

Age-Dependent Differences in the Persistence of Cocaine-Induced Conditioned Activity in Adult and Young Rats: Regional Differences in Fos Immunoreactivity

S.A. McDougall, J.A. Pipkin, T. Der-Ghazarian, A.M. Cortez, A. Gutierrez, R.J. Lee, S.M. Carbajal, J.L. Shaddox, and C.A. Crawford

Department of Psychology, California State University, San Bernardino

Introduction

The neural mechanisms mediating conditioned activity are poorly understood, although the nucleus accumbens (NAcc), amygdala, and hippocampus have been implicated. In a typical experimental design, adult rats are given 4 to 8 cocaine-environment pairings before assessment of conditioned activity; however, we have reported that adult rats show conditioned activity when a single injection of cocaine is given in a novel chamber 24 h before testing. The purpose of this study was to: (a) determine the persistence of one-trial conditioned activity in young and adult rats and (b) assess neural activation by measuring Fos IR on the test day.

Methods

On postnatal day (PD) 19 or PD 79, rats in the Paired condition were injected with 30 mg/kg cocaine immediately before being placed in a novel activity chamber for 60 min. Rats in the Unpaired condition were injected with saline before being placed in the novel activity chamber and then injected with cocaine 30 min after being returned to the home cage. Control rats were injected with saline at both time points.

For adult rats, conditioned activity was assessed 1, 3, 5, 7, 14, or 21 days later; whereas, young rats were assessed 1, 14, or 21 days after cocaine or saline treatment. Brains were removed after testing and processed for Fos IR.

Results

- Adult rats showed robust one-trial conditioned activity that persisted for at least 21 days after cocaine treatment.
- Conditioned activity was entirely context-dependent and did not occur in the unpaired group (i.e., when cocaine was given in the home cage).
- An “incubation-like” effect was not observed, since conditioned activity did not get stronger across time.

Distanced Traveled (cm)

Fig. 1. Mean distance traveled scores (+SEM) of rats given an injection of saline before the 90-min testing session on PD 80, PD 82, PD 84, PD 86, PD 93, or PD 100. * Significantly different from the saline control group. † Significantly different from the Unpaired group.

Fig. 2. Mean number of Fos-positive nuclei (+SEM) in various brain regions on PD 80 (i.e., one day after drug pretreatment). * Significantly different from the Saline Control group ($P < 0.05$). † Significantly different from the Unpaired group ($P < 0.05$).

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■ Young rats did not exhibit conditioned activity when tested 1, 14, or 21 days after a single cocaine-environment pairing (data not shown).

■ When assessed after a 1-day interval, adult rats in the Paired group exhibited elevated Fos IR in the NAcc core and shell. Fos IR did not vary in the dorsolateral striatum, dorsal hippocampus, or basolateral amygdala.

■ Adult rats in the Unpaired group, as well as young rats, did not exhibit elevated Fos IR.

■ Adult rats in the Paired group did not exhibit elevated Fos IR when assessed 3 or more days after the single cocaine-environment pairing (data not shown).

Discussion

- ❖ These results indicate that a single drug-environment pairing is sufficient to induce long-term conditioned activity in adult rats and that the NAcc may be involved in the induction and/or initial expression of conditioned activity.
- ❖ The lack of elevated Fos IR on subsequent test days (i.e., after an interval of 3 or more days) suggests that Fos production and the expression of conditioned activity are dissociable.
- ❖ Cocaine-paired cues often induce greater levels of instrumental responding at longer drug abstinence intervals; however, there was no evidence of an “incubation-like” effect in the present study. The latter result is consistent with research showing that drug incubation is not evident when the experimental paradigm relies on Pavlovian drug-environment associations.
- ❖ A single drug-environment pairing was insufficient to induce conditioned activity in young rats. This age-dependent effect may be due to retention issues or differences in the way young and adult rats perceive and process conditioned stimuli (CSs).