Effects of the retrieval-extinction and extinction-retrieval procedures on cocaine-associated memory

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Introduction
This study examined the effects of the retrieval-extinction (R-E) and extinction-retrieval (E-R) procedures on cocaine-induced conditioned place preference (CPP) memory. Cocaine addiction remains a serious health issue and cannot be thoroughly cured using current pharmacological or behavioral intervention. Previous study found that a behavioral procedure consisting of a brief memory retrieval followed by an extinction procedure (R-E) effectively prevented relapse to cocaine and cocaine. The authors reason why the R-E procedure works is because retrieval renders memory a labile status, hence the following extinction reconsolidates the labile drug memory into a new memory that is dissociated with drug. However, later studies query the validity of the memory reconsolidation mechanism underlying the effect of the R-E procedure. They found that an extinction followed by a retrieval procedure (E-R) is as effective as the R-E procedure to impair reinstatement of alcoholic self-administration. However, the effect of the E-R procedure cannot be explained by the reconsolidation theory since the extinction procedure should not render memory a labile status for reconsolidation. Therefore, the present study aims to elucidate the underlying mechanism of these behavioral procedures using cocaine-induced CPP in mice. We first examined whether the R-E and E-R procedures impaired 10 mg/kg cocaine-induced CPP. Since we previously found that rimonabant differentially modulated cocaine-associated memory, depending on cocaine dosage used. Hence we examined the effects of the R-E and E-R procedures on 40 mg/kg cocaine-induced CPP. Finally, to investigate whether these cocaine-treated mice would return to a naive state, a group of naive mice were compared with cocaine-treated mice undermentioned behavioral procedures.

Experimental procedure
- Cocaine-induced (CPP): Cocaine-induced conditioned place preference (CPP) is a valuable animal model used to study cocaine-associated memory arising from cocaine addictive processes.

Results
1) The effects of different retrieval-extinction procedures on 10 mg/kg cocaine-induced CPP memory.

2) The effects of different retrieval-extinction procedures and re-training on 10 vs. 40 mg/kg cocaine-induced CPP memory.

3) The strength of cocaine-associated memory in CPP is related to the numbers of pairing sessions on 10mg/kg cocaine-induced CPP.

Figure 3. The strength of cocaine-associated memory in CPP is related to the numbers of pairing sessions. A) The experimental procedure used in this study. B) In priming task, mice paired cocaine (10 mg/kg, i.p.) for three times have significantly higher CPP score. Data are presented as mean ± SEM. * p < 0.05, compared with pretreatment; **: p < 0.01, compared with other groups in priming task.

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Conclusions
In conclusion, the findings indicate that there is no significant difference among the extinction only, the retrieval-extinction, and the extinction-retrieval procedures. However, we found that the effects of the behavioral procedures depend on the dosage of cocaine used in the CPP paradigm.