

Emerging Treatments of Anxiety Informed by Scientific Knowledge about the Brain

Outline

- **Psychotherapy, learning, and neuroplasticity**
- **Neural circuitry of therapeutic change**
- **Pharmacological enhancement of psychotherapeutic learning**
 - **D-cycloserine**
 - **SSRIs**
- **Pharmacological interference with psychotherapeutic learning**
 - **Benzodiazepines**
- **Erasing bad memories**

Psychotherapy, Learning, and Neuroplasticity



■ Learning

- Acquiring new information and/or skills: emotional regulation, coping strategies, cognitive structuring, behavioral activation
- Altering/adapting behavior to meet environmental demands or contingencies
- Repetition and practice

■ Neuroplasticity

- Experience-dependent changes in brain structure or function
- Synaptic plasticity (e.g., LTP)
- Neurogenesis
- Repetition and practice

■ Treatment emphasis: learning vs. symptom reduction

- Repetition and practice

Neural Circuitry of Psychotherapeutic Change



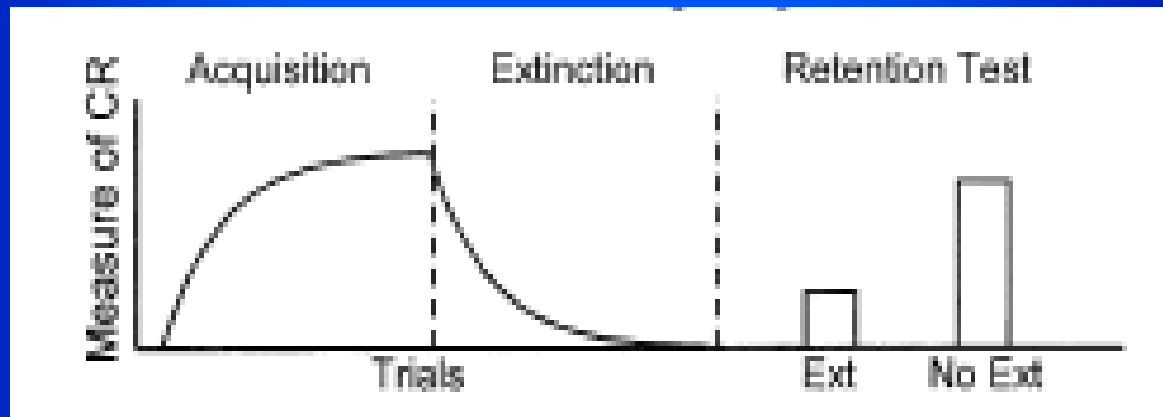
- **Prefrontal cortex**
 - Emotional regulation, coping strategies, cognitive structuring, directing behavioral activation
- **Hippocampus**
 - Learning and memory related to therapeutic change
- **Amygdala**
 - Down-regulation of threat-related activation that is context-inappropriate

Neural Circuitry of Psychotherapeutic Change

- **Neural pathways that support dysfunctional thinking and behavior patterns**
 - Anxiety, panic, worries
 - Depression, self-critical thoughts, suicidal thoughts
 - PTSD, self-blame, safety, trust, power/control, intimacy, esteem
 - Anger, outbursts, abusive behavior
 - Practice/repetition leads to strengthened neural connections
 - Same mechanisms as in learning math, chess, or piano
 - These neural connections will not go away and cannot be excised
 - They are here for the rest of patient's life
 - This is the bad news (but makes evolutionary sense)
 - Anxiety and anger co-opted these evolutionarily preserved and often beneficial mechanisms
- **Psychotherapy develops and strengthens neural pathways that support accurate thinking and adaptive behavior patterns**
 - Thanks to the exact same neuroplastic mechanisms that created the dysfunctional thinking and behavior patterns above

Extinction and Exposure Therapy

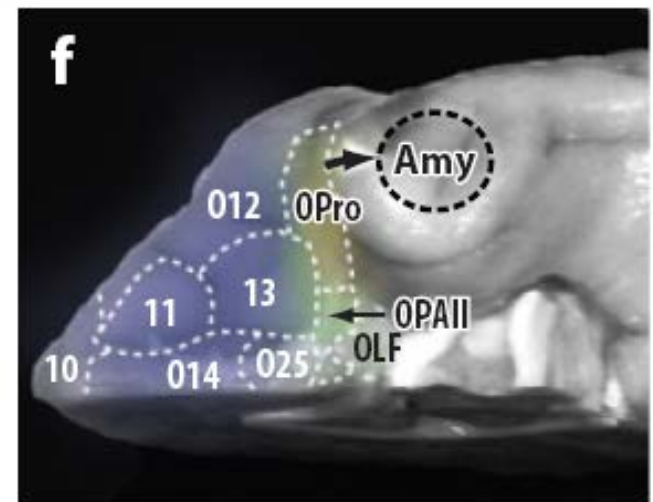
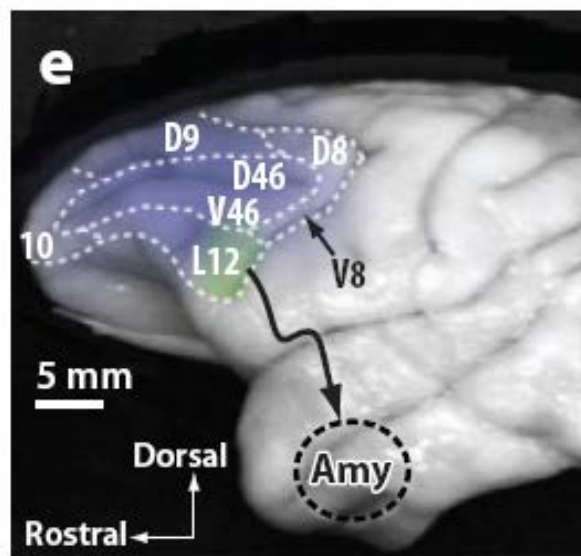
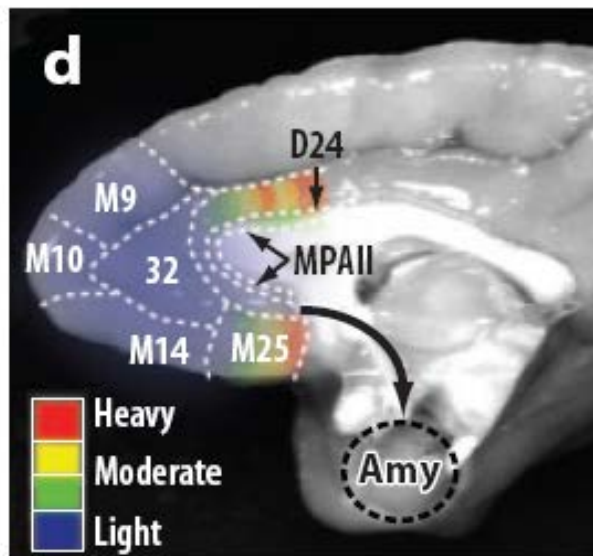
- Extinction is NOT erasing the association between an innocuous cue and danger (shock), but rather learning a new association between that cue and safety (no shock)



- Exposure therapy is NOT erasing the association between an innocuous cue/trigger and danger (rape, mortar attack), but rather learning a new association between that cue/trigger and safety (no harmful event, safe setting)
- This is implemented via activation of the ventromedial PFC that sends inhibitory projections to the amygdala

Extinction and Exposure Therapy

PFC–Amygdala Connectivity



Pharmacotherapy and Psychotherapy

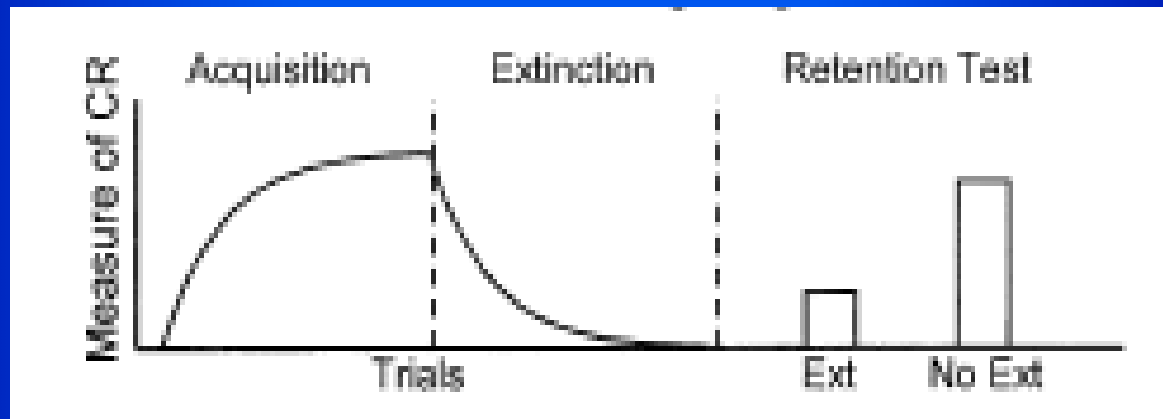
“The joint use of pharmacological and psychotherapeutic interventions might be especially successful because of a potentially interactive and synergistic—not only additive—effect of the two interventions. Psychopharmacological treatment may help consolidate the biological changes caused by psychotherapy.”

Eric R. Kandel, M.D., 1998

Pharmacotherapy and Psychotherapy

D-cycloserine Facilitates Extinction Learning

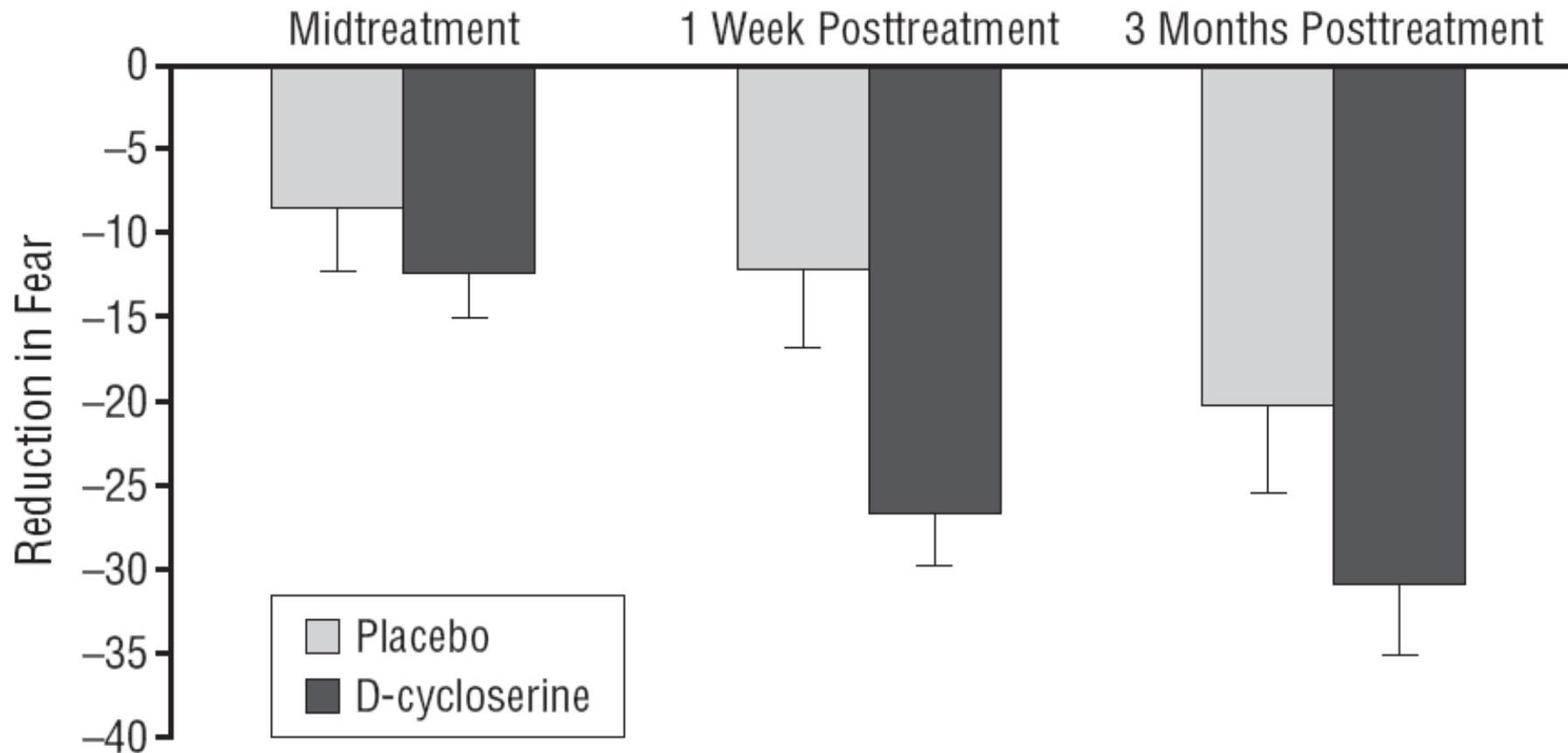
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- D-cycloserine facilitates learning the new association between that cue and safety (no shock)

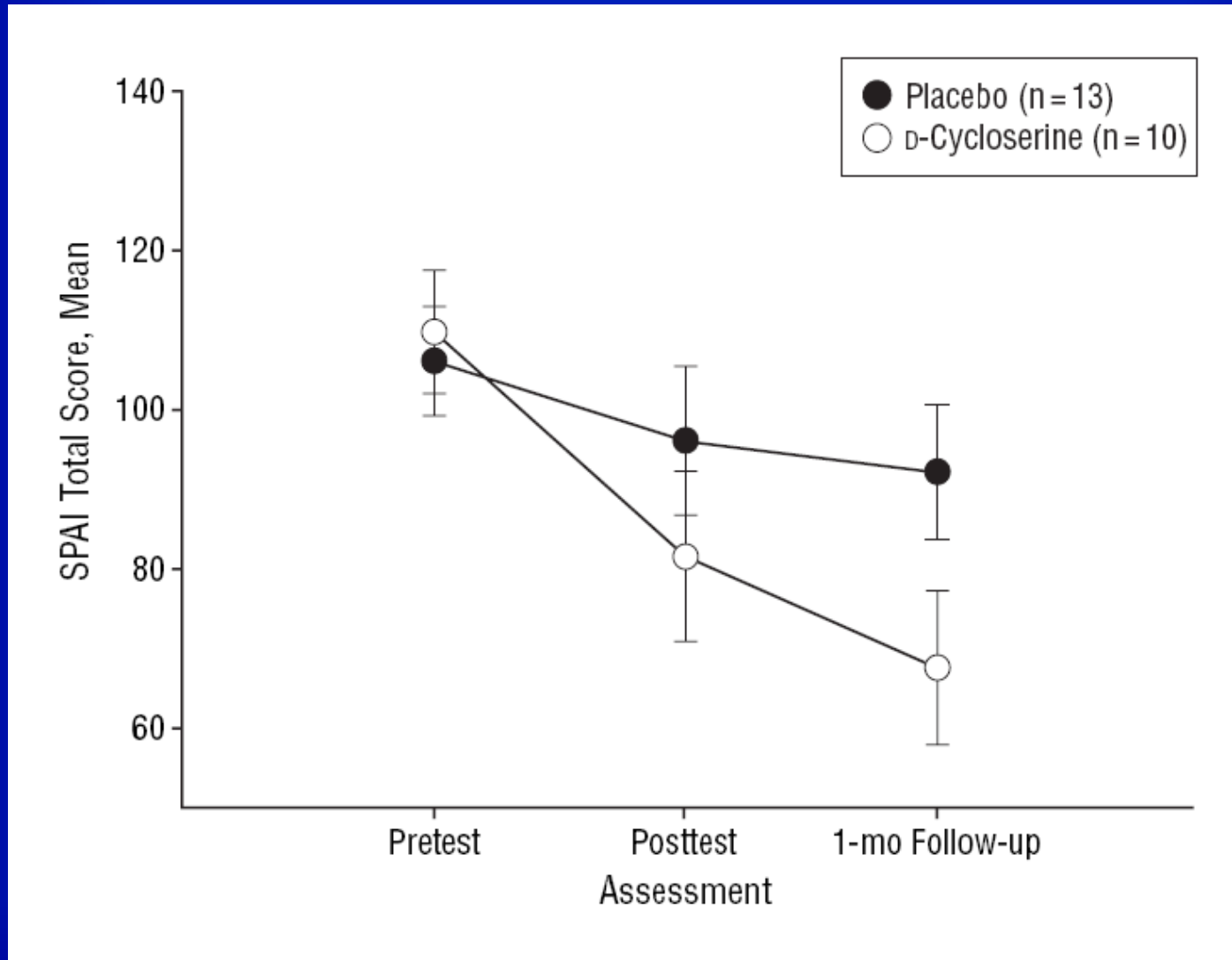
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D-cycloserine, Virtual Exposure Therapy, and Acrophobia



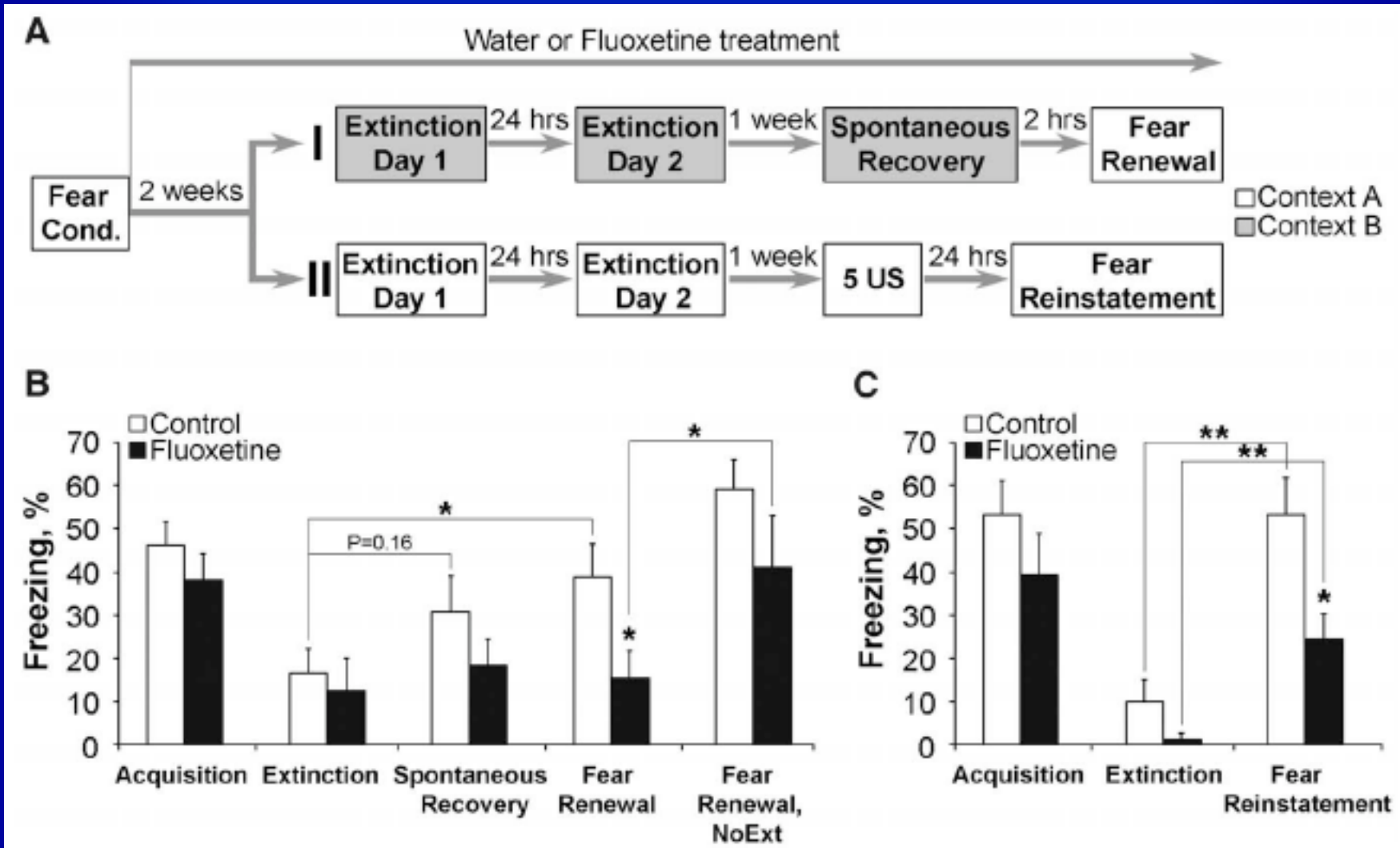
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D-cycloserine, Exposure Therapy, and Social Anxiety Disorder



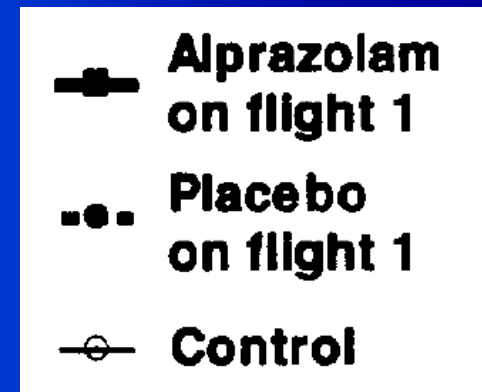
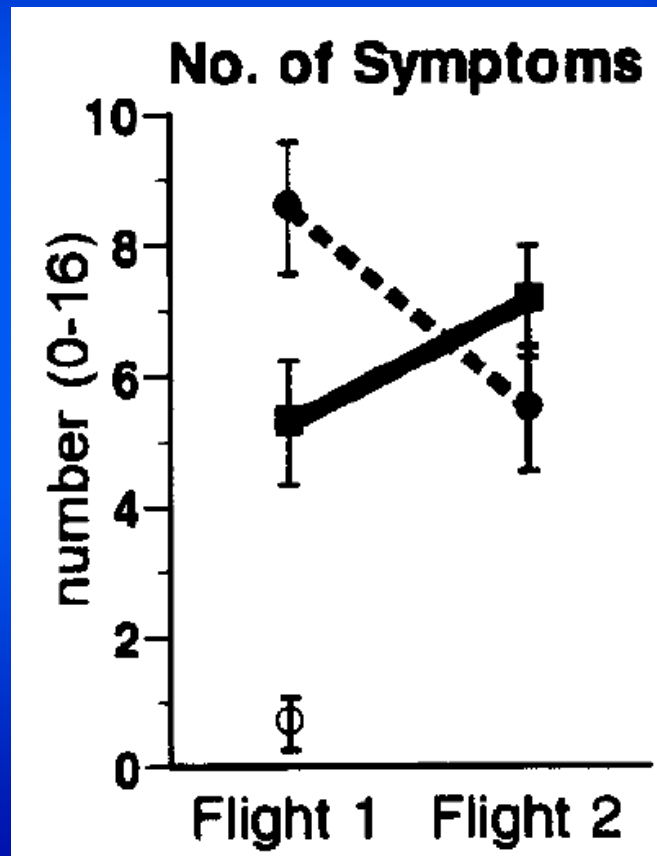
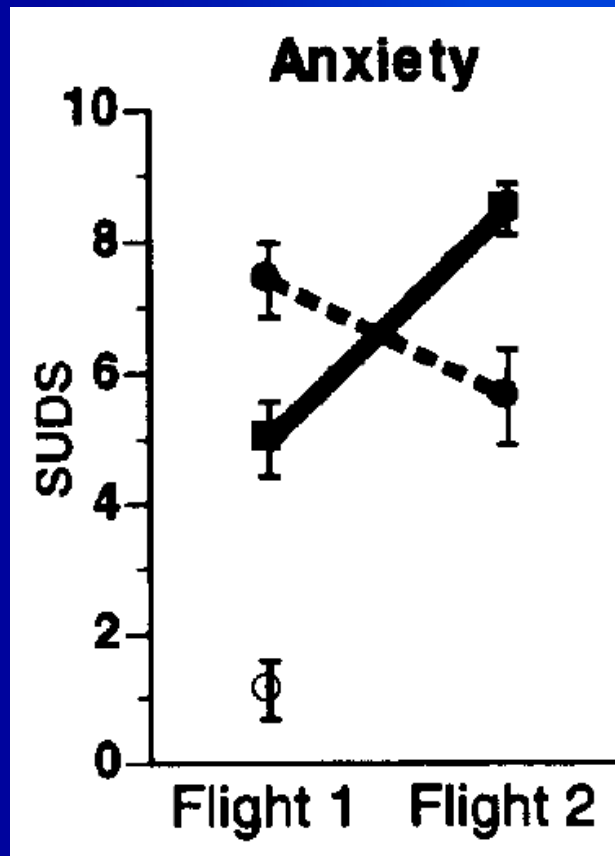
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SSRIs and Extinction



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Benzodiazapines, Exposure, and Fear of Flying



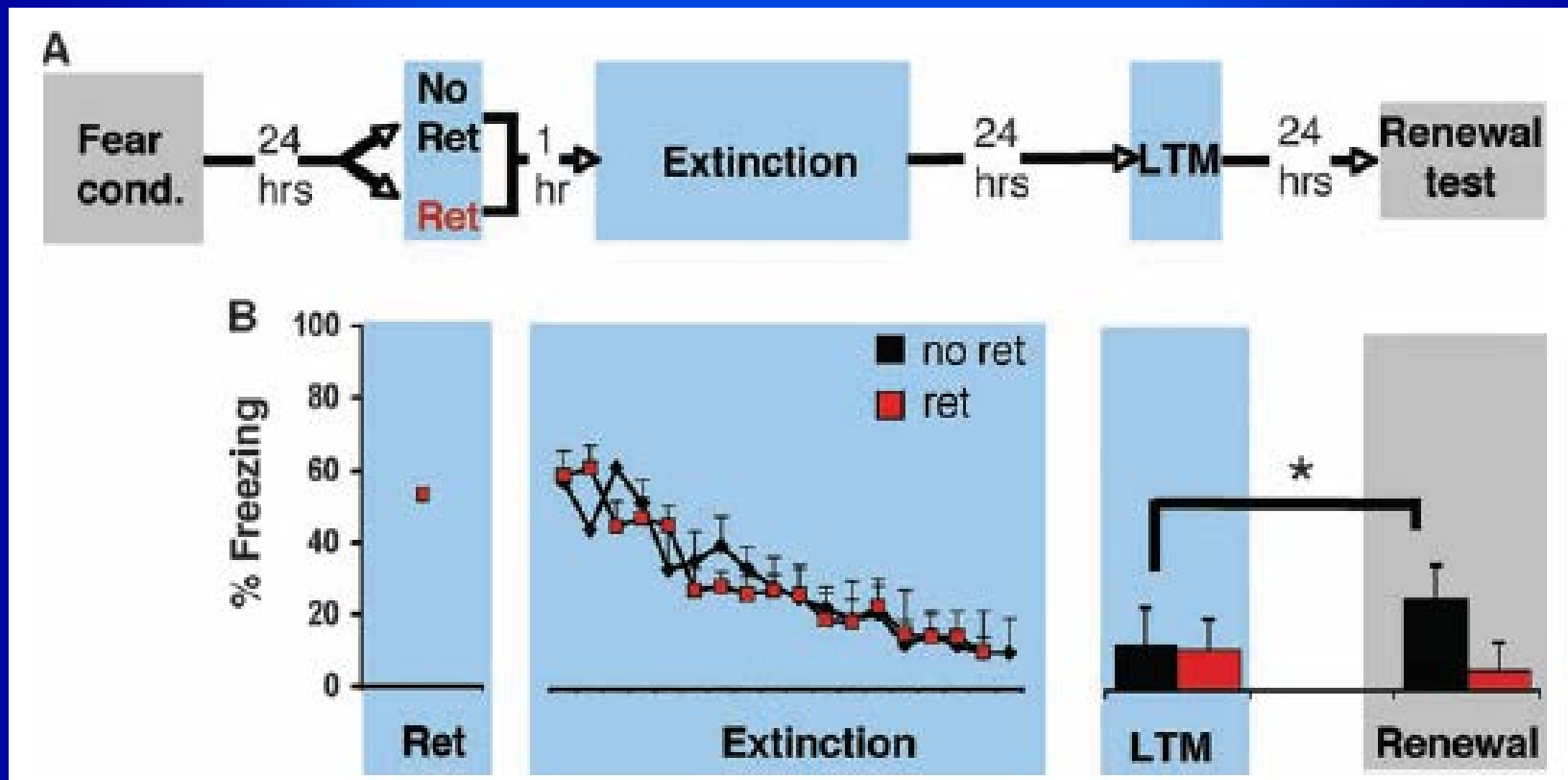
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Erasing Fear Memories

- Is there any way to erase fear memories?
- During memory consolidation, a fear memory is labile and can be erased
- After memory consolidation, a fear memory is indelible and cannot be erased
 - EXCEPT at the time when it is retrieved, during which it becomes labile again and can be erased
- After memory reconsolidation, a fear memory is indelible and cannot be erased
 - EXCEPT at the time when it is next retrieved, during which it becomes labile again and can be erased

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Using Extinction to Erase Fear Memories in Rats



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Using Extinction to Erase Fear Memories in Humans

a	Day 1	Day 2		Day 3
	Group 1: Acquisition	Reminder	10 min → Extinction	Re-extinction
	Group 2: Acquisition	Reminder	6 h → Extinction	Re-extinction
	Group 2: Acquisition	No reminder	→ Extinction	Re-extinction
Spontaneous recovery: (1st trial of re-extinction) – (last trial of extinction)				

Pharmacotherapy and Psychotherapy

Using Extinction to Erase Fear Memories in Humans

