Cannabinoids and Health

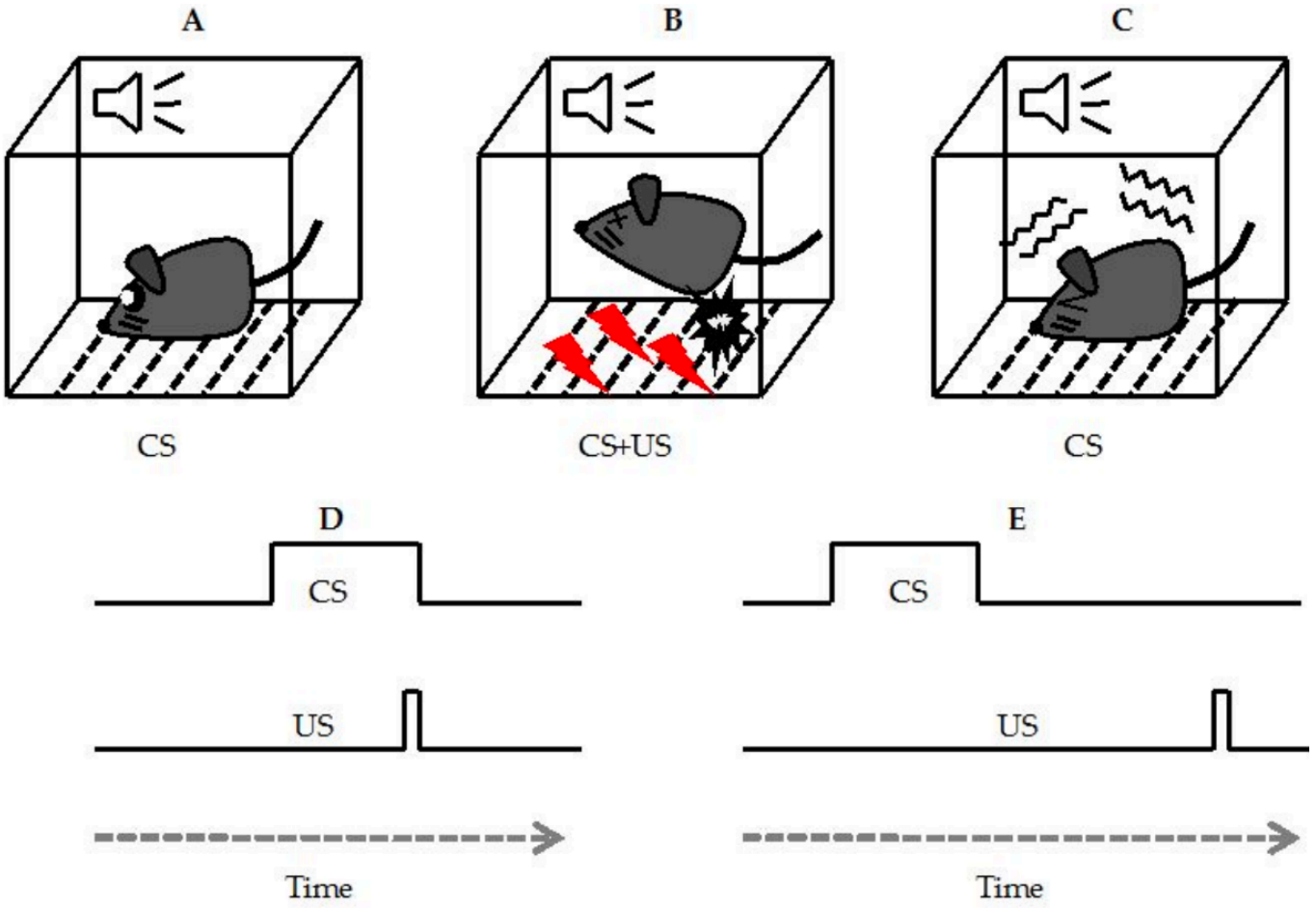
Module 9

Lecture 6: Special Considerations For PTSD

The Role of Fear Extinction in Anxiety Disorders

- Phobias, Post-Traumatic Stress Disorder (PTSD), and other anxiety disorders share an important characteristic
- **A Conditioned Fear Response** (usually to a stimulus that is not actually dangerous or threatening, e.g., going shopping at the grocery store, driving on the interstate, air travel, etc.)
- To study this concept, we can easily create conditioned fear in animals (e.g., mice)

Fear Conditioning in Animal Models



How to “Treat” Conditioned Fear: Extinction Paradigms

- **Fear Extinction** is a decline in the conditioned fear responses following exposure to a feared conditioned stimulus
- In other words, after exposing the mouse to the tone over and over *without* the footshock, the mouse will eventually stop having a fear response to the tone
- This same concept is true in humans, however extinction often doesn’t last long
- **Spontaneous recovery** is return of fear response even after undergoing extinction procedure

Fear Extinction: Clinical Challenges

- First-line approach to treat anxiety disorders is exposure- therapy
- Relies on extinction processes (repeatedly exposing the patient to the feared stimulus until stimulus no longer elicits fear)
- Many patients fail to maintain their treatment gains
  - e.g., fears may return a day, a week, or a month after ending therapy
- Fear extinction is **inhibitory learning** and its maintenance is temporary and conditioned fear responses can return
  - this learning is somewhat “fragile”

Rabinak et al., 2013, *Neuropharmacology*

Cannabinoids and Fear Extinction

- Animal studies show that activation of the cannabinoid system during extinction learning enhances fear extinction and its retention.
- CB1 receptors densely populate areas of the brain associated with fear and emotional memory
- CB1 receptor agonists, such as THC, can facilitate extinction recall by preventing recovery of extinguished fear in rats

Rabinak et al., 2013, *Neuropharmacology*

Human (Clinical) Evidence

- Randomized, double-blind, placebo-controlled, between-subjects design comparing synthetic THC to placebo in 29 healthy adults
- Subjects underwent standard Pavlovian fear conditioning and extinction paradigm
  - received THC or placebo before extinction
- Compared to placebo subjects, THC subjects showed lower fear response to a previously extinguished stimulus 24 h after extinction learning
- Suggests that THC prevented the recovery of fear

Rabinak et al., 2013, *Neuropharmacology*

Research Questions and Future Directions

- How do different cannabinoids or combinations of cannabinoids impact subjective and physiological measures of anxiety?
- CBD vs THC?
- Most of the animal research uses CB1 agonists, and human research usually uses synthetic THC (e.g. dronabinol)
  - How might plant-derived cannabis impact anxiety and facilitate fear extinction?

More Research Questions and Future Directions

- What is the ideal dose?
- How long should treatment last?
- Across which clinically anxious populations are cannabinoids most effective? Most risky?
- How can cannabinoids be integrated into other therapeutic modalities?
  - e.g., used during exposure therapy sessions? Before? After? Both?