The Effects Ovarian Hormones on Heroin Self-Administration in Female Rats

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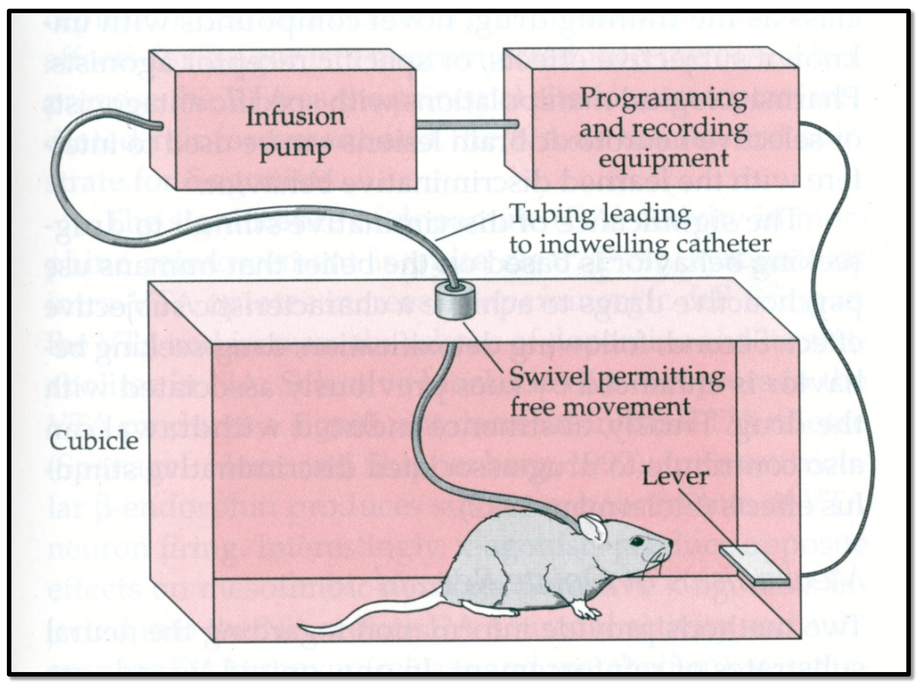
BACKGROUND AND AIMS

- Sex differences in drug use patterns have been consistently reported
- Previous research suggest that gonadal hormones may be driving these differences
- For stimulants, estradiol is facilitative and progesterone is attenuating
- Very few studies have examined the roles of ovarian hormones on opioids such as heroin
- Previous work from our lab suggests that effects of ovarian hormones on cocaine may not generalize to heroin
- The purpose of this study was to experimentally examine the effects of estradiol and progesterone on heroin self-administration

METHODS

- Female rats were obtained as young adults and trained to press a lever following arrival
- Rats were then surgically implanted with intravenous catheters into their right jugular veins to permit drug self-administration
- Rats also underwent ovariectomy procedures to remove their ovaries
- After three days of recovery, rats were randomly assigned to one of four treatment groups: vehicle (VEH), progesterone (PRO), estradiol (EST), or progesterone + estradiol (P+E)
- 30 min prior to each test session, rats in each treatment group received 0.1 ml subcutaneous injections of of estradiol (5 µg), progesterone (125 µg), estradiol + progesterone (5 µg+ 125 µg), or vehicle (peanut oil).
- During 2-hr test sessions, rats pressed a lever to receive a drug infusion on a fixed ratio (FR1) schedule of reinforcement

Self-Administration Procedure



Behavioral Economic Analysis

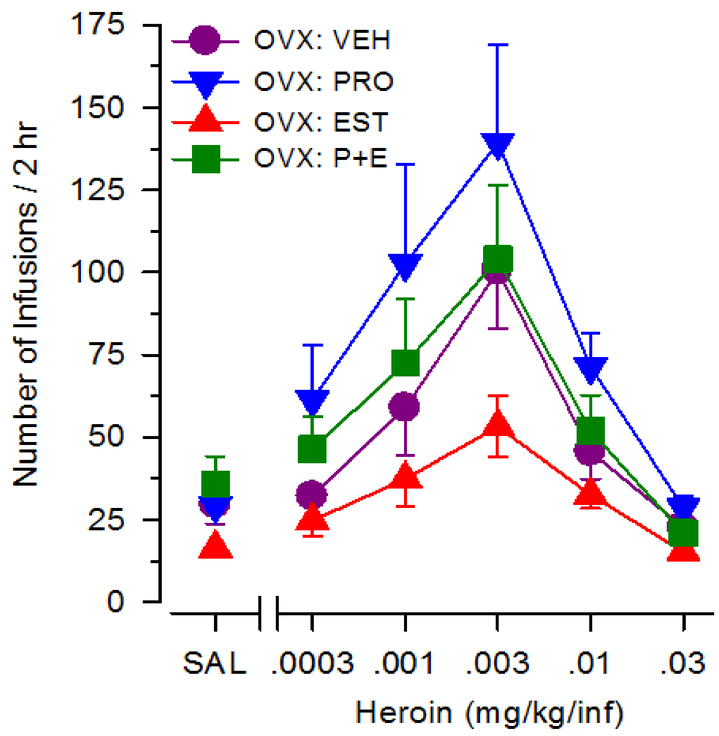
- Behavioral Economic Analysis were applied to the self-administration data to determine the intensity and elasticity of demand using the exponential demand equation (Hursh & Silberberg, 2008):

$$\log_{10}Q = \log_{10}(Q_0) + k(e^{-\alpha * Q0 * C} - 1)$$

- Q = consumption, Q_0 = intensity of demand (consumption when price approaches 0), k = range of possible consumption values in $\log_{10}$ units (set to 3 based on observed range); C = unit price; and α = elasticity of demand.
- Greater values of Q_0 indicate greater consumption when price is unconstrained (i.e. free) while greater values of α indicate greater elasticity (i.e. more sensitive to changes in unit price).

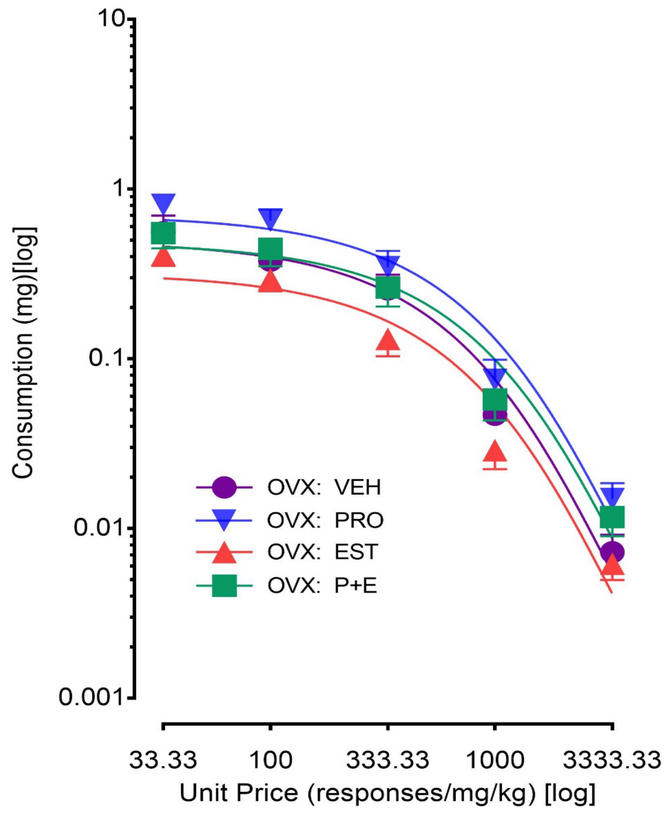
RESULTS

- Heroin self-administration was characterized by an inverted, U-shaped, dose-effect curve
- Self-administration differed significantly between different treatment groups
- EST group self-administered significantly less heroin compared to PRO group.



Dose-response data of heroin self-administration in OVX rats receiving different hormone treatments. Vertical axis depicts number of infusions obtained in a 2-hr test session. Horizontal axis depicts doses of heroin in mg/kg/infusion. Points above "SAL" depicts self-administration of saline. Error bar represent SEM.

- Intensity of demand (Q_0) did not differ across groups
- Elasticity of demand (α) differed significantly across treatment groups.
- Elasticity of demand for EST group was higher than that for PRO group, suggesting that EST group was more sensitive to increases in unit price of heroin



Demand curves computed from dose-response heroin self-administration data. Vertical axis depicts consumption (intake in mg/kg in log units). Horizontal axis depicts price (responses/mg/kg in log units). An exponential demand equation was fitted to the dose-response data and plotted as mean values. Error bars represent SEM; where not indicated, SEM fell within the data point.

Conclusion

- In OVX rats, heroin self-administration was inhibited by estradiol treatment and facilitated by progesterone treatment
- Differences across groups were driven by differences in sensitivity to the unit price of heroin
- These data suggest the ovarian hormones (estradiol) may be effective interventions for heroin use disorders in women, particularly in populations sensitive to price (adolescents and emerging adults)

ACKNOWLEDGEMENTS

Funding for this study was provided by the National Institutes of Health (NIDA Grants DA14255 and DA027485 to MAS) and the Duke Endowment. The authors thank Alexander Casimir, Amy Sullivan, Johanna Ziegler, Meagan Thomas, Chris Van Rooyen and Keith Frye for expert animal care and technical assistance.