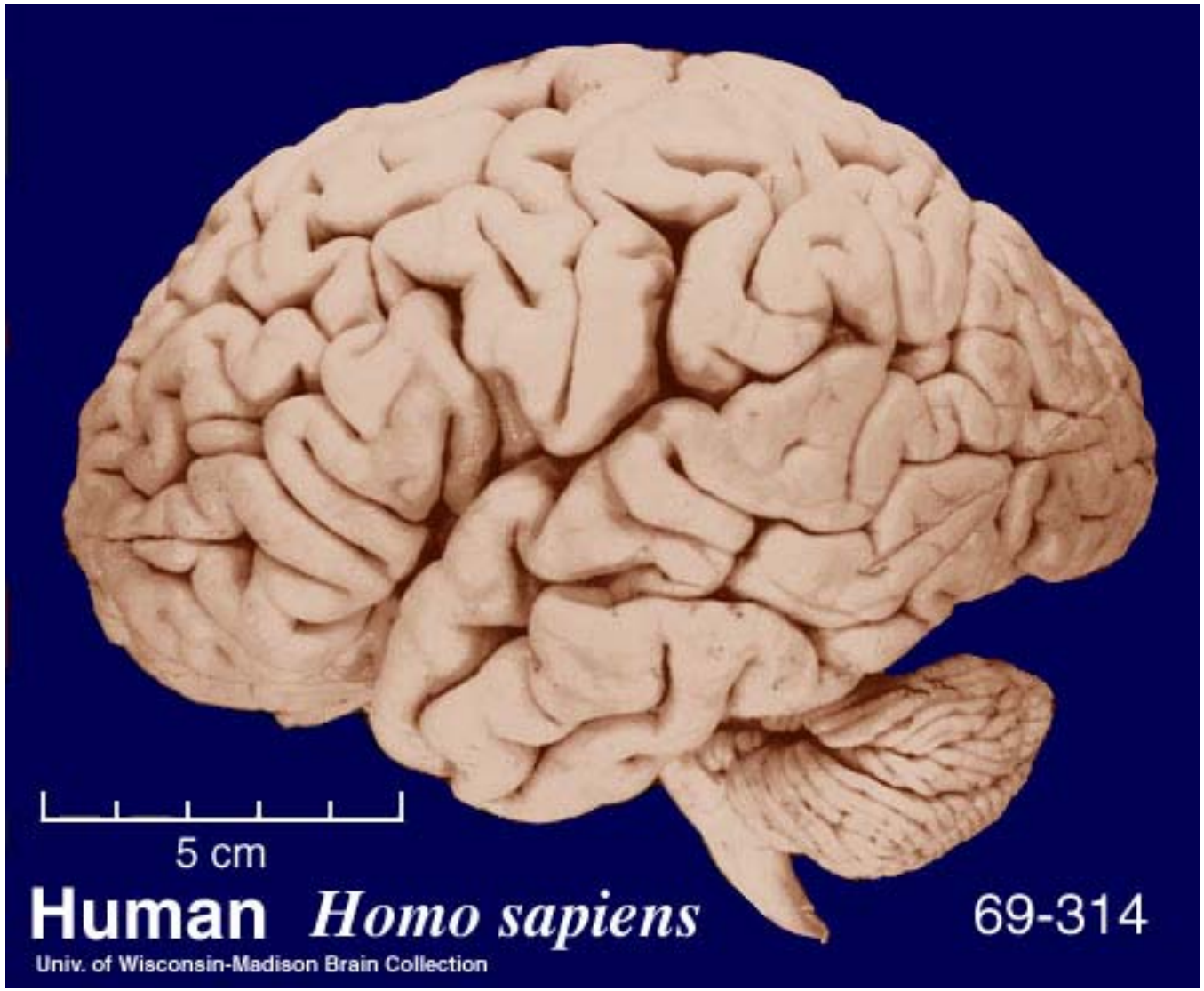
9.00 MEMORY II: AMNESIA & MEMORY SYSTEMS

Professor John Gabrieli



MEMORY

- **Anterograde Amnesia**
- **Retrograde Amnesia**
- **Memory Systems**

Anterograde Amnesia

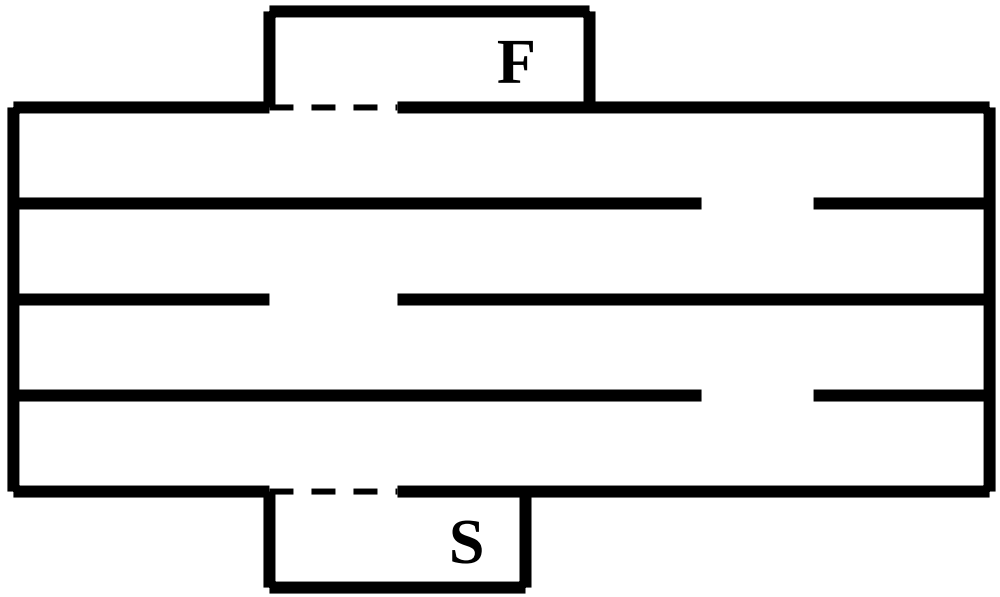
inability to remember new information such as events you experience or facts you encounter

Is memory in the brain *distributed* or *localized*???

"It is not possible to demonstrate the isolated localization of a memory trace anywhere in the nervous system…The engram is represented throughout the region"

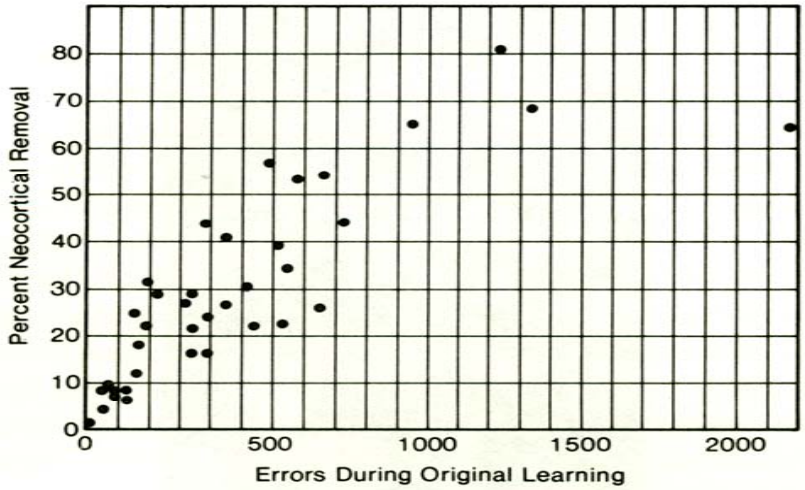
Karl Lashley 1950

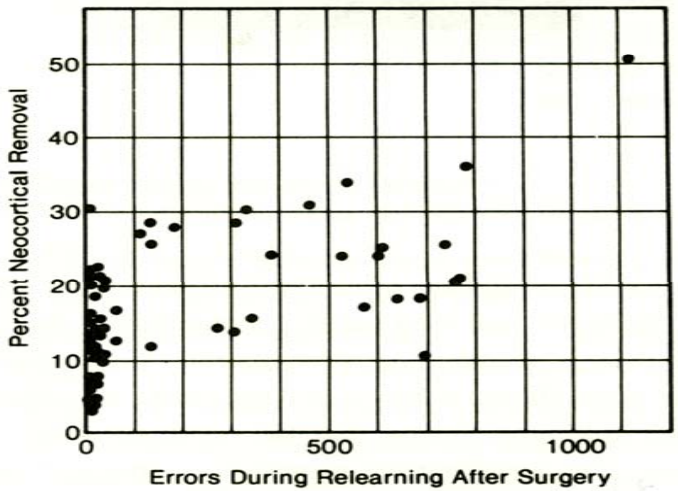
Maze



more cortical brain injury results in worse learning and memory regardless of lesion (injury) location

mass action for distributed memory

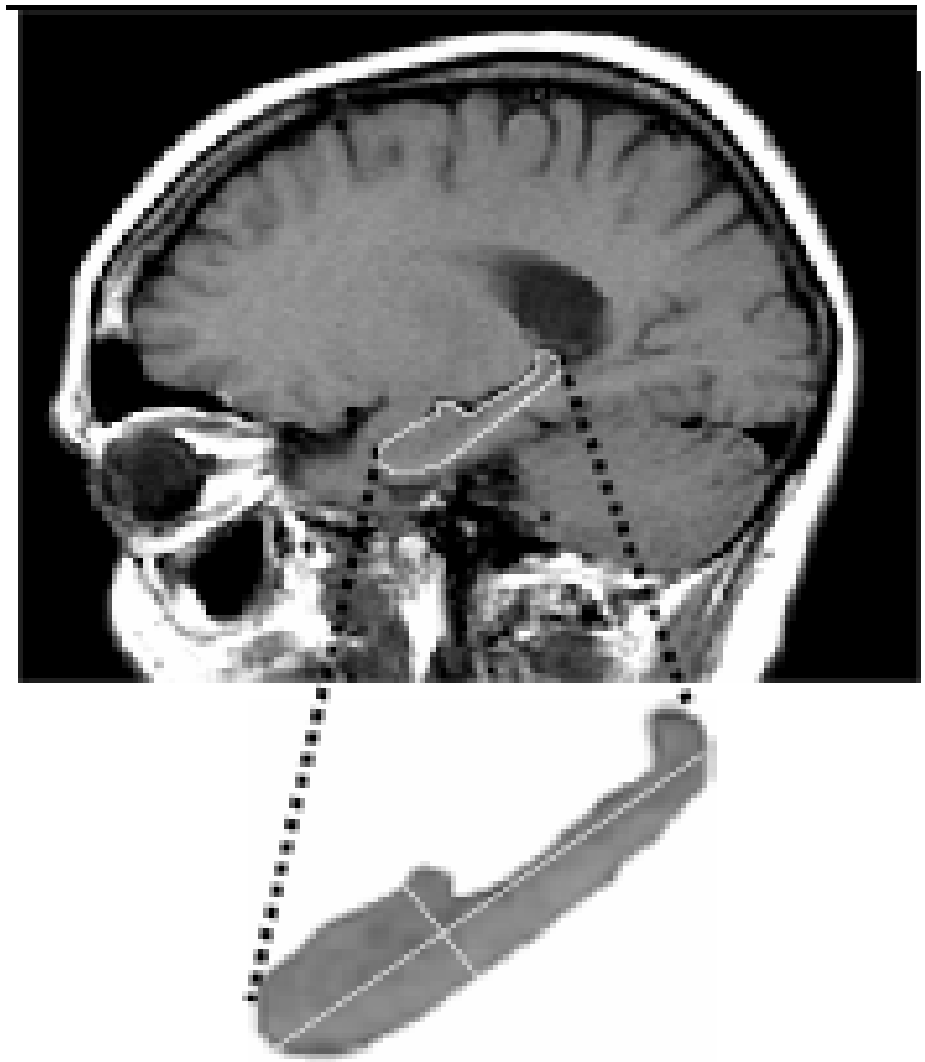




Relationship between extent of injury and errors in learning and relearning the Lashley III maze. Data from Lashley, K.S. "Brain mechanisms and intelligence: A quantitative study of injuries to the brain." University of Chicago Press, 1929.

Location of hippocampus

Image: Public domain (NIH adaptation of Gray's Anatomy).



structural MRI

THE AMNESIC PATIENT H.M.

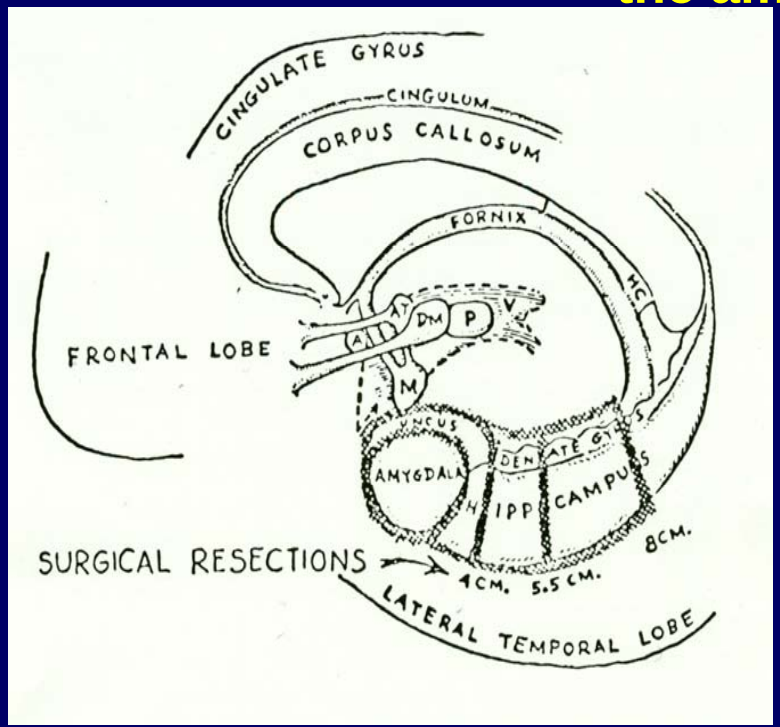
1926 Birth

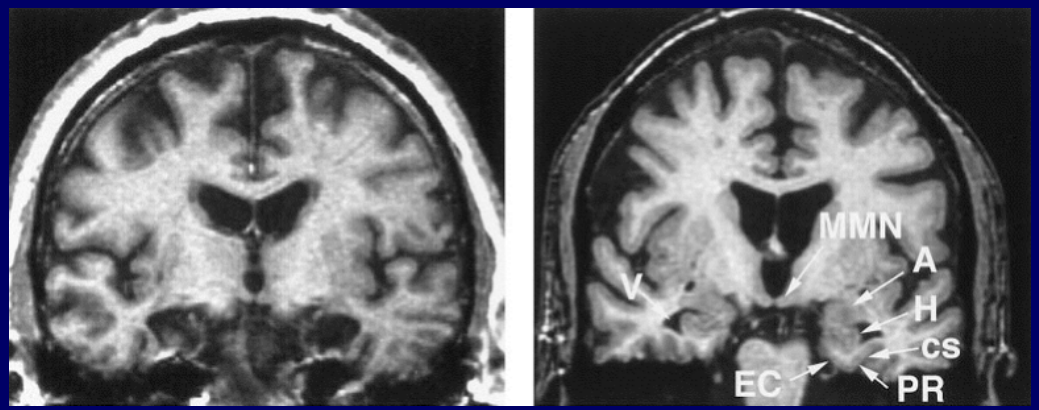
1942 Age 16, First major seizure

1953 Age 27, Bilateral medial temporal-lobe resection

1955 Report of pervasive and profound anterograde amnesia by Dr. Brenda Milner

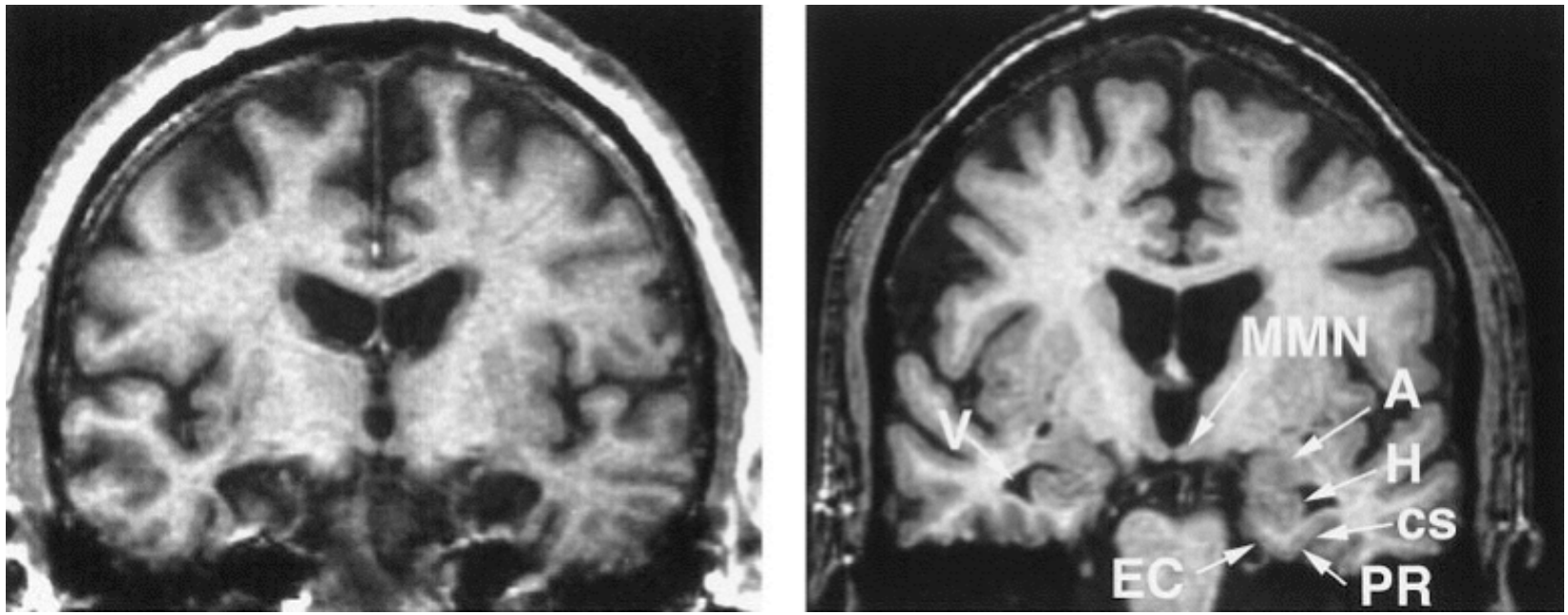
1962 Neuropsychological examinations characterizing the amnesic syndrome





Hippocampus and entorhinal cortex (H and EC) in normal subject (left), but absent in patient H. M. (right)

H.M.



GLOBAL IMPAIRMENT OF LEARNING IN MEDIAL TEMPORAL-LOBE AMNESIA

Assessment of Explicit Remembering	*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**
	Mazes	
Learning to criterion	**Public events, Personal events**	

“Every day is alone in itself, whatever joy I’ve had and whatever sorrow I’ve had.” (Milner et al, 1968)

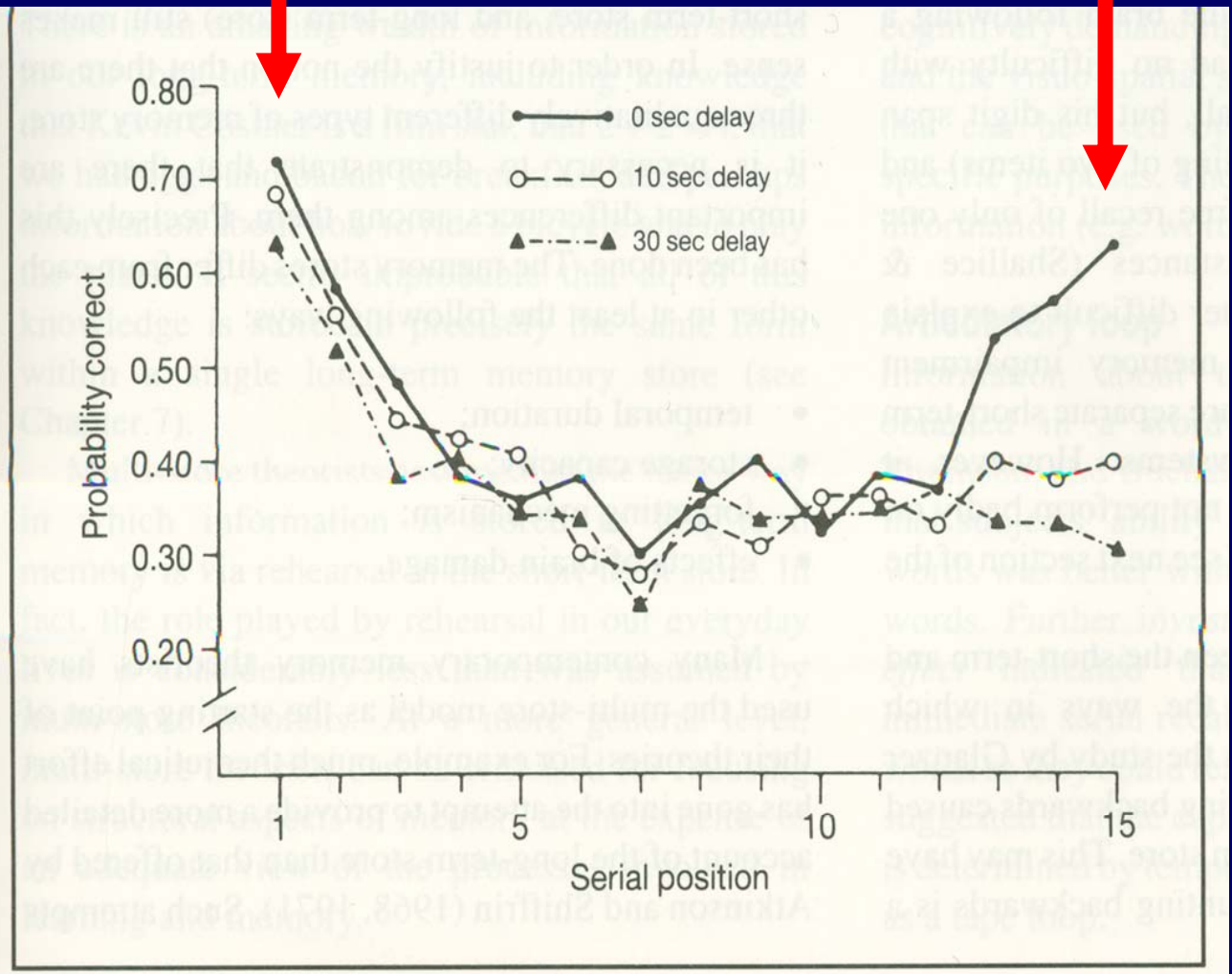
Right now I’m wondering. Have I done or said anything amiss? You see, at this moment everything looks clear to me, but what happened just before? That’s what worries me. It’s like waking from a dream; I just don’t remember.” (Milner, 1970)

HM
Henry Molaison
1926-2008

Photos of patient HM removed due to copyright restrictions.

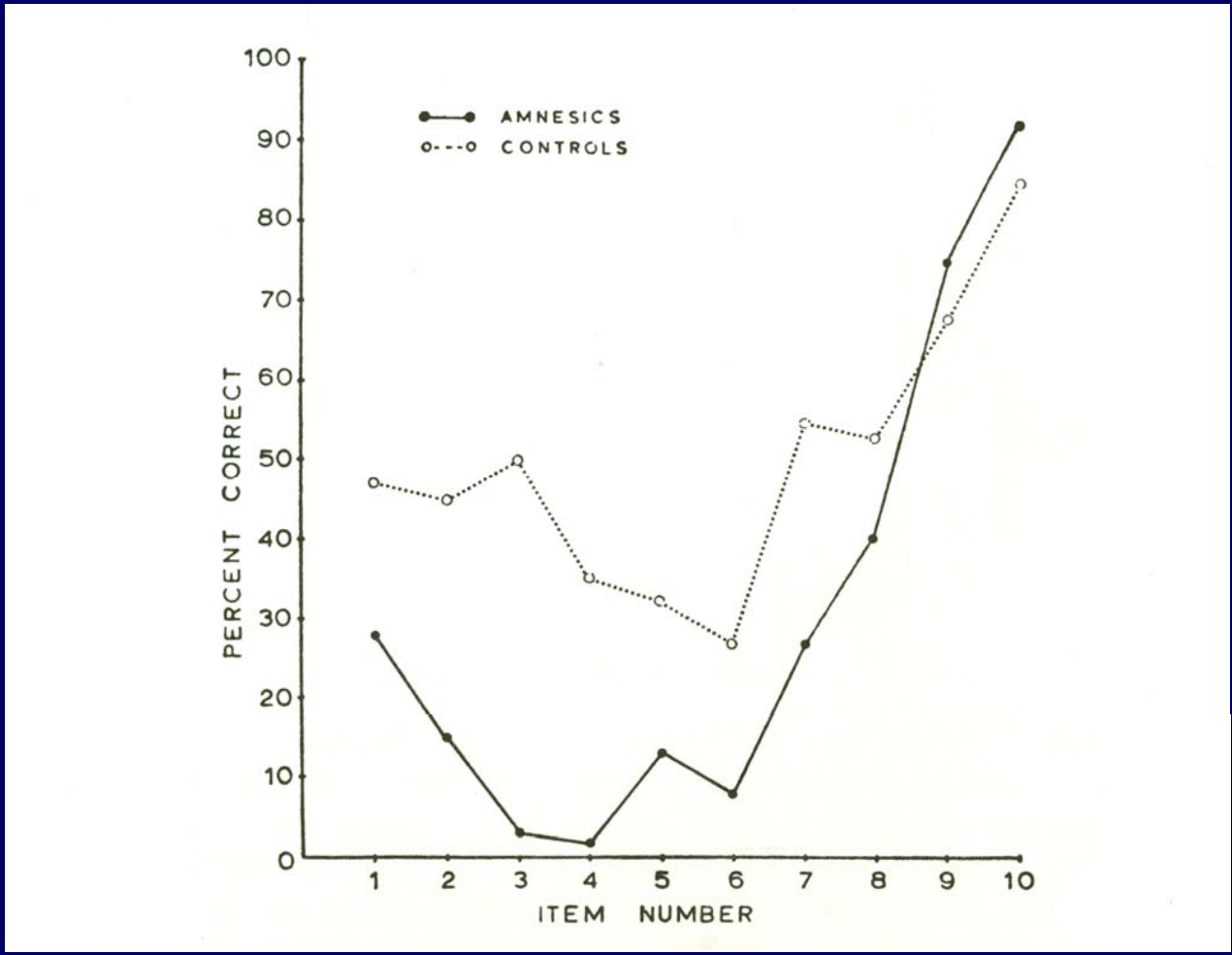
See http://thebrainobservatory.ucsd.edu/content/120209

Primacy Effect = LTM Recency Effect = STM



Intact Recency in Amnesia = Intact STM

Impaired Primacy in Amnesia = Impaired LTM



 Source: Baddeley, A. D., and E. K. Warrington. "Amnesia and the Distinction Between Long- and Short-Term Memory." *Journal of Verbal Learning and Verbal Behavior* 9, no. 2 (1970): 176-89.

Span of 4: 6 1 9 4

Span of 5: 3 7 8 5 2

Span of 6: 9 6 5 2 8 3

Span of 7: 4 2 6 9 8 5 1

Span of 8: 8 1 6 3 7 2 4 9

Span of 9: 6 2 5 7 3 4 9 8 1

Span of 10: 9 3 8 2 4 7 1 5 3 6

Span of 11: 5 8 1 4 7 9 3 2 6 1 7

Digit Span Test: (*hypothetical responses*)

5 7 (correct)
9 1

3 6 1 (correct)
7 2 4

6 1 3 9 (correct)
7 2 5 3

8 4 5 2 6 (correct)
3 6 2 7 5

5 7 4 2 9 8 (correct)
9 3 8 2 7 4 (correct)

5 2 4 8 2 5 7 (correct)
1 7 3 8 5 9 6 (correct)

3 8 4 6 9 1 2 5 (incorrect)
2 6 3 7 4 9 5 1 (incorrect)

3 5 1 7 4 8 2 9 6
8 3 5 1 7 9 6 2 4

Span = 7 digits
Superspan = 8 digits

Hebb Digit Procedure (test at superspan)

8 2 3 6 5 7 9 1 (nonrecurrent sequence)

4 6 1 7 3 8 9 2

2 7 4 3 6 8 5 1 (recurrent sequence)

7 3 5 2 6 1 8 4

2 6 5 9 3 7 1 8

2 7 4 3 6 8 5 1 (recurrent sequence)

7 4 2 6 8 3 1 9

2 9 6 8 1 7 4 3

2 7 4 3 6 8 5 1 (recurrent sequence)

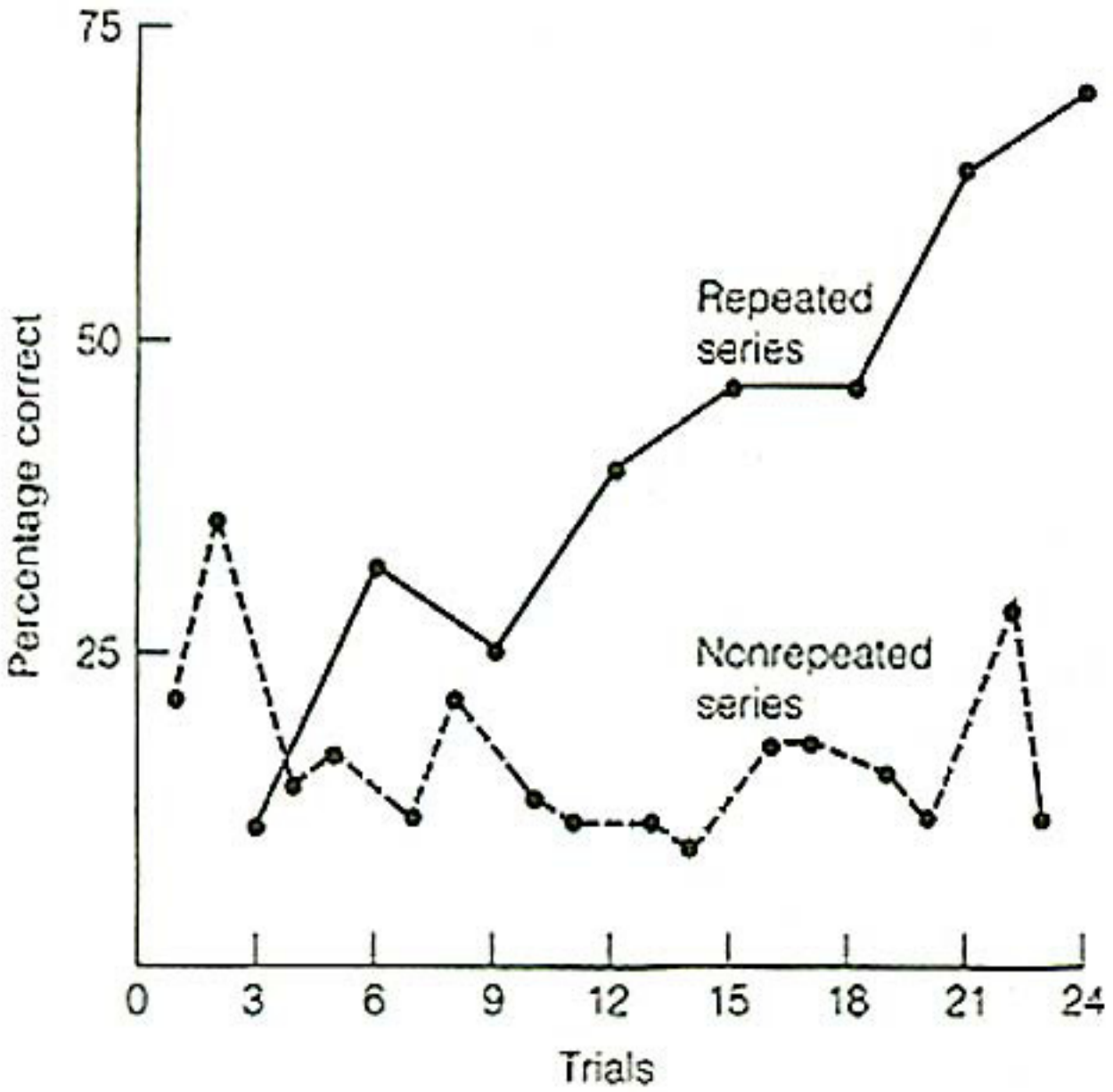
- (nonrecurrent sequence)

  (nonrecurrent sequence)

  (recurrent sequence)
-

repetition makes a LTM beyond STM

but not in HM



VISUO-SPATIAL STM & LTM (repeated superspan sequences)

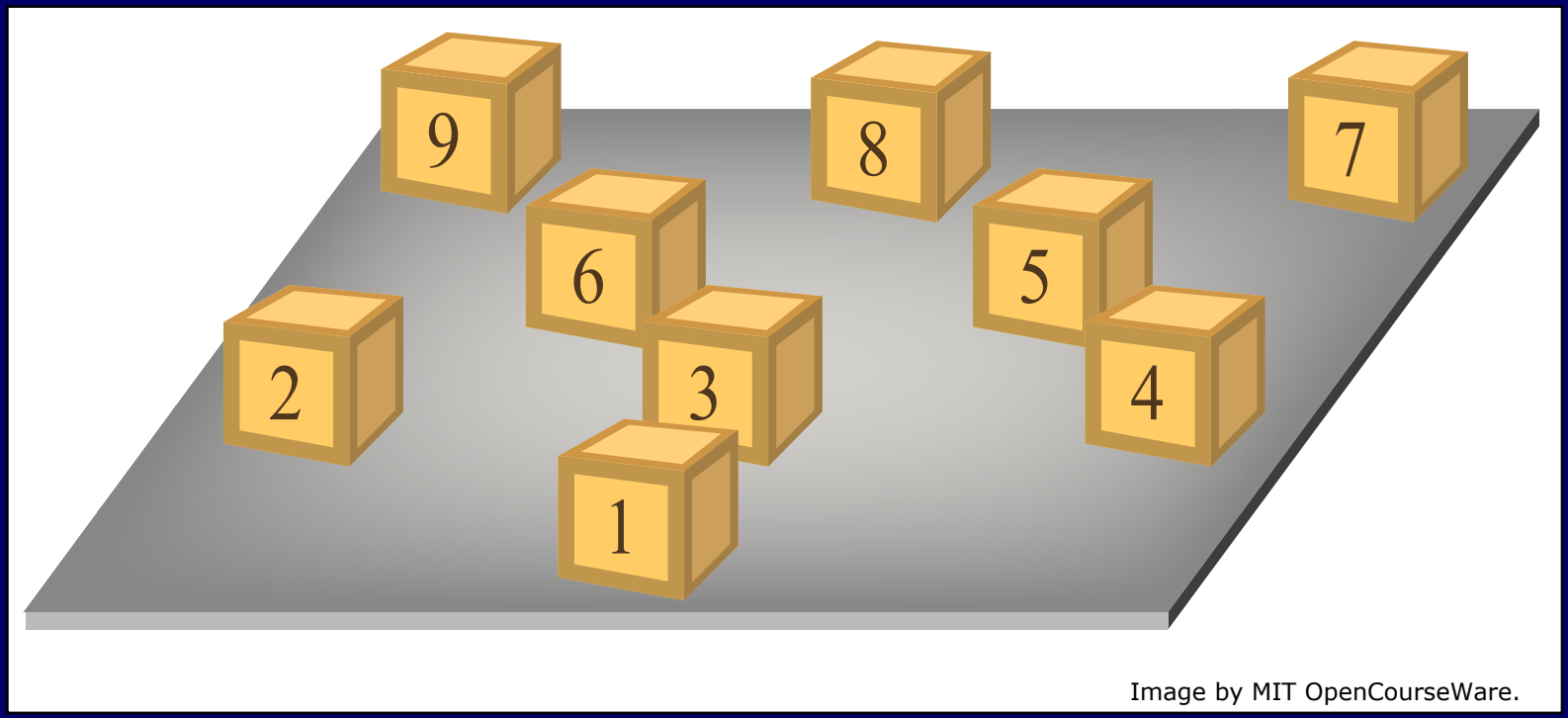


Image by MIT OpenCourseWare.

remove left hippocampus - intact verbal STM, impaired verbal LTM, no effect of removal of right hippocampus

remove right hippocampus - intact spatial STM, impaired spatial LTM, no effect of removal of left hippocampus

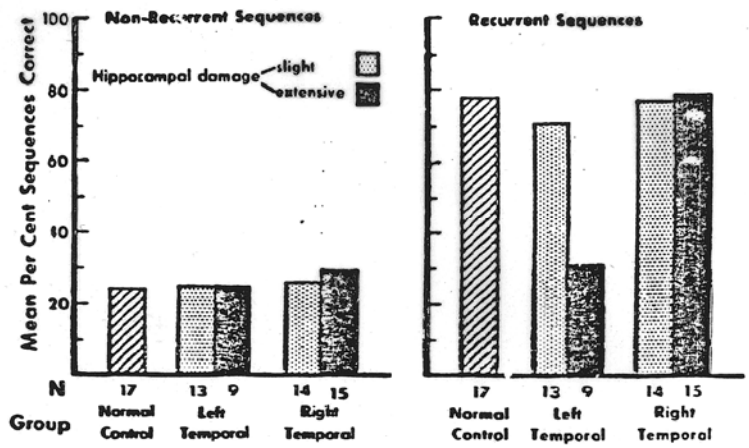


Fig. 6. Digit-sequences task: mean scores for normal control subjects and for left and right temporal-lobe subgroups tested preoperatively. On the left, performance on the non-recurrent sequences; on the right, the more efficient recall of the recurrent sequence by all groups, except those patients with extensive left hippocampal damage.

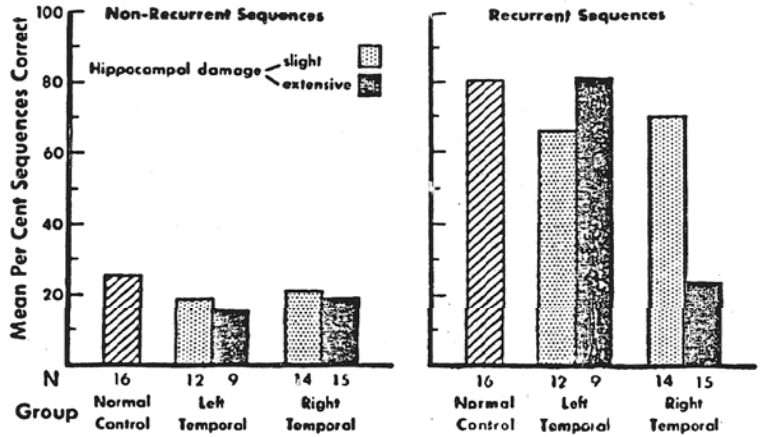
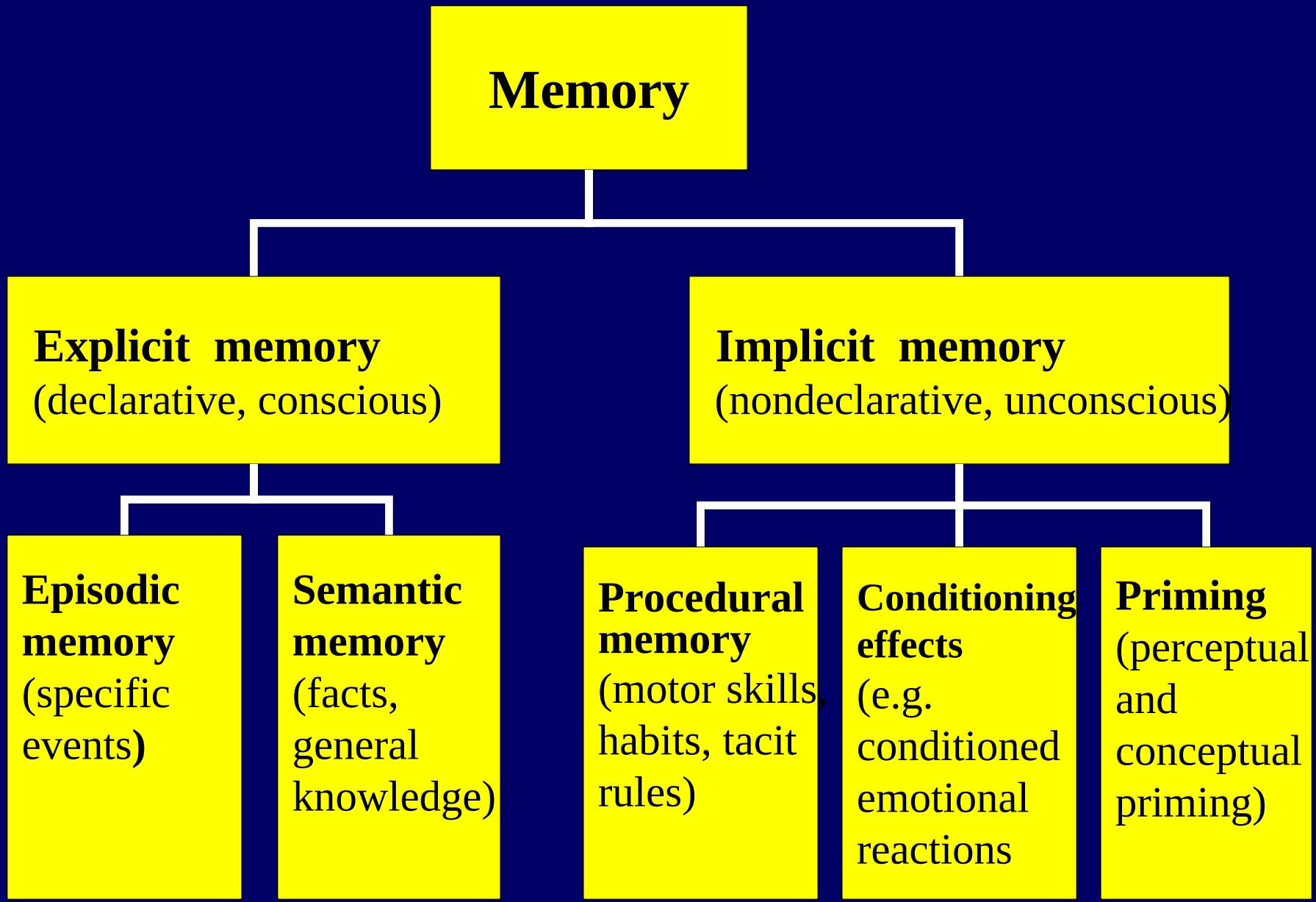


Fig. 7. Block-tapping task: mean scores for normal control groups and for left and right temporal-lobe subgroups tested preoperatively. On the left, performance on the non-recurrent sequences; on the right the more efficient recall of the recurrent sequence by all groups, except those patients with extensive right hippocampal damage.


Memory
Explicit memory
(declarative, conscious)
Implicit memory
(nondeclarative, unconscious)
Episodic memory
(specific events)
Semantic memory
(facts, general knowledge)
Procedural memory
(motor skills, habits, tacit rules)
Conditioning effects
(e.g. conditioned emotional reactions
Priming
(perceptual and conceptual priming)

Episodic Memory

Memory for events

- time

- space

Semantic Memory

Generic knowledge of facts

H.M.'s Definitions for Words and Phrases Entering the Language after the Onset of His Amnesia

WORD/PHRASE	FOUR-CHOICE RECOGNITION
amniocentesis	an infectious, inflammatory disease of the intestines
apartheid	the separation of young cows that have not yet given birth to calves
boat people	people who cater bon voyage parties
brain wash	the fluid that surrounds and bathes the brain
granola	a portable keyboard wind instrument
software	expensive clothing made of a soft, twilled fabric

MEMORY I *Anterograde Amnesia*

1. Lashley & the distributed/localized dichotomy

2. H.M. & anatomy of human amnesia
   - Medial temporal region/hippocampus

3. Spared immediate memory/impaired new learning
   - Primacy/recency distinction
   - Hebb repeating digits

4. Material-specific amnesia
   - left hippocampus & superspan verbal learning
   - right hippocampus & superspan nonverbal learning

5. Semantic/episodic distinction in relation to anterograde amnesia - both kinds of memory impaired

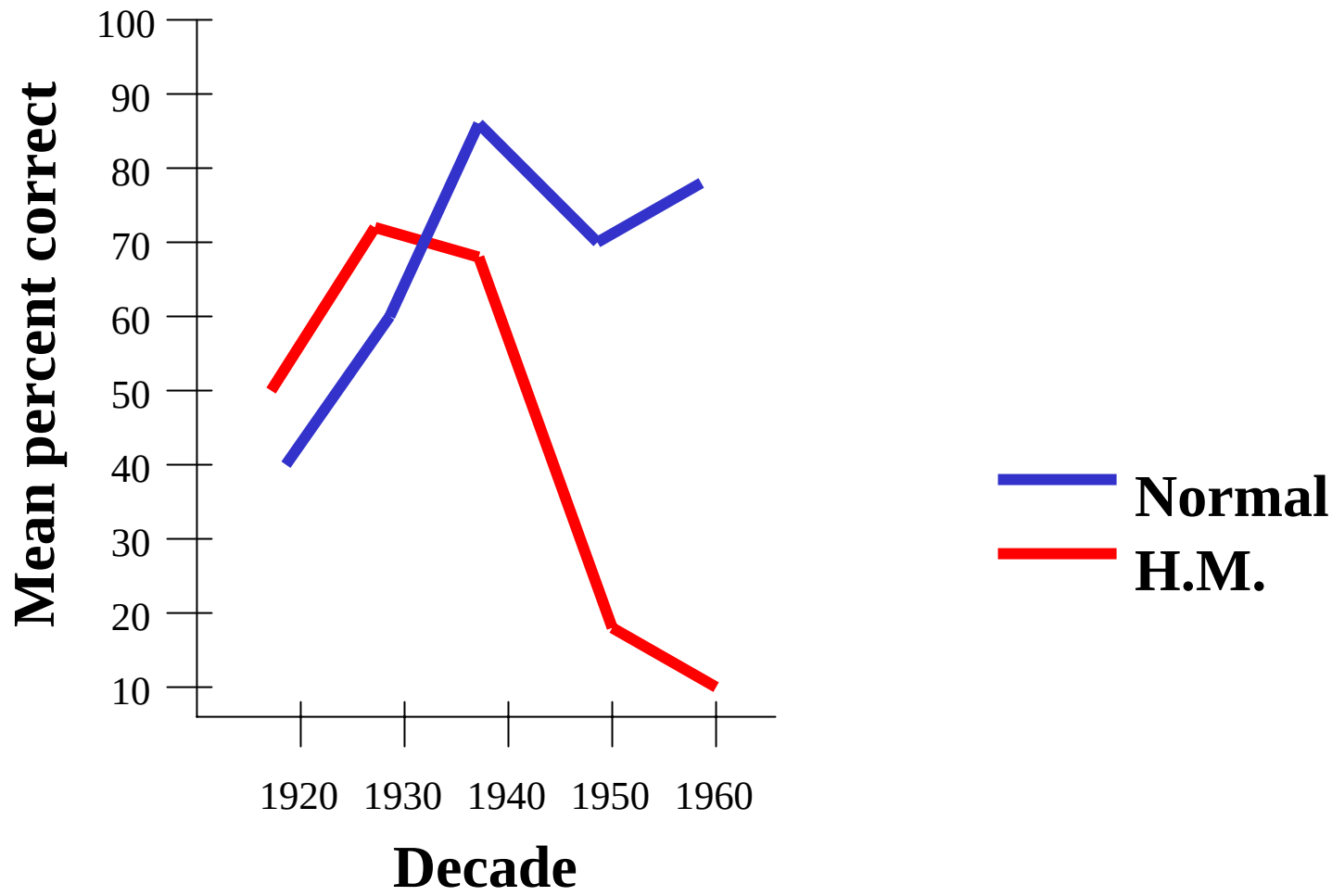
MEMORY II

- **Retrograde Amnesia**

  loss of already known information

Famous Faces

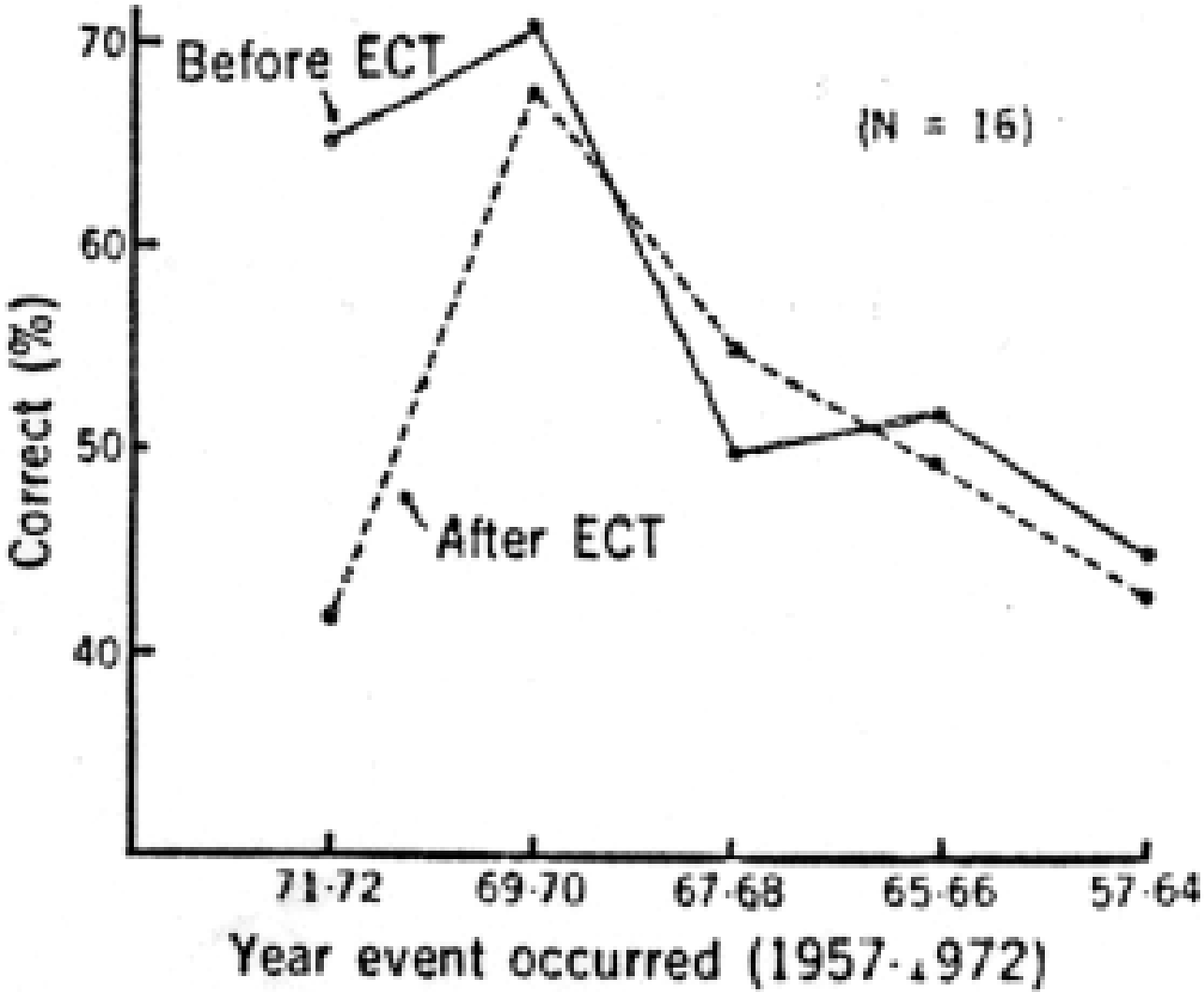
temporally limited retrograde amnesia



**** *** ** *

Bus driver in Washington, DC **drug store Boston** **mattress factory Boston** **hospitalized BostonVA**

- **November 26, 1965** **33 year old male**
  - **-subcutaneous hematoma in right temporal-parietal area**
  - **-stupor, semicomatose, aphasic**
- **December 26, 1965**
  - **-sensorimotor recovery - digit span of 6**
  - **-stated date as 3 or 4 weeks ago**
  - **-severe anterograde amnesia (failed to recognize nurses)**
  - **-believed that he lived in Washington**
- **March 1, 1966**
  - **- anterograde amnesia resolves (learned nurse's names)**
  - **- could not remember moving, accepted living in Boston**
  - **-then that he worked at drug store**
  - **-then that he worked at mattress factory**
  - **-discharged - lost only 24 hours**



 Source: Squire, L. R., and Neal Cohen. "Memory and Amnesia: Resistance to Disruption Develops for Years After Learning." *Behavioral and Neural Biology* 25, no. 1 (1979): 115-25.

evidence in primates for temporally limited retrograde amnesia

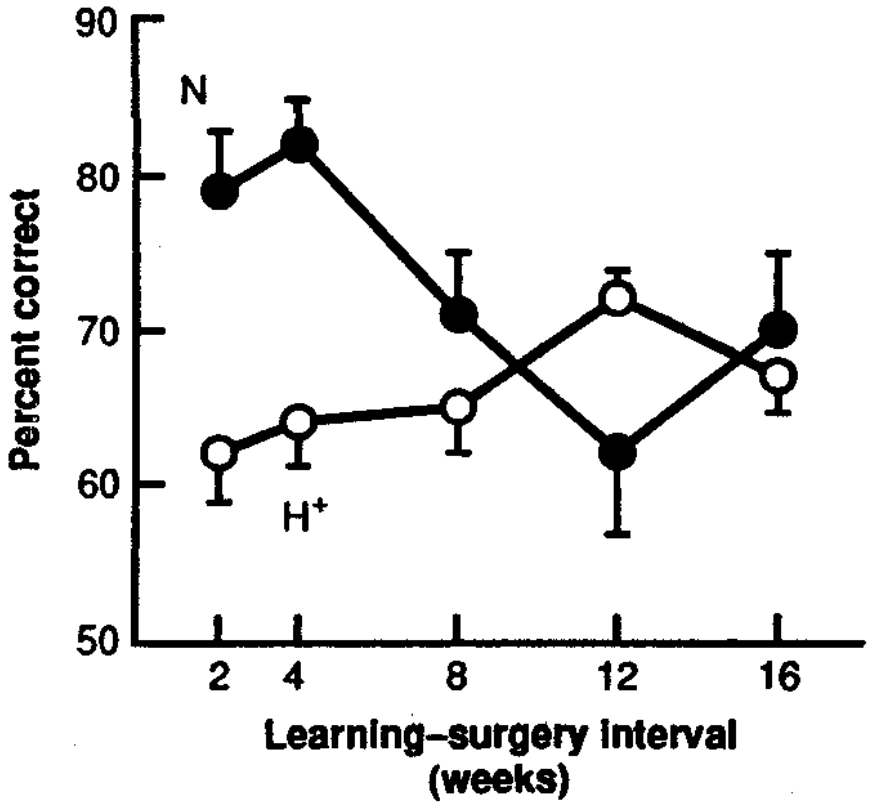
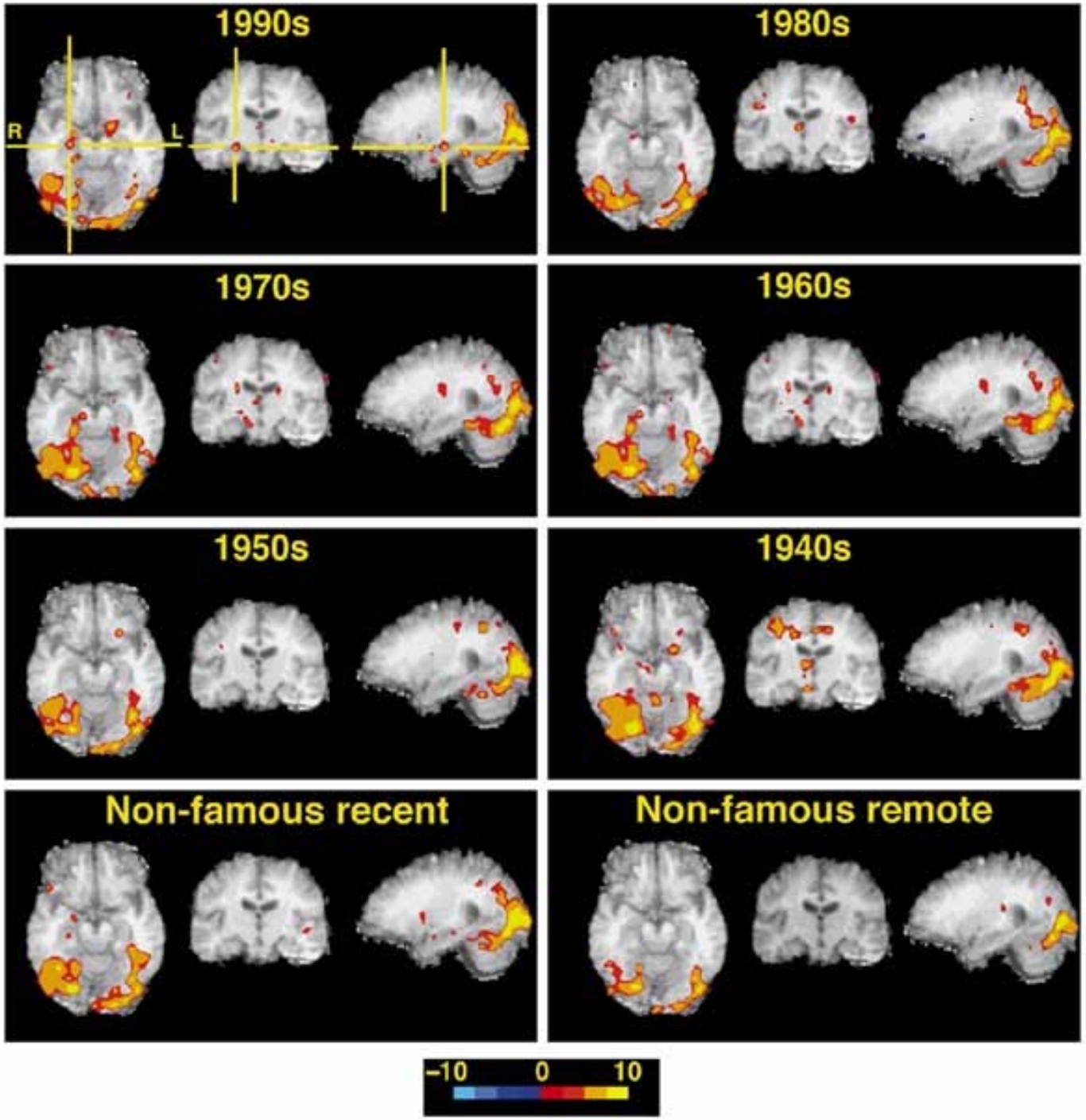


Fig. 2. Retention of 100 object discrimination problems learned approximately 2, 4, 8, 12, and 16 weeks before hippocampal surgery (20 pairs per time period). Retention was assessed 2 weeks after surgery in monkeys with lesions (H^+) (○) ($n = 11$) or after an equivalent interval in unoperated animals (N) (●) ($n = 7$). Brackets show standard error of the mean.

imaging activations for famous faces for different decades



B. Retrograde Amnesia

1. H.M. & Famous Faces
   - remote memory spared in amnesia
   -- hippocampus *not* the long-term site of memory storage
2. Shrinking retrograde amnesia
   - Link between anterograde and retrograde amnesia
3. ECT study
4. Squire & Zola-Morgan monkey study
   -- hippocampus necessary for consolidating a memory for an extended period- once consolidated, hippocampus no longer involved
5. fMRI evidence with famous faces from different decades

MEMORY III

- **Memory Systems**

  specific neural networks that record, retain, and retrieve particular kinds of memory

Memory System

- ***particular*** **neural network**
- ***specific*** **mnemonic process**

Measures of Memory

Explicit (direct)

- Recall
- Cued Recall
- Recognition

Implicit (indirect)

- Skill learning
- Repetition priming
- Conditioning

DECLARATIVE/PROCEDURAL MEMORY DISTINCTION

Declarative Memory

- directly accessible to conscious recollection
- facts and episodes
- knowing that

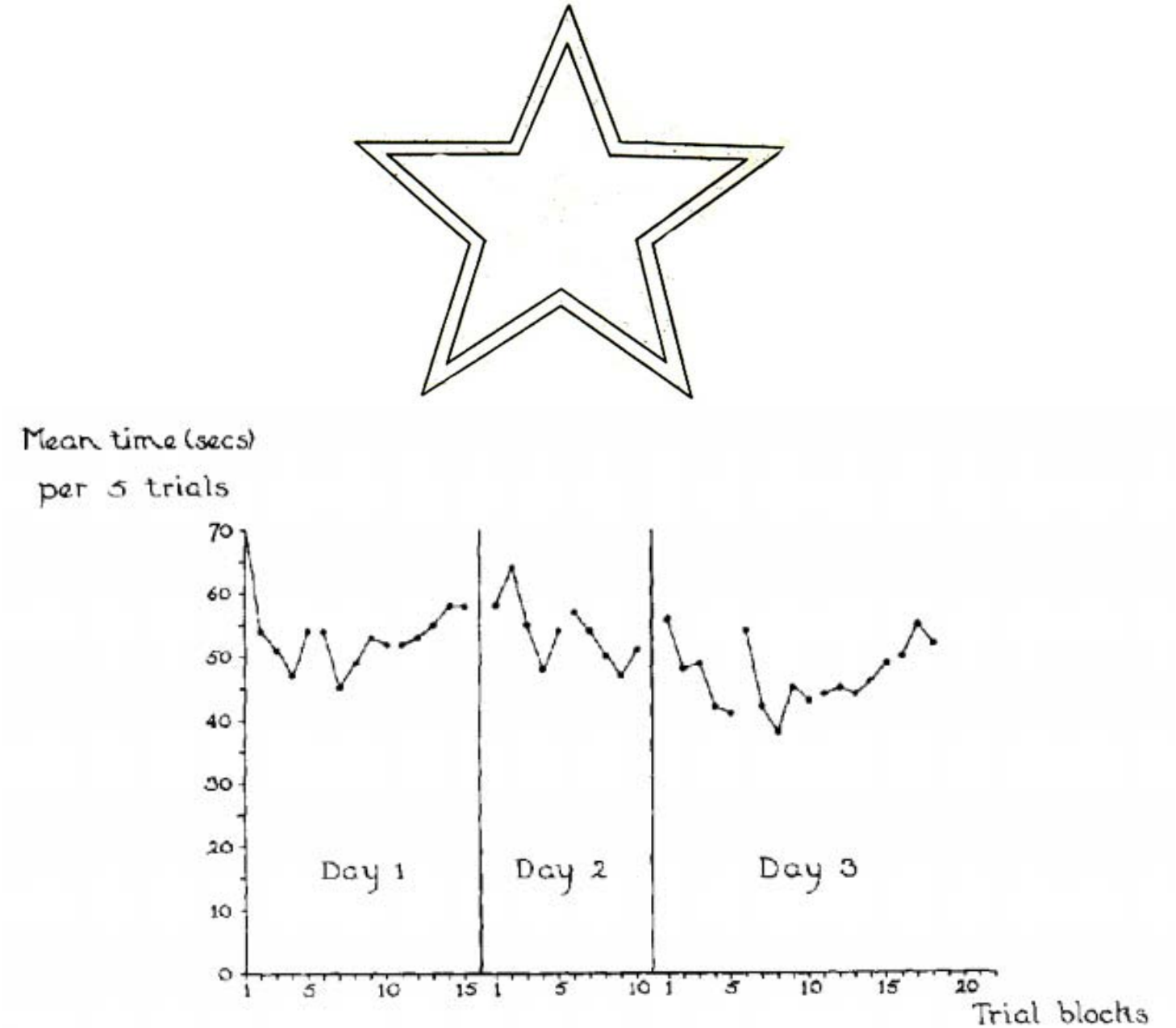
Procedural Memory

- accessible only through performance
- knowing how

SKILL LEARNING

- **Improved performance (accuracy, speed) with practice on a motor, perceptual, or cognitive task**

Image by MIT OpenCourseWare.



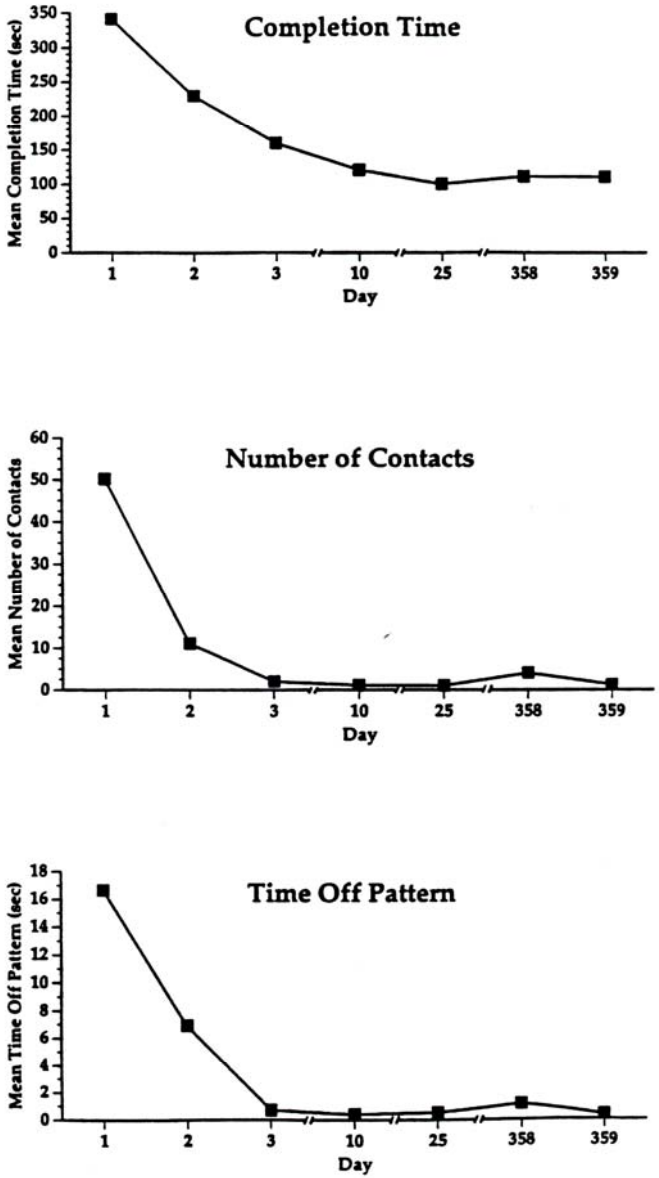
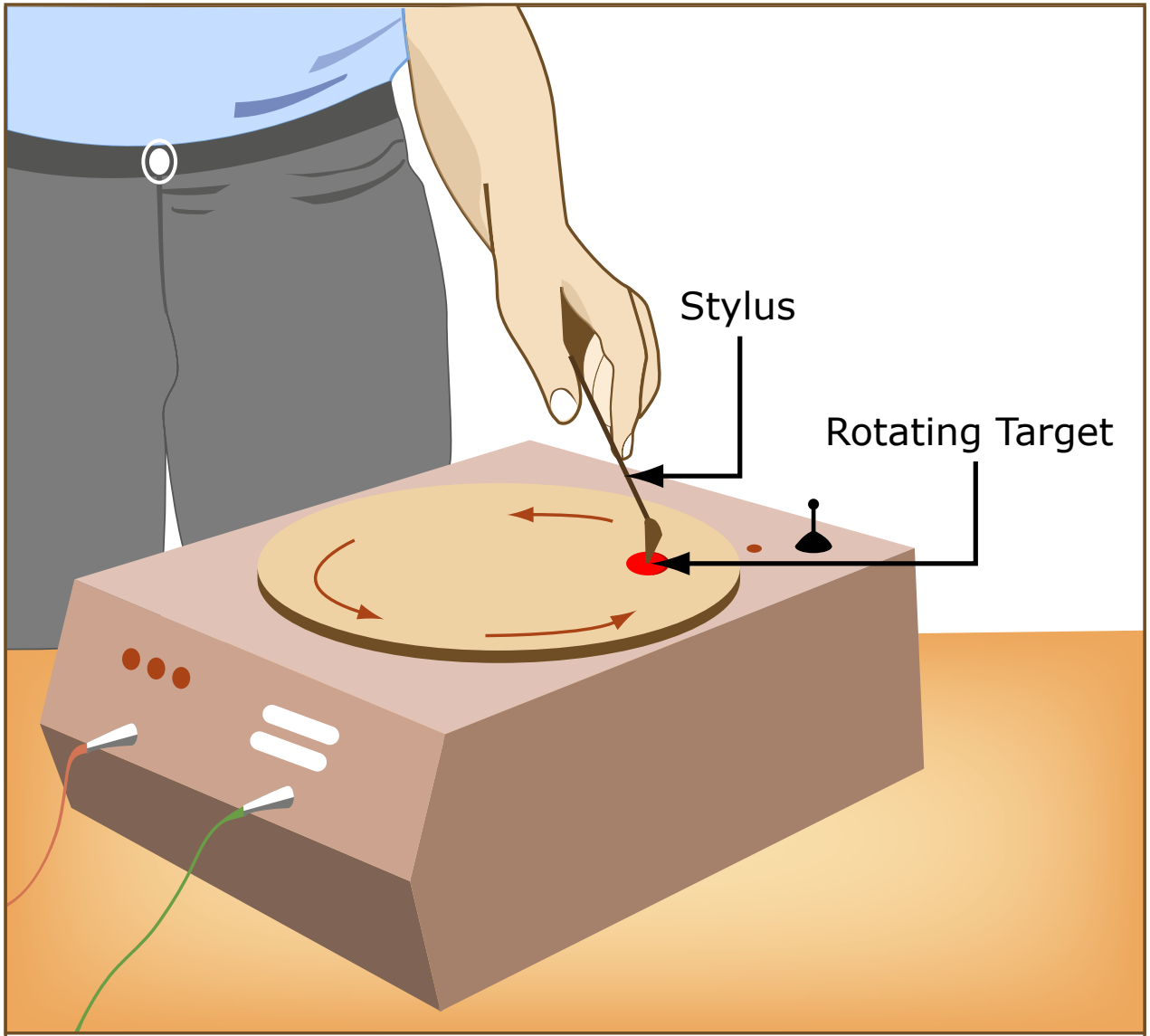


Figure 3.. Mirror-tracing results for H.M. (Top: Mean completion time per day for 3 consecutive days and after intervals of 1 week, 2 weeks, and nearly 1 year. Middle: Mean number of contacts for the same trials. Bottom: Mean time spent off pattern for the same trials.)



Rotary-pursuit task. While the target rotates, the subject tries to keep the stylus in contact with it.

HUNTINGTON'S DISEASE (HD)

Etiology

- genetic (autosomal dominant)

Frequency

- 5/1,000,000
- usual onset in 30s or 40s

Symptoms

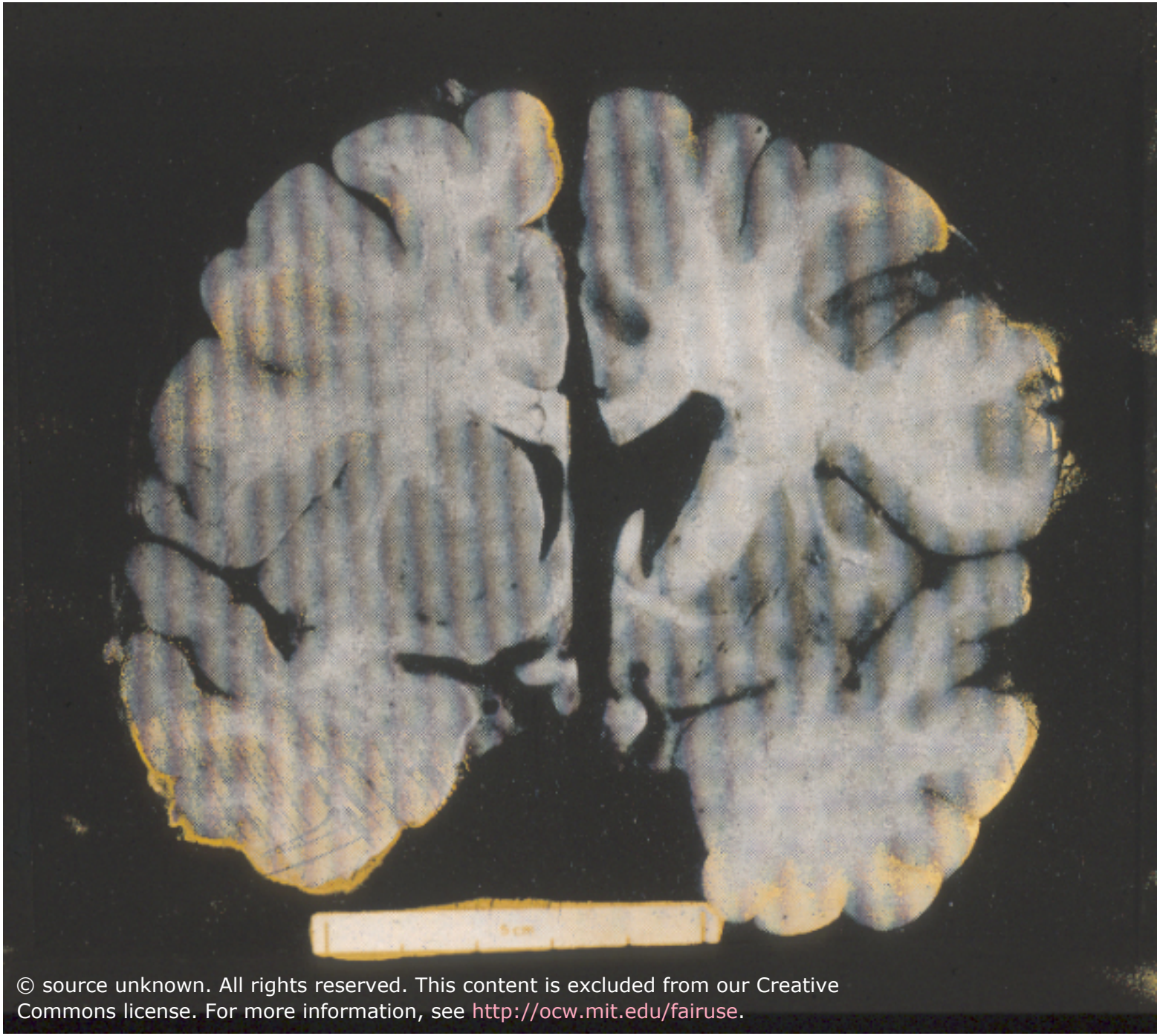
- Motoric
  - Choreiform movements
  - Athetosis
- Cognitive
  - Progressive dementia
- Psychiatric
  - Depression, disinhibition, mood disturbance

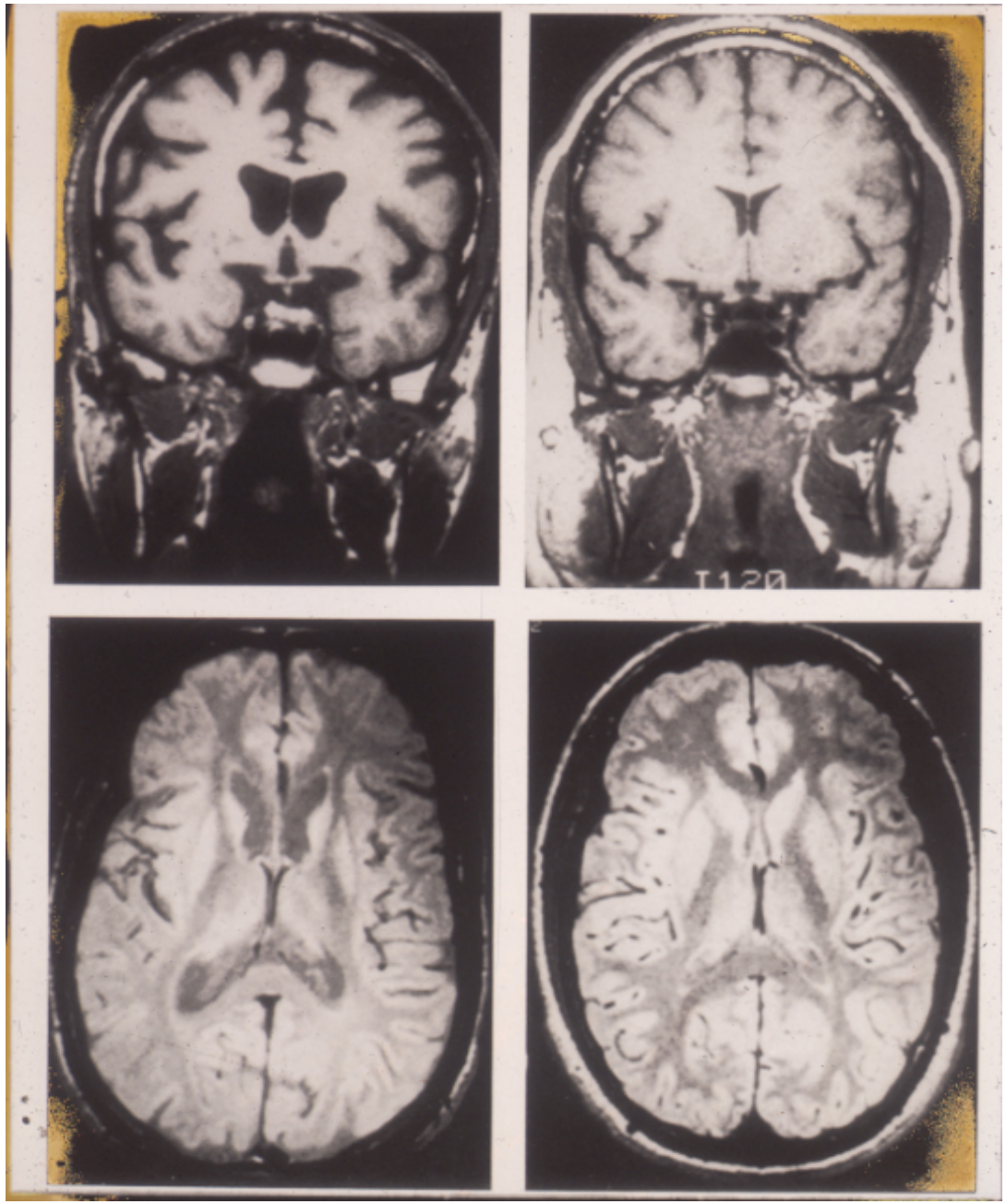
Neural Systems

- Caudate and putamen
  - (putamen may be more affected in earliest stages)
- More moderate frontal and temporal gyral atrophy

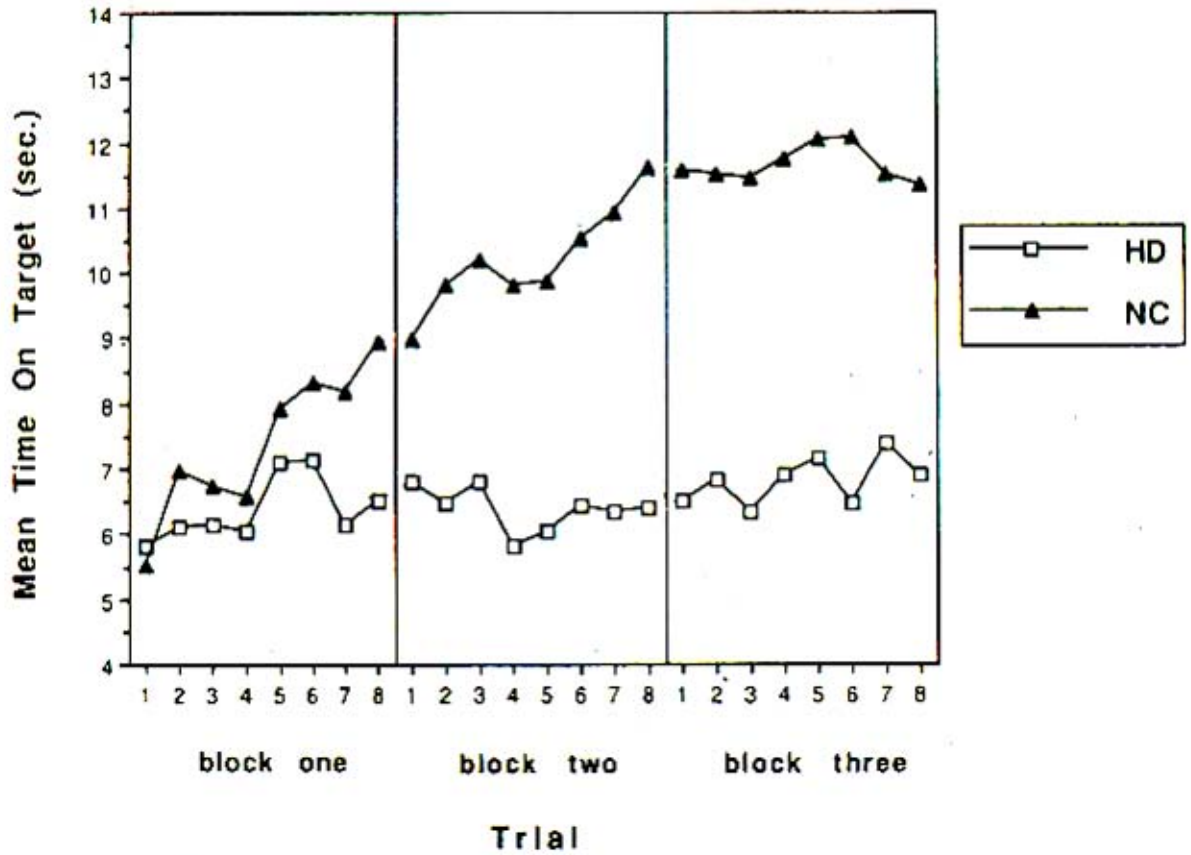
Treatment

- none





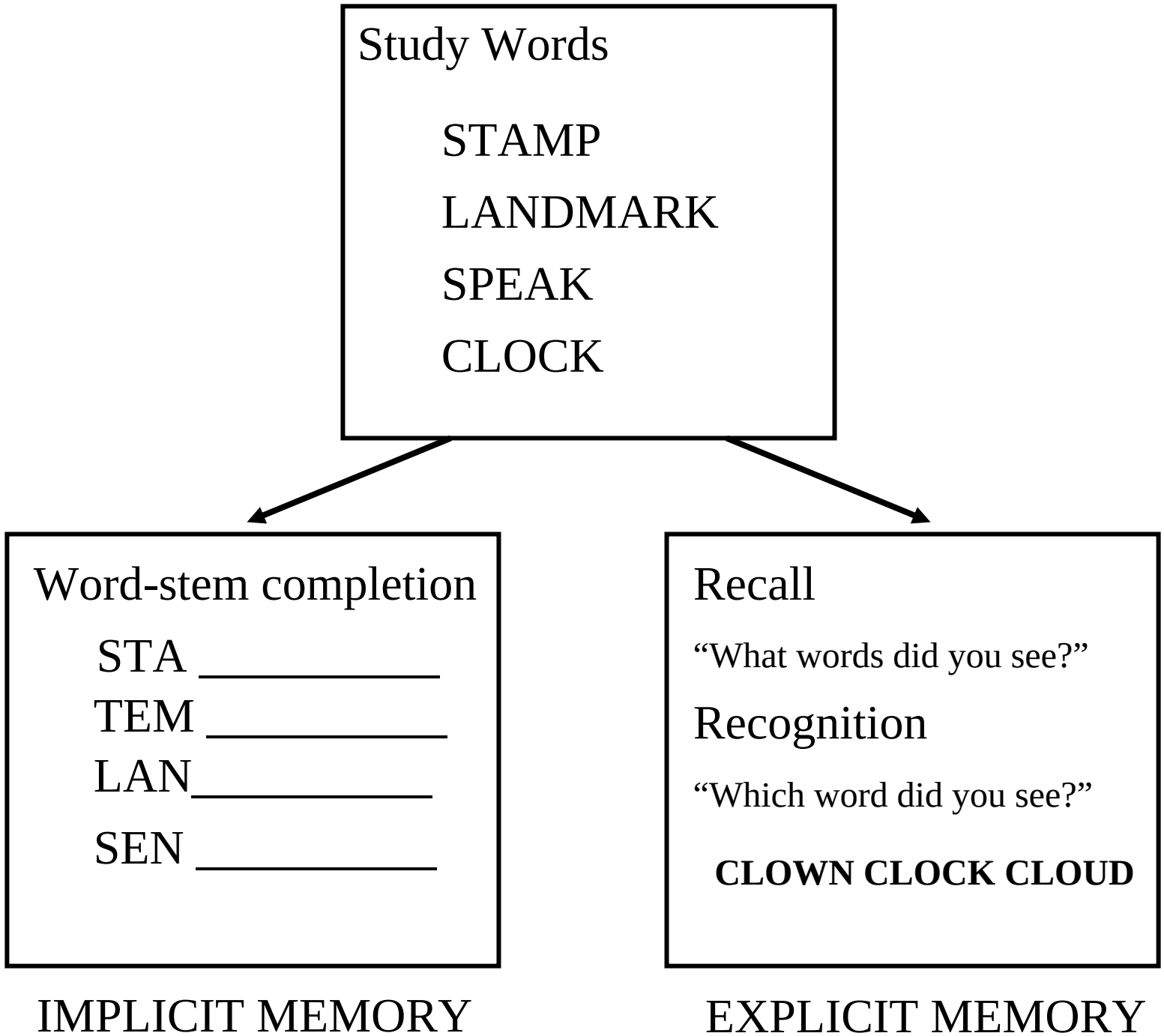
ROTARY PURSUIT LEARNING IMPAIRED IN HD



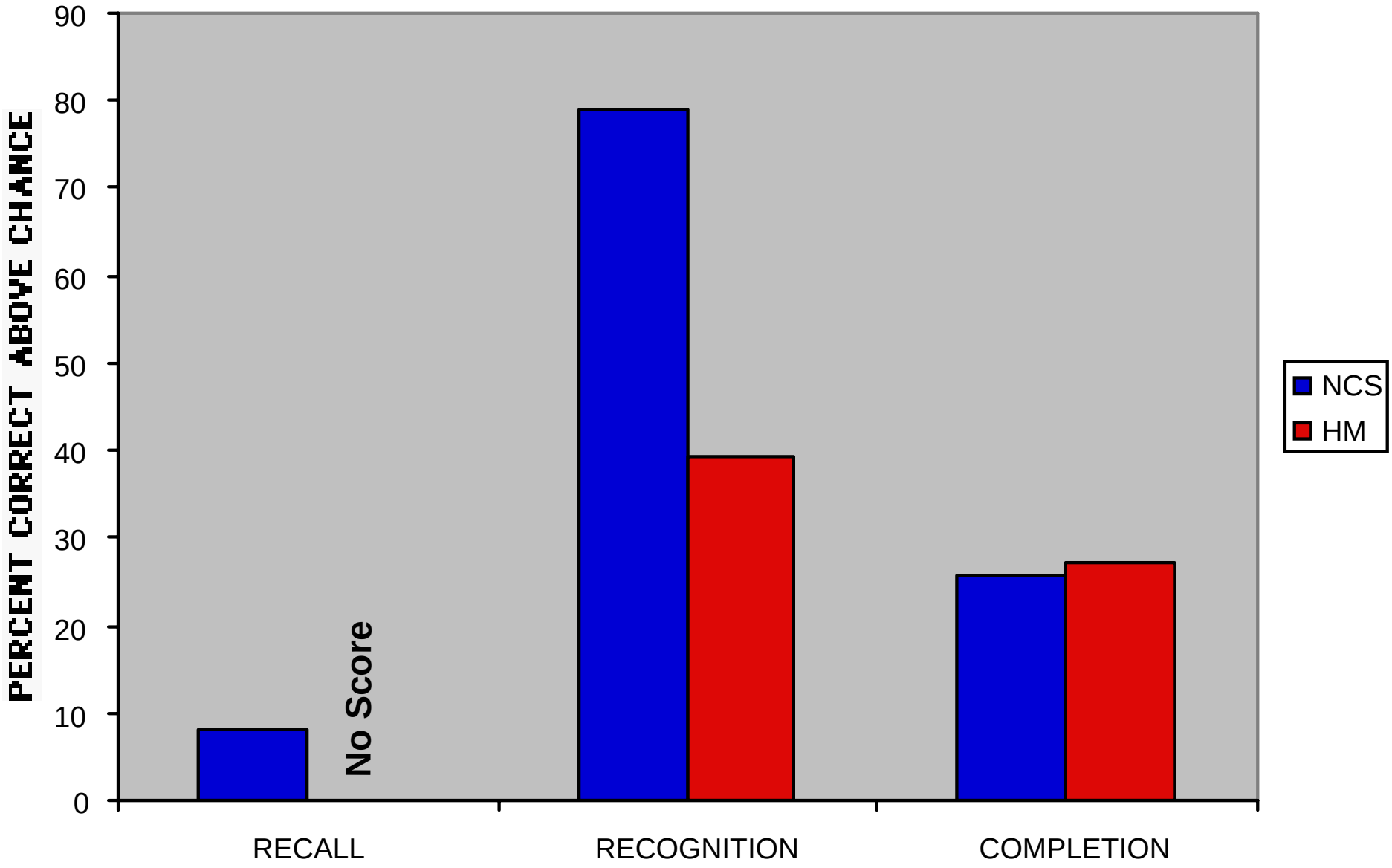
See Gabrieli, J. D. E., et al. *Neuropsychology* 11, no. 2 (1997): 272-81.

REPETITION PRIMING

- Change in performance (accuracy, speed) with a stimulus (e.g., word or picture) due to prior processing of that stimulus or a related stimulus


Study Words
STAMP
LANDMARK
SPEAK
CLOCK
Word-stem completion
STA _____
TEM _____
LAN_____
SEN _____
Recall
"What words did you see?"
Recognition
"Which word did you see?"
CLOWN CLOCK CLOUD
IMPLICIT MEMORY
EXPLICIT MEMORY

Intact Repetition Priming in HM



Behavioral Pathology in Alzheimer's Disease

- insidious and progressive dementia
- * memory (amnesia) *
- language (aphasia)
- thinking, planning, judgement
- concentration, attention
- spatial thinking
- mood and personality

MULTIFOCAL NEUROPATHOLOGY IN ALZHEIMER'S DISEASE

DENSE NEUROPATHOLOGY

- **hippocampal complex**
- **association neocortex**
  temporal lobes, parietal lobes, frontal lobes

MILD NEUROPATHOLOGY

- **basal ganglia**
- **cerebellum**
- **primary motor cortex**
- **primary sensory cortices**

  occipital lobe (vision)

  temporal lobe (audition)

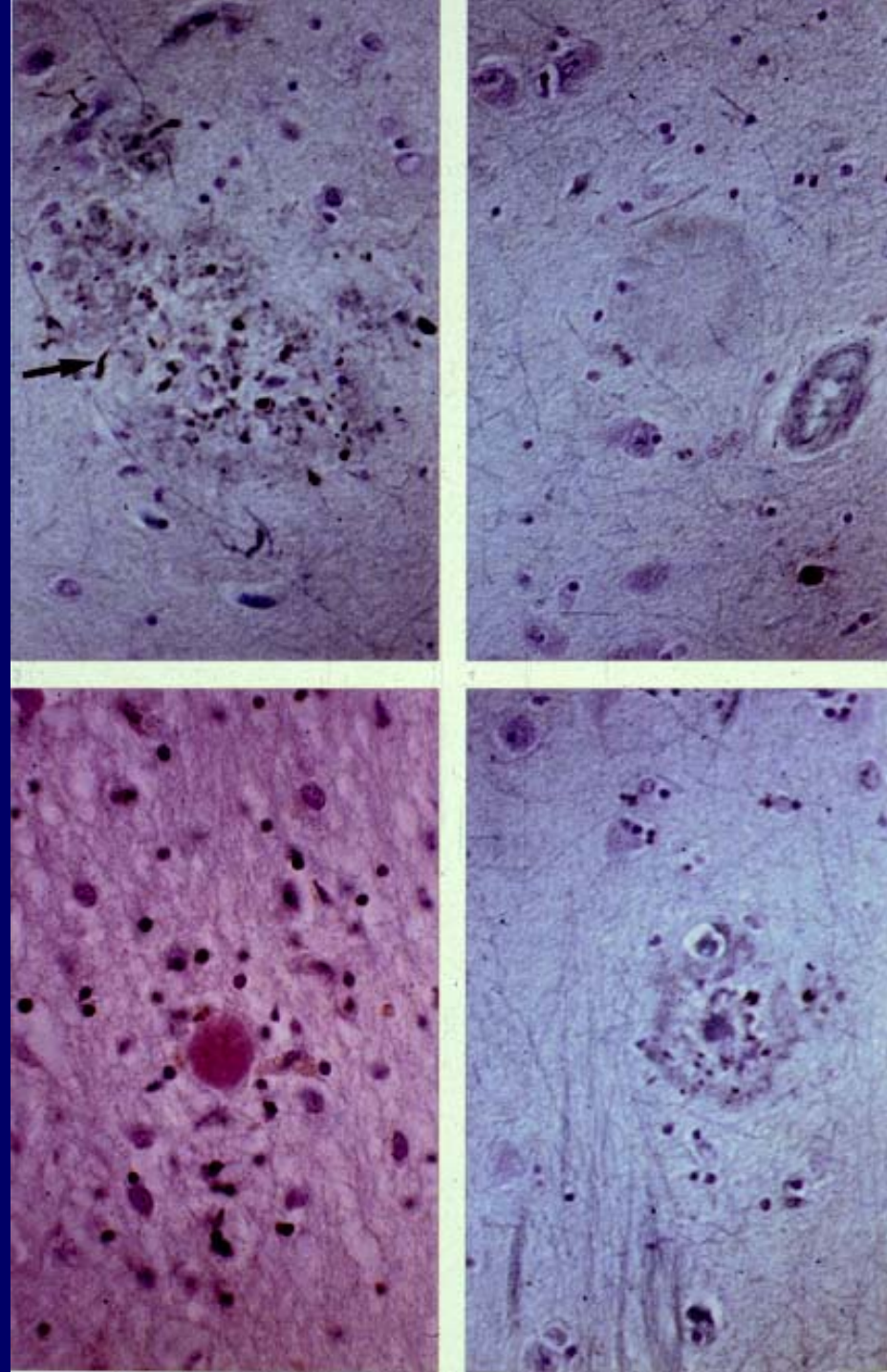
  parietal lobe (touch)

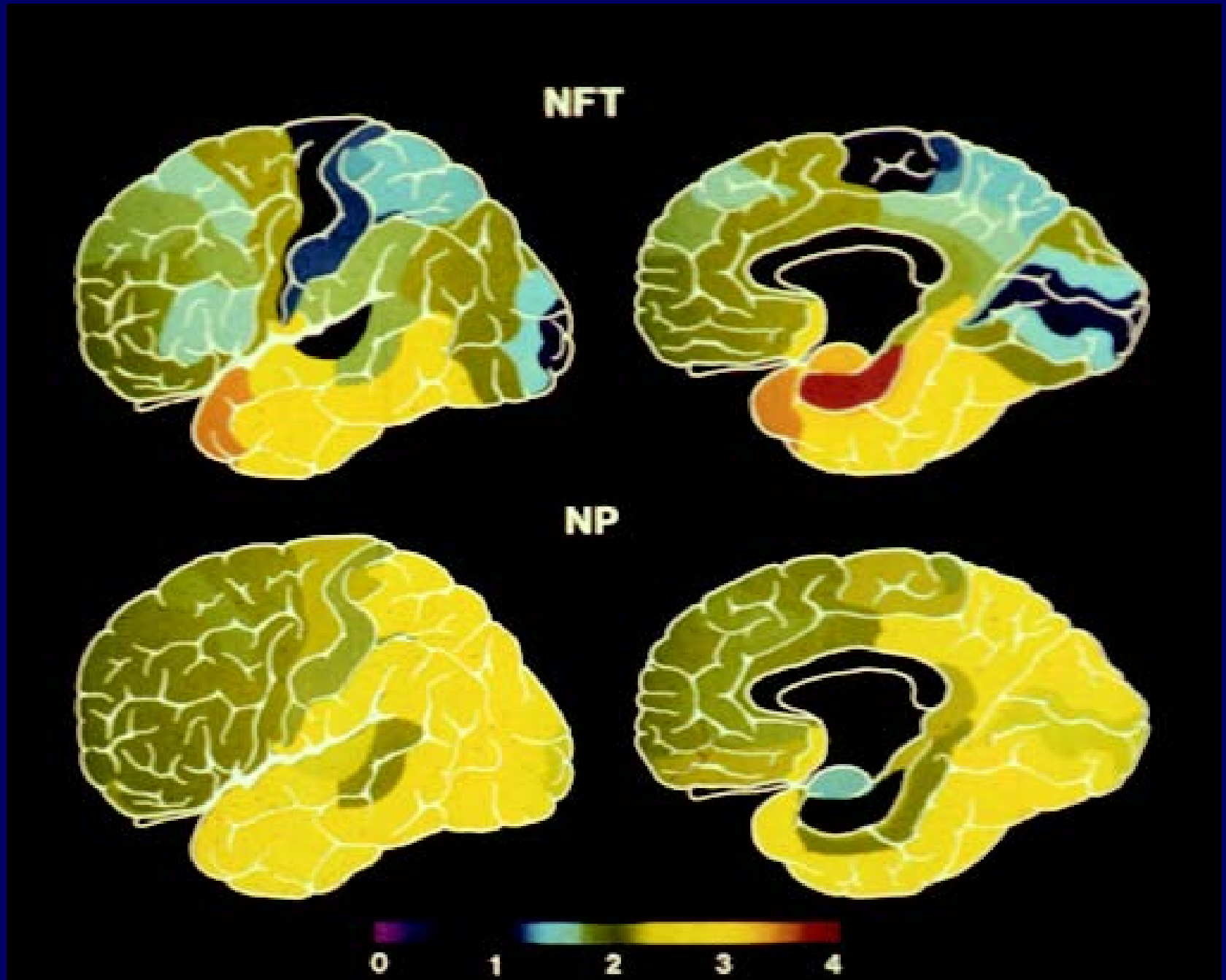
AD Patient **Control**

Cellular Pathology of AD

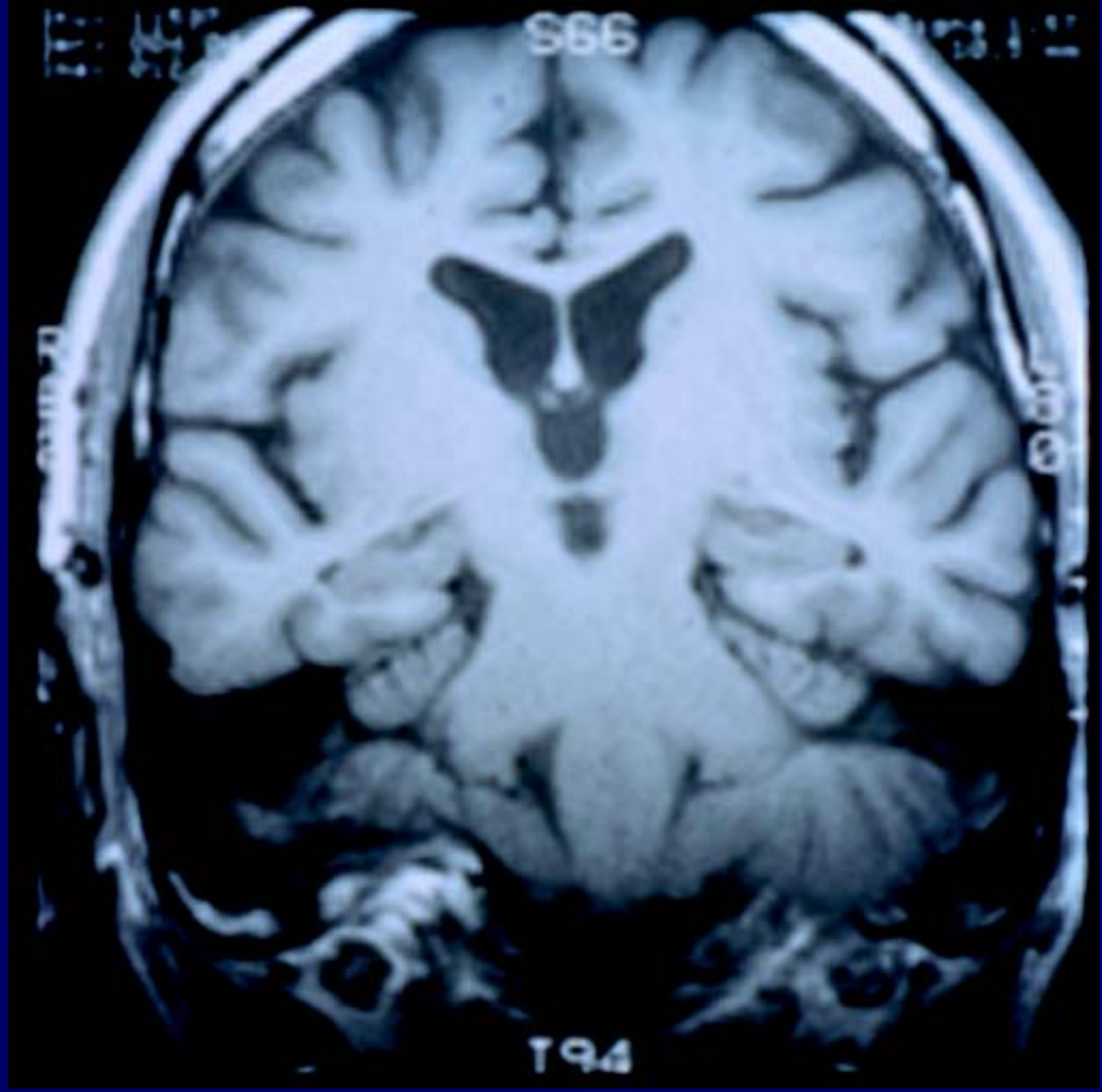
neurofibrillary tangles

amyloid plaques



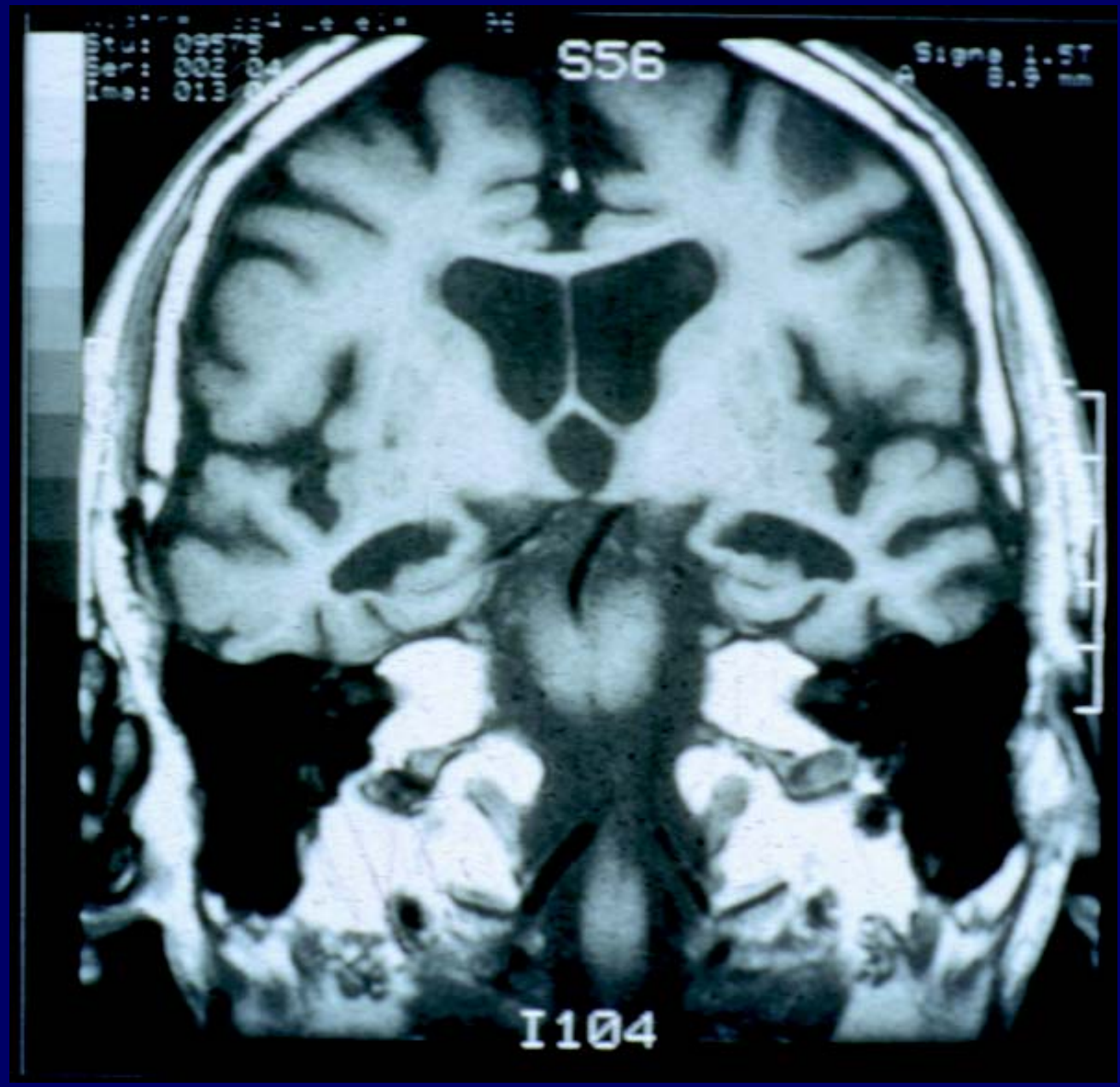


Healthy 81 year old structural MRI



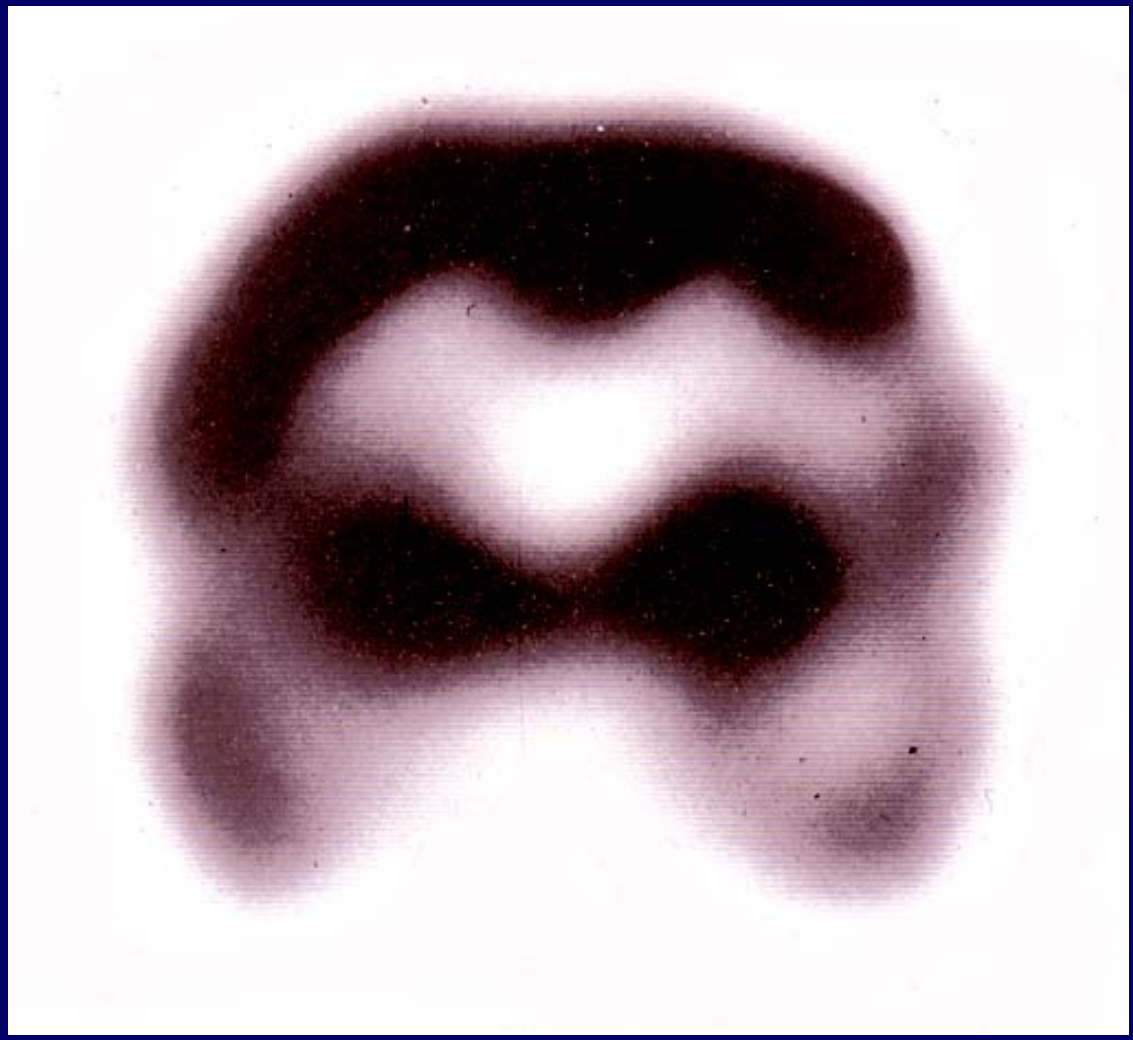
Courtesy of Leyla de Toledo-Morrell. Used with permission.

AD patient
80 years old
structural
MRI



Courtesy of Leyla de Toledo-Morrell. Used with permission.

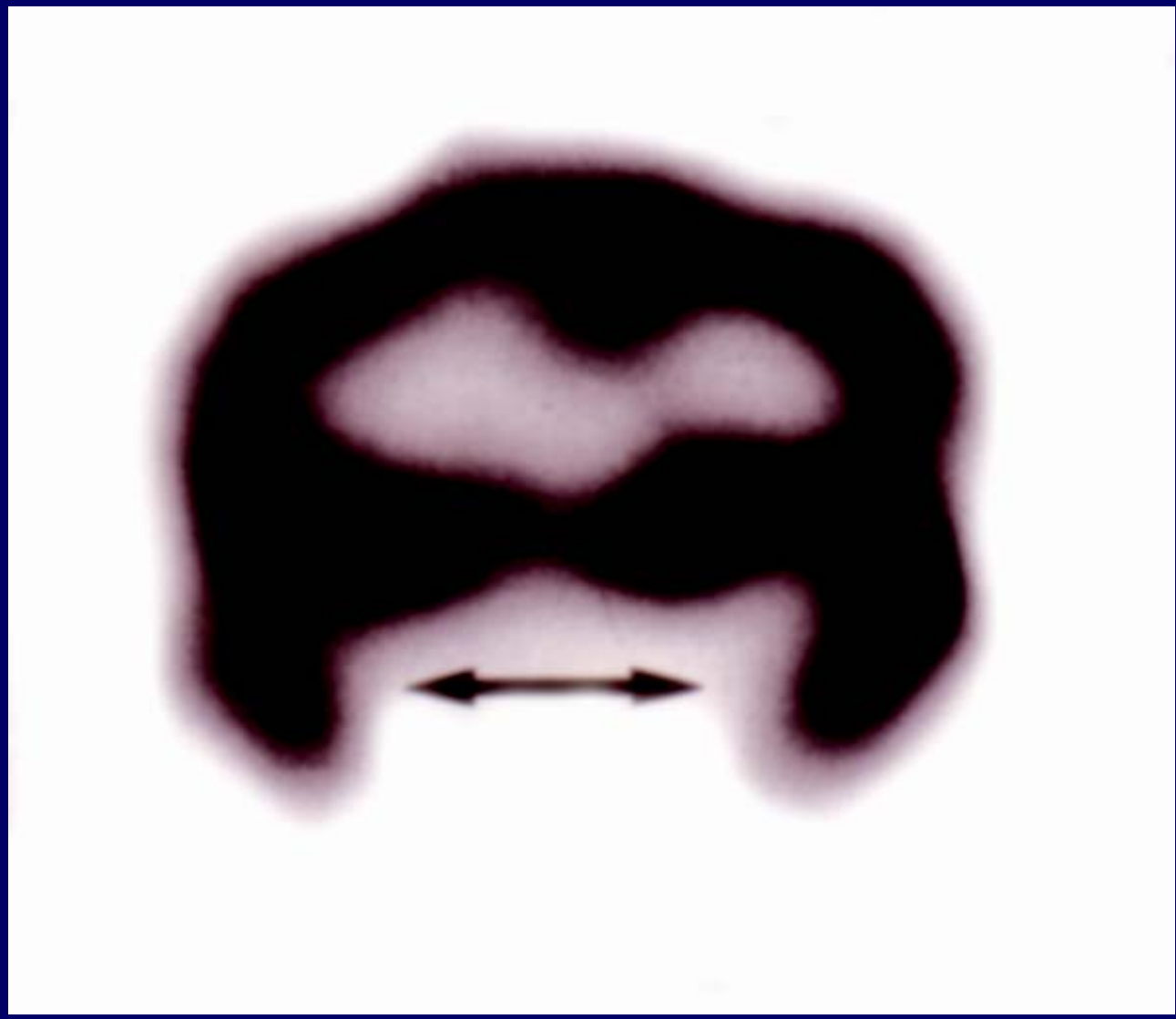
Healthy Elderly Adult



blood flow & metabolism

Single Photon Emission Computed Tomography - SPECT

H.M.

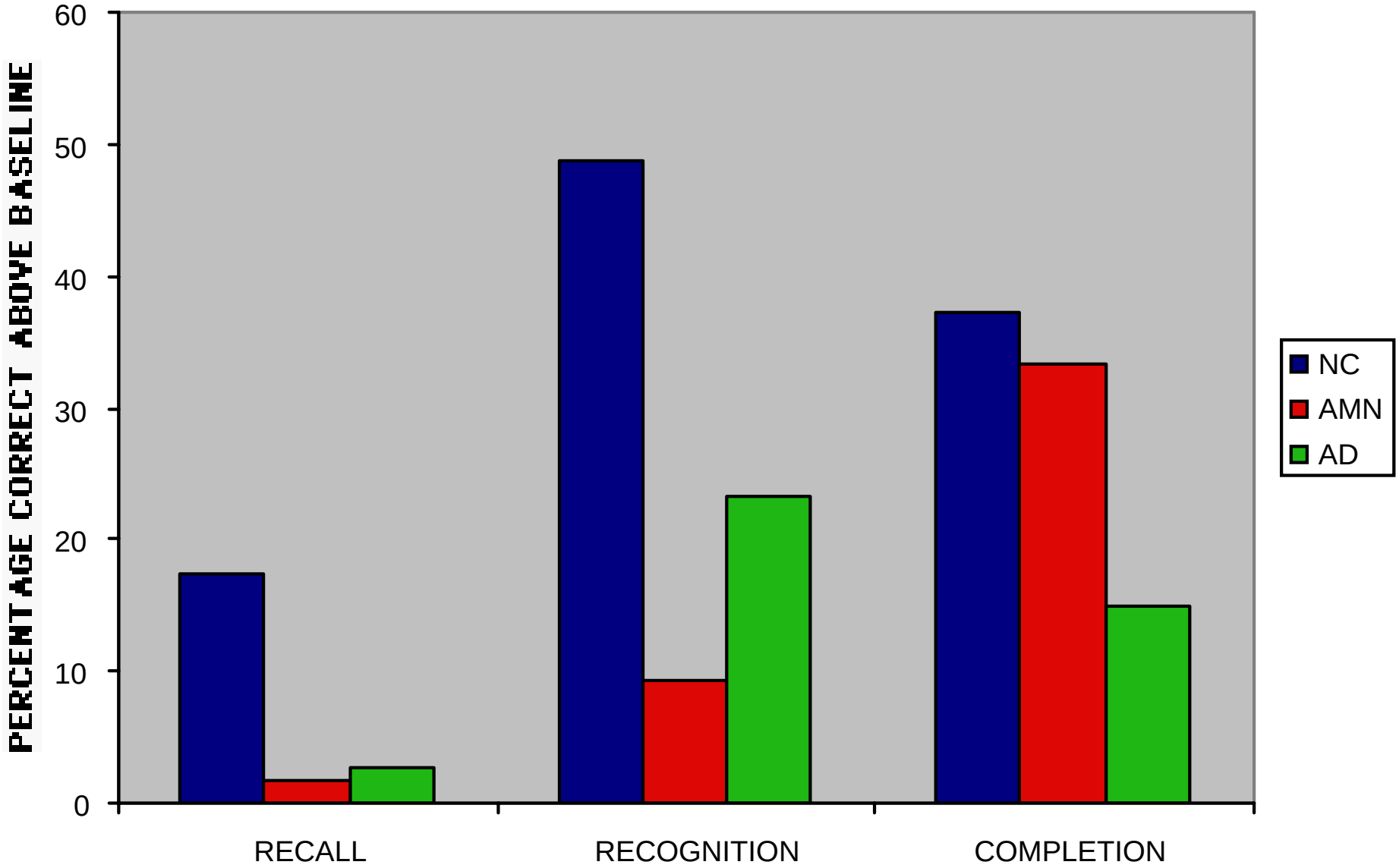


Single Photon Emission Computed Tomography - SPECT

AD Patient

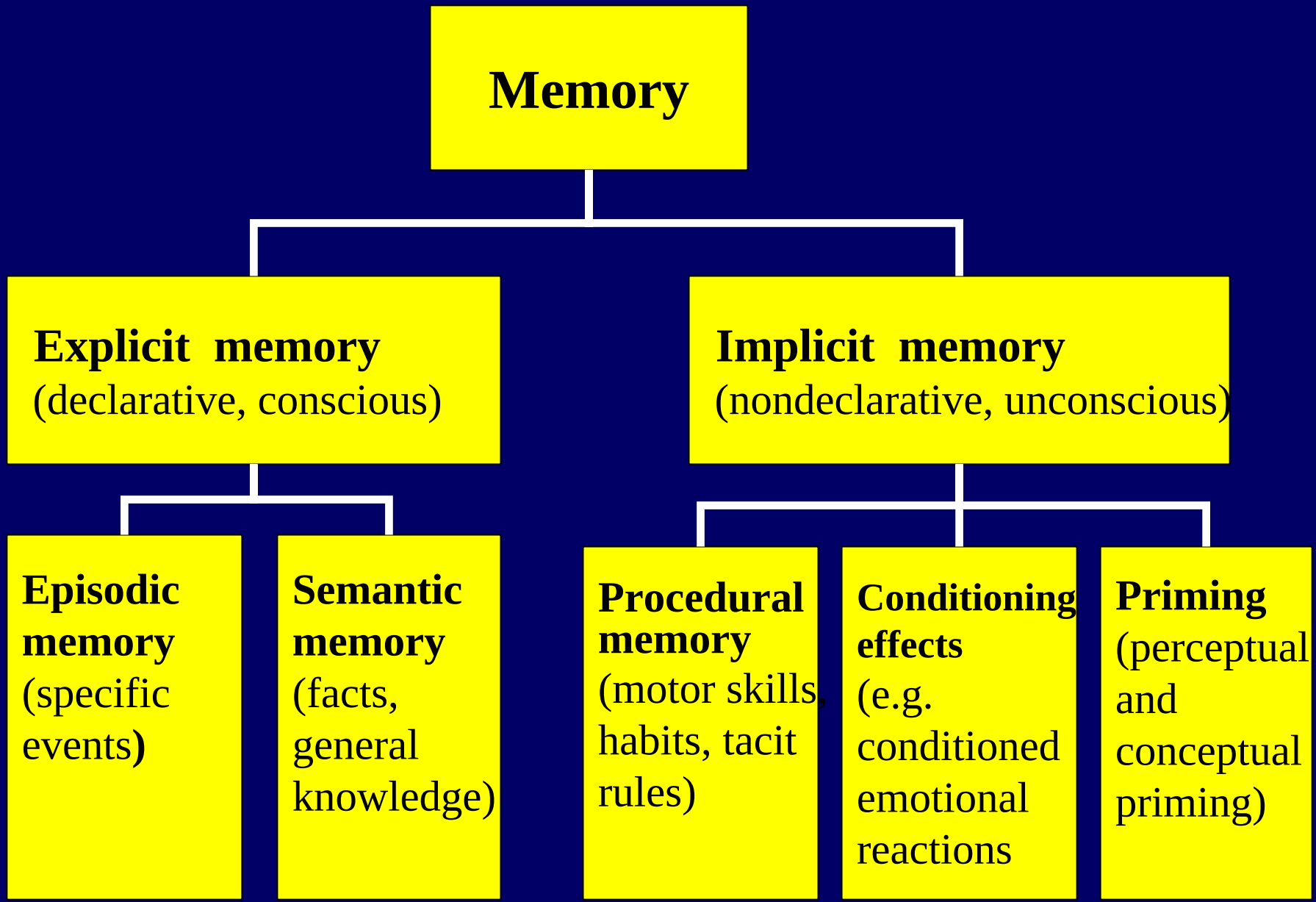
Single Photon Emission Computed Tomography - SPECT

Impaired Repetition Priming in AD



THREE MEMORY SYSTEMS

Kind of Memory	*Patient Information*	*Neural System*
Explicit / Declarative	**Amnesia**	**Medial Temporal Lobe**
Skill Learning *(rotary pursuit)*	**Huntington's Disease**	**Basal Ganglia**
Repetition Priming *(word-stem completion)*	**Alzheimer's Disease**	**Neocortex**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Conditioning effects
(e.g. conditioned emotional reactions
Priming
(perceptual and conceptual priming)

Is memory in the brain *distributed* or *localized*???

"It is not possible to demonstrate the isolated localization of a memory trace anywhere in the nervous system…The engram is represented throughout the region"

Karl Lashley 1950

9.00SC Introduction to Psychology
Fall 2011