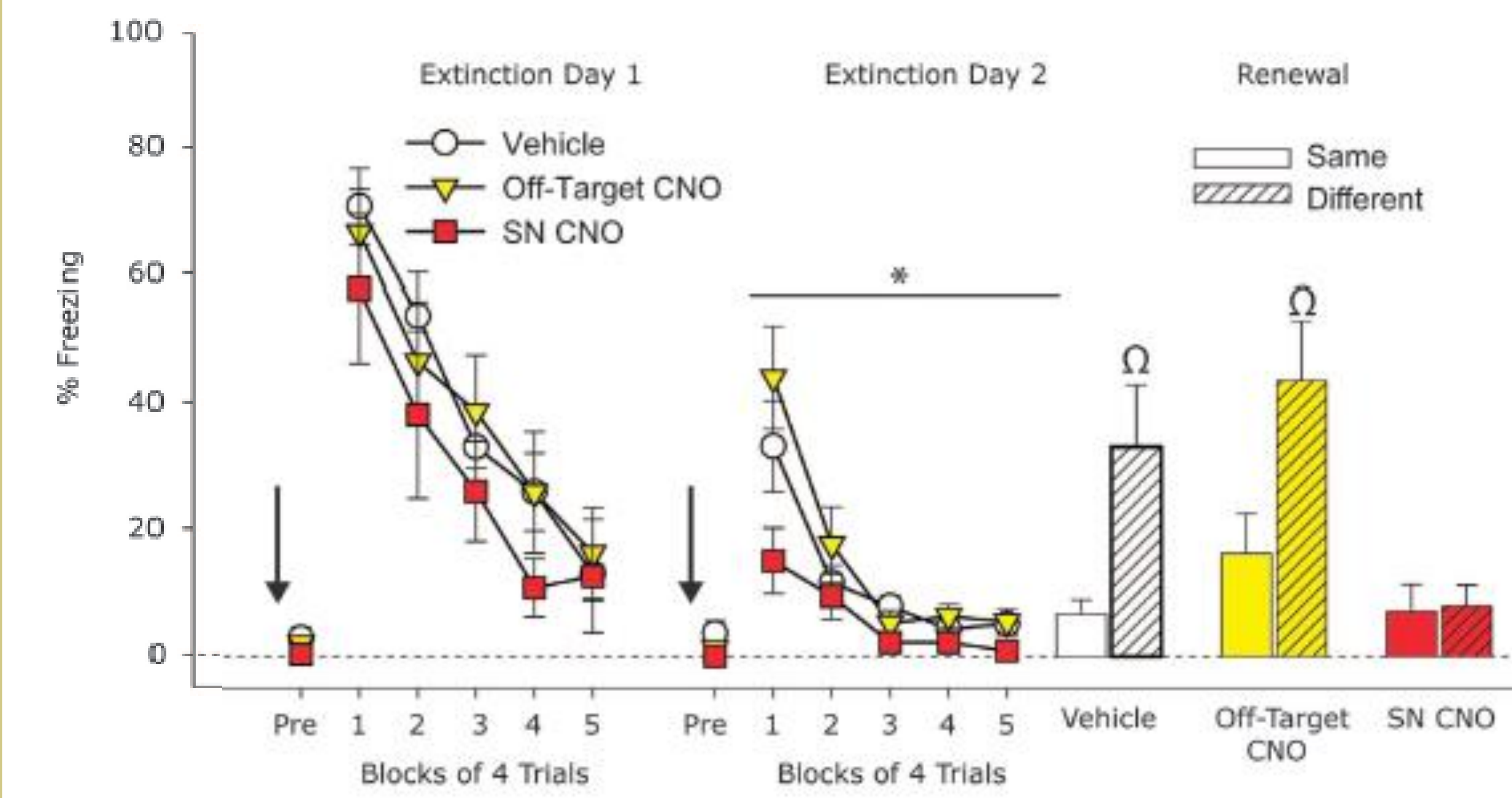
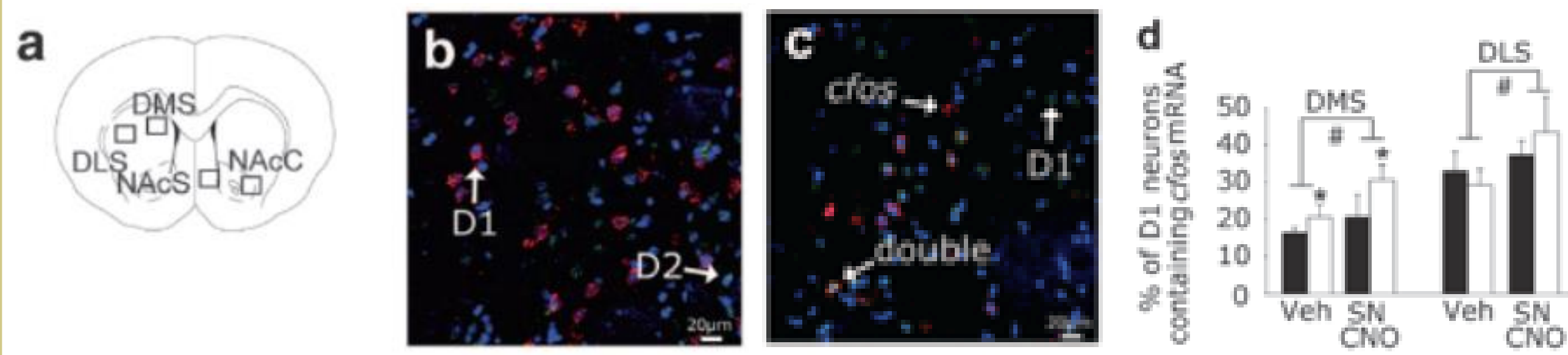


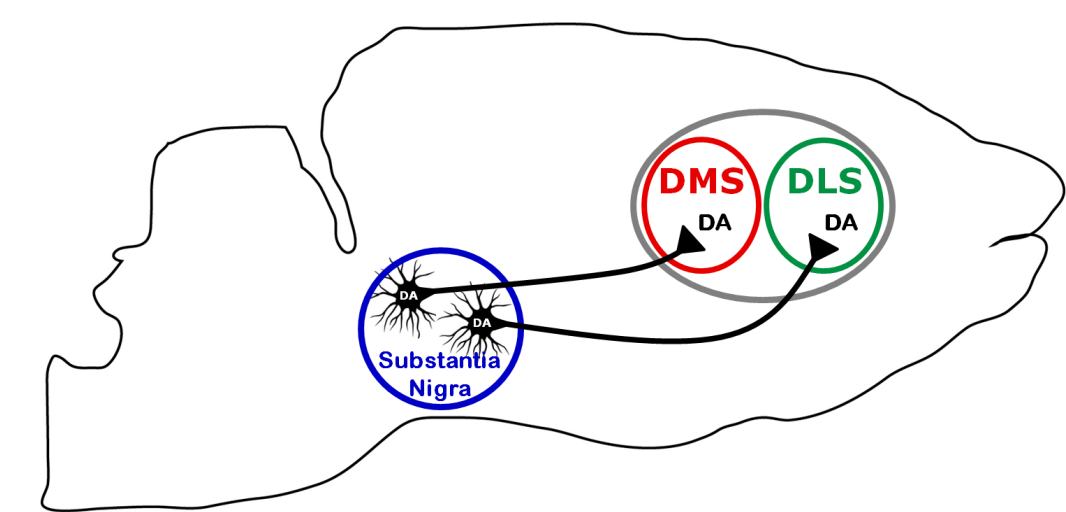
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**Background**

- ❖ Relapse of previously extinguished fear plays a role in the poor long-term success of fear extinction-based exposure therapy for PTSD rodent models.
- ❖ We have observed that fear extinction recruits D1-expressing neurons in the dorsal striatum, and activation of the nigrostriatal dopamine (DA) pathway during fear extinction enhances extinction and prevents fear renewal (Bouchet et al. 2018).



Nigrostriatal dopamine pathway

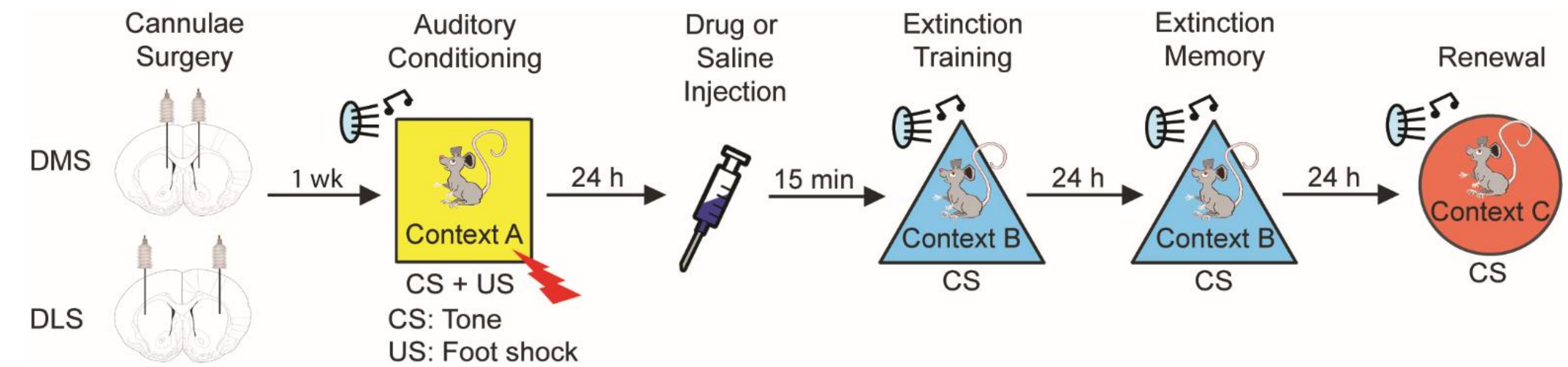


- ❖ These data suggest that the dorsal striatum, the main target of nigrostriatal dopamine, could be an important brain site not before considered in fear extinction.
- ❖ The DMS supports learning that remains sensitive to changes in contextual contingencies, while the DLS supports more rigid, habitual learning strategies.
- ❖ It is possible that dopamine in either the DMS or DLS can enhance fear extinction, but fear extinction enhanced by the DMS or DLS might differ in susceptibility to fear renewal.

The goal of the current study was to begin to investigate the role of dopamine signaling in the DMS and DLS in fear extinction and renewal.

**Methods**

- ❖ Experiments 1 and 2: A GABA<sub>A</sub>/GABA<sub>B</sub> agonist drug cocktail (0.03/0.3 nmol/μl Muscimol/Baclofen) was injected bilaterally into the DMS or DLS.
- ❖ Experiment 3: A D1 antagonist, SCH-233965 (1.0 μg/μl), was injected bilaterally into the DMS.

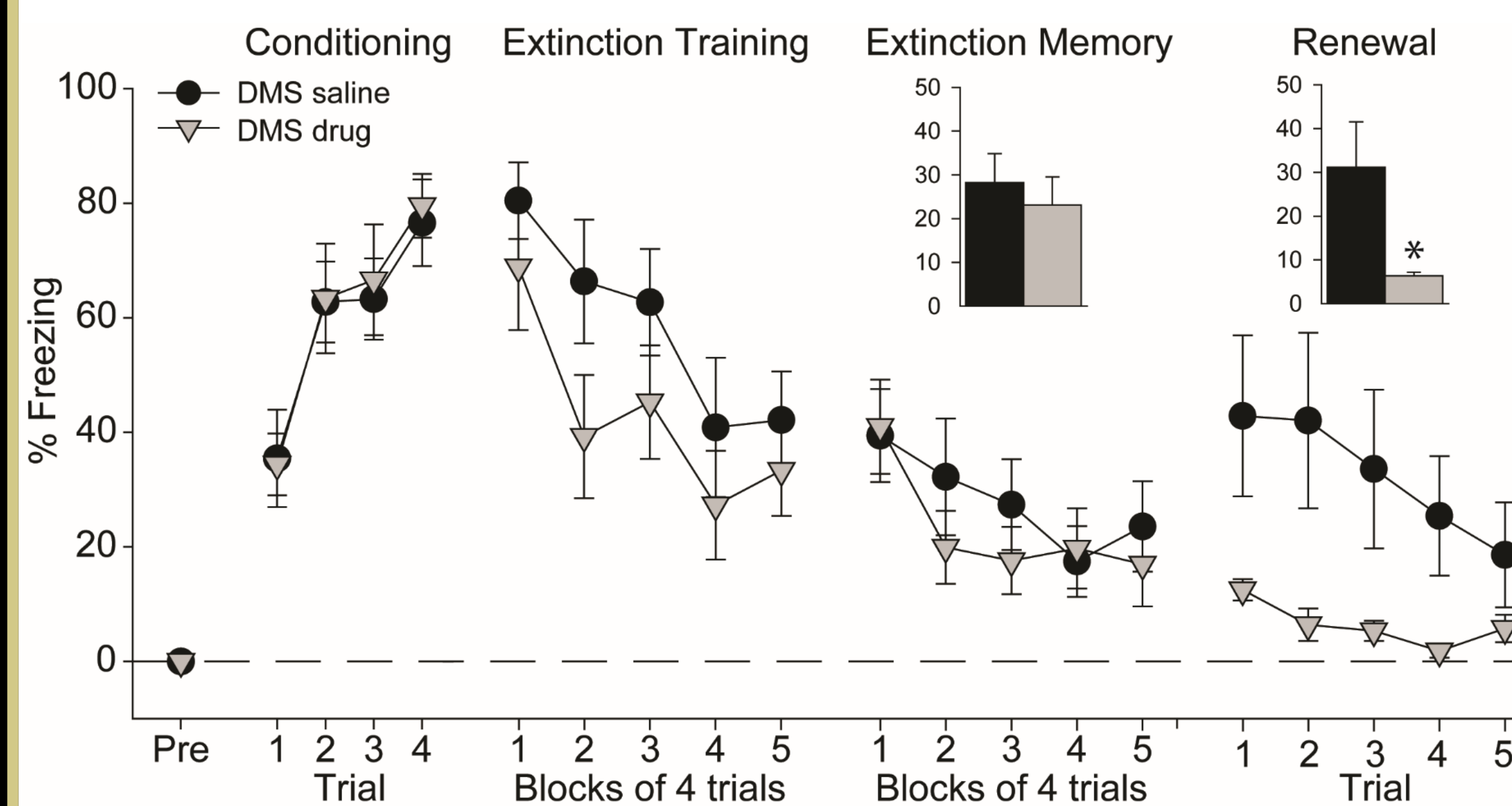


**Experiment 1**

- Goal**
- ❖ To investigate the role of the DMS in fear extinction.
- Hypothesis**
- ❖ Inhibition of the DMS will increase the reliance on the habit learning strategy involving the DLS, thereby rendering fear extinction resistant to fear renewal.

**Results**

Fear extinction supported by the DLS (DMS inactivation) is resistant to renewal

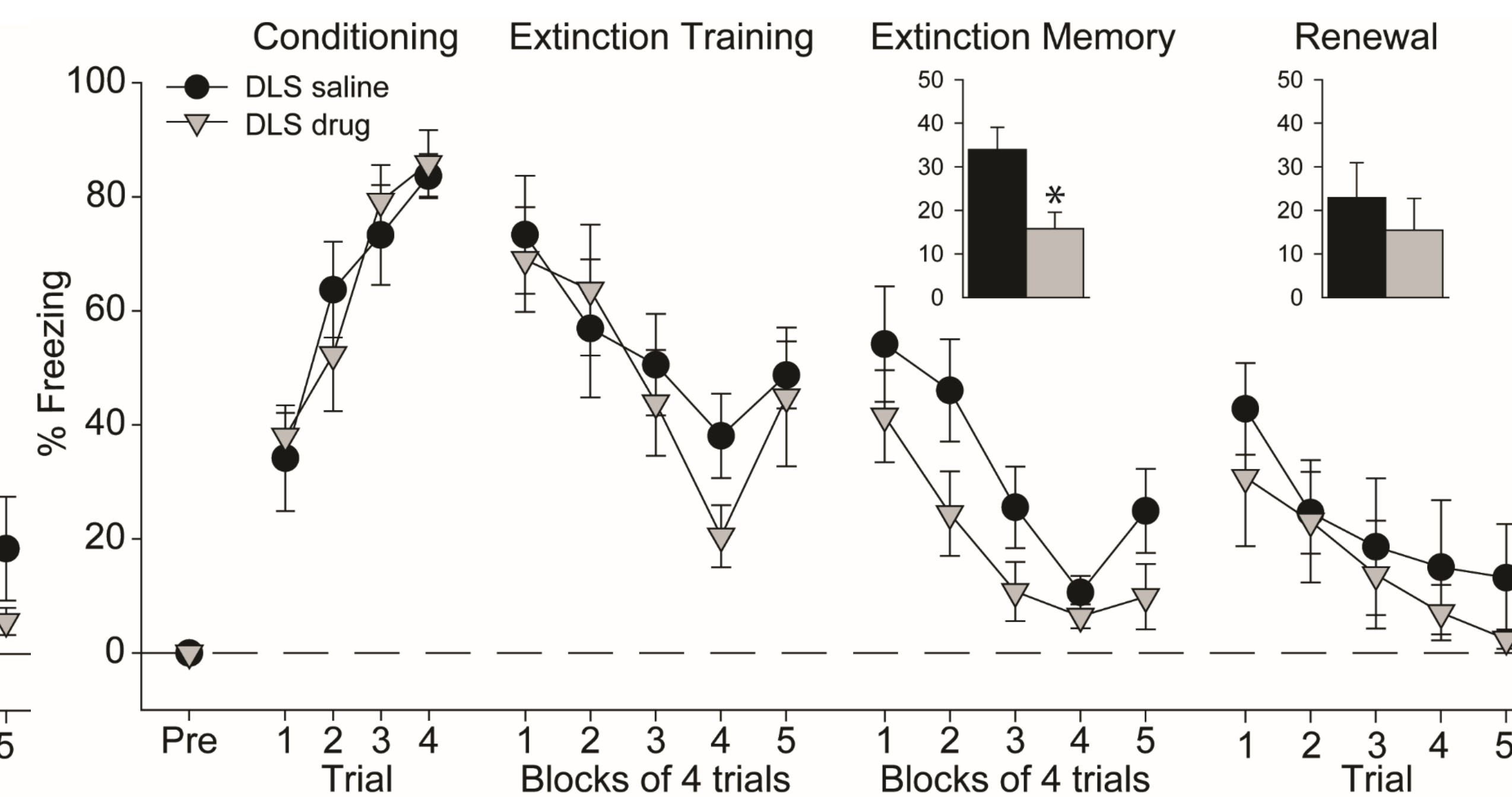


**Experiment 2**

- Goal**
- ❖ To investigate the role of the DLS in fear extinction.
- Hypothesis**
- ❖ Inhibition of the DLS will increase reliance on the goal-directed learning strategy involving the DMS, thereby enhancing fear extinction in a context-dependent manner.

**Results**

Fear extinction supported by the DMS (DLS inactivation) is strengthened but remains context-dependent

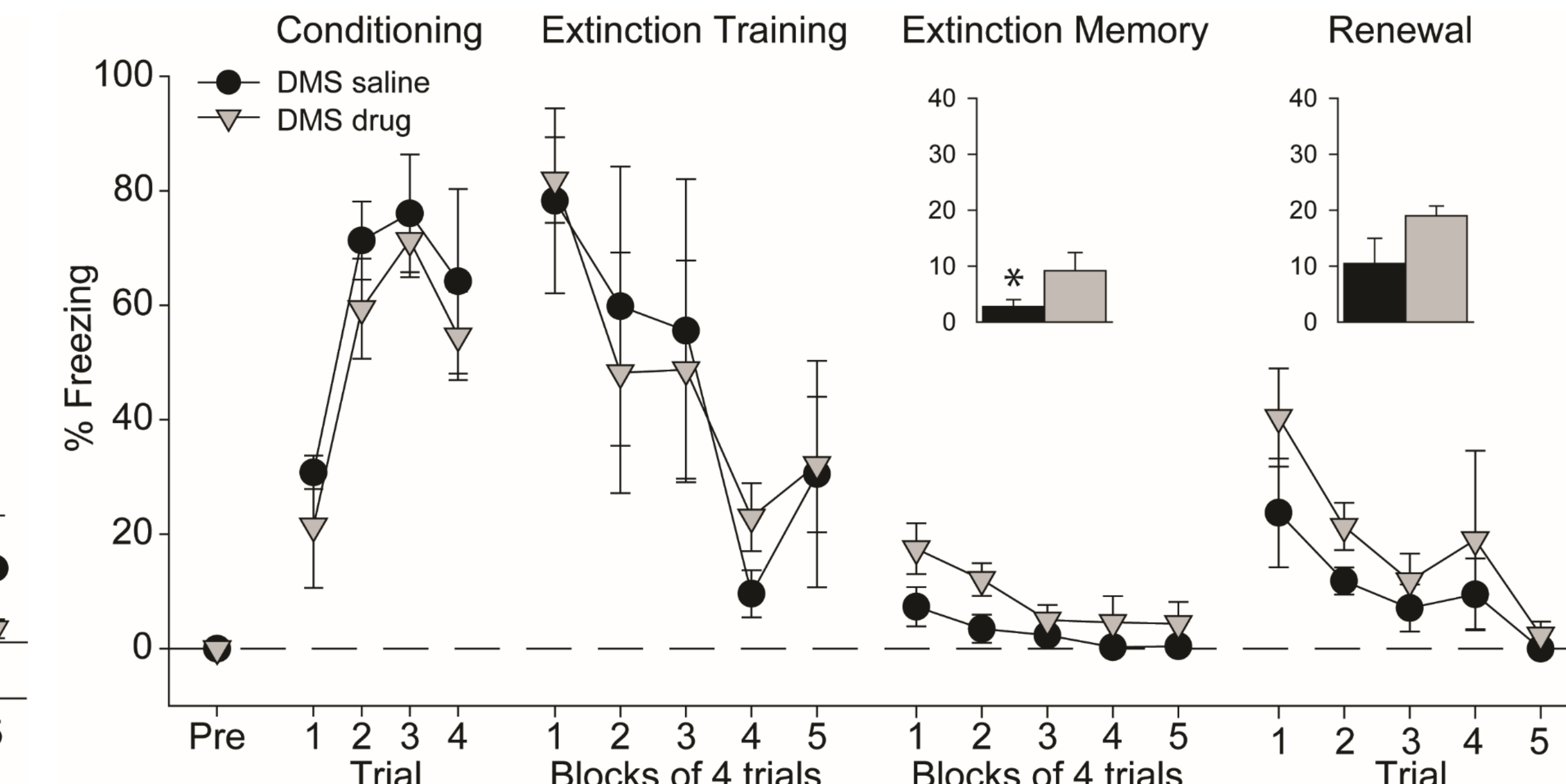


**Experiment 3**

- Goal**
- ❖ To investigate the role of D1 signaling in the DMS and DLS in fear extinction.
- Hypothesis**
- ❖ Based on our prior work, blocking D1 signaling in the DMS will impair fear extinction memory.

**Results**

D1 receptor signaling in the DMS, but not DLS (not shown) contributes to fear extinction learning



**Conclusions**

- ❖ Fear extinction learning supported by DLS, habit strategies (DMS inactivation) is resistant to fear renewal, whereas fear extinction learning supported by DMS, goal-directed strategies (DLS inactivation) improves extinction retention, but the extinction memory remains context-dependent.
- ❖ D1 receptor signaling in the DMS contributes to the role of the DMS in supporting fear extinction, but mechanisms other than D1 receptor signaling contribute to the role of the DLS.
- ❖ Results suggest that substantia nigra activation enhances extinction memory through D1 signaling in the DMS and renders the extinction memory resistant to renewal through a D1-receptor independent mechanism in the DLS.

