Environmental Enrichment as a Treatment for Cocaine Relapse

Shreyya Malik, Allison R. Bechard

Department of Psychology and Neuroscience, State University of New York at Geneseo

Background

- **Cocaine Use Diosorder (CUD) is a chronic relapsing disorder affecting millions of people; however, we still lack an effective pharmacological treatment**
- **CUD is characterised by compulsive drug-seeking behaviour which marks difficulties in remaining abstinent, with a high risk of relapse**
- **Environmental cues associated with cocaine use are capable of generating cravings in cocaine-dependent humans, even after extended period of abstinence**
  - **Often, a return to the drug-seeking environment results in relapse**
  - **Visual stimuli such as location, peers, often act as cues to induce relapse**
- **Pharmacological interventions have been unsuccessful in reducing this context-induced relapse**
  - **This is potentially due to specific neuronal circuitry that differs from that mediating drug-primed relapse**
- **Relapse in animal models can be triggered the same way as in humans (context, cues, drug, stress)**
  - **Environmental Enrichment (EE) is an animal paradigm that maintains complexity and novelty in the environment by systematic rotation of toys, tunnels, and a running wheel (see Fig. 1a)**
- **The current research focused on the interaction bewtween post-drug environment and cue-induced drug-seeking by testng one potential environmental treatment, EE, to reduce the reactivity of animals due to motivational effects of cocaine and environmental stimuli**

Results

- **Mice spent more time in the drug-associated room than in the saline-associated room in the cue- and coc-primed test of drug-conditioned preference ((1.16) = 87.7, $p<0.0001$; Fig 4)**

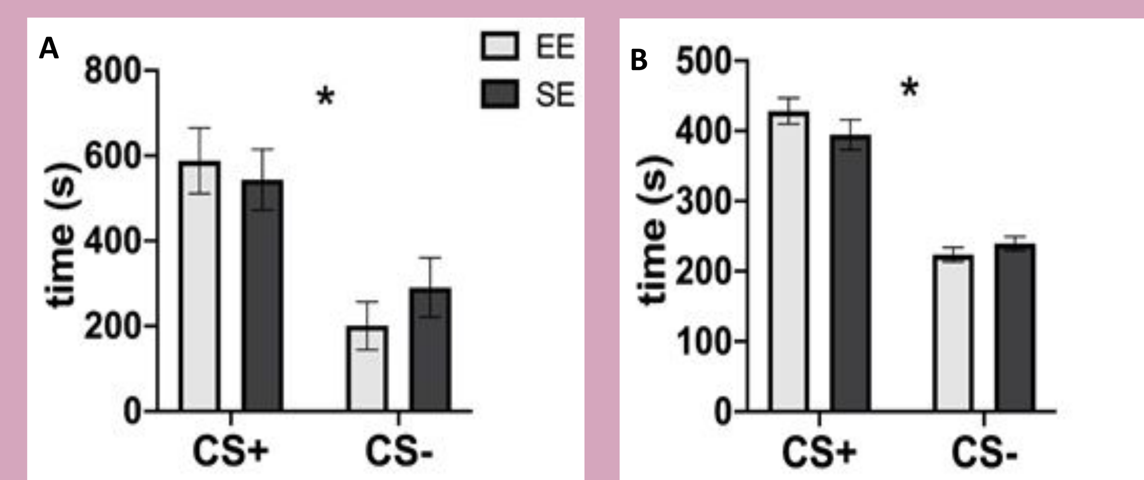

Fig. 4. Shows the time spent in the drug-paired (CS+) and saline-paired (CS-) sides of the arena during a 15-minute session of free exploration for enriched (EE) and standard (SE) mice 24 h after the final conditioning session in A) a cue-primed test of conditioned preference and B) a cocaine-primed test * indicates $p < 0.05$ for CS+ vs CS-

- **After a 2 week period of withdrawal, there was no preference for the drug-associated room or differences due to housing in cue-primed test (Fig 5a). When primed with a cocaine injection, a strong conditioning effect returned that did not differ by housing ($F(1,16)=7.26$, $p=0.016$, Fig5b)**

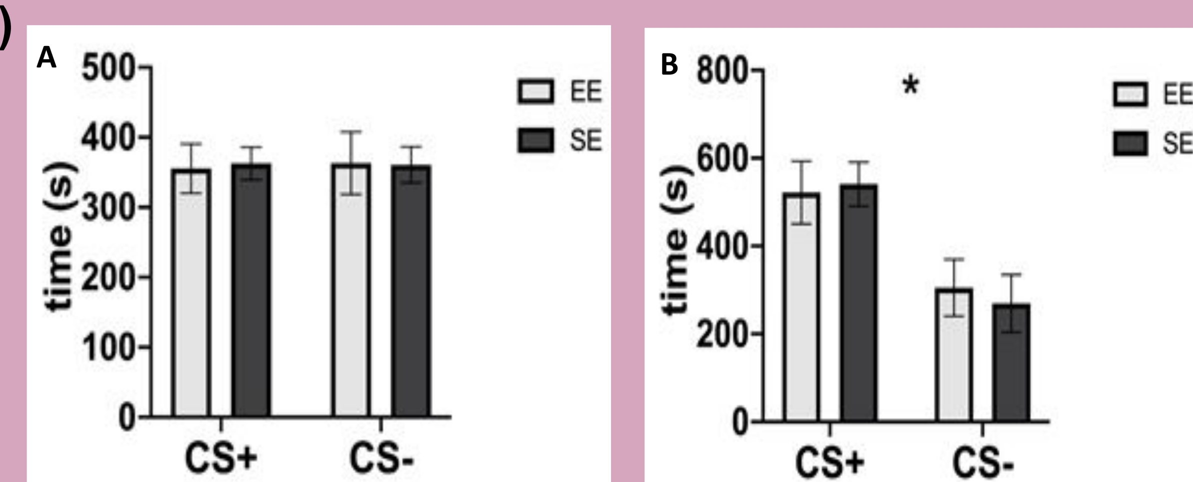

Fig. 5. Shows the time spent in the drug-paired (CS+) and saline-paired (CS-) sides of the arena during a 15-minute session of free exploration for enriched (EE) and standard (SE) mice after a 2 week period of withdrawal + EE. A) A cue-primed and B) a cocaine-primed test of conditioned preference 2 weeks after the last conditioning session * indicates $p < 0.05$ for CS+ vs CS-

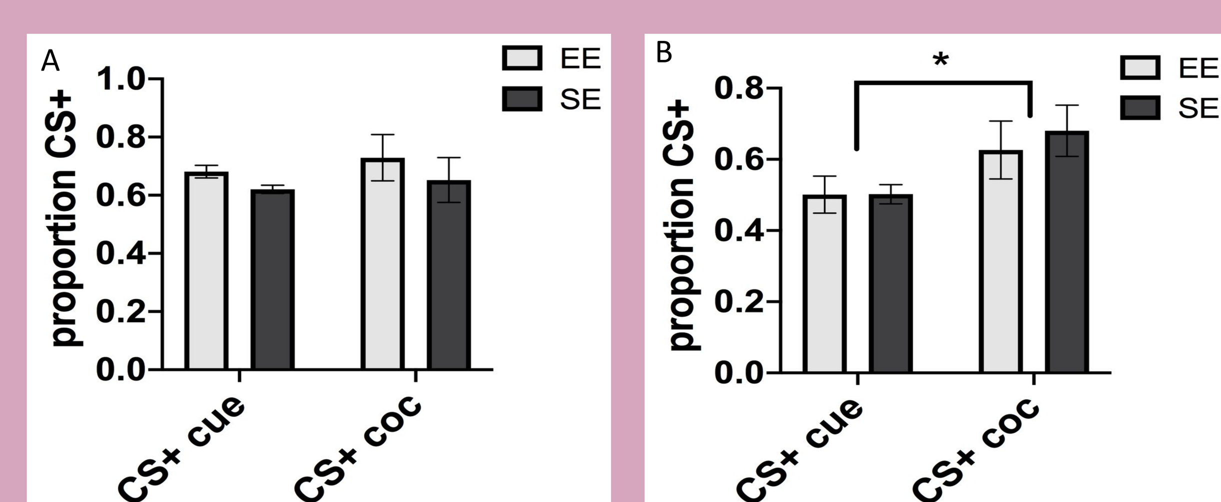

Fig. 6. Shows the proportion of time spent in the drug-paired (CS+) side relative to the saline-paired side (neutral chamber not considered) of the arena during a 15-minute session of free exploration for enriched (EE) and standard (SE) mice A) 24h after the last conditioning session and B) after 2 weeks of withdrawal + enrichment. * indicates $p < 0.05$ for CS+ cue vs CS+ coc

Methods

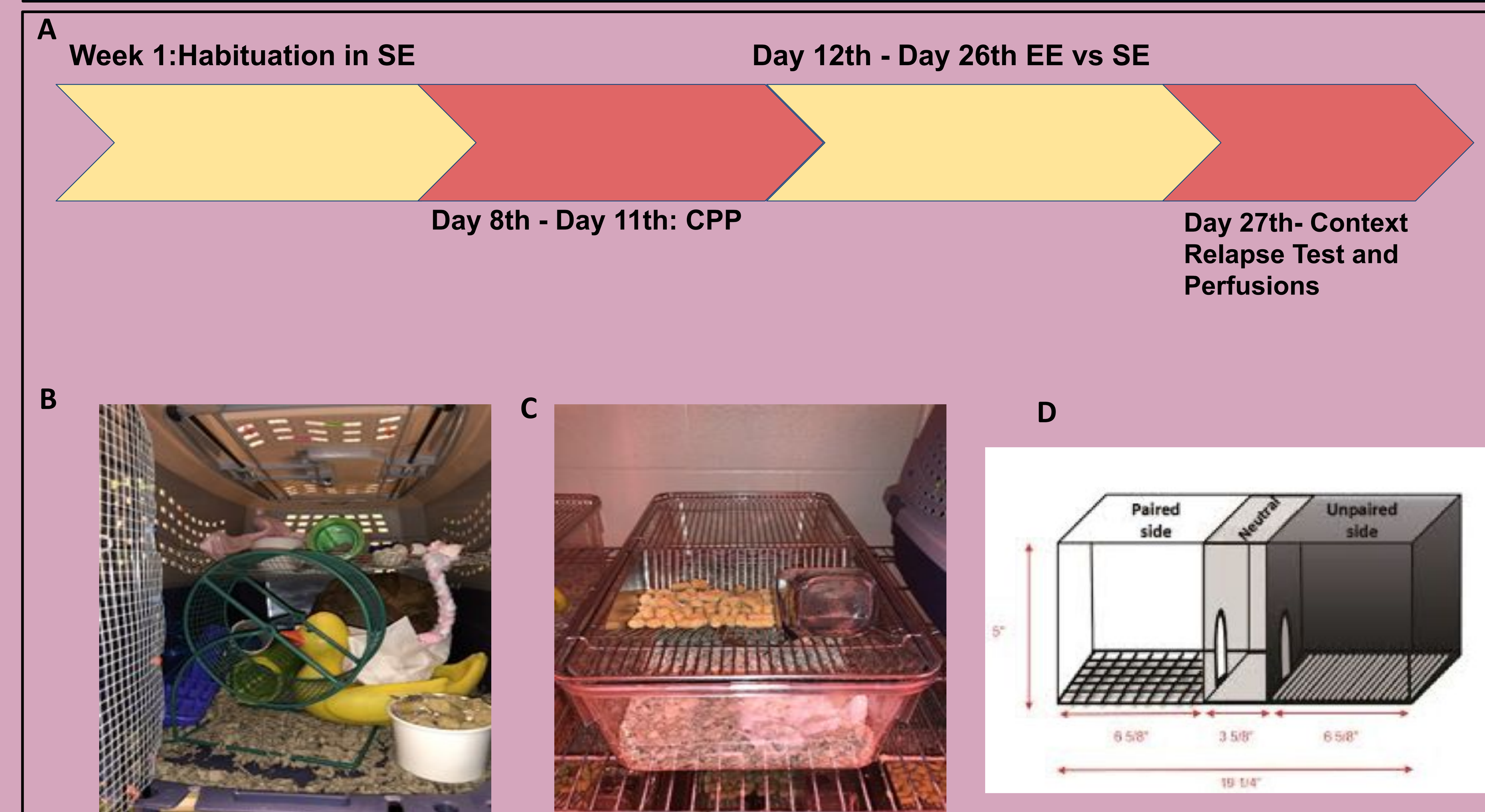

Fig. 1. A) Graphic representation of the protocol used for the CPP procedure. B) Shows the enriched (EE) housing compared to C) standard (SE) housing, and D) the 3-chambered CPP arena.

Conclusions & Future Directions

- **In conclusion, we did not find a therapeutic effect of EE to prevent cocaine-seeking**
- **Relative to earlier findings that EE could reduce time in the CS+ (Sotnikov et al. 2014) we used a bigger dose (20 mg/kg vs 10 mg/kg) of cocaine and a shorter amount of time (14 days vs 30 days)**
- **Future directions include repeating our study using the same duration of EE treatment (2 weeks) but reducing the dose used during conditioning**

Acknowledgements: This work was funded by the Undergraduate Summer Fellowship awarded by the Office of Sponsored Research at SUNY Geneseo.