Disruption of Reconsolidation as a Treatment for PTSD

Psychology 355: Cognitive Psychology
Instructor: John Miyamoto
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This Powerpoint presentation may contain macros that were used to create the slides. The macros aren’t needed to view the slides. If necessary, you can disable the macros without any change to the presentation.
• Comment about sleep and memory consolidation
• Undoing fear conditioning in the rat
• Disruption of memory reconsolidation at a treatment for PTSD
• Role of sleep in consolidation is not understood, but there seems to be a significant relationship between sleep and consolidation.

• Sleep (dreaming?) plays a functional role in promoting consolidation.
  - Rat brain cells that fire together while exploring a location also show increased firing during subsequent sleep. Not true of other cells that did not fire during exploration.
  - Disruption of dreaming seems to disrupt consolidation.
  - Similar effects with humans who are learning to play tetris.

• Some evidence suggests that if a subject expects to be tested on Topic A but not on Topic B, then sleep (possibly, dreaming) enhances future memory of Topic A more than Topic B.
Consolidation & Reconsolidation

Fact to be discussed in remainder of this lecture:

- When a memory is retrieved, it is vulnerable to change.
- After retrieval of a memory, it is necessary to store the memory again to return it to a permanent state.

- **Consolidation** refers to processes that change an initially encoded memory into a permanent memory.

- **Reconsolidation** refers to processes that restore a memory to a more permanent form after it has been retrieved.

Sometimes consolidation & reconsolidation are referred to together as “consolidation.”
Memories Representations Are Malleable At Time of Retrieval

• Hypothesis:
  When memories are retrieved, they are vulnerable to change.

• Under special circumstances, when memories are retrieved, memories can be wiped out.
  ♦ Can these ideas be used to develop a treatment for PTSD?
Undoing Fear Conditioning in the Rat


• If a tone is paired with an electric shock, a rat will learn to freeze when it hears the tone (classical conditioning of fear).

• Anisomycin – antibiotic that inhibits protein synthesis that is required in the formation of new memories.

• Administering anisomycin to a rat can cause it to fail to learn.
**Experimental Design**

**Condition 1:**
- Day 1: Tone + Shock + anisomycin
- Day 2: No drug; no tone; no shock
- Day 3: Does not freeze to tone
  (shows no learning)

**Condition 2:**
- Day 1: Tone + Shock
- Day 2: Drug; no tone; no shock
- Day 3: Freezes to tone (shows learning)

**Condition 3:**
- Day 1: Tone + Shock
- Day 2: Drug + tone, no shock.
- Day 3: Does not freeze to tone
  (shows no learning)

![Figure 7.20](image-url)
Experimental Design

**Condition 1:**
Day 1: Tone + Shock + anisomycin
Day 2: No drug; no tone; no shock
Day 3: Does not freeze to tone
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Summary of Results
Summary of Main Finding

Condition 1:
Day 1: Tone + Shock + anisomycin
Day 2: No drug; no tone; no shock
Day 3: Does not freeze to tone
(shows no fear conditioning)

Condition 2:
Day 1: Tone + Shock
Day 2: Drug; no tone; no shock
Day 3: Freezes to tone
(shows fear conditioning)

Condition 3:
Day 1: Tone + Shock
Day 2: Drug + tone, no shock.
Day 3: Does not freeze to tone
(shows no fear conditioning)

Combining drug with tone & shock on Day 1 prevents fear conditioning.

Drug on Day 2 does not undo fear conditioning.

Combining drug with retrieval on Day 2 of memory of fear conditioning undoes fear conditioning.
• Retrieval makes the fear conditioning from Day 1 vulnerable to damage. Combining retrieval with drug causes loss of conditioning.

• Nader et al. (2000) state that the memory trace is "labile" during retrieval, i.e., its form can be changed at that time.

Figure 7.20
Using Fragility of Memories During Retrieval to Treat PTSD

• Post-traumatic stress disorder (PTSD): Strong fear and stress responses are evoked by reminders of the initial traumatic event.

• Brunet et al. asked whether human PTSD patients can lose or at least diminish their fear and stress conditioning by techniques that are similar to Nader et al.'s demonstration that rats can lose their fear conditioning.
  - Study used propranolol, a drug that is used to prevent traumatic memories if administered immediately following a traumatic event. Propranolol reduces the fear & stress conditioning of trauma.
Brunet et al.'s Study of PTSD Subjects

- PTSD patients: Childhood sexual abuse, motor vehicle accident, rape, being taken hostage.
  - Comorbid mental disorders included: major depressive disorder, panic disorder, social phobia, bulimia, generalized anxiety disorder.

- Two scripts were prepared for each patient that described the events that produced the trauma for that patient.

- 19 PTSD patients were randomly assigned to either a treatment condition or a placebo control condition.
  - Both Conditions: Patient hears a 30-second recording describing their traumatic experience.
  - Treatment Condition: Patient is injected with propranolol immediately following recording.
  - Control Condition: Patient is injected with a placebo that has no active ingredients.

Analogy Between Brunet’s Treatment of PTSD & Fear Deconditioning in Rats
Test of Treatment

• One week later, the patients listened to a taped version of the scripts that described their traumatic experience, and are asked to imagine the traumatic events while listening to the tape.
  - Physiological measures of stress and anxiety are taken while patients listen to the tape.

• Question: When the patients hear the taped version of traumatic experience, will they experience fear, anxiety, etc. of PTSD?
  - I.e., has the drug treatment reduced or eliminated their tendency to associate fear responses with these memories.
Human traumatic experience

Listen to taped description of traumatic experience

Injection of propranolol immediately after recall

Later, will the human seem to have unlearned the fear conditioning to the traumatic memories?

Rat tone + shock conditioning in the rat

Rat hears tone without the shock

Injection of anisomycin immediately after rat hears tone

Later, the rat seems to have unlearned the fear conditioning to the tone.
Brunet et al. Results

- Grey = placebo group; Black = propranolol group

- Result: Therapy reduces original fear conditioning.
Brunet et al. Results

- Grey = placebo group; Black = propranolol group
- Result: Therapy reduces original fear conditioning.

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Tensing of Frowning Muscles

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Return to Malleability of Memory During Retrieval
Malleability of Memories During Retrieval

• Learned associations can be lost during retrieval
  ✦ Rats unlearned tone-shock connection
  ✦ Humans unlearn (to some degree) the association between a traumatic episodic memory and the emotional response

• Consolidation & Reconsolidation – memories can be strengthened during retrieval
  ✦ Practice testing (retrieval) produces better future recall

• Do these results contradict each other? No!

• Stored representations can change during retrieval.
  ✦ Usually the change makes the memory stronger, better organized, more linked to other memories, especially to retrieval cues.
  ✦ The opposite can also happen, e.g., rats unlearn their fear conditioning, or humans become desensitized to memories of trauma. This special case is based on the injection of drugs that would not normally be present.
Conclusion re Consolidation

• Consolidation occurs through reactivation of memories.

• Hippocampus plays a major role in reactivation for recent memories. After the memories have been consolidated, the hippocampus plays a reduced role in retrieval of memories.

• Memories are malleable during or shortly after retrieval.