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).

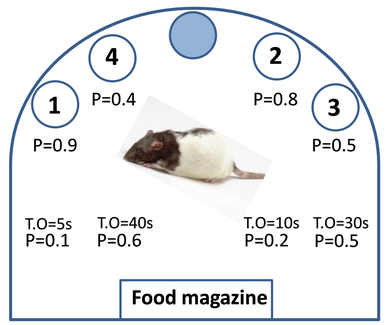

Figure 1. Different schedules of the rewarding/punishment probabilities (T.O., time out)

RESULTS

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

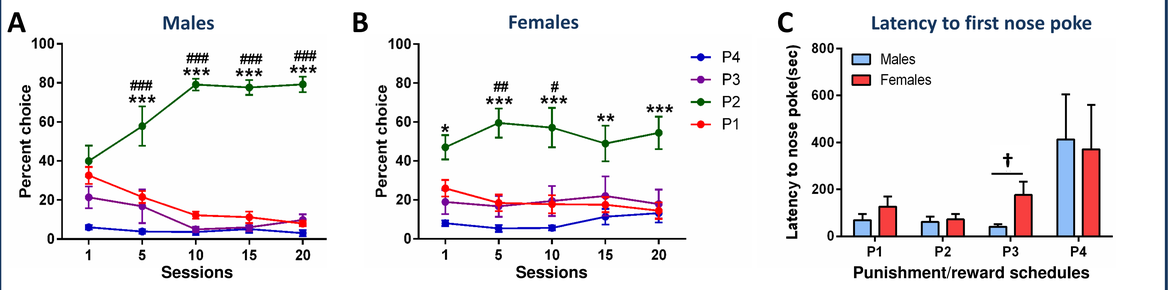

Figure 2. Acquisition of choice patterns in the rat gambling task in **(A)** male and **(B)** female rats. **(C)** Choice latency during the first session of the rat gambling task. Data are expressed as the mean ± SEM (n=8-9/group). *$p<0.05$, **$p<0.01$, ***$p<0.001$ *vs* P1, P3 and P4; #$p<0.05$, ##$p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

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

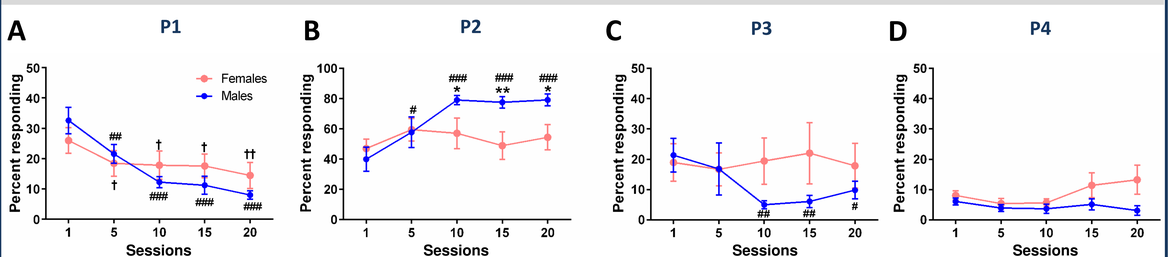

Figure 3. Sex differences in **(A)** P1; **(B)** P2; **(C)** P3 and **(D)** P4 punishment/reward schedules in the rat gambling task. Data are expressed as the mean ± SEM (n=8-9/group). *$p<0.05$, **$p<0.01$ *vs* females; #$p<0.05$, ##$p<0.01$, ###$p<0.001$ *vs* males' session 1; †$p<0.05$, ††$p<0.01$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

Sex differences in measures of impulsivity

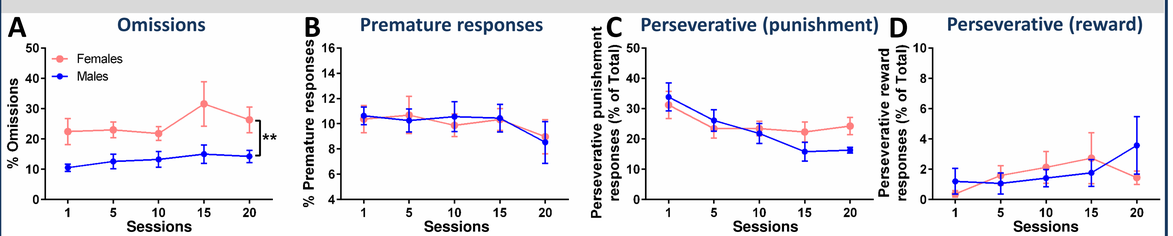

Figure 4. Sex differences in **(A)** % omissions **(B)** % premature responses, **(C)** % perseverative punishment responses and (D) % perseverative reward responses in the rat gambling task. Data are expressed as the mean ± SEM (n=8-9/group). **$p<0.01$ *vs* males

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

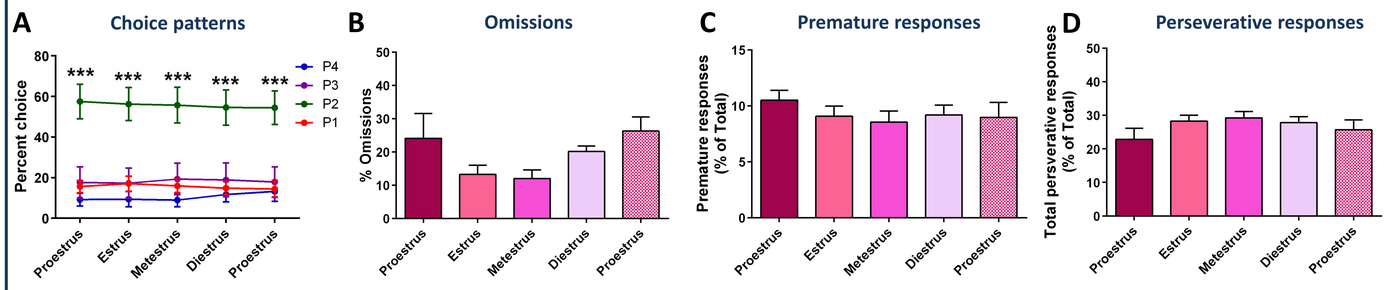

Figure 5. Estrous cycle effect on **(A)** choice patterns; **(B)** % omissions; **(C)** % premature responses and **(D)** % perseverative responses in female rats. Data are expressed as the mean ± SEM (n=9/group). ***$p<0.001$ *vs* P1, P3 and P4.

Effects of dopamine D_2 receptor antagonism on the rat gambling task

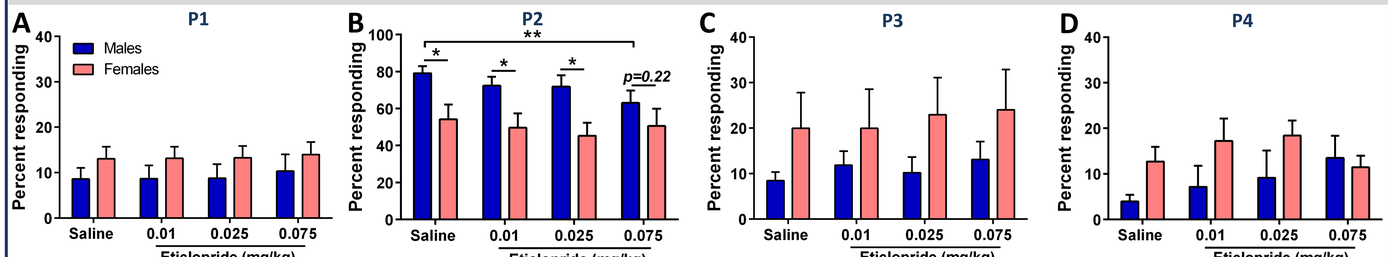

Figure 6. Effects of dopamine D2 receptor antagonism on **(A)** P1, **(B)** P2, **(C)** P3 and **(D)** P4 punishment/reward schedules in male and female mice during the rat gabling task. Data are expressed as the mean ± S.E.M (n=8-9 per group) **$p<0.05$, **$p<0.01$, ***$p<0.001$ (A, B, C, D, F: two-way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

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.
- Hormonal changes characteristic of estrous cycle (estrogen and progesterone) do not affect decision-making and impulsivity in female rats.
- Increased dopaminergic neurotransmission dose-dependently negatively affected decision-making of male, but not female rats.

References: Brand et al., *Psychiatry Research*, 133, 91-99 (2005); Cavedini et al., *Biological Psychiatry,* 51, 334-341 (2002); van den Bos et al., *Behavioral Brain Research,* 238, 95-108 (2013); Wong et al., *Journal of Gambling Studies*, 29, 171-189 (2013).

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