

Sex-dependent modulation of decision-making in the rat gambling task

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BACKGROUND

- Problem or pathological gambling is characterized by impaired decision-making, higher impulsivity and risk-taking behaviors (Brand et al., 2005)
- In humans, the prevalence of problem gambling among men is higher than that for women suggesting possible sex-related differences in several aspects of pathological gambling, which may include risk-taking and impulsivity (Wong et al., 2013).
- Sex differences have been observed in the human Iowa Gambling Task, which involves learning to differentiate between advantageous and disadvantageous decks of cards (Cavedini et al., 2002)
- Men show greater preference for the long-term advantageous options compared to women in the human Iowa Gambling Task (van den Bos, et al., 2013)

Aim:

- Assess whether there are sex differences in decision-making and choice impulsivity associated with the addictive gambling behavior in a rat model of the Iowa gambling task.

METHODS

- Food-deprived rats were trained to nose-poke for sucrose pellet rewards.
- As in the human Iowa Gambling Task, four different options associated with different amounts of reward and with different probability and duration of punishing time-out periods were presented to male and female rats.
- The four different schedules consisted of the following rewarding/punishment probabilities: (i) 90% reward (1 pellet)/ 10% punishment (5 sec time-out); (ii) 80% reward (2 pellet)/ 20% punishment (10 sec time-out); (iii) 50% reward (3 pellet)/ 50% punishment (30 sec time-out); (iv) 40% reward (4 pellet)/ 60% punishment (40 sec time-out); Fig. 1.
- The schedules were designed such that the options linked with larger rewards result in fewer pellets earned per unit time and the most optimal option was the 2-pellet schedule.
- Rats typically learn to avoid risky options to maximize their reward (i.e., earnings).

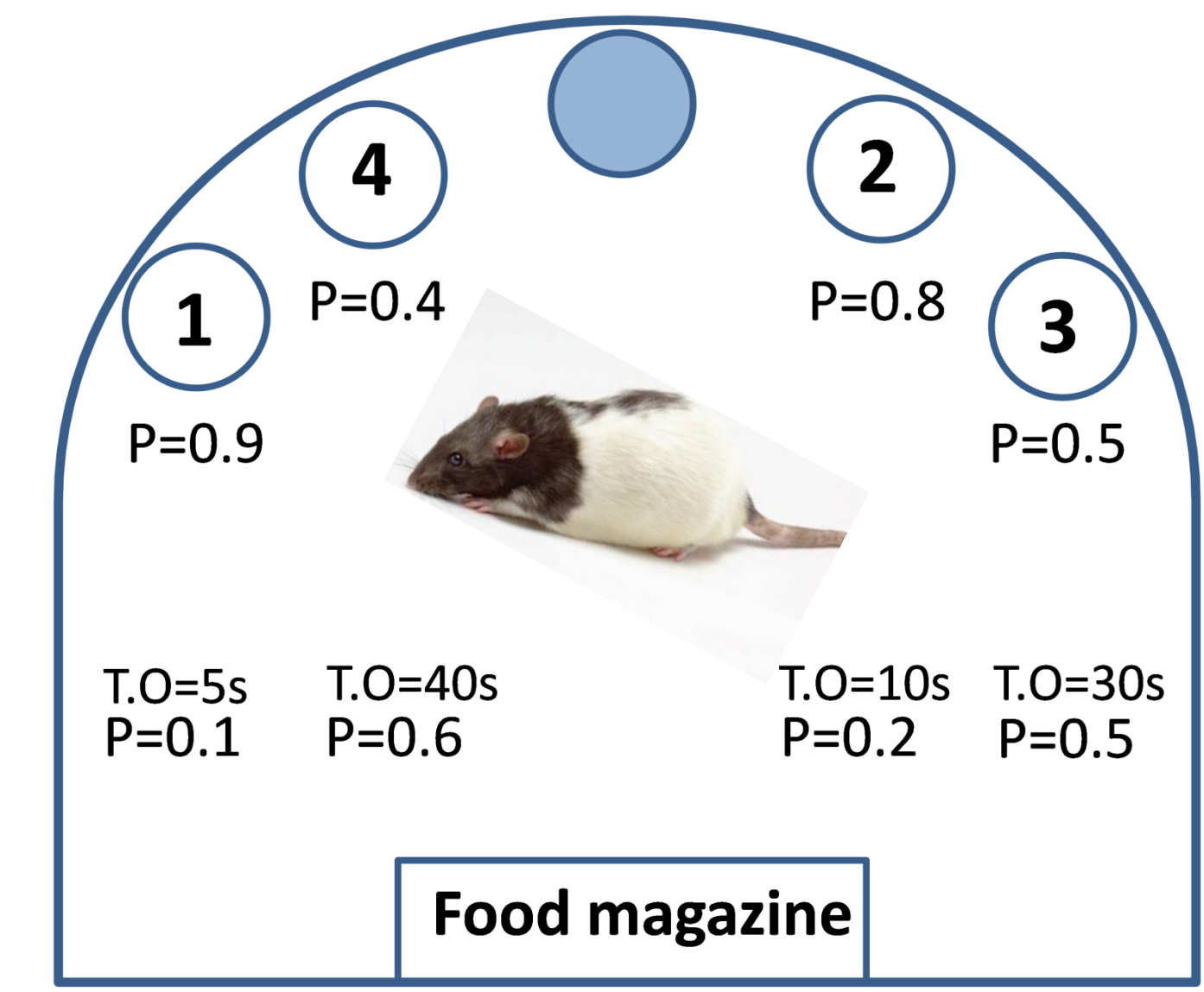


Figure 1. Different schedules of the rewarding/punishment probabilities (T.O., time out)

RESULTS

Females performed better during the first session of the rat gambling task

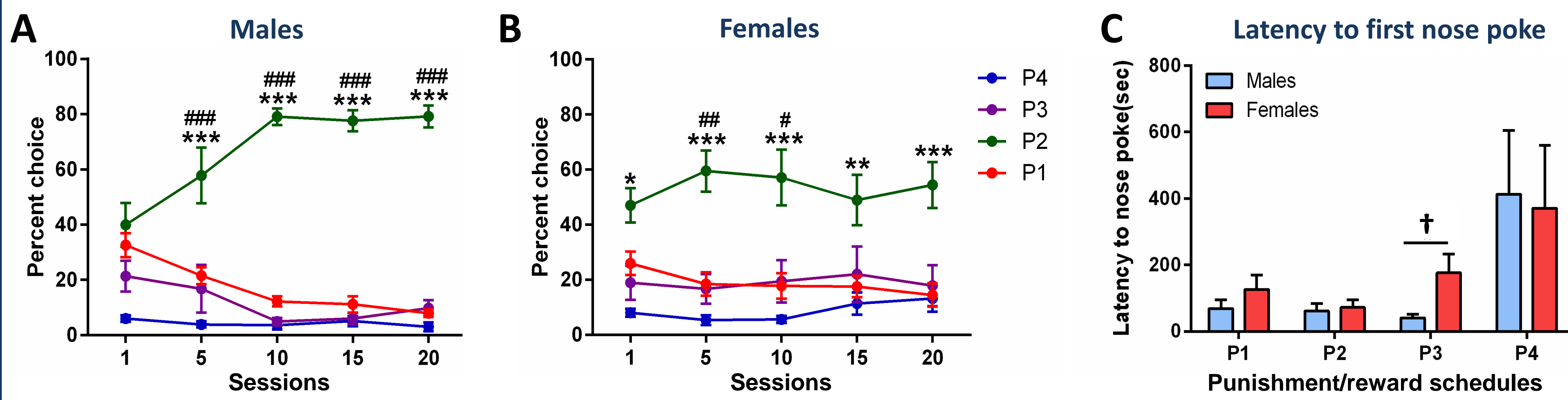


Figure 2. Acquisition of choice patterns in the rat gambling task in (A) male and (B) female rats. (C) Choice latency during the first session of the rat gambling task. Data are expressed as the mean \pm SEM (n=8-9/group). * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs P1, P3 and P4; # $p < 0.05$, ### $p < 0.01$, #### $p < 0.001$ vs session 1; † $p < 0.05$ vs males.

No effect of estrous cycle on rat gambling task performance in females

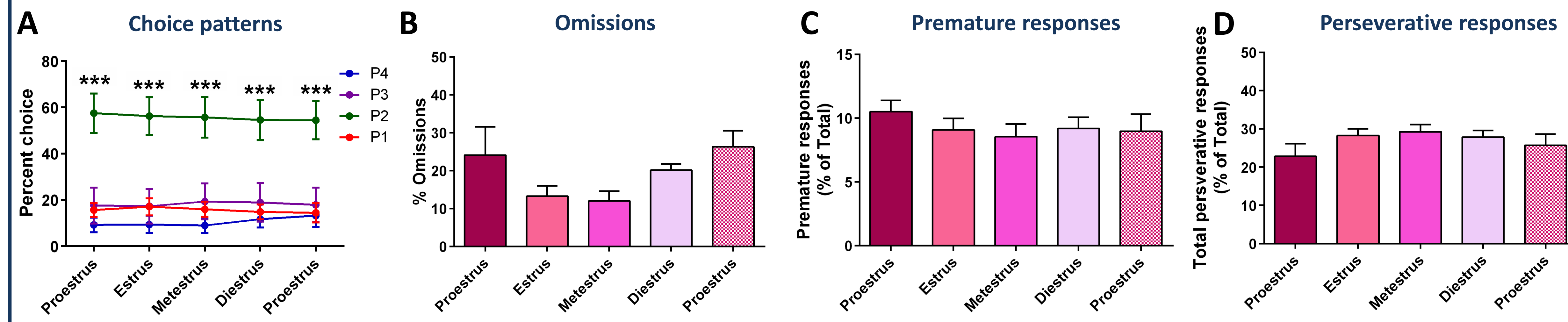


Figure 5. Estrous cycle effect on (A) choice patterns; (B) % omissions; (C) % premature responses and (D) % perseverative responses in female rats. Data are expressed as the mean \pm SEM (n=9/group). *** $p < 0.001$ vs P1, P3 and P4.

Improvement of performance of males but not females in the rat gambling task

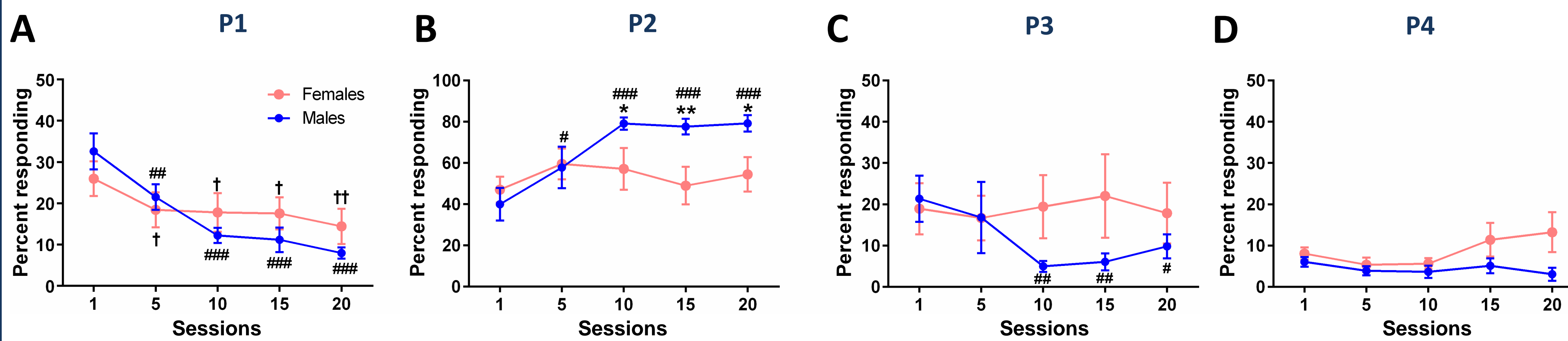


Figure 3. Sex differences in (A) P1; (B) P2; (C) P3 and (D) P4 punishment/reward schedules in the rat gambling task. Data are expressed as the mean \pm SEM (n=8-9/group). * $p < 0.05$, ** $p < 0.01$ vs females; # $p < 0.05$, ## $p < 0.01$, ### $p < 0.001$ vs males' session 1; † $p < 0.05$, †† $p < 0.01$ vs females' session 1.

Effects of dopamine D₂ receptor antagonism on the rat gambling task

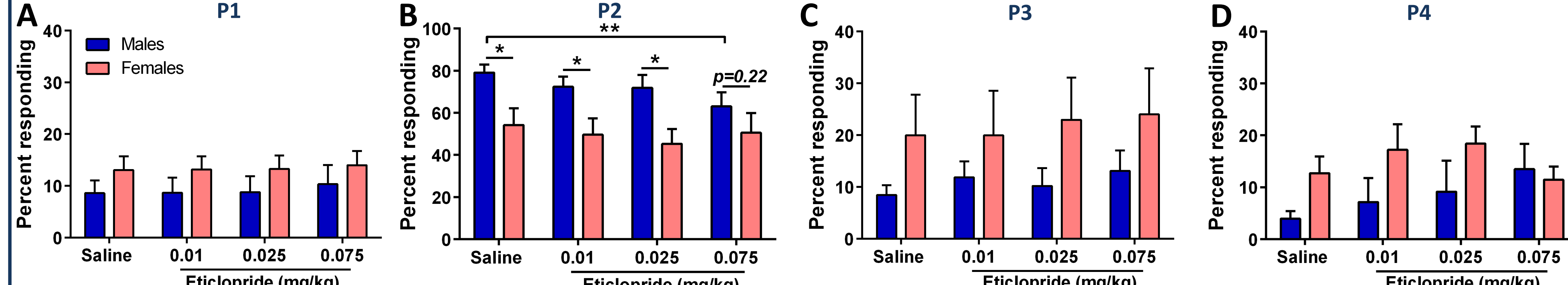


Figure 6. Effects of dopamine D₂ receptor antagonism on (A) P1, (B) P2, (C) P3 and (D) P4 punishment/reward schedules in male and female mice during the rat gambling task. Data are expressed as the mean \pm S.E.M (n=8-9 per group) *** $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ (A, B, C, D, F: two-way repeated measures ANOVA, E: one-way ANOVA; Bonferroni *post-hoc* test).

Sex differences in measures of impulsivity

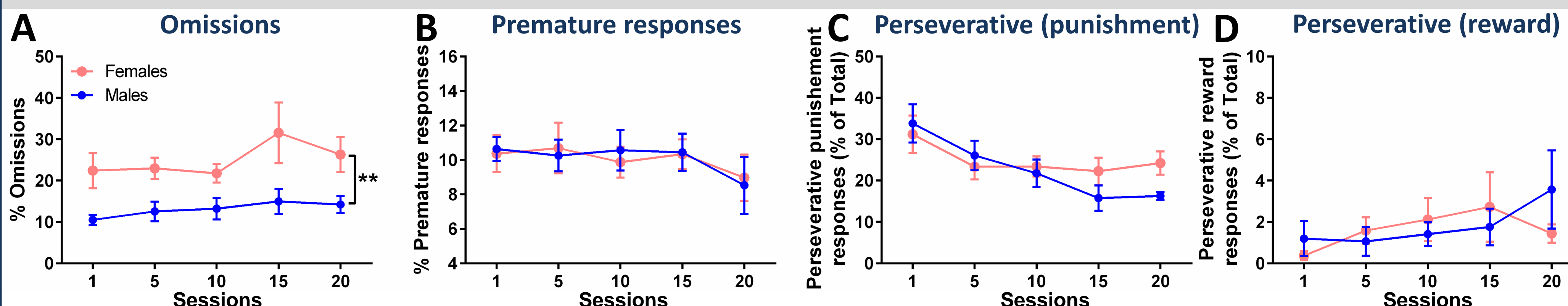


Figure 4. Sex differences in (A) % omissions (B) % premature responses, (C) % perseverative punishment responses and (D) % perseverative reward responses in the rat gambling task. Data are expressed as the mean \pm SEM (n=8-9/group). ** $p < 0.01$ vs males

CONCLUSIONS

- These results show direct sex differences in various aspects of the rat gambling task.
- While females show a better decision-making performance during the first session of the test, only males have a progressive improvement of performance, indicating possible differential mechanisms underlying short- and long-term decision-making in males vs females.
- No sex differences were observed in impulsivity measures
- Sex-differences are not dependent on physiological effects of the estrous cycle hormonal changes in females
- Increased dopaminergic neurotransmission dose-dependently negatively affected decision-making of male, but not female rats.