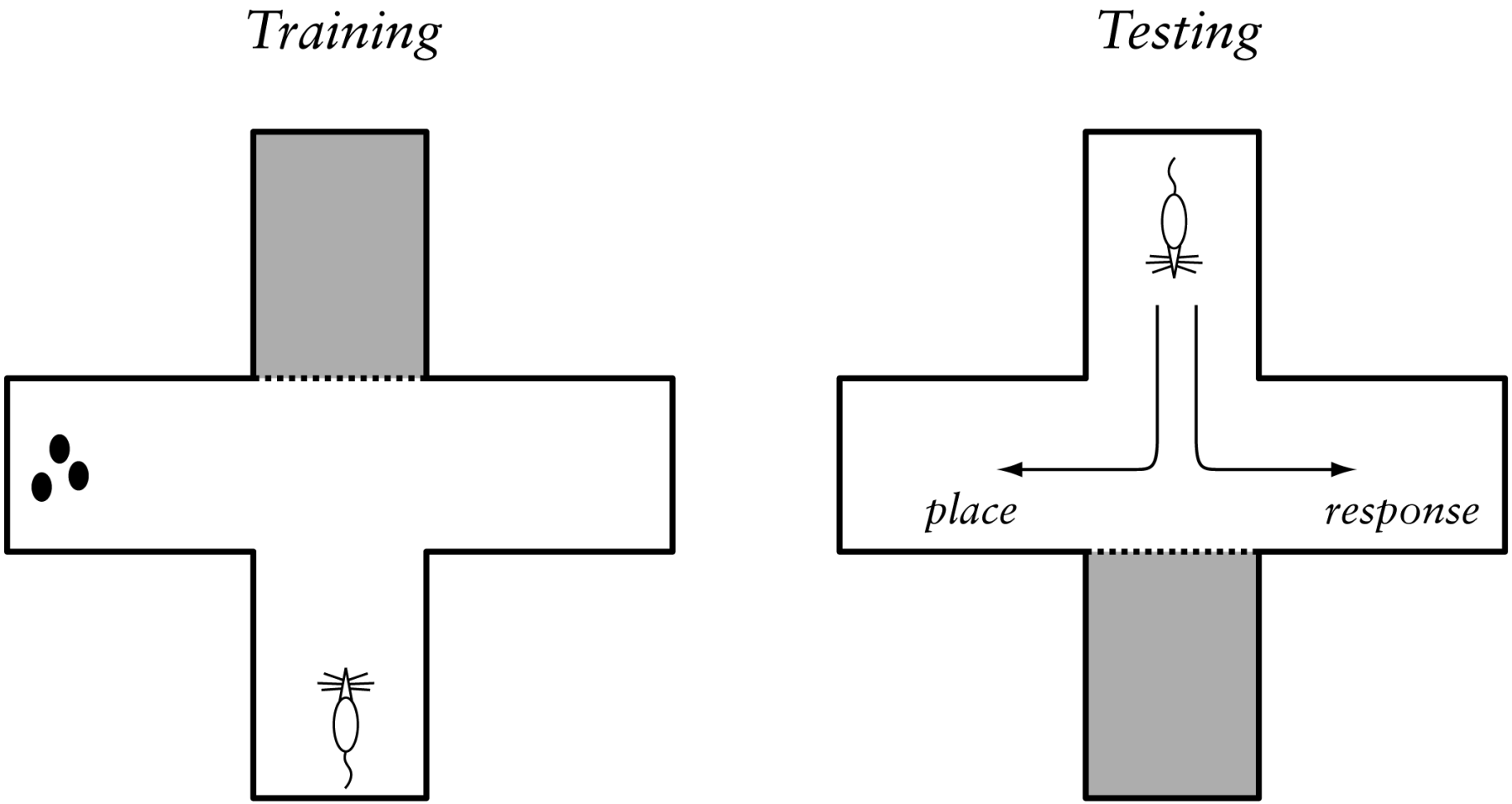
A double dissociation between PD and amnesiacs (2)



- ***PD patients:*** *impaired on probabilistic classification task, not declarative. (PD* = severe.)*
- ***Amnesic patients (with bilateral hippocampal damage or midline diencephalic damage):*** *impaired on declarative task, not probabilistic classification.*

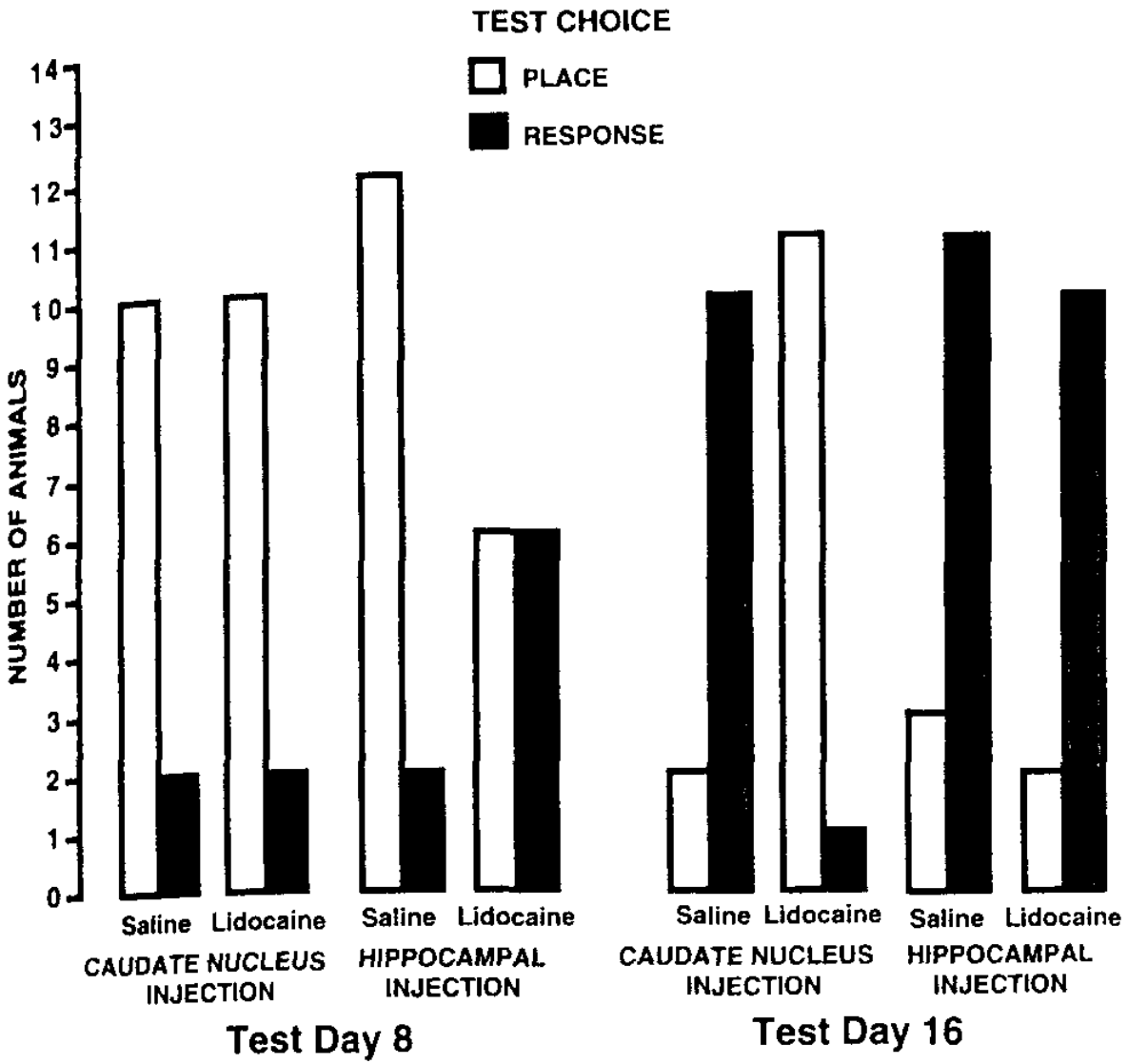
Knowlton et al. (1996)

Habits and the dorsal striatum (1)



Packard & McGaugh (1996)

Habits and the dorsal striatum (2)



Packard & McGaugh (1996)