



*The University of Texas
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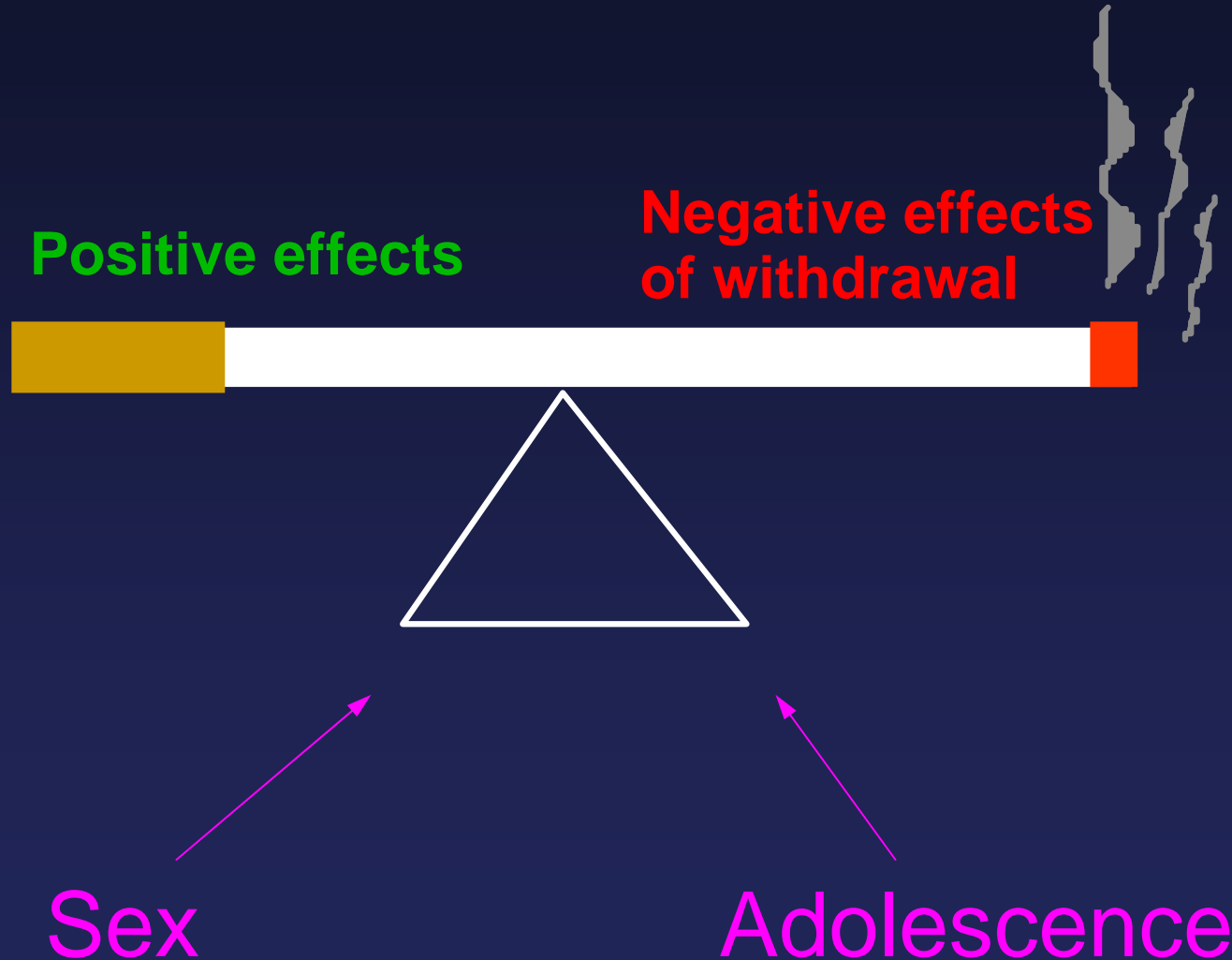
**“Oh Rats!”:
Implications of Adolescent
Rodent Studies for Humans**

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Factors Influencing Smoking Behavior





Nicotine Withdrawal in Rats

- Dependence Induction:

Chronic administration of nicotine via subcutaneous mini pump for 7-14 days
(*Equivalent doses=3.2 mg/kg/day in adults; 4.7 mg/kg/day adolescents; base*)

- Precipitated Withdrawal:

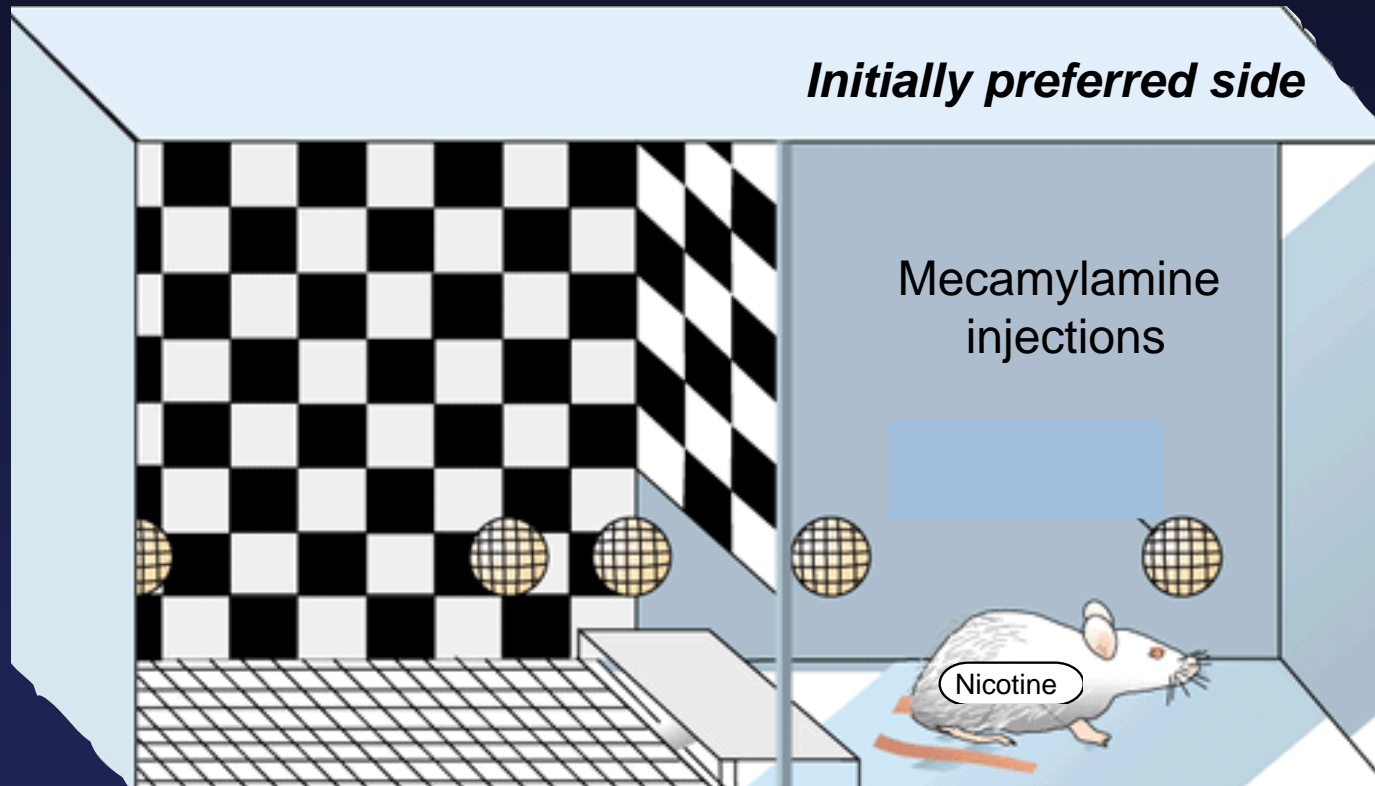
Administration of the nicotinic antagonist mecamylamine



Goal: To compare Nicotine Withdrawal and Rewarding Effects in Adolescent and Adult Rats

- Aversive effects of nicotine withdrawal
Conditioned Place Aversion Paradigm
- Rewarding effects of nicotine
Conditioned Place Preference Paradigm

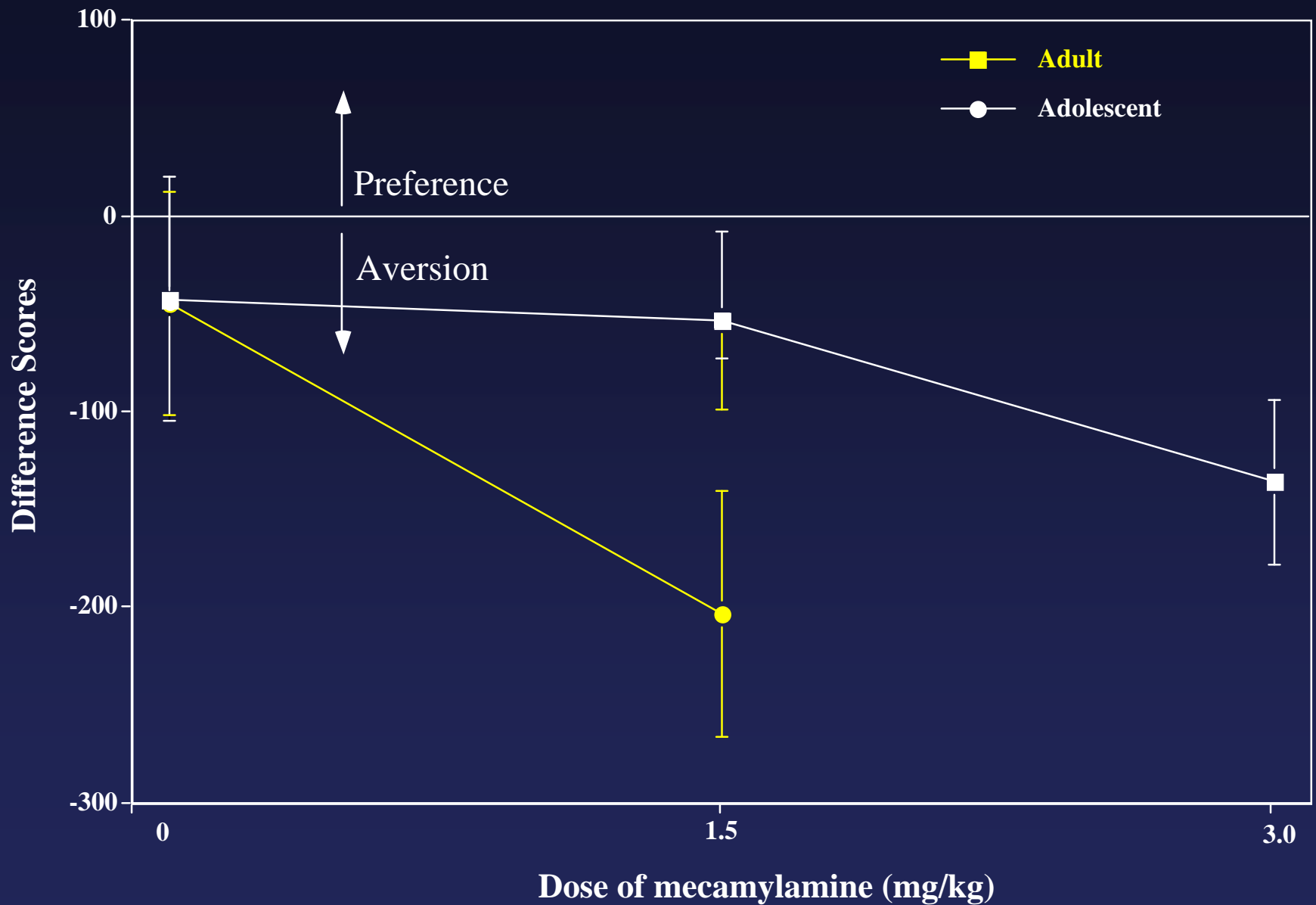
Conditioned Place Aversion



Neutral side

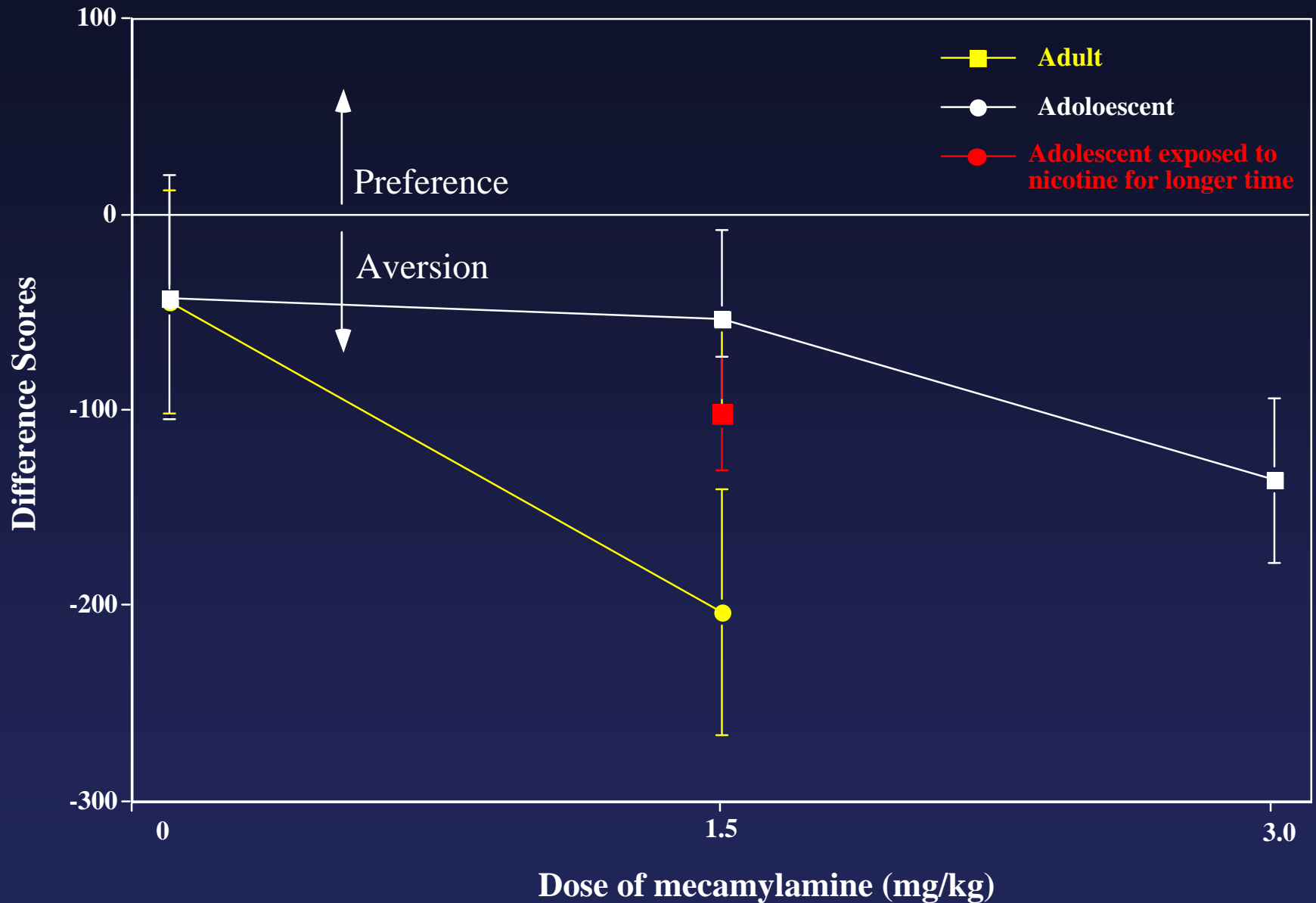
"Withdrawal" side

Nicotine withdrawal is lower in adolescent rats



O'Dell LE, Torres OV, Natividad LA, Tejeda HA. (2007). Adolescent nicotine produces less affective measures of withdrawal relative to adult nicotine exposure in male rats. *Neurotoxicol Teratol.* 29(1):17-22.

Nicotine withdrawal is lower in adolescent rats



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SUMMARY

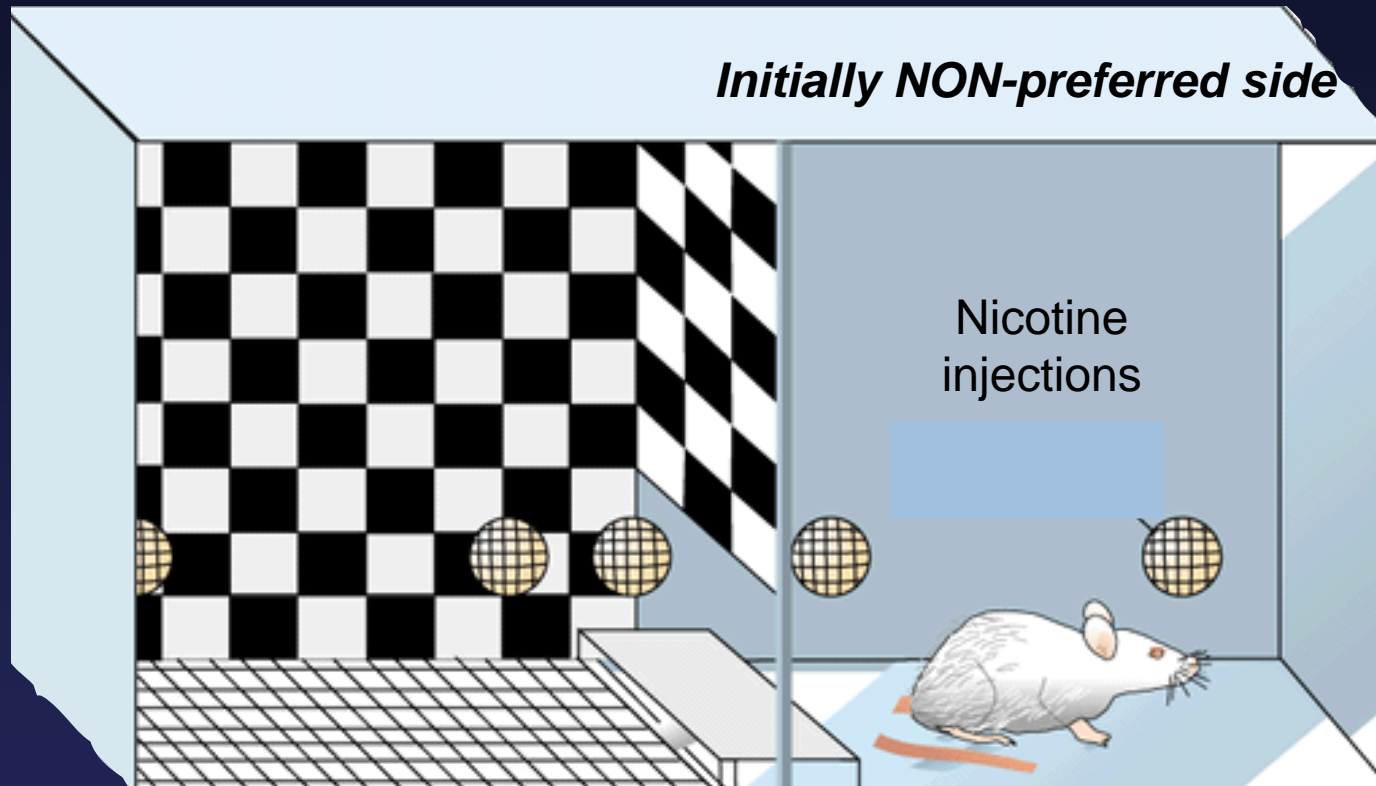
- **Affective properties of nicotine withdrawal are lower during adolescence.**



Goal: To compare Nicotine Withdrawal and Rewarding Effects in Adolescent and Adult Rats

- Aversive effects of nicotine withdrawal
Conditioned Place Aversion Paradigm
- Rewarding effects of nicotine
Conditioned Place Preference Paradigm

Conditioned Place Preference

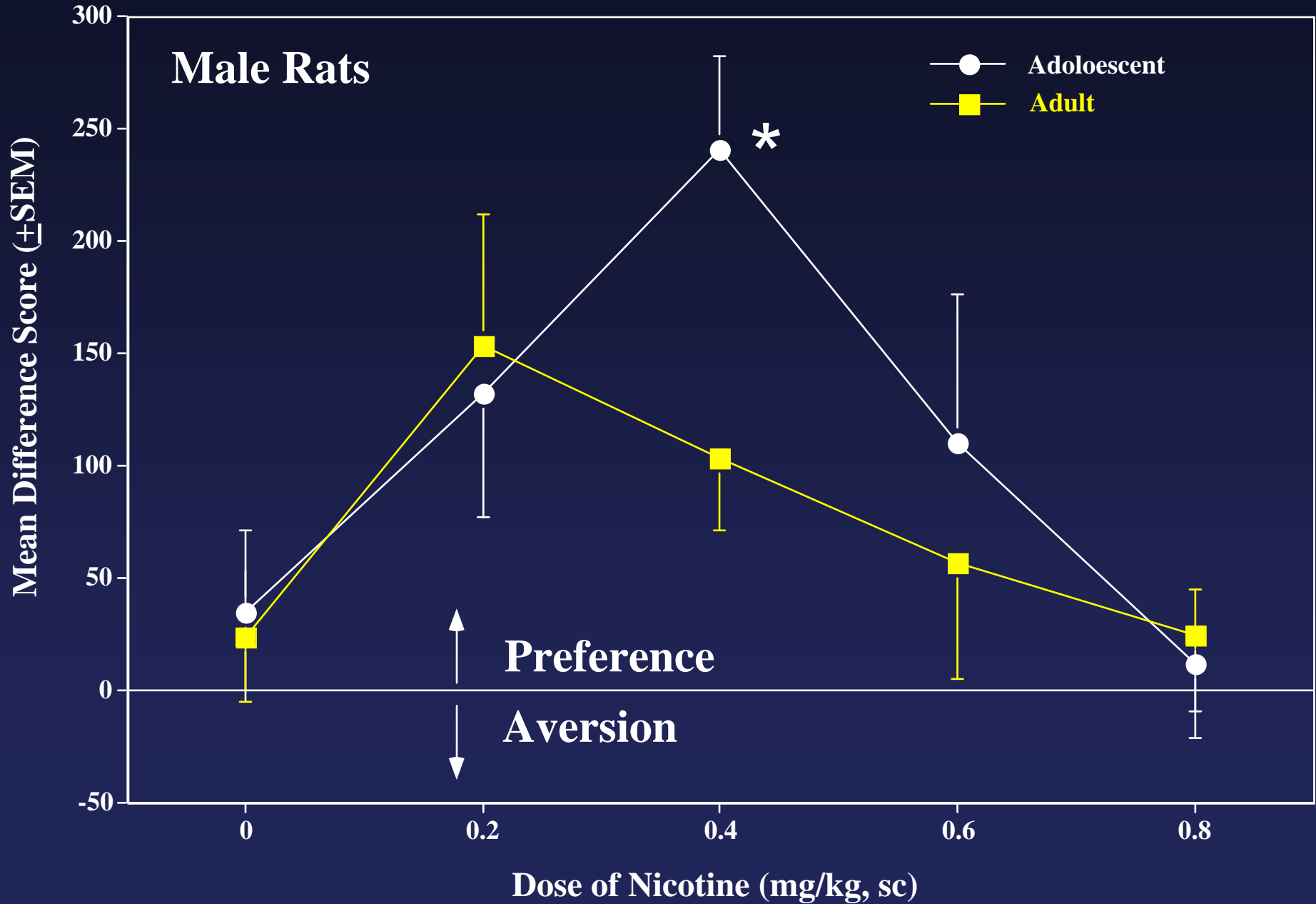


Neutral side

"Reward" side

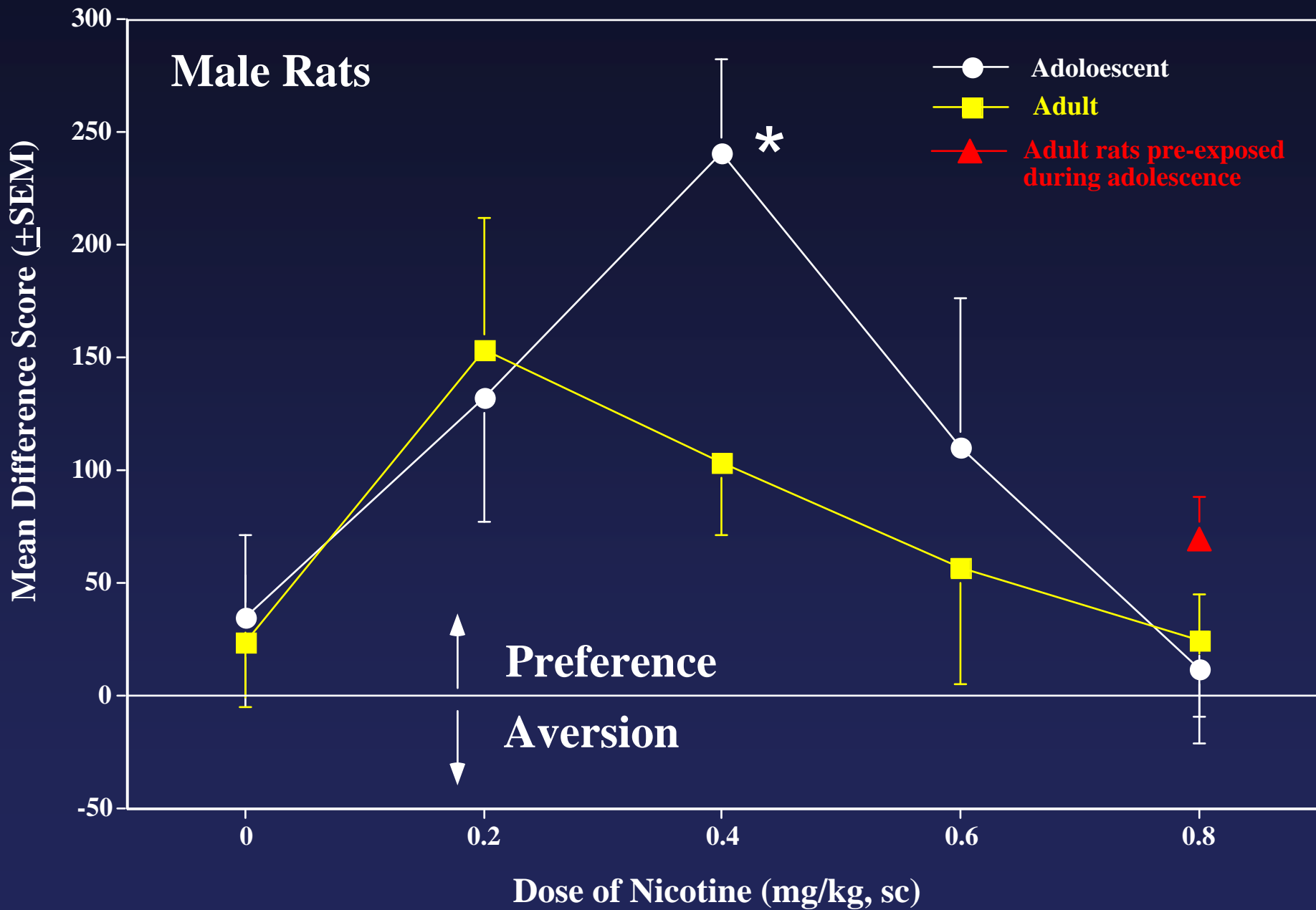
Nicotine Place Preference is enhanced in adolescent rats

Male Rats



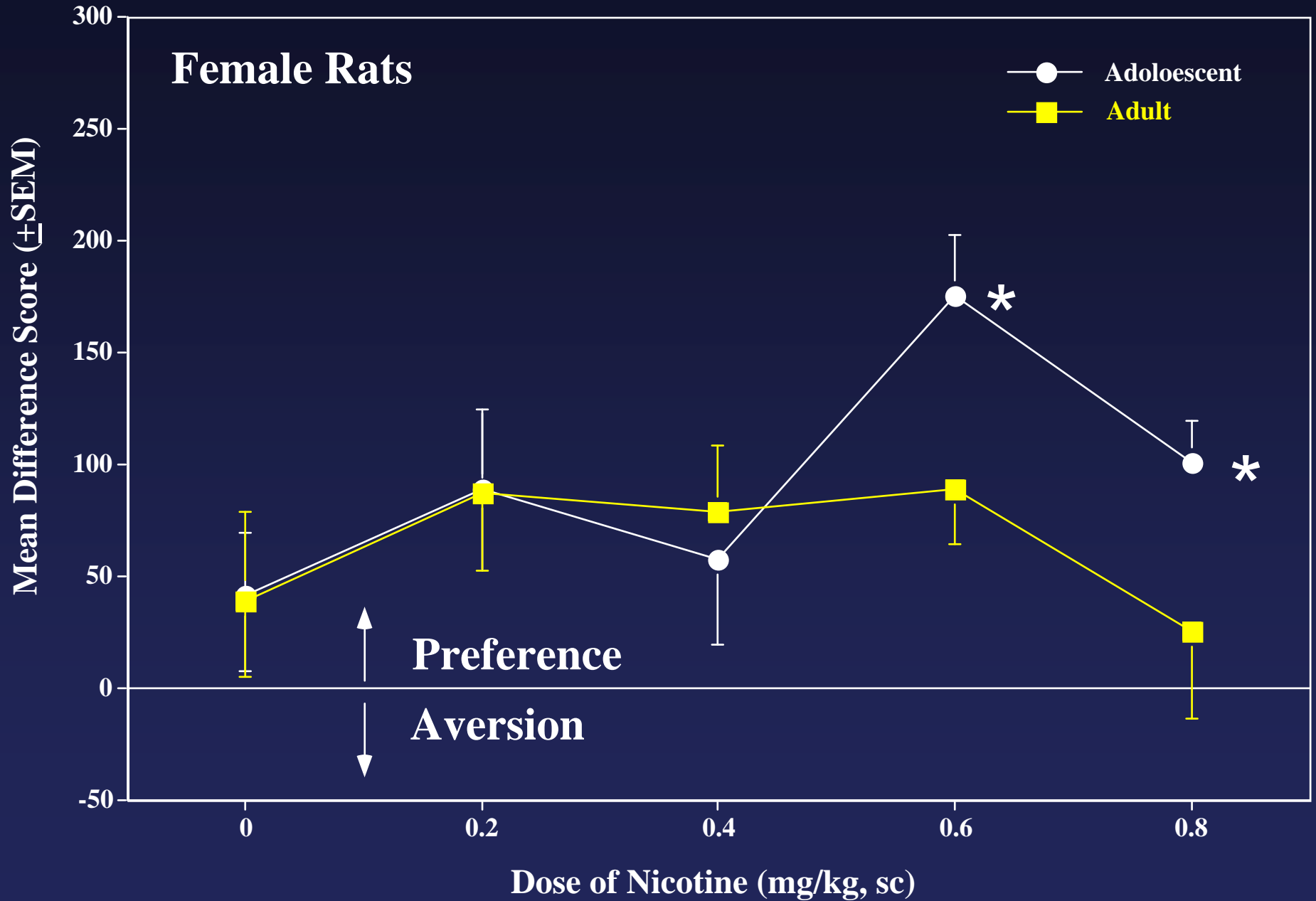
Nicotine Place Preference is enhanced in adolescent rats

Male Rats

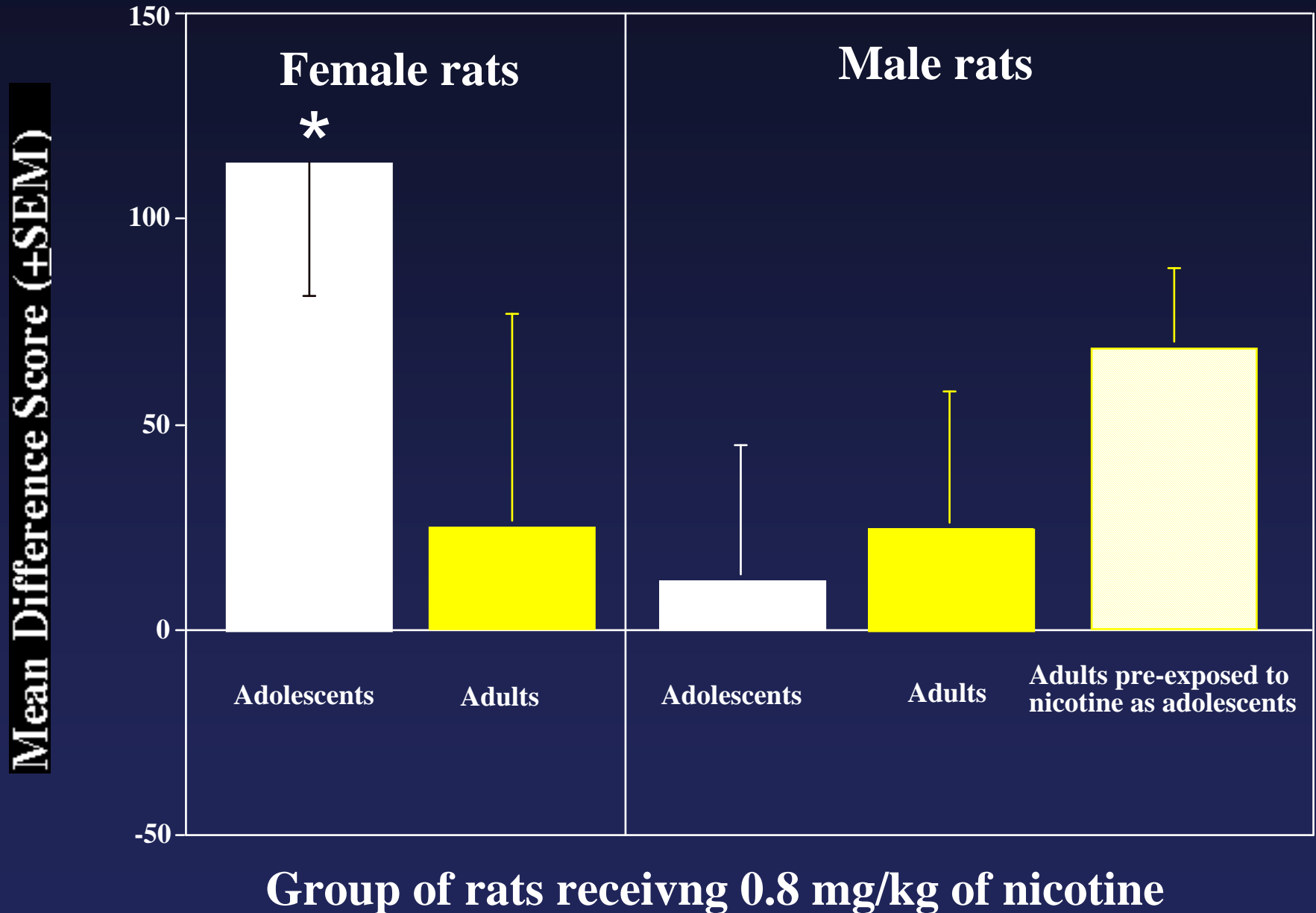


Nicotine Place Preference is enhanced in adolescent rats

Female Rats



Adolescent females display a large preference at a high dose that appears to be aversive in males





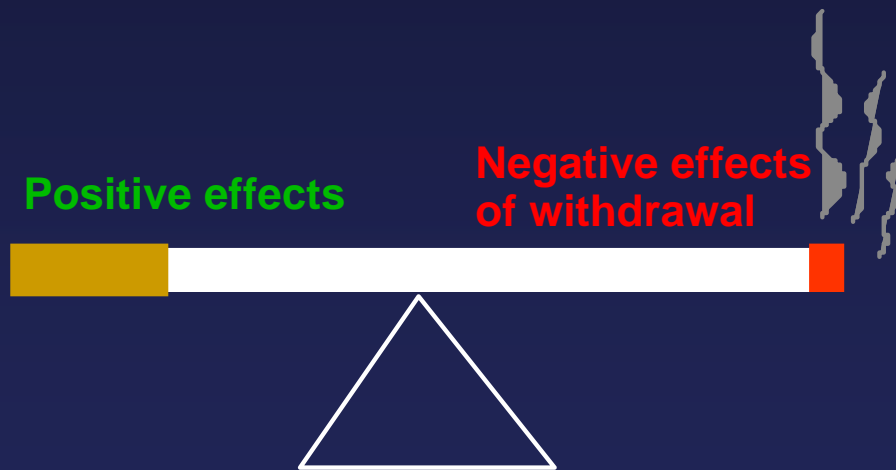
Summary

- The rewarding effects of nicotine are enhanced during adolescence in male and female rats.
- The rewarding effects of nicotine are enhanced by pre-exposure to nicotine during adolescence.
- Preference produced by high nicotine doses is enhanced in females and adult males pre-exposed to nicotine during adolescence.



CONCLUSION

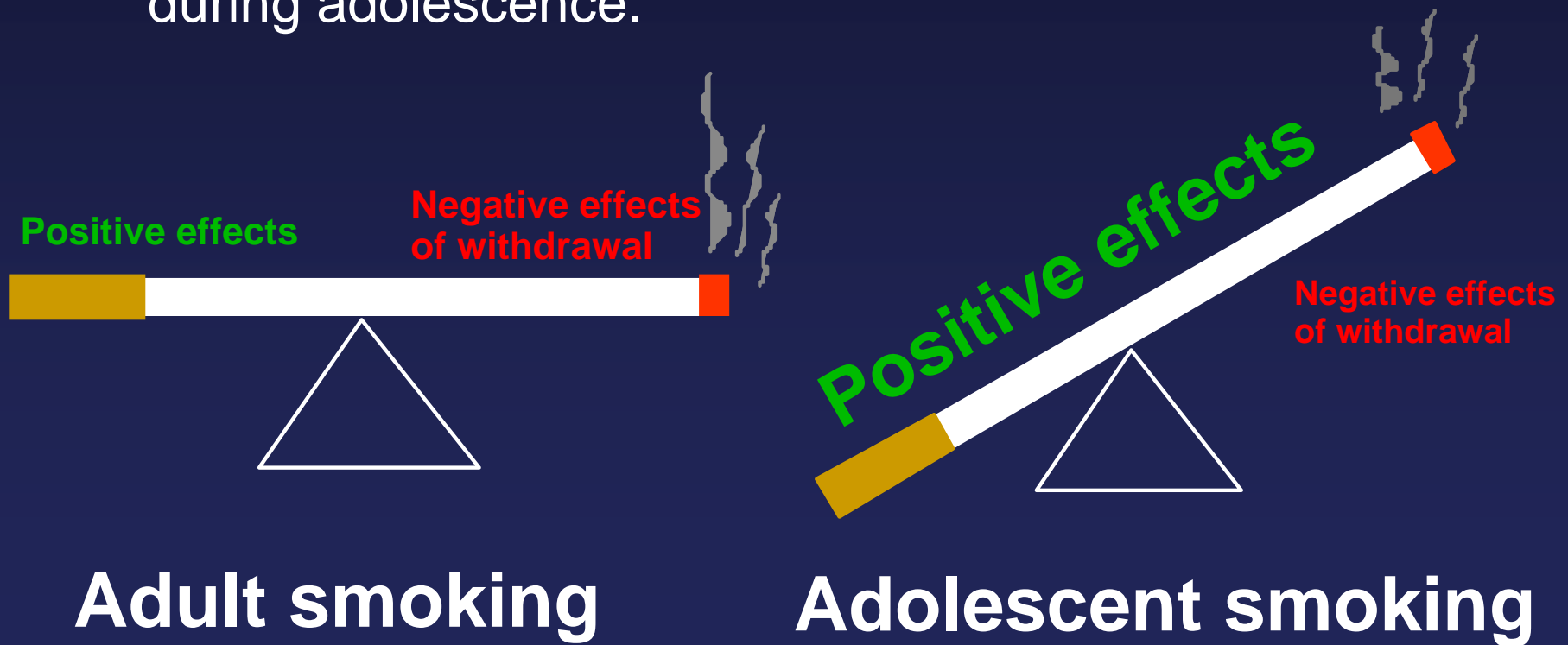
- Adult smoking is mediated by a balance between the positive effects of nicotine and avoiding the negative consequences of nicotine withdrawal.



Adult smoking

CONCLUSION

- Adolescent smokers experience enhanced positive effects of nicotine and decreased negative effects of withdrawal.
- These likely both contribute to enhanced tobacco abuse during adolescence.





Clinical implications

- We may need to apply different treatment strategies for smokers at different stages of development.
- Treatment strategies that focus on alleviating withdrawal (NRT) may be ineffective in treating adolescent smokers who do not experience withdrawal.
- NRT appears to be ineffective at reducing abstinence rates in adolescent smokers (see Hurt et al. 2000; Moolchan et al. 2006; Smith et al. 1996).

Collaborators

Scripps Research Institute

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Dr. Adrie Bruijnzeel

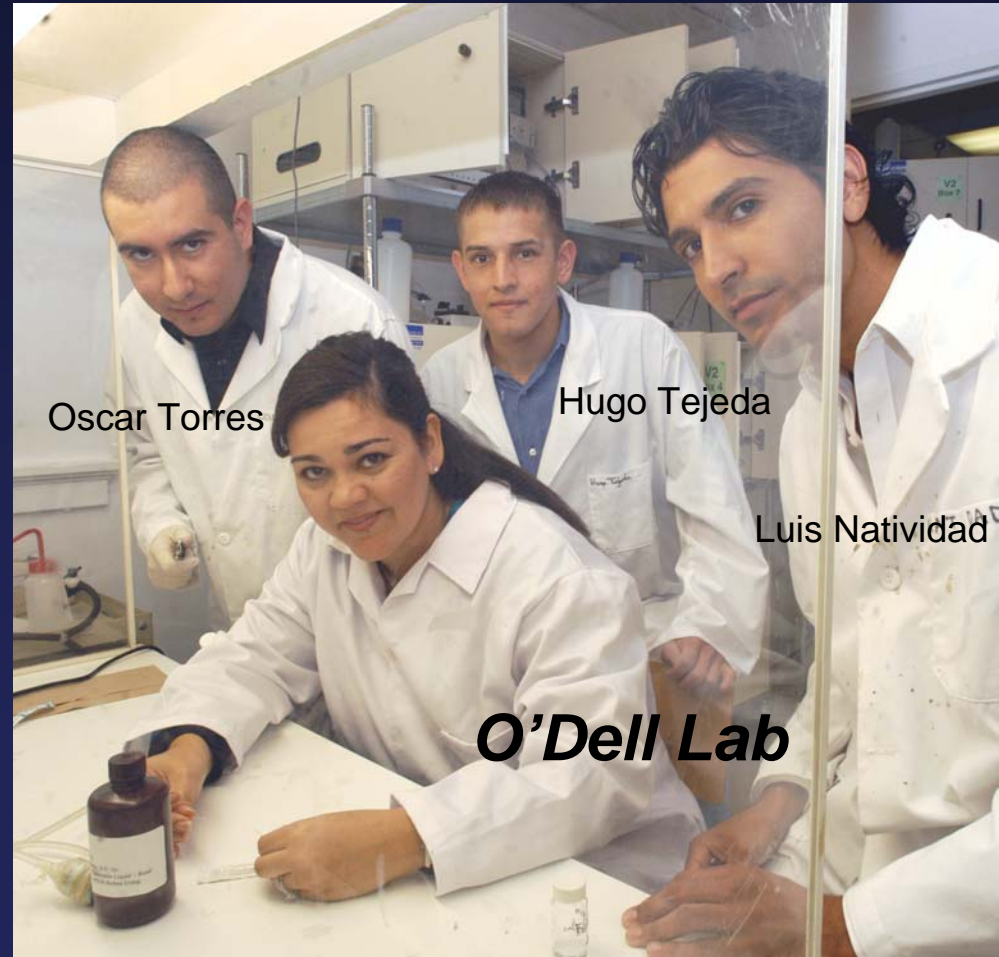
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