

Effect of adolescent and adult nicotine exposure on methamphetamine self-administration in male rats

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INTRODUCTION

90% of American nicotine users begin smoking before the age of 18.

This fact is particularly concerning, because nicotine is believed to be a “gateway” to other drugs of abuse in adulthood; particularly METH.

Because a majority of juvenile smokers continue to smoke as adults, understanding the nature of the relationship between early nicotine use and later METH use is difficult.

As such, the goal of the present study was to examine the individual and combined roles of adolescent and adult nicotine exposure on METH self-administration, extinction, and reinstatement.

It was hypothesized that exposure to nicotine during adolescence would increase METH-seeking in adulthood. Moreover, it was hypothesized that rats pretreated with nicotine as adolescents and adults would have decreased METH intake, METH-seeking behavior, and METH reinstatement.

METHODS

Subjects. Subjects consisted of 43 male rats of Sprague-Dawley descent (Charles River Laboratories, Hollister, CA), born and raised at California State University, San Bernardino (CSUSB).

In Vivo Drug Treatment. On PD 35, rats were weighed and injected with saline or nicotine (0.16 or 0.64 mg/kg, sc) once a day for 16 days until PD 50. On PD 51, rats that had received the low or high nicotine doses were either switched to saline or continued to receive the same nicotine dose they received as adolescents. Thus, there were five groups based on their adolescent/adult nicotine exposure: SAL/SAL, 0.16/0.16, 0.16/SAL, 0.64/0.64, and 0.64/SAL.

Acquisition: METH acquisition (.05 mg/kg, IV) occurred across three weeks, with a minimum of one week on an FR1 schedule and two weeks on an FR3 schedule. Furthermore, rats on FR1 also had to meet the criterion of receiving 10 infusions for at least two days..

Extinction: Extinction (i.e., active lever presses result in no infusions) occurred after the two weeks of FR3. Subjects remained on extinction until active lever responses were below 10% of the last day of FR3 acquisition for two consecutive days (e.g., subjects with 200 active presses on the final day of FR3 reached extinction when they pressed the active lever ≤ 20 time for two consecutive days).

Reinstatement: Following extinction, subjects were primed with METH (1.0 mg/kg, IP) five minutes before being placed in chambers. Reinstatement sessions lasted two hours, and active presses resulted in no drug).

Data Analysis. All data (active lever presses, inactive lever presses, number of days to reach criteria, number of METH infusions earned, and timeout sessions) from acquisition, extinction, and reinstatement sessions were analyzed by separate one-way ANOVAs, with group being the independent variable. Tukey’s tests were used to make post hoc comparisons ($p < .05$).

RESULTS

METH Acquisition

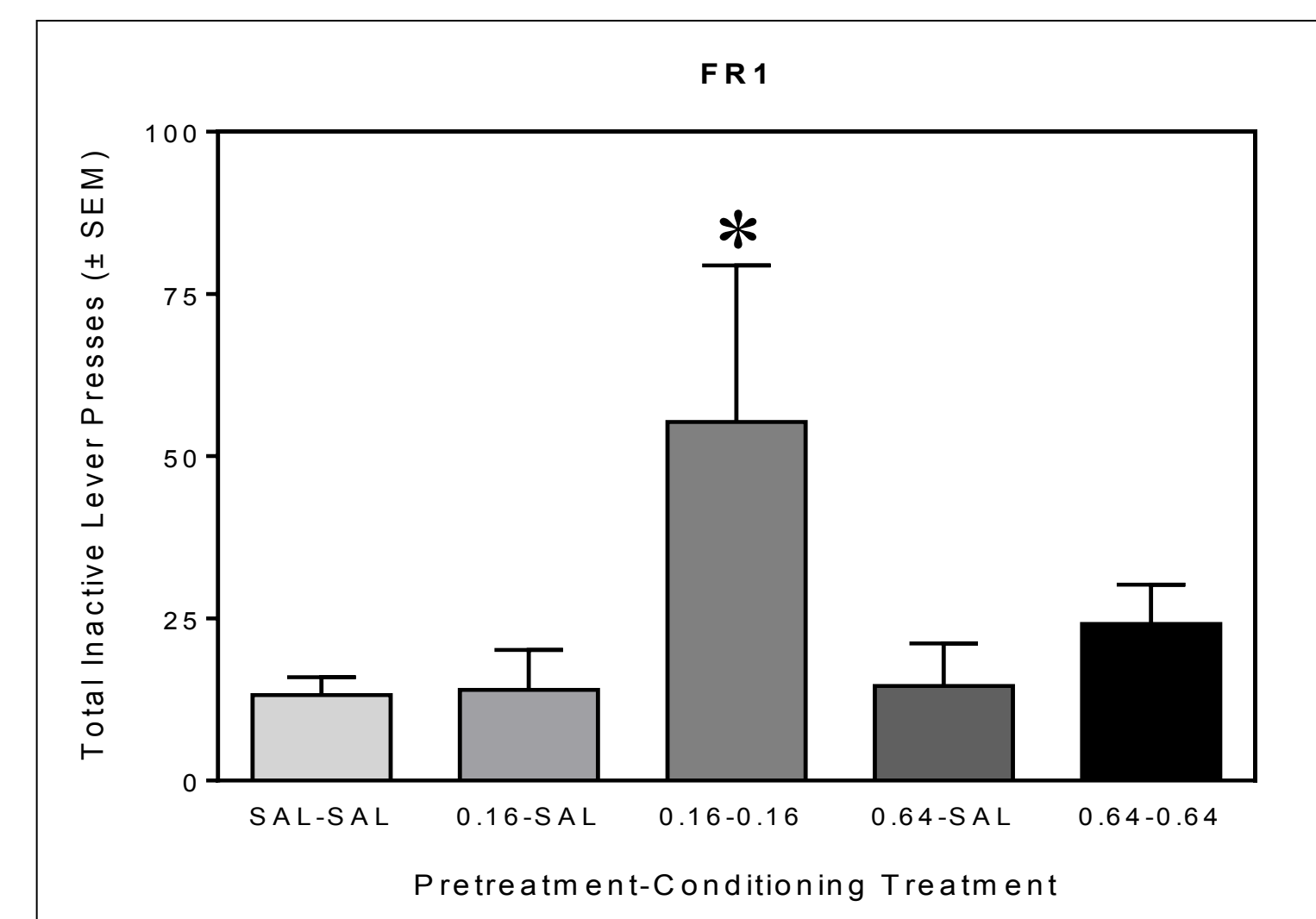


Fig. 1. Mean Total Number of Inactive Lever Presses (± SEM) Made by Adult Rats During Self-Administration Training for METH on an FR 1 Schedule of Reinforcement. Rats were Exposed to Nicotine (0.16 or 0.64 mg/kg) or Saline during Adolescence (PD 35-50) and Adulthood. * Indicates Statistical Difference from SAL-SAL Group

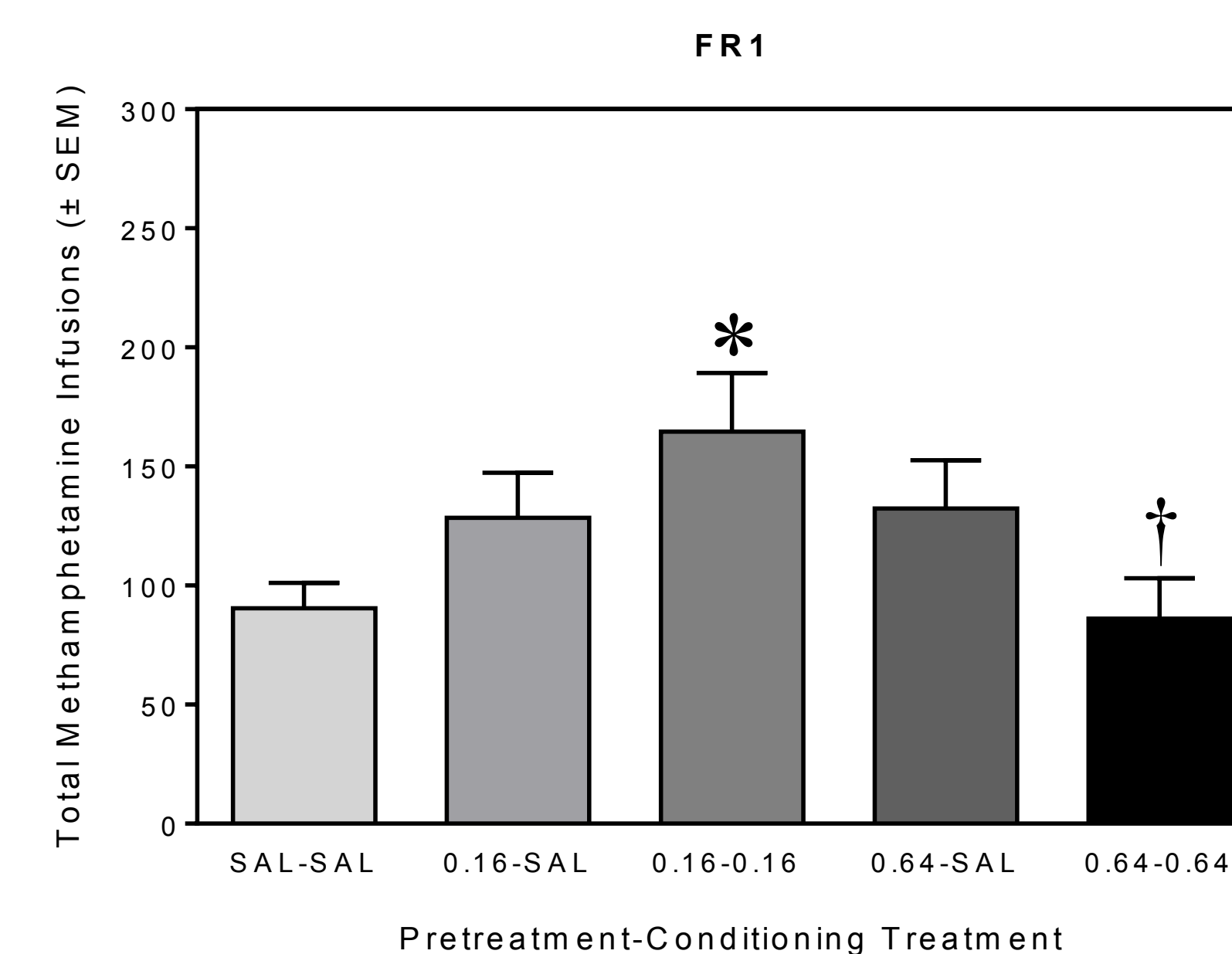


Fig. 2. Mean Total Number of METH Infusions (± SEM) Made by Adult Rats During Self-Administration Training for METH on an FR 1 Schedule of Reinforcement. Rats were Exposed to Nicotine (0.16 or 0.64 mg/kg) or Saline during Adolescence (PD 35-50) and Adulthood. * Indicates a Statistical Difference from SAL-SAL group. † Indicates a Statistical Difference from 0.16-0.16 Group.

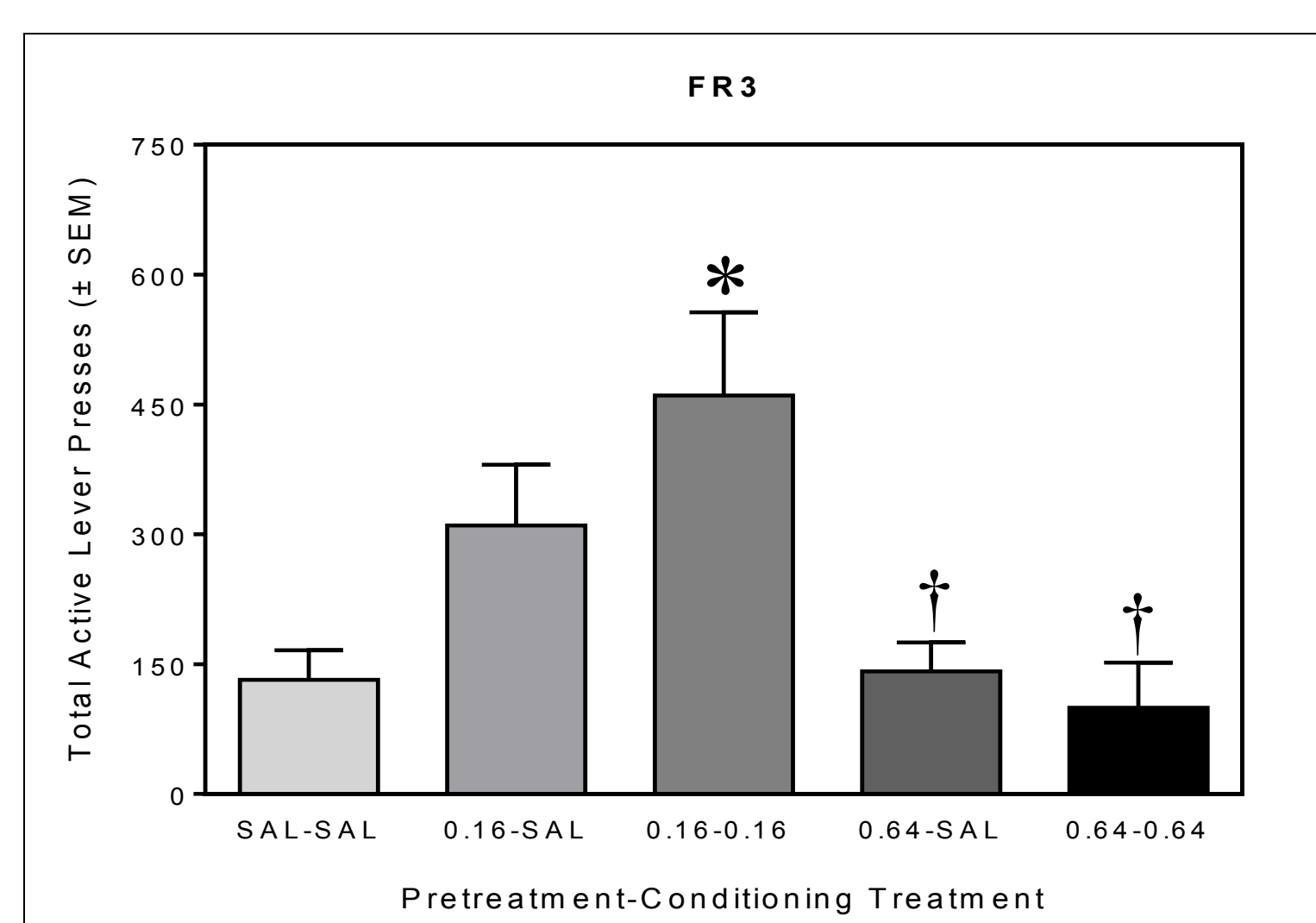


Fig. 3. Mean Total Number of Active Lever Presses (± SEM) Made by Adult Rats During Self-Administration Training for METH on an FR 3 Schedule of Reinforcement. Rats were Exposed to Nicotine (0.16 or 0.64 mg/kg) or Saline during Adolescence (PD 35-50) and Adulthood. * Indicates a Statistical Difference from SAL-SAL group. † Indicates a Statistical Difference from 0.16-0.16 Group.

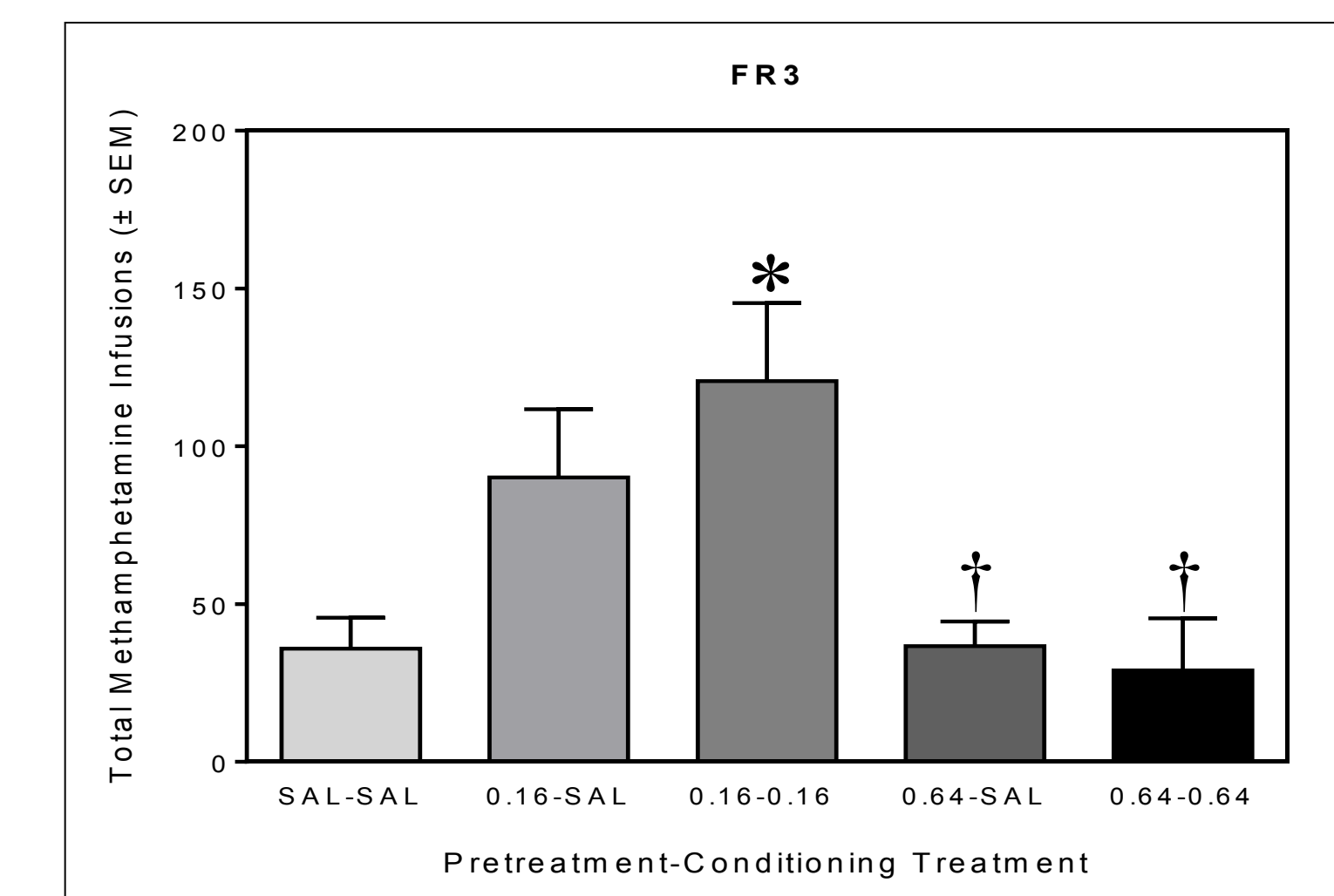


Fig. 4. Mean Total Number of METH Infusions (± SEM) Made by Adult Rats During Self-Administration Training for METH on an FR 3 Schedule of Reinforcement. Rats were Exposed to Nicotine (0.16 or 0.64 mg/kg) or Saline during Adolescence (PD 35-50) and Adulthood. * Indicates Statistical Difference from SAL-SAL Group; † Indicates Different from 0.16-0.16 Group.

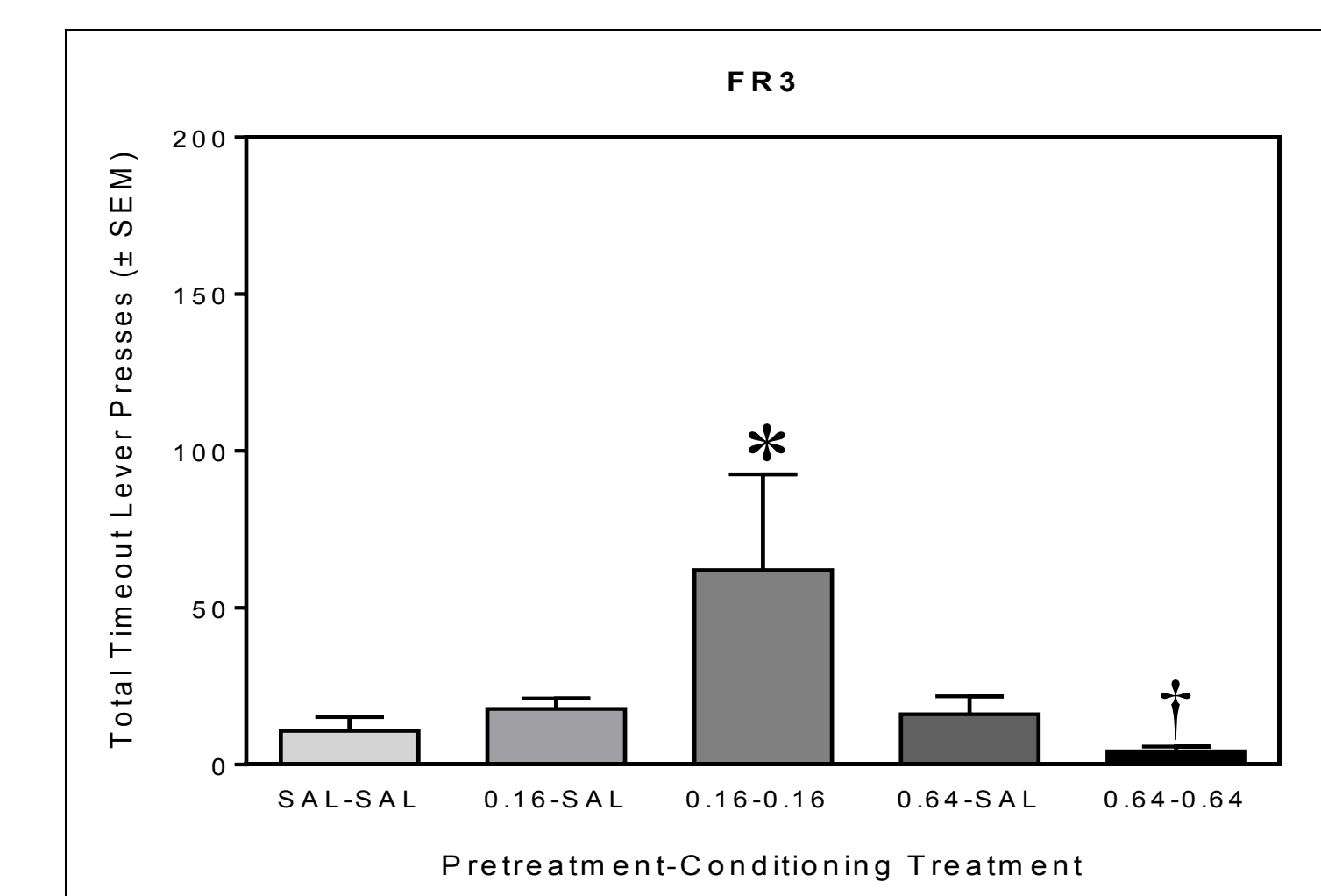


Fig. 5. Mean Total Number of Timeout Periods (± SEM) Made by Adult Rats During Self-Administration Training for METH on an FR 3 Schedule of Reinforcement. Rats were Exposed to Nicotine (0.16 or 0.64 mg/kg) or Saline during Adolescence (PD 35-50) and Adulthood. * Indicates a Statistical Difference from SAL-SAL Group; † Indicates a Significant Difference from 0.16-0.16 Group.

Extinction

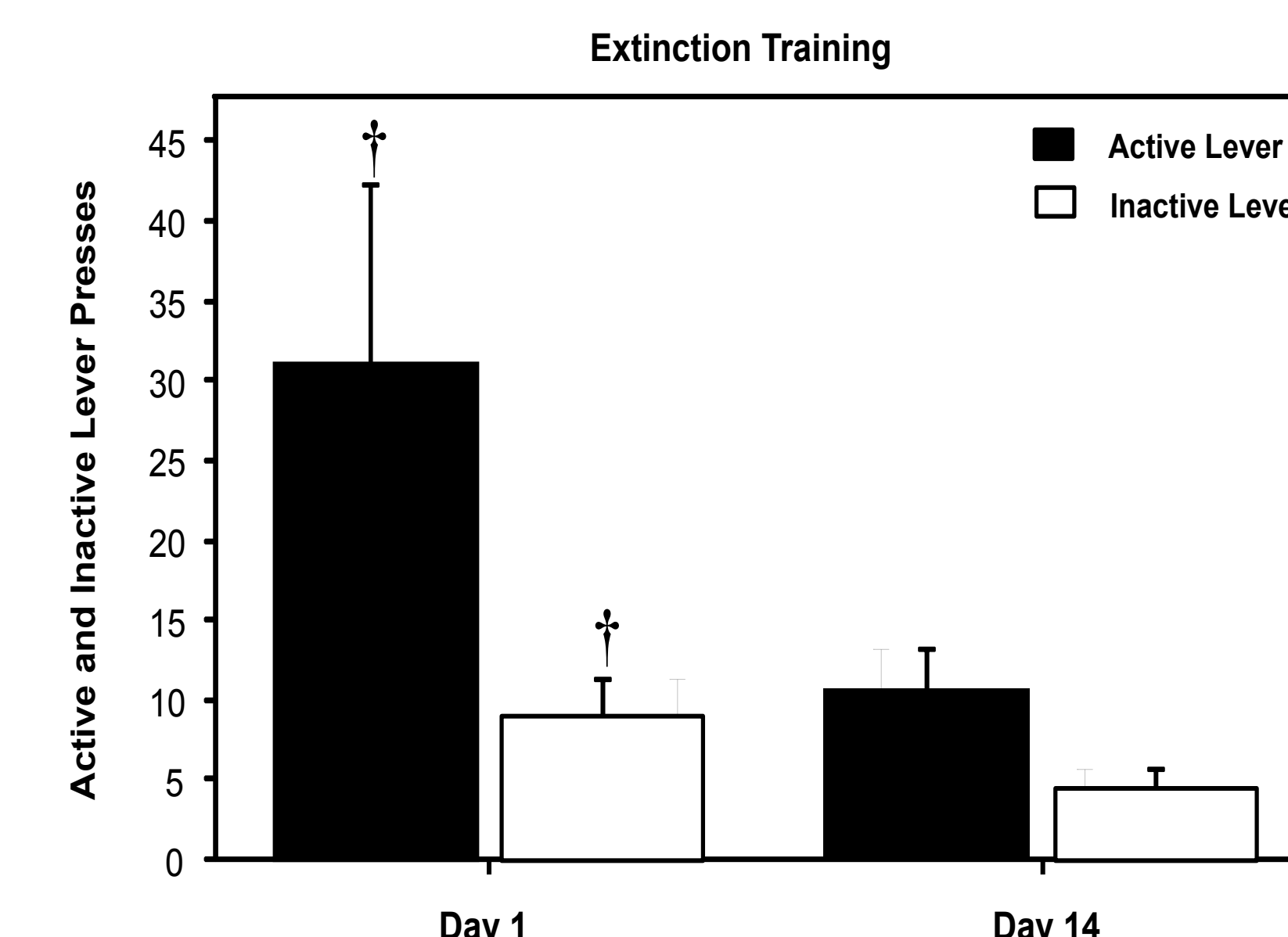


Figure 6. Mean Total Number of Active and Inactive lever press (± SEM) Made by Adult Rats During the First and Last Day of Extinction Training. * Indicates a Statistical Difference from the Last Day of Extinction Training

Reinstatement

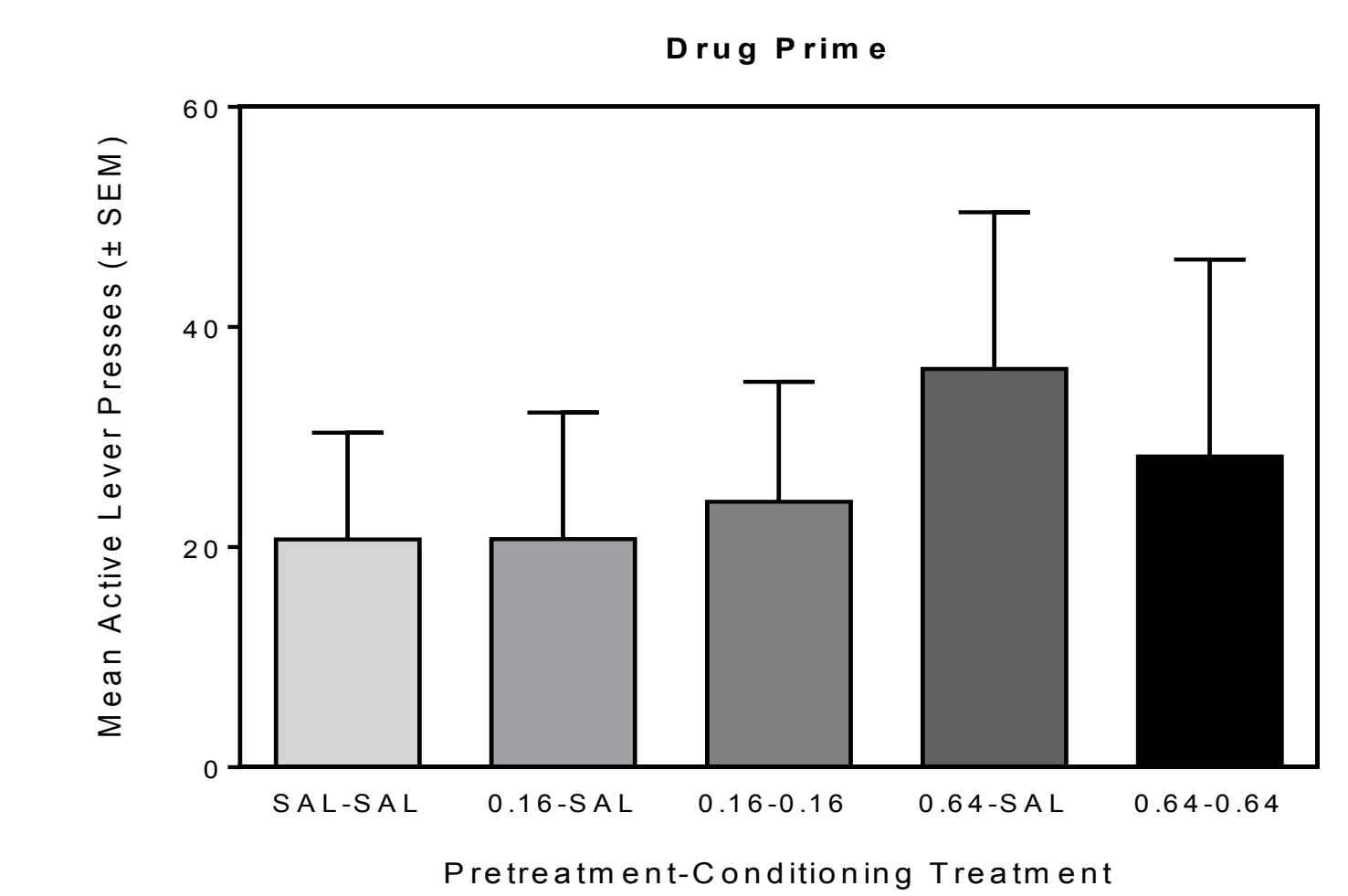


Table 1. Drug Prime Reinstatement Active and Inactive Lever Presses (± SEM).

DISCUSSION

IMPLICATIONS

- ❖ These data suggest that nicotine use is an important contributor to the abuse of METH, and that METH rehabilitation programs should also assess nicotine use in designing treatment plans.
- ❖ Novel pharmacotherapies altering cholinergic and dopaminergic interactions may be key in preventing METH relapse in humans.

Acknowledgments

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