

Is Methamphetamine Conditioned Place Preference Due to More Visits or Longer Visit Duration?

Behavioral Microanalysis of Pre vs Post Conditioning Data for Study CPP5.

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Abstract

Conditioned placement preference (CPP) is a commonly used preclinical behavioral model consisting of a specially crafted enclosure that holds a minimum of 2 separate chambers featuring opposing stimulus cues. The multi-phase CPP approach is especially useful in the study of drug therapy options for methamphetamine/ other drugs of abuse as it allows the species to form a connection between the chamber and the administered substance. Thus, drug-seeking behaviors can be analyzed in the presence and absence of the drug of abuse and are then compared to behavior post-administration of the experimental substance.² The use of CPP as an experimental protocol has been debated as the criteria for determining preference (and magnitude of preference) is unclear.¹

Introduction

A microanalysis of behavioral changes in the mice pre vs post conditioning will help us to broaden our current understanding of CPP and outline the basis of inclusion/exclusion standards of conditioning.

Some important questions include:

- Do the mice make more trips to the METH side during post-conditioning?
- Do the mice make less or the same number of trips to the METH chamber, but stay in the METH chamber for a longer duration?
- Is there an increase or decline in exploratory behavior?
- Is there an increase or decline in anxious behavior?

Answering these critical questions would allow us to better understand the behavioral effects of Methamphetamine use and streamline the CPP model.

Materials & Methods

Subjects: 20 Male C57BL/6J mice (*Mus musculus*) were obtained from our breeding colony at Indiana University of Pennsylvania.

Methods: Subjects from the CPP trial 5 were monitored based on the following criteria and evaluated pre vs post conditioning:

- Number of trips to the Meth/ Saline chamber.
- Duration of stay in each room.
- Number of rearing incidents.

Materials: *Microsoft Excel* software was be used to record and manage the data. *Prism* (GraphPad) was used to generate graphs and perform statistical analyses (paired T-tests).

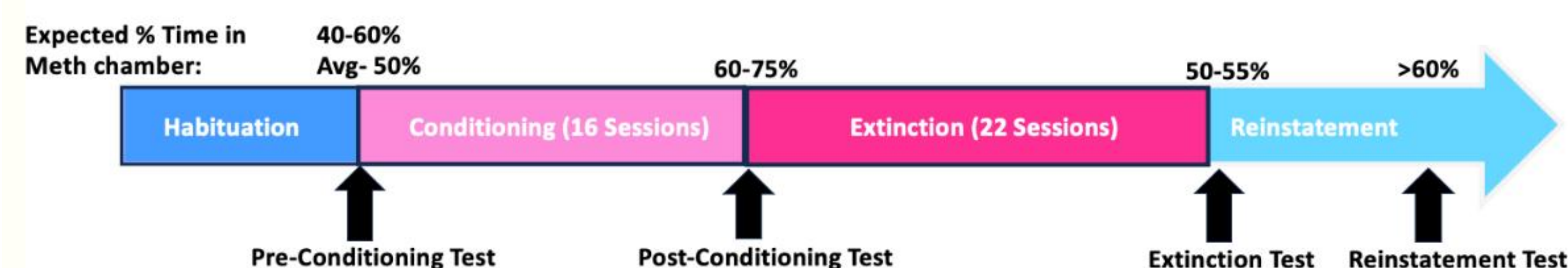
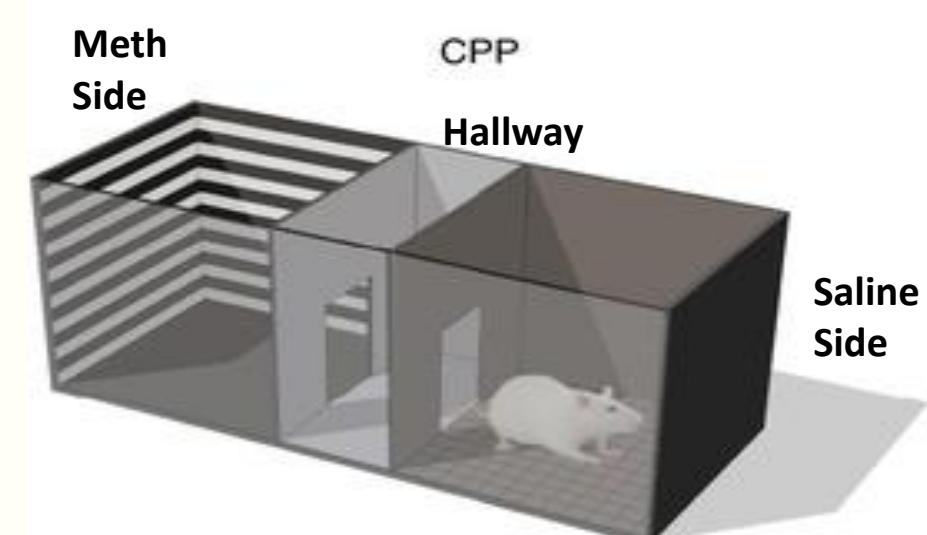


Figure 1: Left Panel – diagram of test apparatus. Right Panel - Experimental design and timeline showing different phases of CPP experiments.

Results

Meth Room Visits

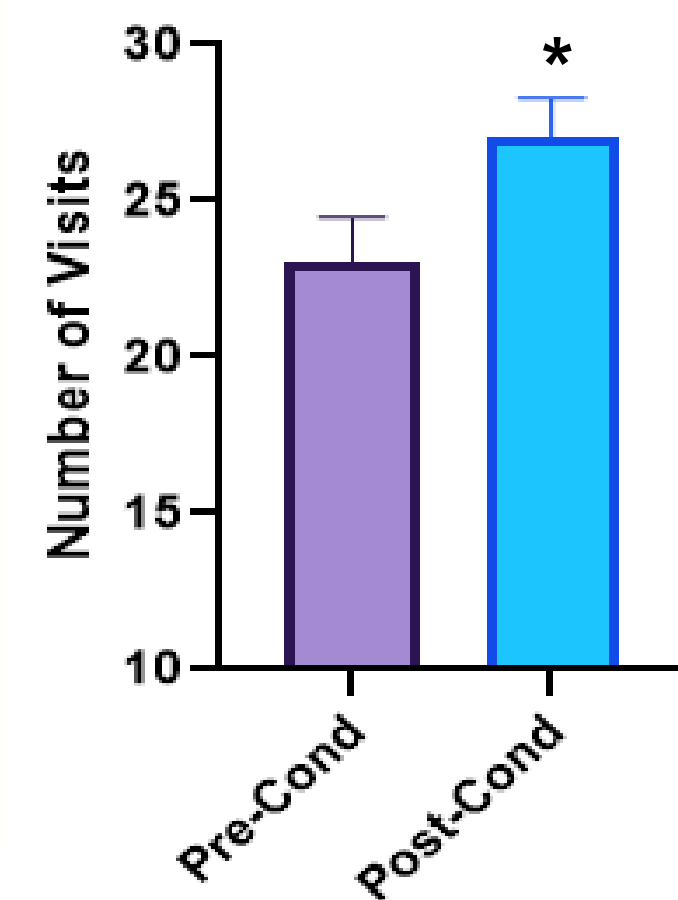


Figure 2: Number of Visits to Meth Room Pre vs. Post Conditioning. Note * indicates $P < 0.05$ paired T-test.

Saline Room Visits

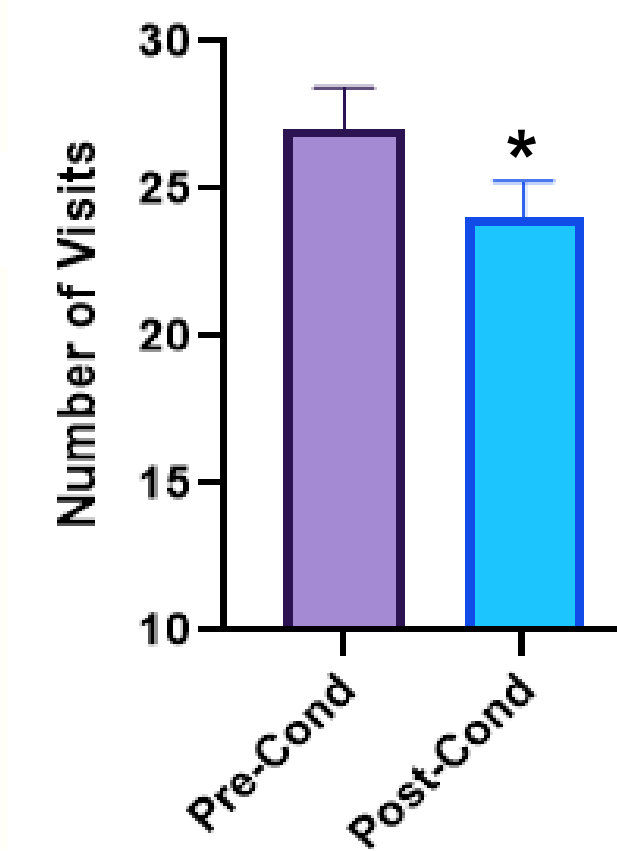


Figure 3: Number of Visits to Saline Room Pre vs. Post Conditioning. Note * indicates $P < 0.05$ paired T-test.

Meth Room Visit Duration

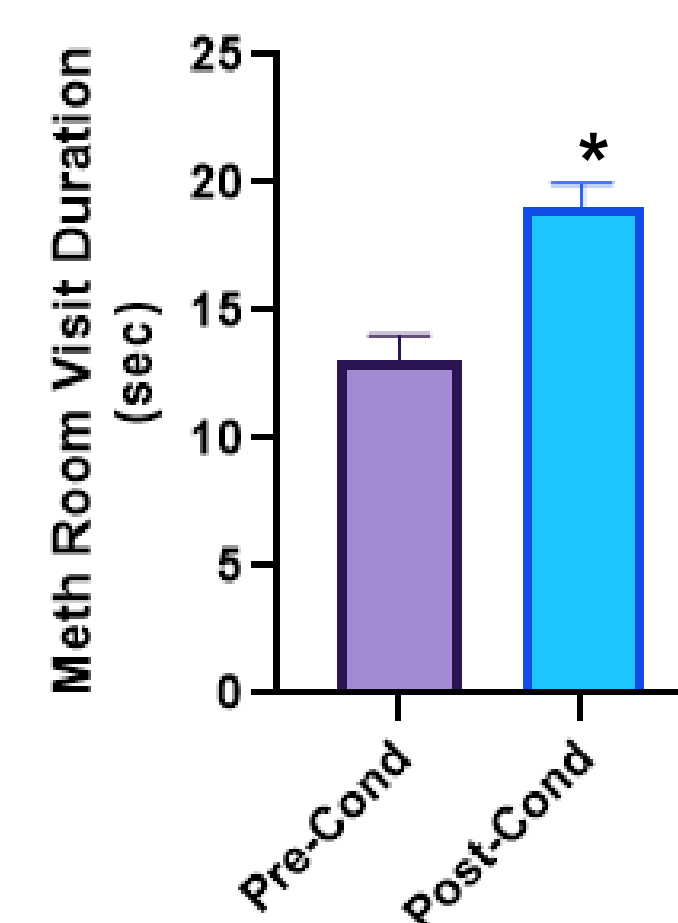


Figure 4: Meth Room Visit Duration in Seconds Pre vs. Post Conditioning. Note * indicates $P < 0.05$ paired T-test.

Saline Room Visit Duration

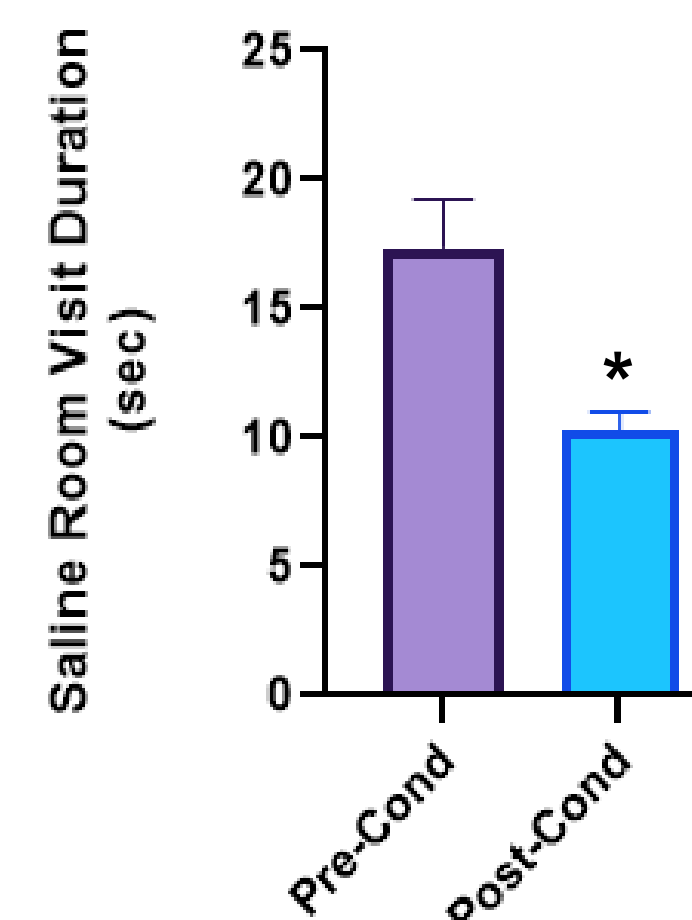


Figure 5: Saline Room Visit Duration in Seconds Pre vs. Post Conditioning. Note * indicates $P < 0.05$ paired T-test.

Rearing Saline vs. Meth

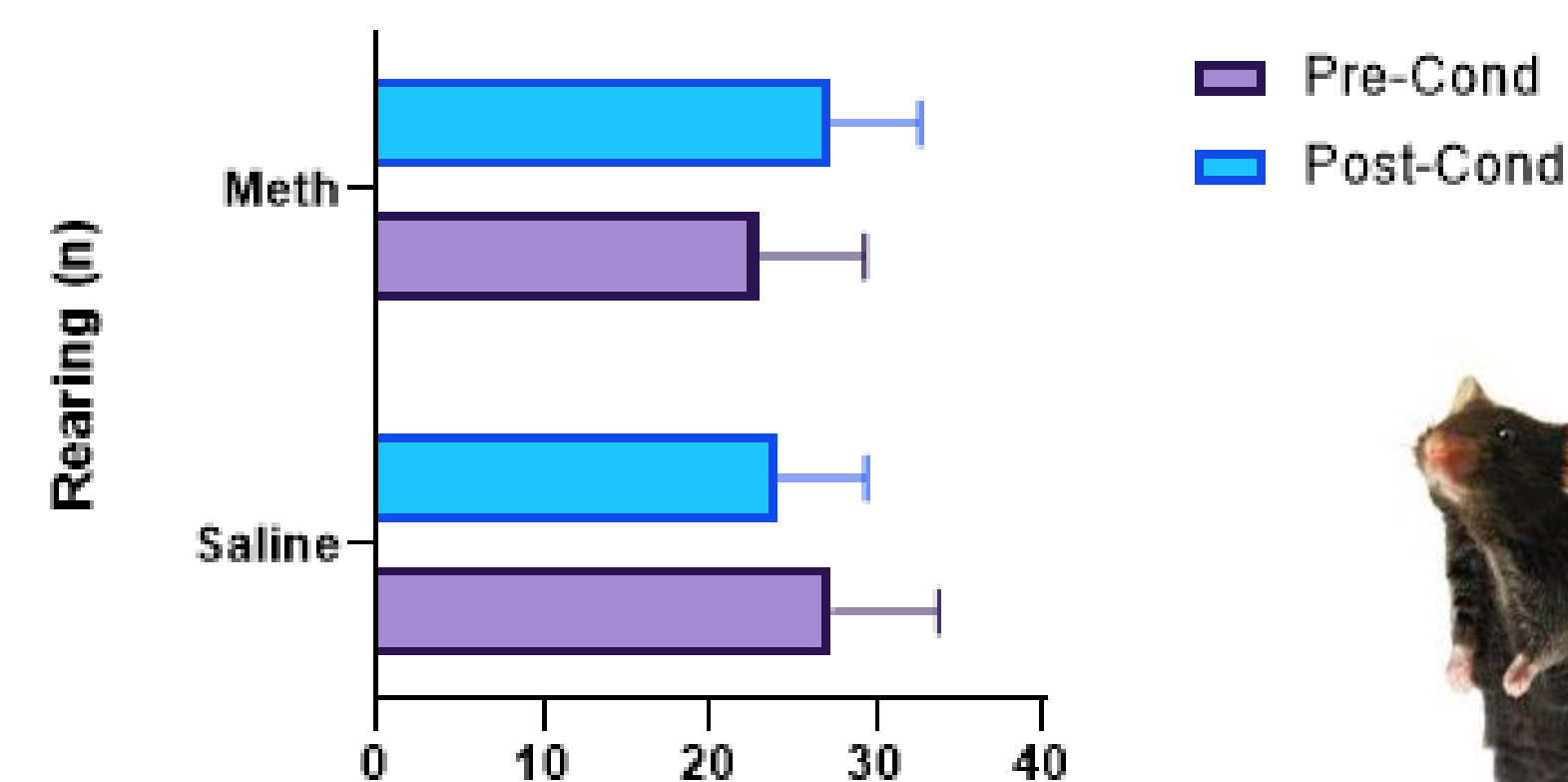
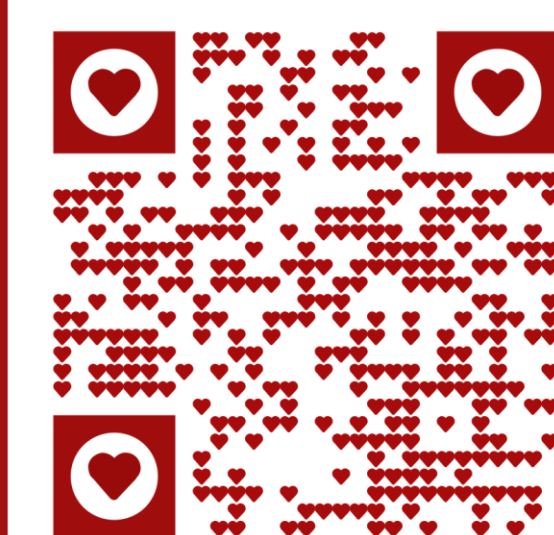


Figure 6: Bouts of Rearing in Saline and Meth Rooms Pre vs. Post Conditioning. Note * indicates $P < 0.05$ paired T-test.



SCAN ME



Conclusions

- The microanalysis of number of trips made to both S and M rooms pre vs post conditioning indicates that mice made more trips to the M room and less trips to the S room during post-conditioning than pre-conditioning.
- The microanalysis of the visit duration in both S and M rooms pre vs. post conditioning revealed that mice spend more time in the M room and less time in the S room during post conditioning. The T test revealed that the reduction in time spent in the S room during post-conditioning was significant (P value = 0.0008).
- The microanalysis of bouts of rearing in both S and M rooms pre vs post-conditioning revealed that mice rear more in the M room during post conditioning and less in the S room during post-conditioning as compared to pre-conditioning.
- Considering the totality of the data collected from the microanalysis, it is fair to say that conditioning is achieved by both an increase in the frequency of trips to the M and an increase in the amount of time spent in the M room during post-conditioning.
- The increase in the amount of rearing in the M chamber that was observed during post-conditioning may be indicative of increased spatial awareness that was a result of successful conditioning.

Discussion

- While more research is still needed to determine the underlying mechanism of conditioning, conditioned placement preference continues to be an optimal method for discovering pharmacological interventions to drugs of abuse such as methamphetamine.
- Future studies could involve the use of functional magnetic resonance imaging to identify which areas of the brain are affected by conditioning.

Literature Review

The article: *Conditioned place preference: what does it add to our preclinical understanding of drug reward?* by T. Bardo and A. Bevins provides a theoretical overview of some of the advantages and limitations of CPP. What they found was that despite some limitations including difficulty determining preference, CPP can provide useful information about the contextual cues associated with a drug stimulus.¹

References

1. Bardo, M. T., & Bevins, R. A. (2000). Conditioned place preference: What does it add to our preclinical understanding of drug reward? *Psychopharmacology*, 153(1), 31–43. <https://doi.org/10.1007/s002130000569>
2. Rodríguez-Arias M, Castillo A, Daza-Losada M, Aguilar MA, Miñarro J. 2009, Mar 23. *Effects of extended cocaine conditioning in the reinstatement of place preference*. *Physiol Behav*. doi: 10.1016/j.physbeh.2008.12.011.