

The effects of environment on the development of cocaine-seeking

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Background

- Cocaine use disorder is a major individual and societal issue. Currently, we are in great need for more effective treatment options.
- Animal models are useful for studying neurobiological mechanisms underlying addiction and relapse. One paradigm that has profound and persistent effects on brain development in rodents is the Enriched Environment (EE). While a typical Standard Environment (SE) may include only bedding, food, and water, an EE will generally include toys for lab animals to play with, places for them to climb, and ways for them to exercise.
- EE is linked to resistance of neurotoxic effects caused by cocaine (Freese et al., 2018). However, there is some dispute as to if EE is more effective for reducing cocaine preference if used before or after cocaine addiction is established (Galaj et al. 2017).
- How much socialization an animal receives during rearing is a major developmental factor, and there is evidence to suggest that socialization may even be more influential in attenuating drug seeking behavior than housing type (Zakharova et al., 2009).
- This study aimed to investigate the environmental and social factors that influence the development of cocaine addiction

Research Hypotheses

- H1: Adult mice reared in enriched environments will have reduced preference of a cocaine-associated context relative to adult mice reared in standard cages
- H2: Adult mice reared in larger groups will have reduced preference of cocaine-associated context relative to adult mice reared in smaller groups

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Results

- During cue-primed testing EE mice spent significantly more time in the CS+ than in the CS-. This result was not found in SE subjects when gender was not considered (see Figure 2A). During cocaine-primed testing, all mice preferred the CS+ (See Figure 2B).

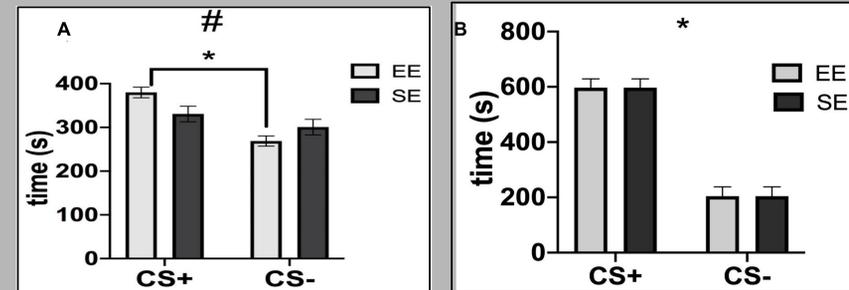


Figure 2 A) During cue prime testing, an interaction between housing type and side resulted [$F(1, 28) = 4.58, p = 0.0412$]. Sidak's Post Hoc testing revealed that only subjects reared in EE spent more time in the CS+ as compared to the CS- $p=0.0006$. B) All mice preferred the CS+ after a cocaine-prime (10 mg/kg).

- Further testing revealed sex differences in cocaine preference in cue-primed testing. Males subjects preferred the CS+ during cue-primed testing (see Figure 3A) but only EE females, and not SE females, similarly preferred the CS+.

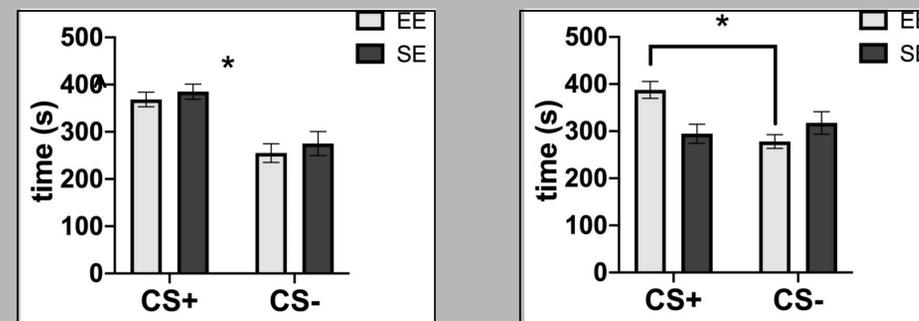


Figure 3: A) Both standard (SE) and enriched (EE) male subjects spent significantly more time in the CS+ compared to the CS-. but without any significant differences between housing groups. B) Enriched female subjects spent significantly more time in the CS+ compared to the CS-. However, standard females did not show a CS+ preference.

- Group size did not correlate with cocaine-seeking.

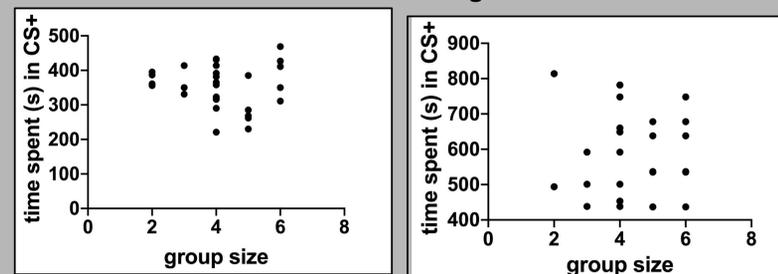


Figure 4: No relationship was found between group size and time spent in the CS+ and group size in either A) cue-primed or B) cocaine-primed testing.

Methods

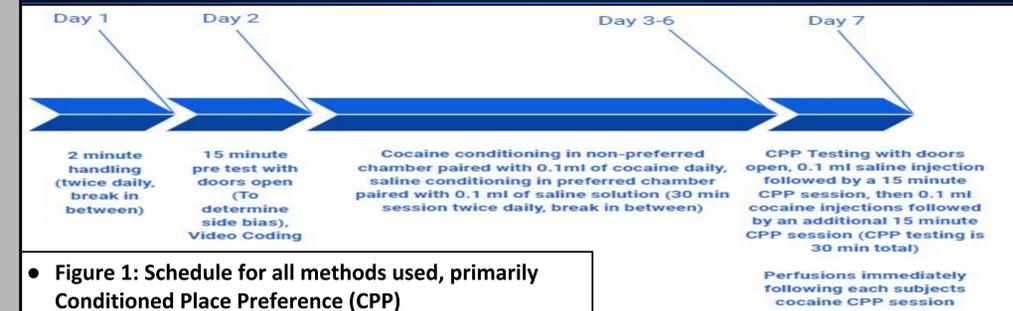
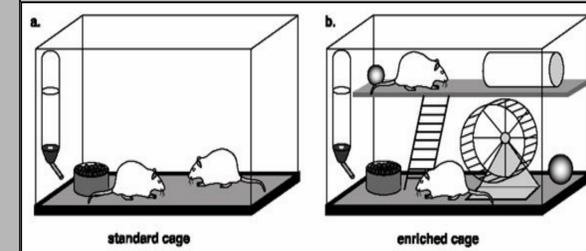
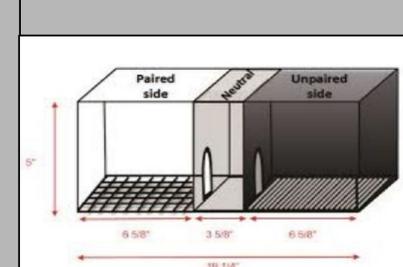


Figure 1: Schedule for all methods used, primarily Conditioned Place Preference (CPP)



Environmental Enrichment (EE): Kennels were used to house subjects in the EE condition. Mesh was used to create multiple levels, which were connected by a ramp. Toys, tunnels, birdseed, and items that the mice can chew on were rotated on a systematic basis to ensure novelty and complexity.



The CPP consists of two equally sized main areas, connected by a smaller center room. The two outer chambers differ in the color of walls (e.g. Light or Dark), pattern on the floor (checkerboard or grey), and smell (vanilla scent or no scent). Subjects are given cocaine injections in only one of the chambers. Thus, cocaine injections become associated with the environmental context in which they were received (known as the CS+). The subject is similarly exposed to the other side of the arena (the unconditioned side known as a CS-) but is given injections of saline.

- Statistical analysis: A two-way ANOVA with Housing Group (EE, SE) and Side (CS+, CS) was run for cue primed and coc-primed testing separately.

Conclusions & Future Directions

- Contrary to expectations, mice reared in enriched environments displayed greater preference for cocaine-seeking in cue primed tests. This may be attributed to the better memory that is often associated with EE (Harati et al., 2011). Future studies will investigate neuronal activation across brain regions, including the hippocampus.
- Testing for sex effects revealed differences in the cue-primed test. Specifically, standard females were the only group not to show increased time spent in the CS+ during the cue primed test. This effect warrants further investigation. I plan on testing several more groups of standard females in order to determine if this is a consistently observable effect.