One-Trial Behavioral Sensitization in Preweanling Rats: Importance of the D1 Receptor

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Introduction

In adult rodents, the impact of D1 receptor blockade on cocaine-induced behavioral sensitization is more complex than for other DA-acting drugs. More specifically, SCH23390 does not block the induction of cocaine-induced behavioral sensitization when a multi-trial procedure is employed; however, the sensitized responding of adult rats and mice is completely eliminated if SCH23390 is injected before a single pretreatment administration of cocaine. In contrast, SCH23390 blocks the induction of amphetamine-, MAP-, and apomorphine-induced behavioral sensitization using either a multi- or one-trial procedure.

Preweanling rats also exhibit behavioral sensitization after one or more psychostimulant exposures; however, the sensitized responding of young animals differs from adults in some important respects. This has led some researchers to speculate that the neural mechanisms underlying behavioral sensitization differ across ontogeny. The purpose of the present study was to determine the importance of the D1 receptor for the one-trial behavioral sensitization of preweanling rats.

Methods

Experiment 1. Because indirect DA agonists preferentially induce sensitized responding at different ages, cocaine-induced behavioral sensitization was assessed on PD 20–21, while MAP- and NPA-induced sensitization was assessed on PD 16–17. On the pretreatment day, rats were injected with SCH23390 (0, 0.1, 0.5, 1, or 5 mg/kg) followed, 15 min later, by an injection of cocaine (30 mg/kg), MAP (4 mg/kg), or NPA (2 mg/kg). Rats in the acute control group were given two injections of saline. After the second injection, rats were placed in activity chambers and distance traveled was measured for 30 min. On the test day, rats were injected with cocaine (20 mg/kg), MAP (2 mg/kg), or NPA (0.5 mg/kg) and placed in activity chambers for 120 min.

Experiment 2. The pretreatment day procedures were the same as just described, with the exception that rats were injected with 0.5 mg/kg SCH23390 either 0, 30, or 60 min before receiving a single injection of cocaine (30 mg/kg), MAP (4 mg/kg), or NPA (2 mg/kg). Behavioral assessment and test day procedures were identical to Experiment 1.

Results

On the pretreatment day, all DA agonists increased the locomotor activity of preweanling rats. This effect was only partially blocked by SCH23390 (Fig. 1). On the test day, cocaine-, MAP-, and NPA-induced one-trial behavioral sensitization was evident. D1 receptor blockade was unable to attenuate the induction and ultimate expression of the sensitized response (Fig. 2 and 3).

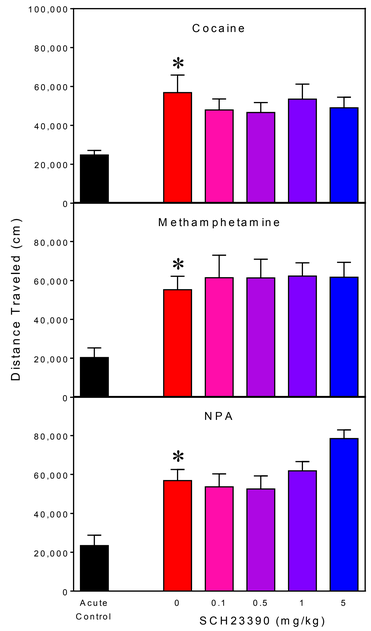

Fig. 2. Test day performance of rats injected with SCH23390 15 min before DA agonist administration on the pretreatment day. * Significantly different from the acute control group.

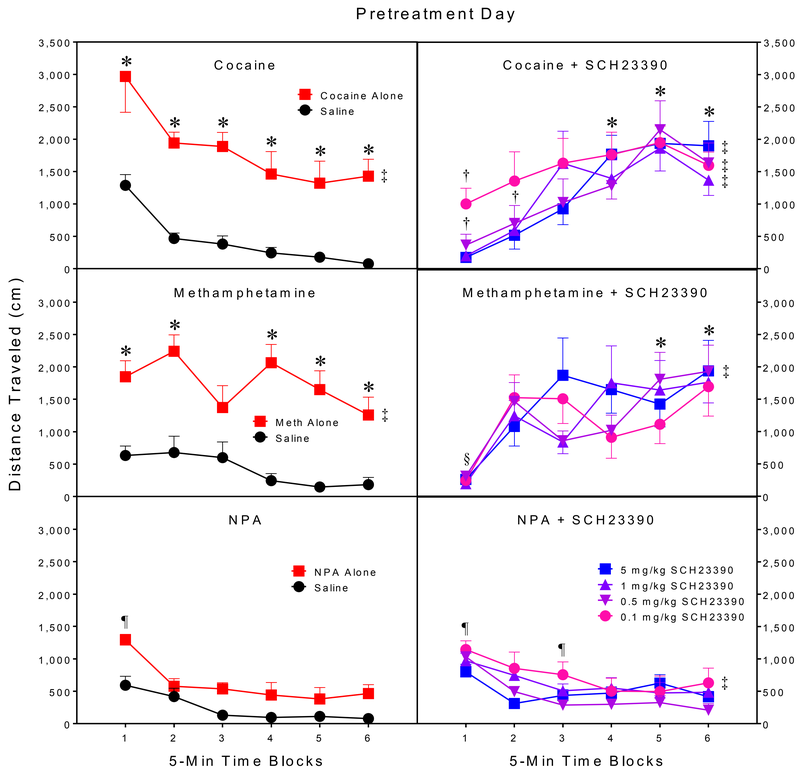

Fig. 1. Mean distance traveled scores of rats (n = 8 per group) injected with saline, cocaine (30 mg/kg), methamphetamine (4 mg/kg), or NPA (2 mg/kg) immediately before a 30-min placement in activity chambers on the pretreatment day (left panels). Additional groups of rats were injected with SCH23390 (0.1, 0.5, 1, or 5 mg/kg) 15 min before DA agonist pretreatment (right panels).
* Significantly different from the saline control group on the same time block.
‡ Significantly different from the saline control group when collapsed across time blocks 1–6.
† Significantly different from the cocaine alone group on the same time block.
§ Significantly different from the methamphetamine alone group on the same time block.
¶ Significantly different from the NPA alone group on the same time block.

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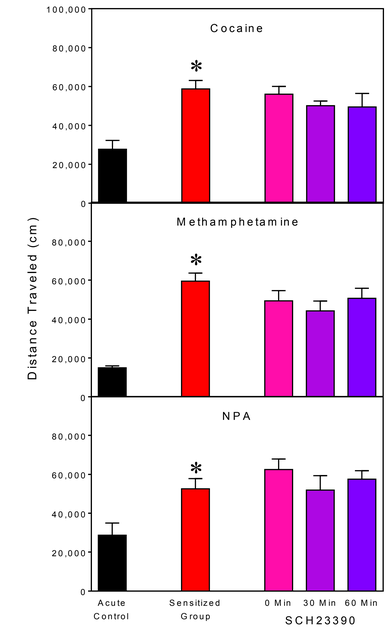

Fig. 2. Test day performance of rats injected with SCH23390 0, 30, or 60 min before DA agonist administration on the pretreatment day. * Significantly different from the acute control group.

Discussion

- Cocaine, MAP, and NPA caused robust behavioral sensitization in preweanling rats.
- The inability of SCH23390 to prevent the sensitized responding of preweanling rats suggests that the D1 receptor is not necessary for the induction of behavioral sensitization during early ontogeny.
- In contrast, SCH23390 blocks MAP- and apomorphine-induced sensitization in adult rats. Cocaine-induced behavioral sensitization is typically not affected by D1 receptor blockade except when a one-trial paradigm is used.
- When all of the relevant evidence is considered together, it appears that the mechanisms mediating one-trial behavioral sensitization differ markedly between the preweanling period and adulthood.