

MCB/Neuro 80 Fall 2019

Section 8

Activity 1: Long-Term Plasticity and Alzheimer's Disease

Alzheimer's disease (AD) is a form of dementia (brain disorder that affects negatively a person's ability to perform daily tasks), characterized by mild cognitive impairments and a slow loss of memory (short-term, then long-term). AD symptoms usually appear at old ages (after 60). As the disease evolves, patients accumulate amyloid beta plaques, formed by the aggregation of misfolded amyloid beta proteins, in the extracellular environment of their brain.

In 2008, Bernardo Sabatini's lab at Harvard Medical School tested the effect of amyloid beta plaques on LTP and LTD in the mouse hippocampus. Below are the results they obtained.

- 1- Define LTP, LTD. Which panel is LTP / LTD?

LTP: long-lasting increase in synaptic strength

LTD: long-lasting decrease in synaptic strength

- 2- NMDA receptor is often called "coincidence detector". Explain.

- *captures you about pre/post-synaptic information similarity*

- 3- Explain how the authors obtained their results.

- *stimulate @ presynaptic, measure at post-synaptic*

- *slice hippocampus and add amyloid beta*

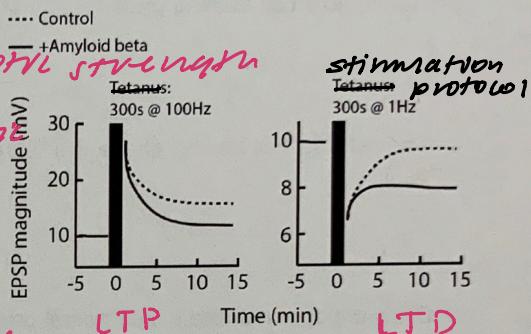
- 4- Describe, then interpret the results.

- *after 300s stimulation at 100Hz, EPSP magnitude is lower w/ β-amyloid than control*

- *β-amyloid inhibits LTP but facilitates LTD*

- 5- How do the results relate to AD symptoms?

- *✓ EPSP magnitude = ↓ synaptic strength = ↓ long-term potentiation = ↓ long-term memory*



Shankar et al. Nat Med. 2008 Aug;14:837-42

Activity 2: Retroactive Emotional Learning

Elizabeth A. Phelps, Professor of Human Neuroscience at Harvard, is the guest speaker of this Friday lecture. Prof. Phelps' research focuses on how emotions affect the way our brain works. This week in section we will go over the main results of an article Prof. Phelps published in Nature in 2015.

Here is an excerpt from the first paragraph of the article:

People are motivated to remember the episodic details of emotional events, because this information is useful for predicting and controlling important events in the future. (...) Here, we provide evidence of a generalized retroactive memory enhancement in humans that is selective to information conceptually related to a future emotional even.

- 1- What is episodic memory? Give an example of "episodic details of emotional event".

Episodic memory is long-term memory about events.

- 2- What is the main goal of the study?

Effect of emotions on retroactive memory in humans.

Here is a summary of the experimental procedure:

Training phase 1: Subjects are shown a series of pictures, one at a time, representing either an animal or a tool.

Training phase 2: Subjects are shown a novel series of pictures of animals or tools. Images of animals are paired with an unpleasant electric shock.

Testing phase: Subjects are shown a series of pictures, one at a time, representing either an animal or a tool. Half of the pictures

are a mix from the training phases 1 and 2, while the other half are novel pictures. Subjects report whether the images are new. Note that, during the training phases, subjects were never explicitly asked to remember the images they were shown.

Subjects are divided in two groups. Group A was tested right after the end of training phase 2, while group B was tested 6h later.

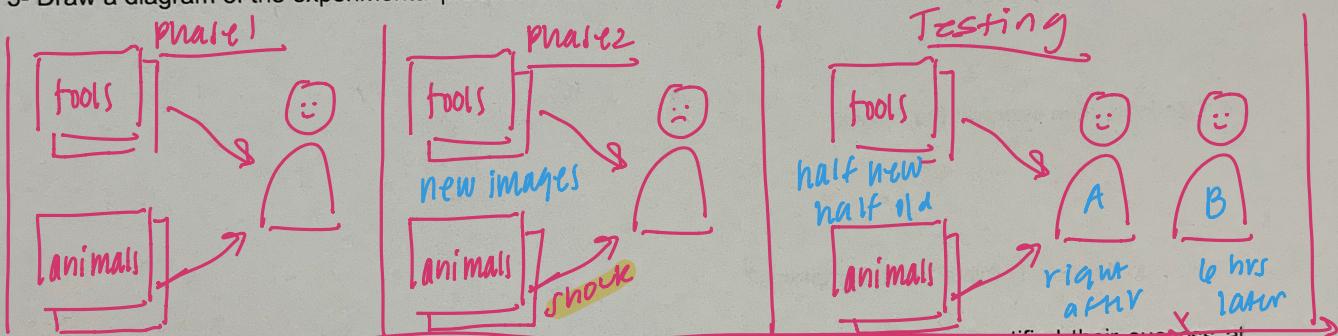
3- The authors call training phase 2 a "trial-unique form of Pavlovian" learning. Discuss and explain.

Making an association between two things (animals + shocks)

4- The authors call testing phase 3 a "surprise recognition memory test". Explain (how would a non-surprise test differ?).

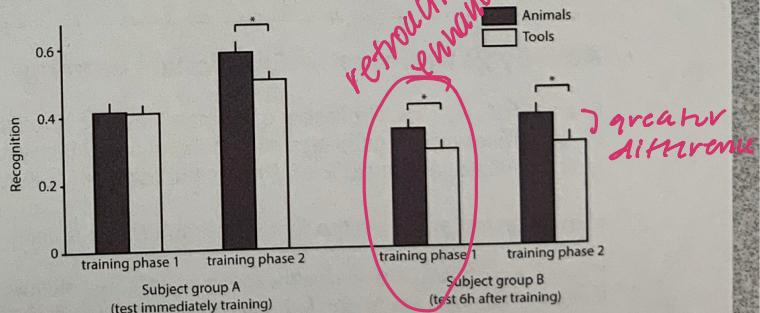
A non-surprise learning test would be independent of emotion. A surprise learning test means subjects only recall the images that were inherently remembered.

5- Draw a diagram of the experimental procedure.



Finally, the authors analyzed the recognition performance of subjects. In brief, they quantified their success at recognizing whether the images were new. They separated the recognition performance of images from training phases 1 and 2 separately. The results are below.

6- Describe, then interpret the results.



7- The authors see this as evidence of "retroactive enhancement of episodic details". What does that mean? Would you add any conditions to this enhancement?

NMDA (N-Methyl D-Aspartate receptor)

- respond to post-synaptic depolarization
- excitation
- glutamate receptor
- need pre-synaptic glutamate release
- voltage-gated
- at rest, Mg^{2+} blocks