

# **Emerging Treatments of Anxiety Informed by Scientific Knowledge about the Brain**

# Outline

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- **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

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## ■ Learning

- **Acquiring new information and/or skills: emotional regulation, coping strategies, cognitive restructuring, mindfulness, acceptance, 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

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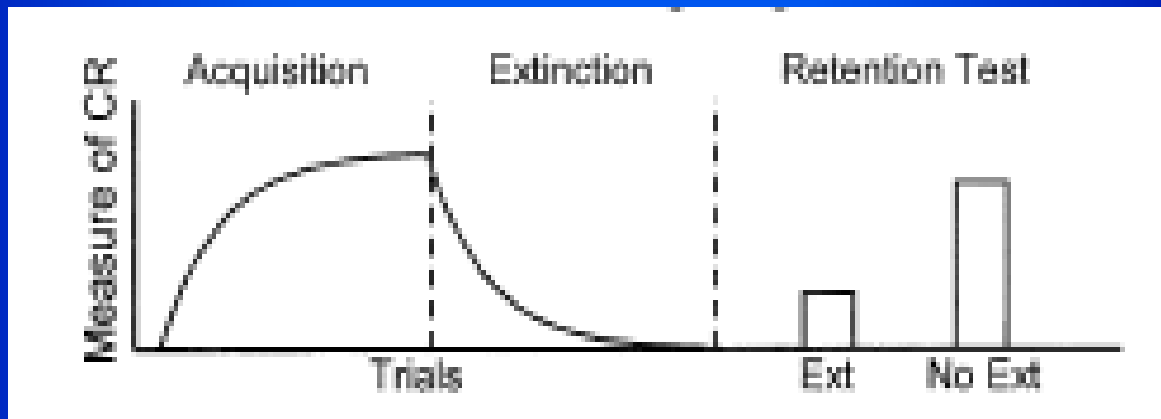
- **Prefrontal cortex**
  - Emotional regulation, coping strategies, cognitive structuring, directing behavioral activation
- **Hippocampus**
  - Learning and memory related to therapeutic change
- **Amygdala**
  - Threat-related activation that is maladaptive, which can be affected by therapeutic change

# Neural Circuitry of Psychotherapeutic Change

- **Neural pathways that support dysfunctional thinking and behavior patterns**
  - **Anxiety, panic, worries, phobias, obsessions**
  - **Depression, self-critical thoughts, suicidal thoughts**
  - **PTSD, self-blame, safety, trust, power/control, intimacy, esteem**
  - **Anger, irritability, 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, depression, 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)

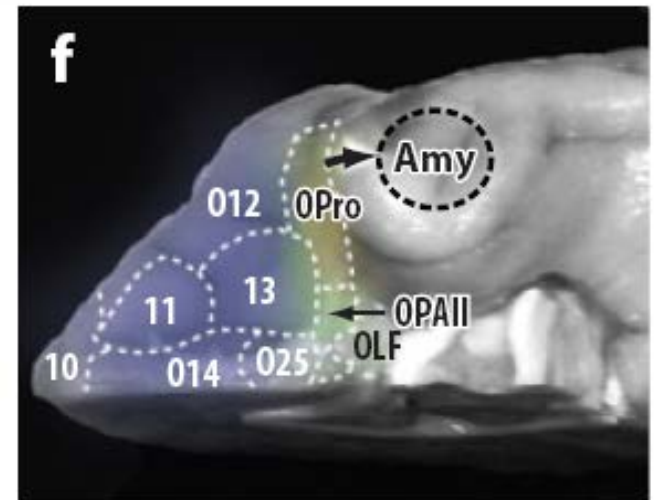
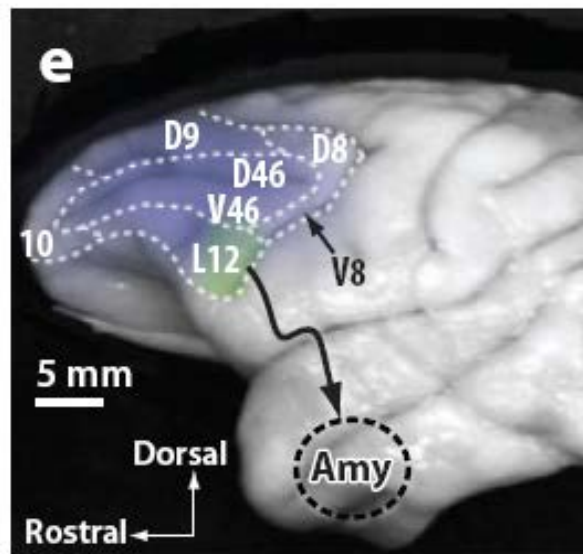
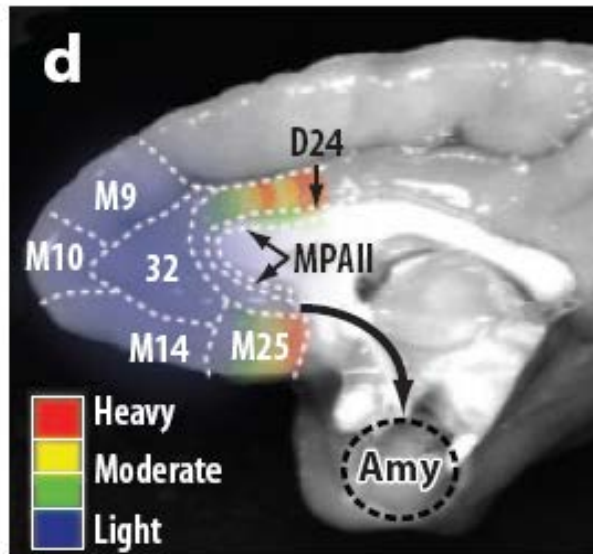


- Exposure therapy is **NOT** erasing the association between an innocuous cue/trigger and danger (rape, mortar attack), but rather learning a new association between that cue/trigger and safety (no harmful event, safe setting)
- This is implemented via activation of the ventromedial PFC that sends inhibitory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



# Extinction and Exposure Therapy

## PFC–Amygdala Connectivity



# Pharmacotherapy and Psychotherapy

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**“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.”**

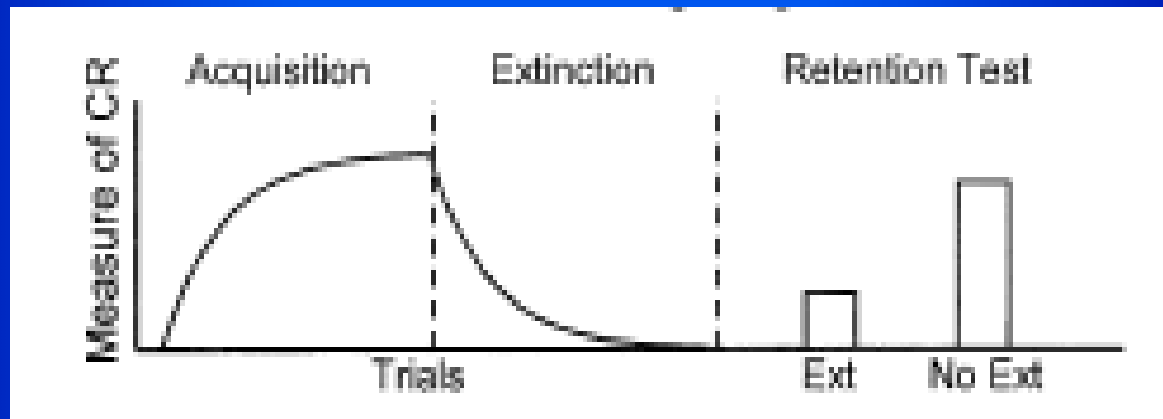
**Eric R. Kandel, M.D., 1998**



# Pharmacotherapy and Psychotherapy

## D-cycloserine Facilitates Extinction Learning

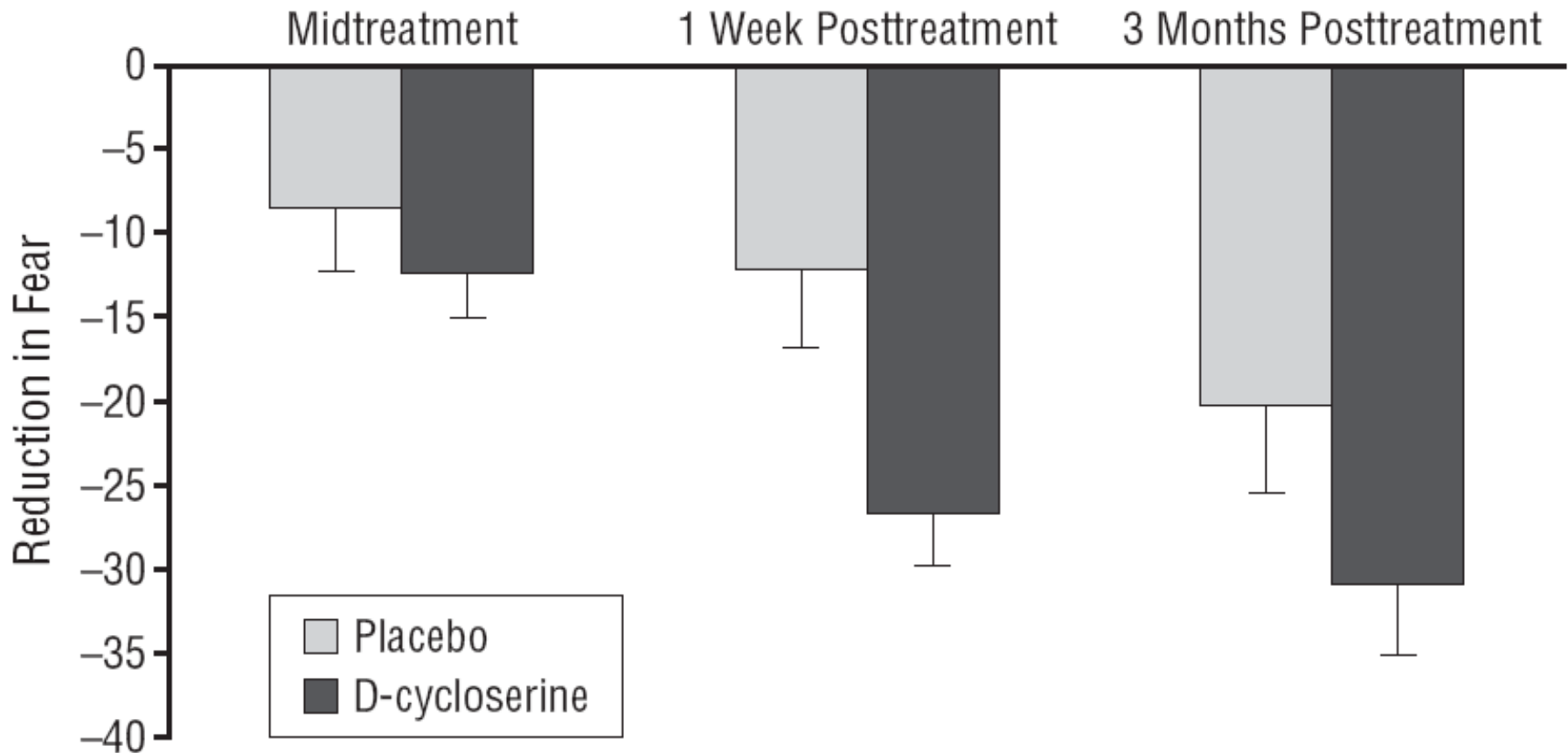
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- D-cycloserine facilitates learning the new association between that cue and safety (no shock)

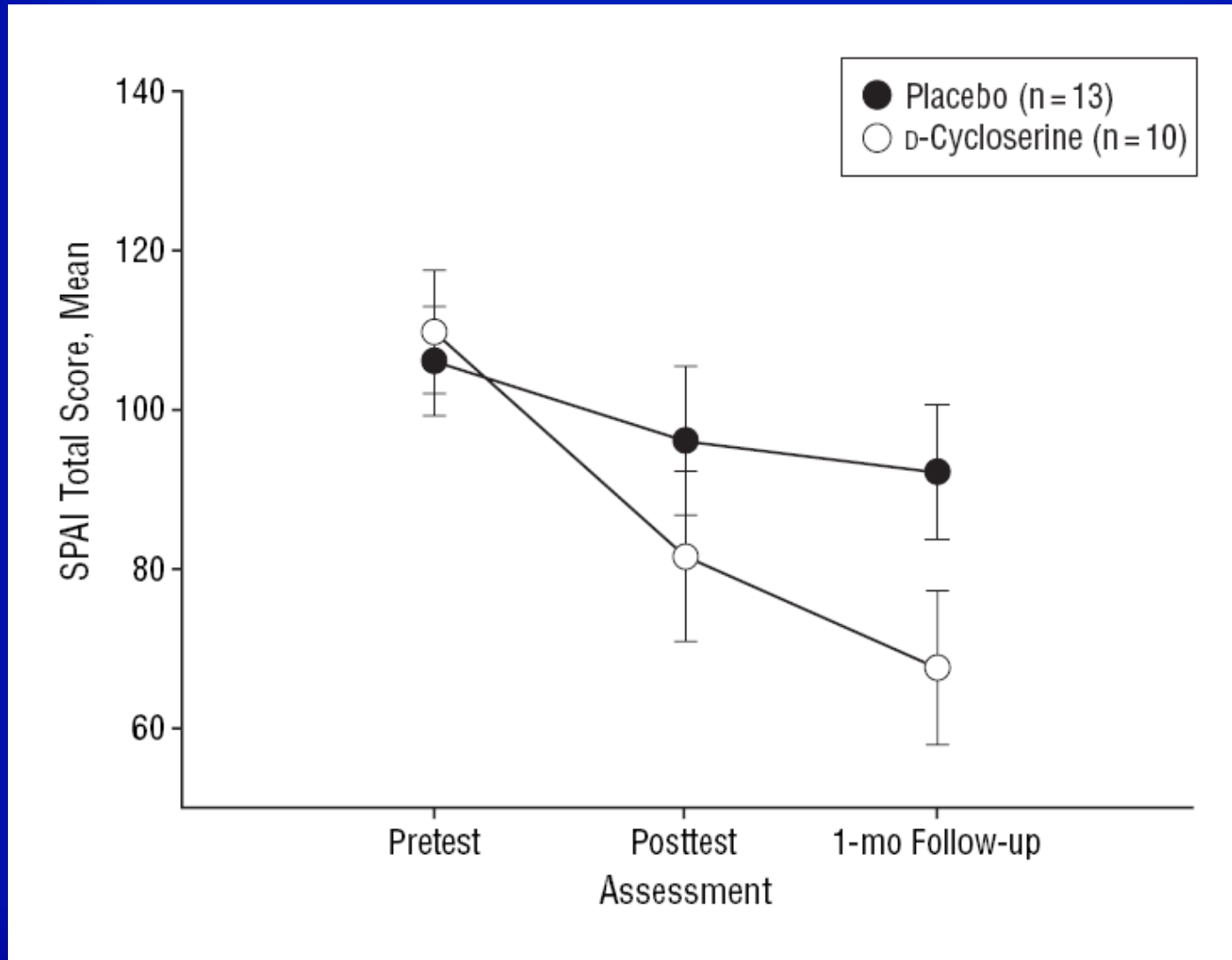
# Pharmacotherapy and Psychotherapy

## D-cycloserine, Virtual Exposure Therapy, and Acrophobia



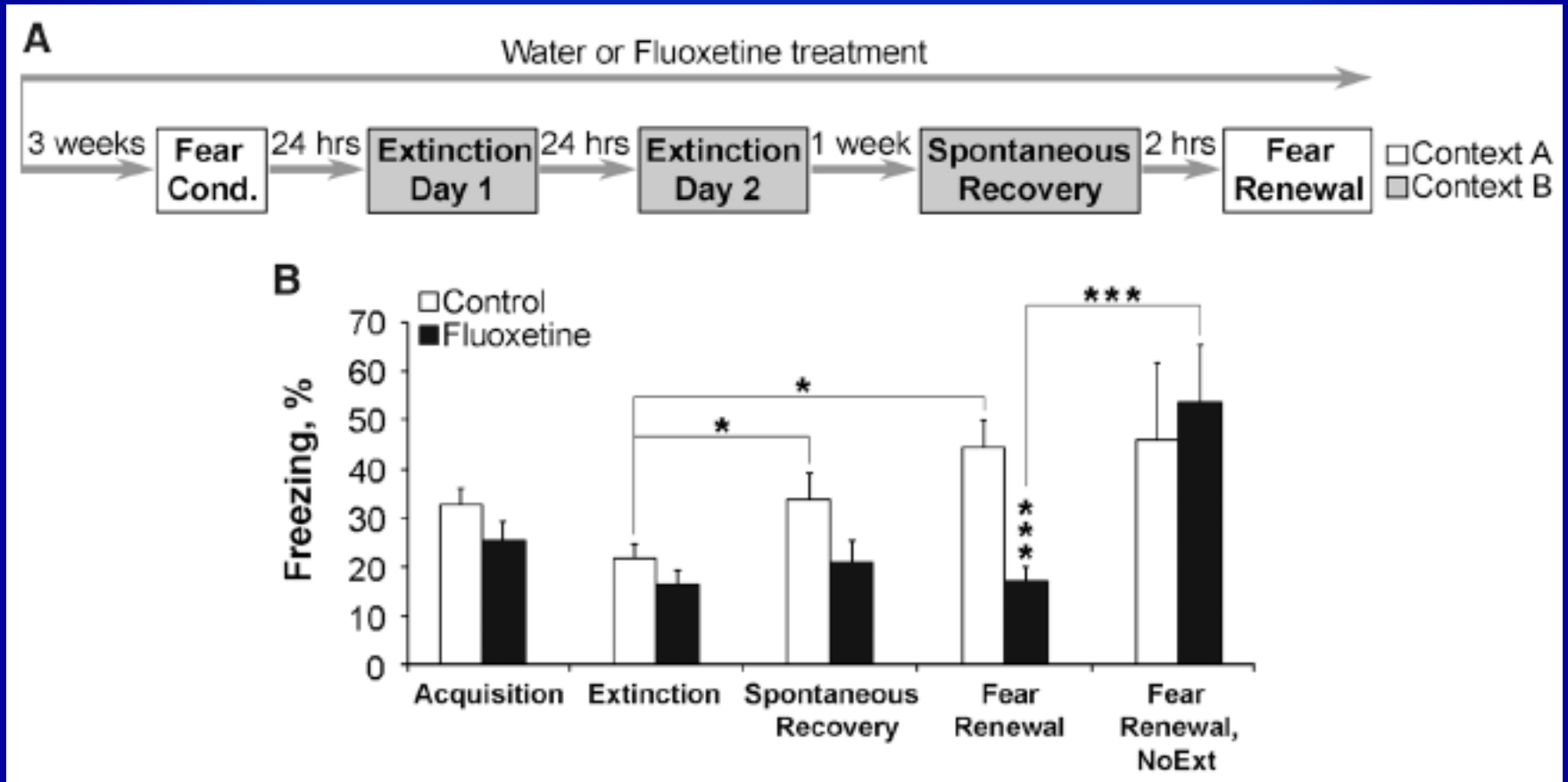
# Pharmacotherapy and Psychotherapy

## D-cycloserine, Exposure Therapy, and Social Anxiety Disorder



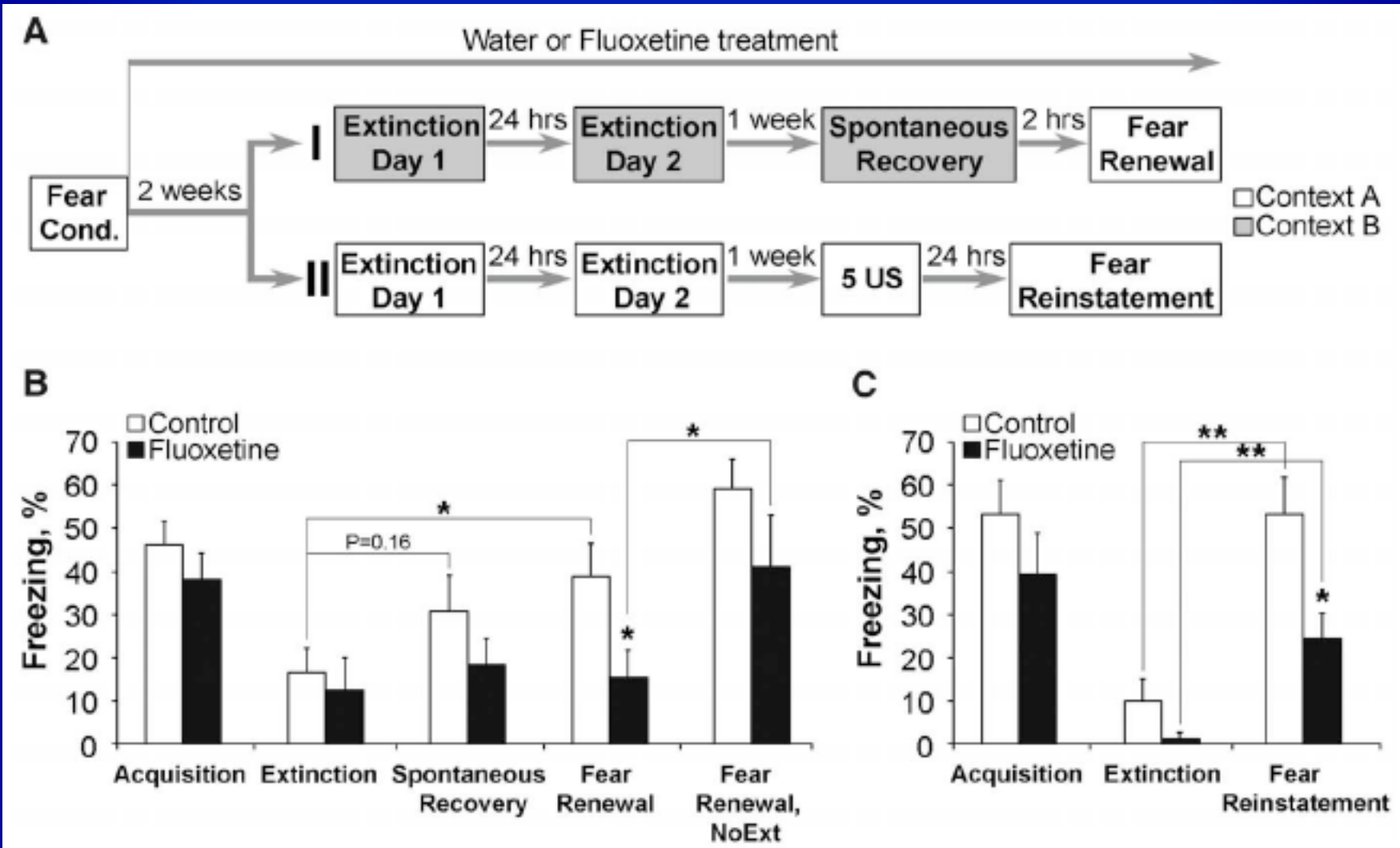
# Pharmacotherapy and Psychotherapy

## SSRIs and Extinction



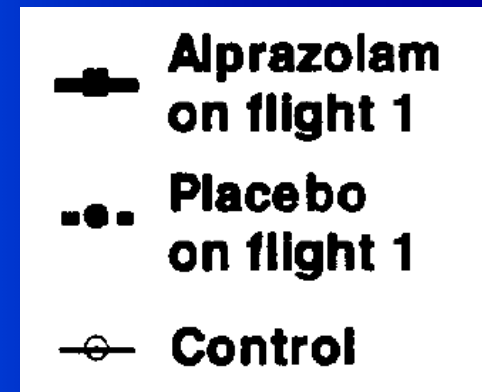
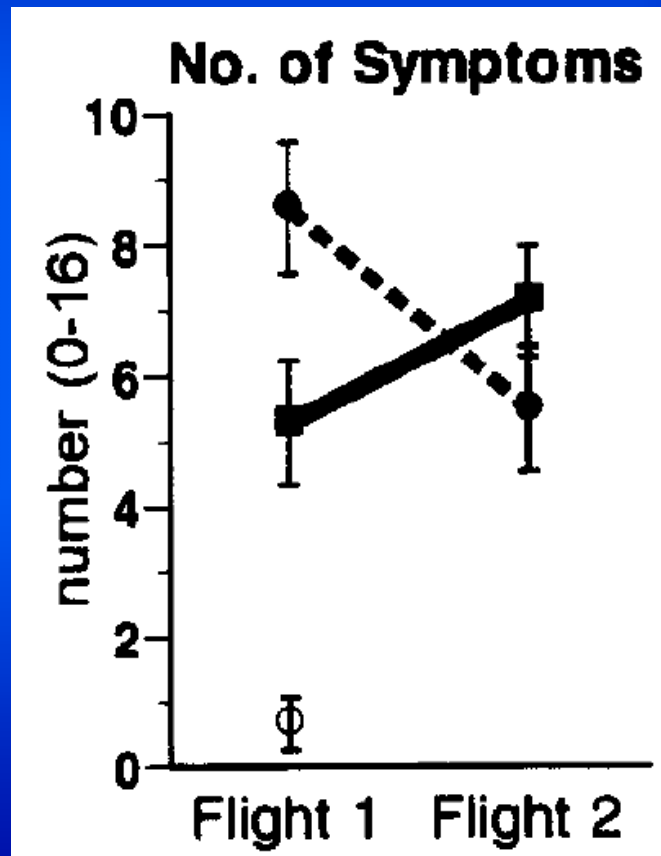
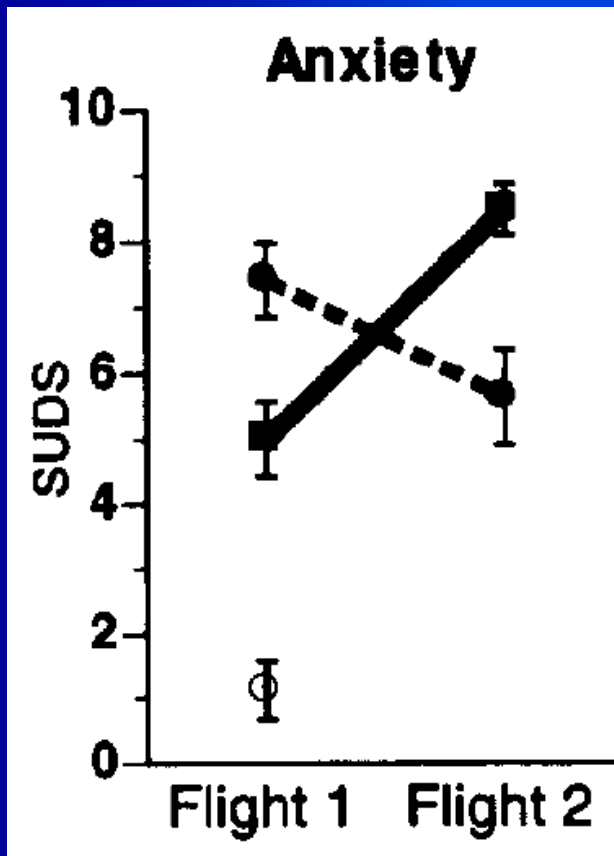
# Pharmacotherapy and Psychotherapy

## SSRIs and Extinction



# Pharmacotherapy and Psychotherapy

## Benzodiazapines, Exposure, and Fear of Flying





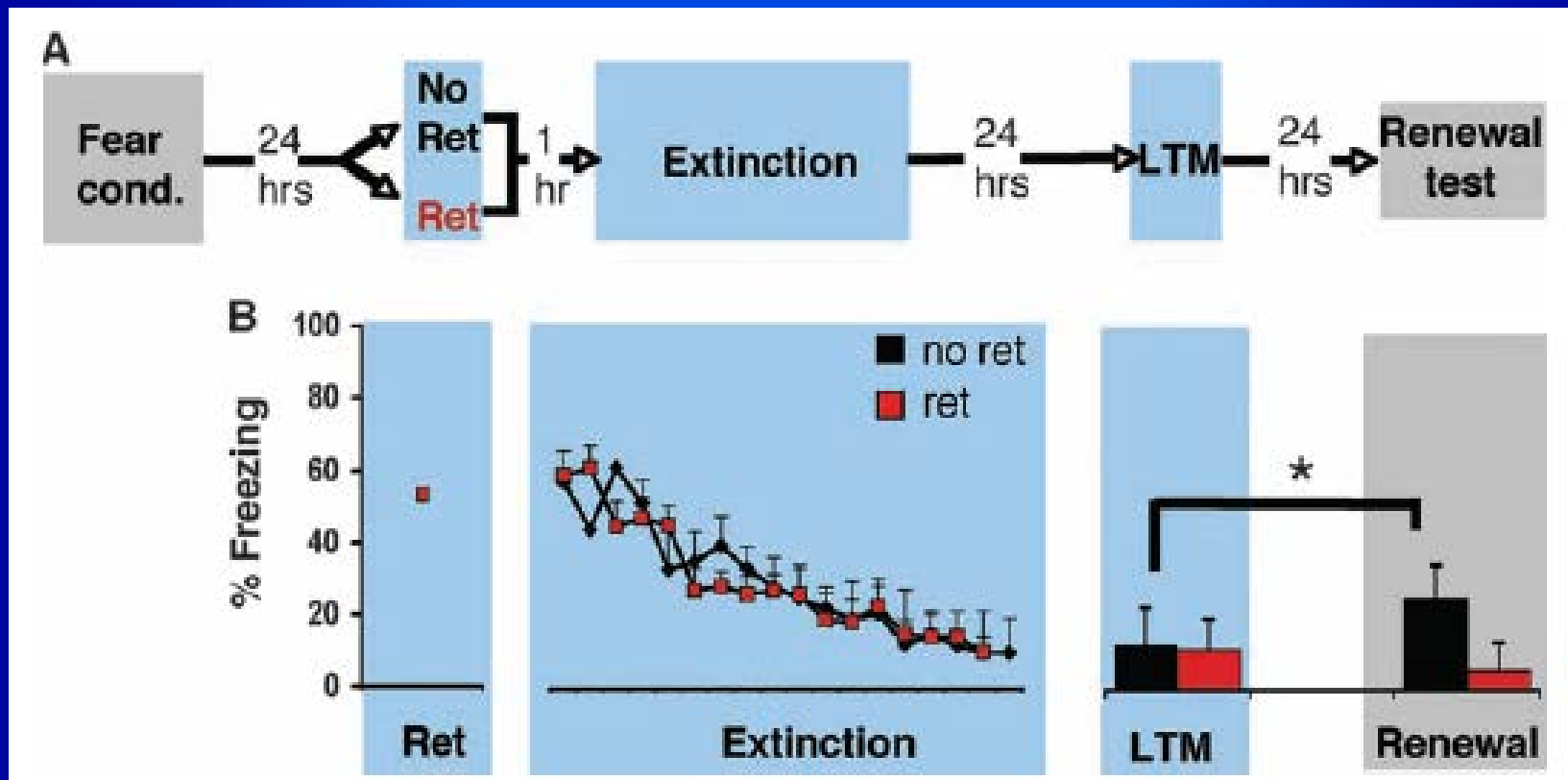
# Pharmacotherapy and Psychotherapy

## 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**

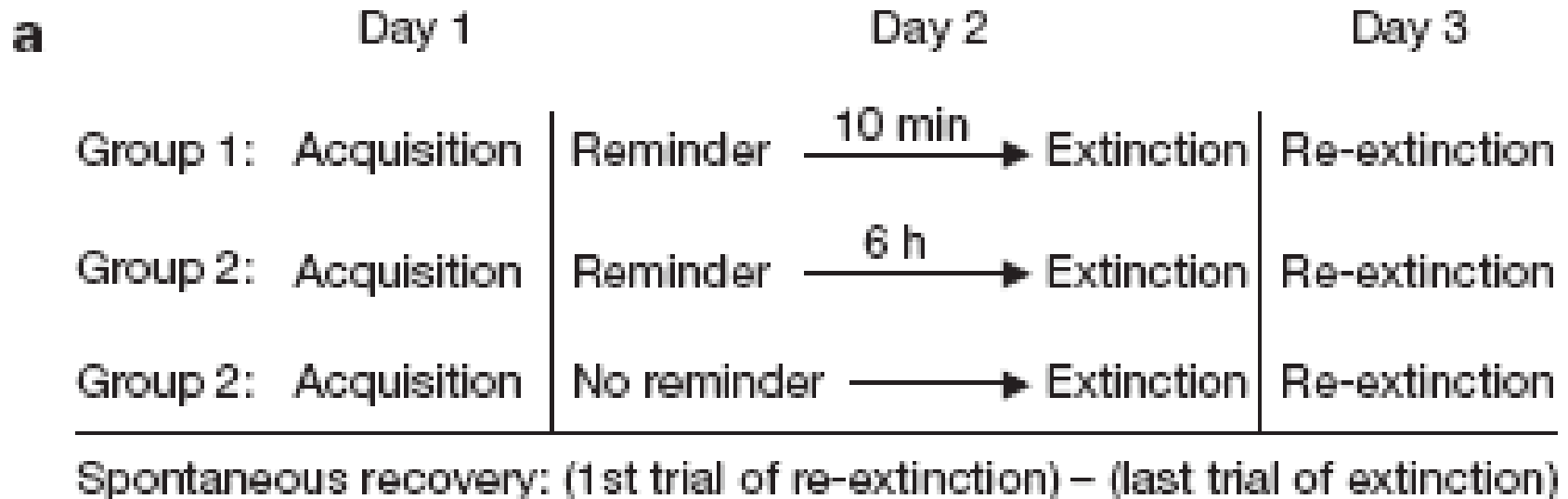
# Pharmacotherapy and Psychotherapy

## Using Extinction to Erase Fear Memories in Rats



# Pharmacotherapy and Psychotherapy

## Using Extinction to Erase Fear Memories in Humans



# Pharmacotherapy and Psychotherapy

## Using Extinction to Erase Fear Memories in Humans

