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SEX AND AGE DIFFERENCES IN ONE-TRIAL METHAMPHETAMINE SENSITIZATION IN SPRAGUE-DAWLEY RATS

Background: Methamphetamine (METH) behavioral sensitization is a phenomenon in which previous administration to METH elicits a heightened behavioral response in subsequent exposures. Research has found that even one previous pairing is enough to elicit sensitization. In adult rats, sensitization is context-dependent, in which a sensitized response is only evident in the area in which they had previously received the drug. Juvenile rats (postnatal day [PD] 24 or younger), however, exhibit context-independent sensitization, a heightened response regardless of what environment the METH was previously paired. Adolescent rats (PD 25-50) do not exhibit sensitization to METH. Prior studies have examined a wide range of doses of METH (1-6 mg/kg), but doses lower than 1 mg/kg METH have not been used. Thus, the present study examined one-trial sensitization in juvenile, adolescent, and adult rats using 0.1 and 0.3 mg/kg of METH.

Methods: During the pretreatment phase, PD 18, 28, 38, or 68 male and female rats were injected with saline or 3 mg/kg METH and placed in a novel activity chamber, where their locomotor activity (distance traveled in m) was assessed for 60 min. Rats were then taken to their home cage. 45 min later, a subgroup of rats that had been given saline in the activity chamber were then injected with 3 mg/kg METH and, placed back in their home cage. During the challenge test, PD 19, 29, 39, or 69 male and female rats were injected with saline or METH (0.1 or 0.3 mg/kg) before being placed in the activity chamber, during which distance traveled was assessed for 90 min.

Results: The results show that PD 29 and 39 adolescent male and female rats exhibited context-dependent sensitization. Interestingly, sex-related differences were observed as PD 39 female rats exhibited behavioral sensitization only when challenged with 0.3 mg/kg METH, while male rats exhibited behavioral sensitization only at 0.1 mg/kg METH. In contrast, PD 19 and 69 male and female rats did not exhibit behavioral sensitization at any dose.

Conclusion: In contrast to prior studies that failed to show that adolescent rats exhibit one trial sensitization with METH (1-6 mg/kg), we found that adolescent rats exhibited context-dependent sensitization using low doses of METH. These findings highlight the need to examine a wide range of doses and different age periods to understand the development of sensitization in rats.