260-2017-11-29-memory

2017-11-28 09:48:45

Prelude

Memento Original 35 mm Anamorphic Trailer (HD) (CC)

Today's topics

- Biological basis of learning & memory

Coming up…

- Quiz 4, review Exam 3 on Fri
- In-class lab next Mon
- Review for Exam 4 next Wed
- Exam 4, Mon 12/11, 12:20-2:10 pm in 302 Boucke

How do synapses change strength?

Donald Hebb's Insight

(Hebb, 1949, p. 62)

(Lowell & Singer, 1992, p. 211).

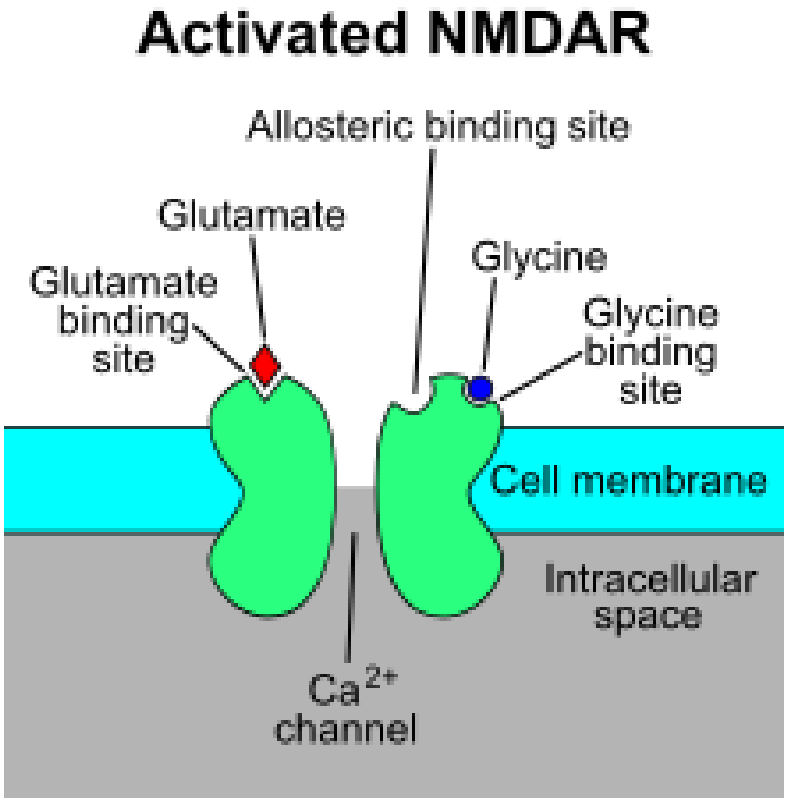
'Hebbian' learning via NMDA receptor

- receptor (NMDAR)
- 'Coincidence' detector
  - Sending cell has released NT
  - Receiving cell is/has been recently active

Example mechanism for 'Hebbian' learning

- Chemically-gated AND
  - Ligand- (glutamate/aspartate + glycine) gated
  - Sending cell active
- Voltage-gated
  - Zn^{++} or Mg^{++} ion 'plug' removed under depolarization
  - Na^{+} & Ca^{++} influx; K^{+} outflux
  - Receiving cell responds

NMDA receptor figure



https://upload.wikimedia.org/wikipedia/commons/thumb/0/00/Activated_NMDAR.svg/220px-Activated_NMDAR.svg.png

NMDA receptors contribute to associative learning

- Associate (link)
  - Concept A -> Concept B
  - Neuron A -> Neuron B

Donald

Donald

- Trump
- Duck
- Draper

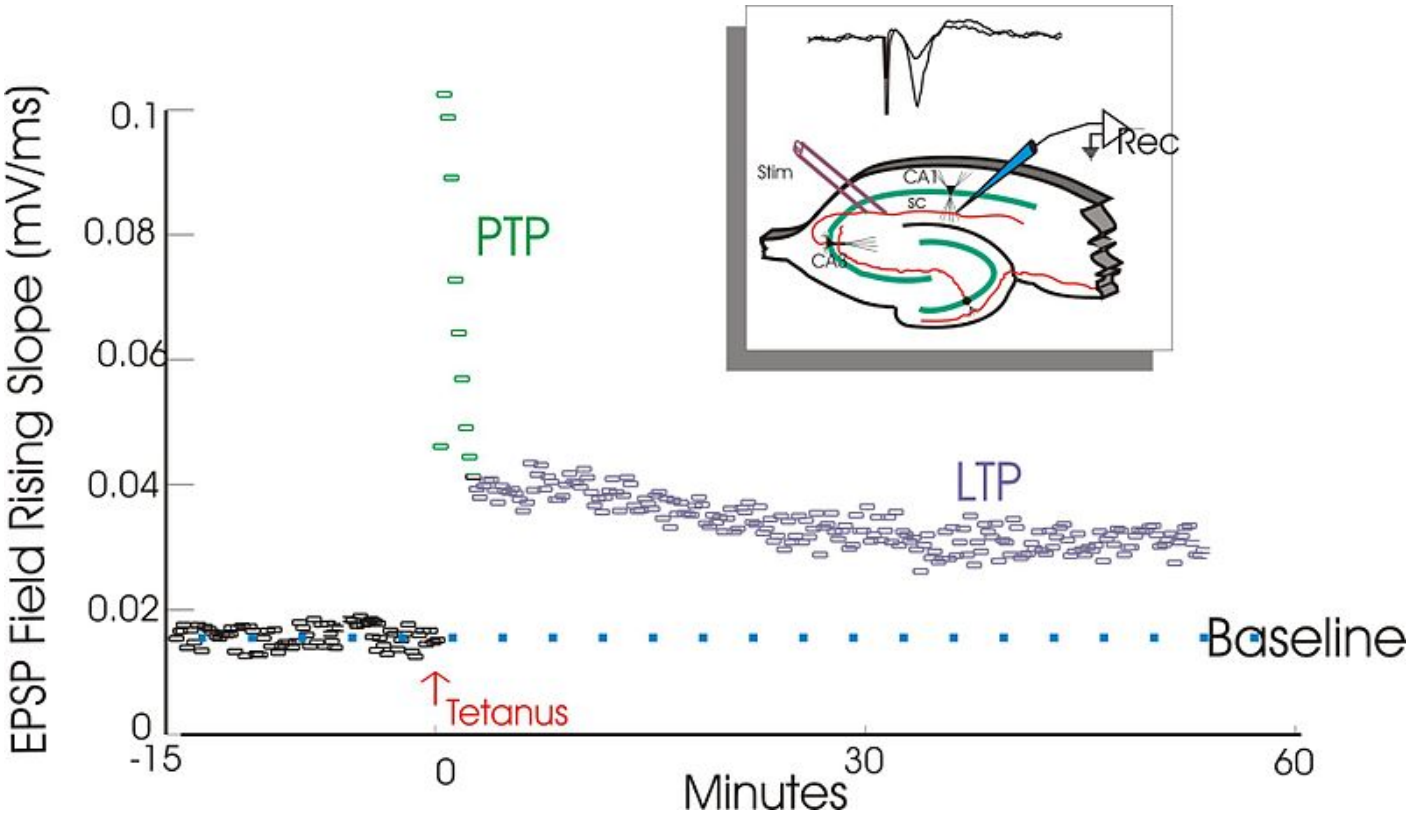
NMDA clinical significance

- (Alzheimer's Disease treatment) blocks NMDAR
  - Controls over-activation and Ca^{++} excitotoxicity?
- Implicated in effects of (PCP)
  - Link to glu hypothesis of schizophrenia?

NMDA clinical significance

- is NMDA receptor antagonist
  - anesthesia, sedation pain relief
  - possible short-term relief for depression
- Analgesic effects of nitrous oxide (laughing gas; NO)
- Ethanol inhibits (Ron et al., 2011)

Long-term potentiation (LTP)



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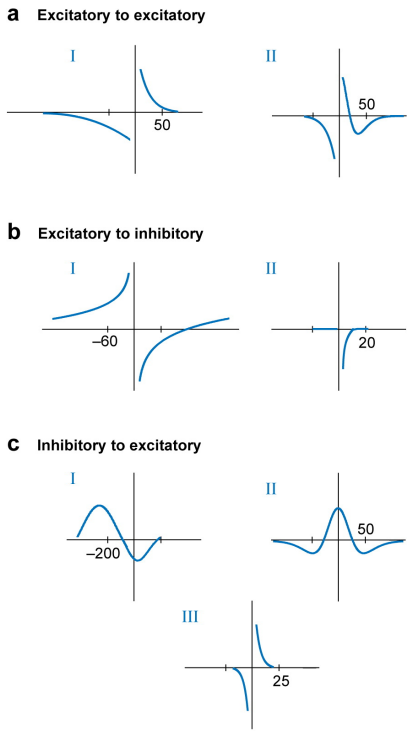
Long-term potentiation (LTP)

- Increase in synaptic strength based on recent activity.
- But how to learn/remember "causal chains"?
  - e.g., lightning THEN thunder
  - unusual food THEN indigestion

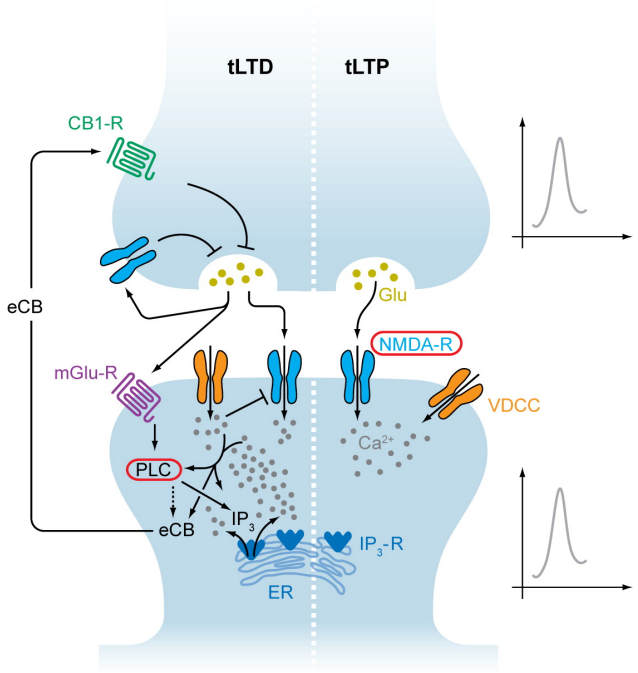
Spike-timing-dependent plasticity



Caporale N, Dan Y. 2008.
Annu. Rev. Neurosci. 31:25–46.

(Caporale and Dan 2008)

Spike-timing-dependent plasticity



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(Caporale and Dan 2008)

Spike-timing-dependent plasticity

- A before B: strengthen A->B
- A after B: weaken A->B
-
    - Lasting changes in neural firing, connectivity

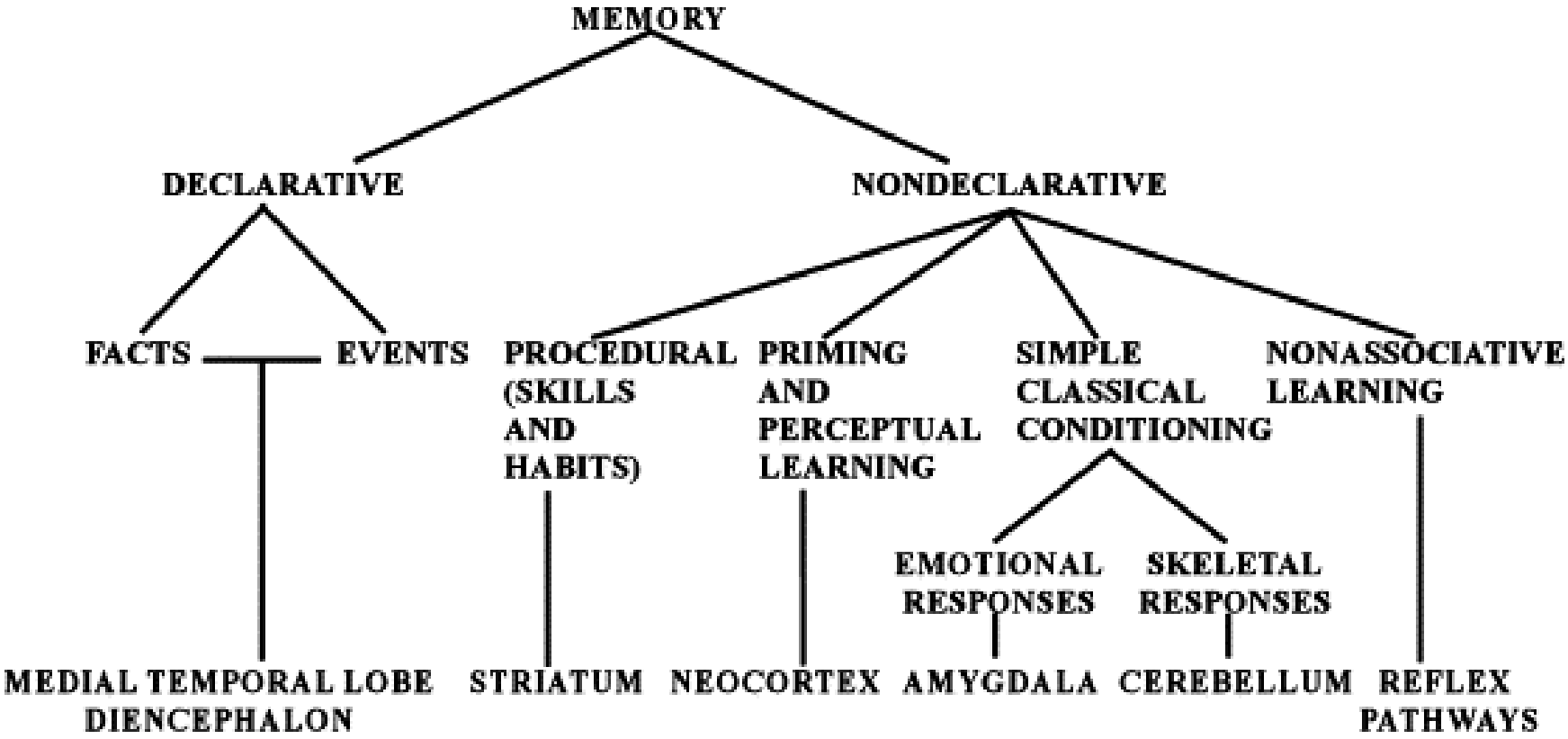
How does LTP (& LTD) work?

- NMDA receptor one molecular mechanism for implementing LTP, LTD and spike-timing-dependent plasticity
- Ca++ entry triggers biochemical cascade
- Existing (AMPA) glutamate receptors made to stay open longer
- New AMPA Glu receptors synthesized, inserted into postsynaptic membrane
- Change in quantity of glutamate released presynaptically

Dimensions of stored info

- Memory of what?
  - Facts/events/places vs. skills
- Memory of when?
  - Immediate vs. distant past
- Memory for how long?
  - Seconds vs. years

Memory systems in the brain



(Squire 2004)

Summary thus far

- Learning and memory involve changes in neural firing, circuitry
- Hebbian learning a type of associative learning
- NMDA receptor as coincidence detector
    - Molecular basis of one form of long-term potentiation (LTP)
- Different types of information stored in different brain systems

Disorders of memory

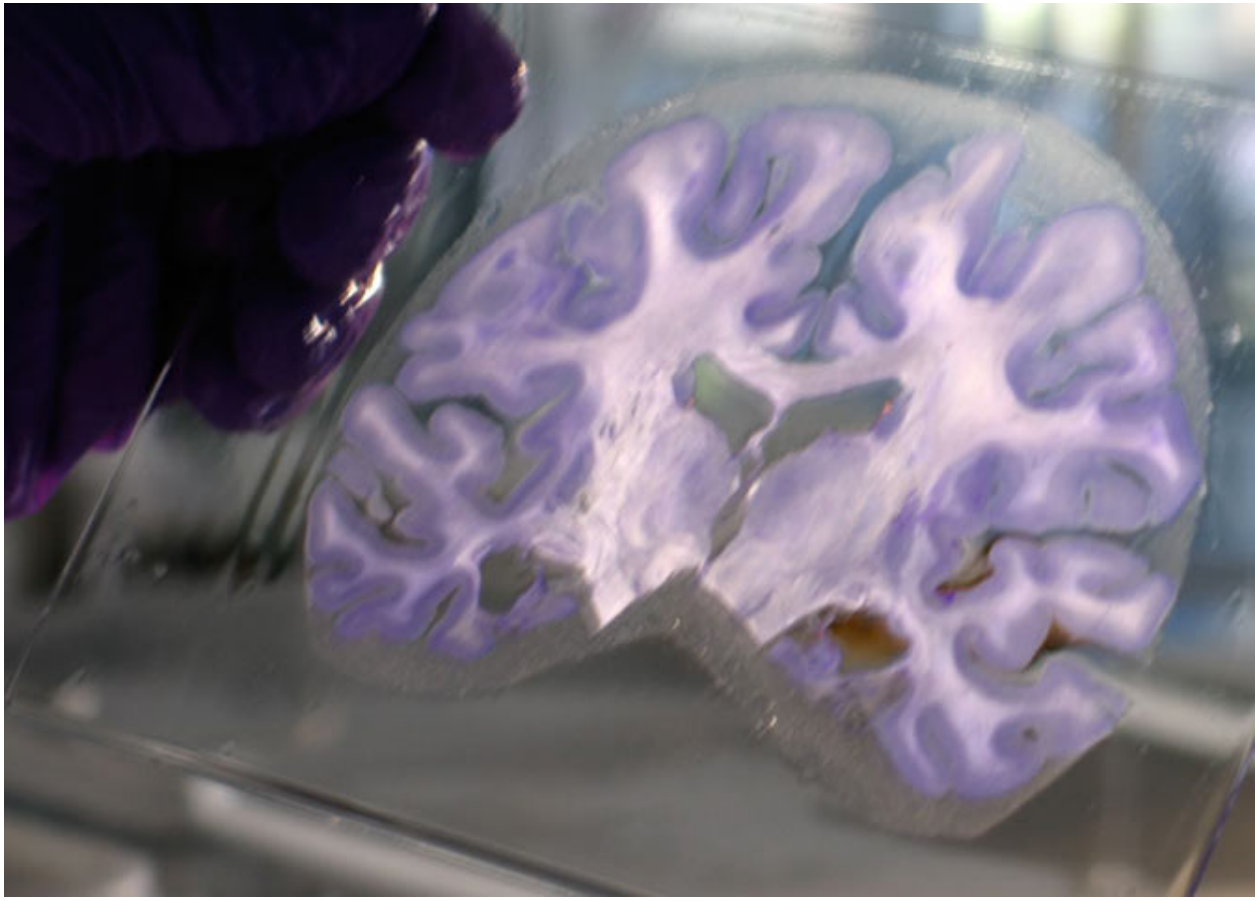
Patient HM (Henry G. Molaison)

- Intractable/untreatable epilepsy
- Bilateral resection of medial temporal lobe (1953)
- Epilepsy now treatable
- But, memory impaired
- Lived until 2008

Brenda Milner tells the story

Brenda Milner, Neuropsychologist

HM's surgery



Amnesia

- Acquired loss of memory
- ≠ normal forgetting
- Note: computers don't forget

HM's amnesia

- Retrograde amnesia
  - Can’t remember 10 yrs before operation
  - Distant past better than more recent
- Severe, global anterograde amnesia
  - Impaired learning of new facts, events, people
- But, skills (mirror learning) intact

Types of amnesia

- Retrograde ('backwards' in time)
  - Damage to information acquired pre-injury
  - Temporally graded
- Anterograde ('forward' in time)
  - Damage to information acquired/experienced post-injury

What it's like

Other causes of amnesia

- Disease
  - Alzheimer's, herpes virus
- Korsakoff's syndrome
  - Result of severe alcoholism
  - Impairs medial thalamus & mammillary bodies

Patient NA

- Fencing accident
- Damage to medial thalamus
- Anterograde + graded retrograde amnesia
- Are thalamus & medial temporal region connected?

Patient NA

Larry Squire's Amnesic Patient NA

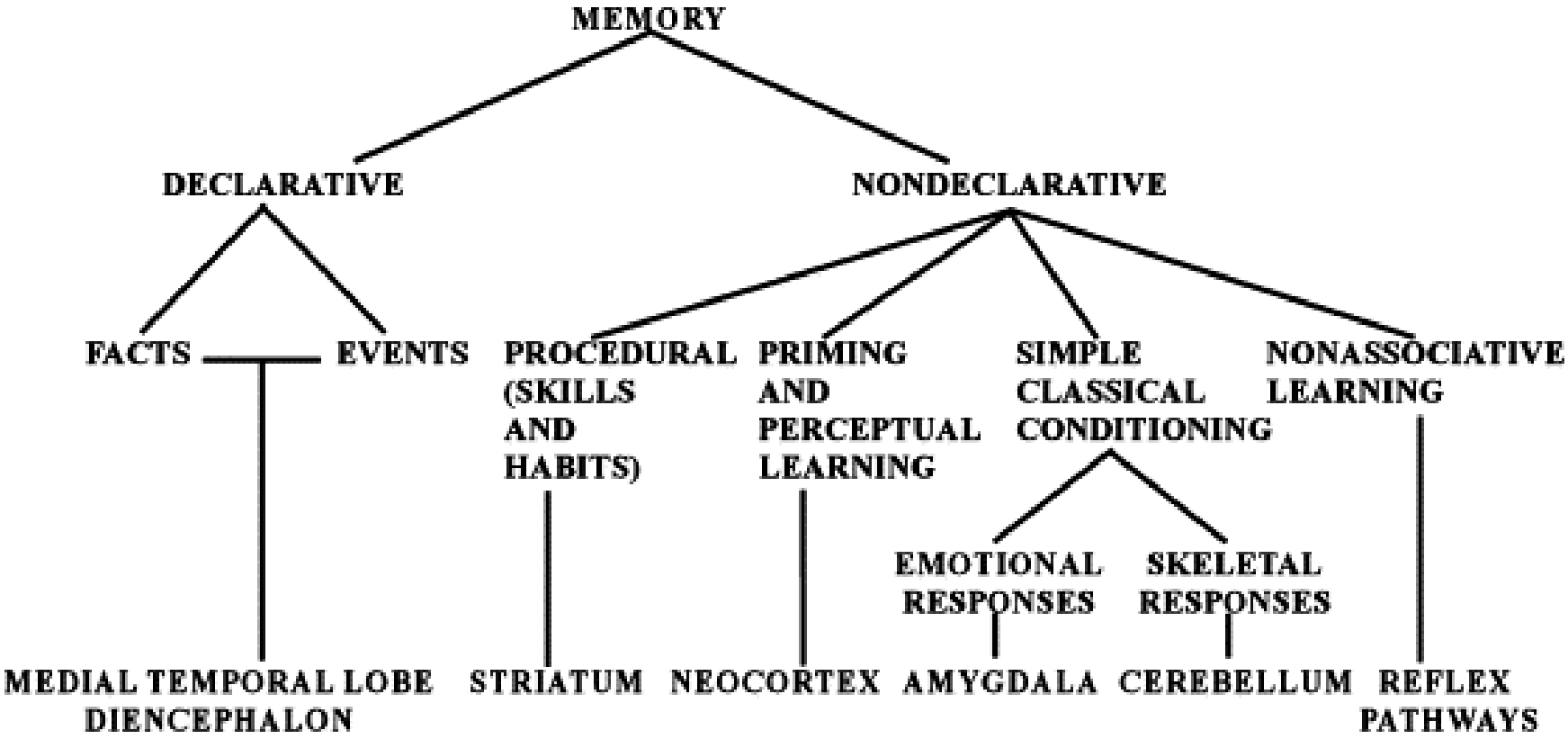
Spared skills in amnesia

- Skill-learning
- Mirror-reading, writing
- Short-term memory
- “Cognitive” skills
- Priming

What does amnesia tell us?

- Long-term memory for facts, events, people
- ≠ Short-term memory
- ≠ Long-term memory for “skills”
- Separate memory systems in the brain?

Memory systems in the brain



(Squire 2004)

Next time…

- Quiz 4
- Go over Exam 3

References

Caporale, Natalia, and Yang Dan. 2008. “Spike Timing-Dependent Plasticity: A Hebbian Learning Rule.” 31. Annual Reviews: 25–46. doi:10.1146/annurev.neuro.31.060407.125639.

Squire, Larry R. 2004. “Memory Systems of the Brain: A Brief History and Current Perspective.” , Multiple Memory Systems, 82 (3): 171–77. doi:10.1016/j.nlm.2004.06.005.