
Figures and figure supplements

Sex differences in discrimination behavior and orbitofrontal engagement during context-gated reward prediction

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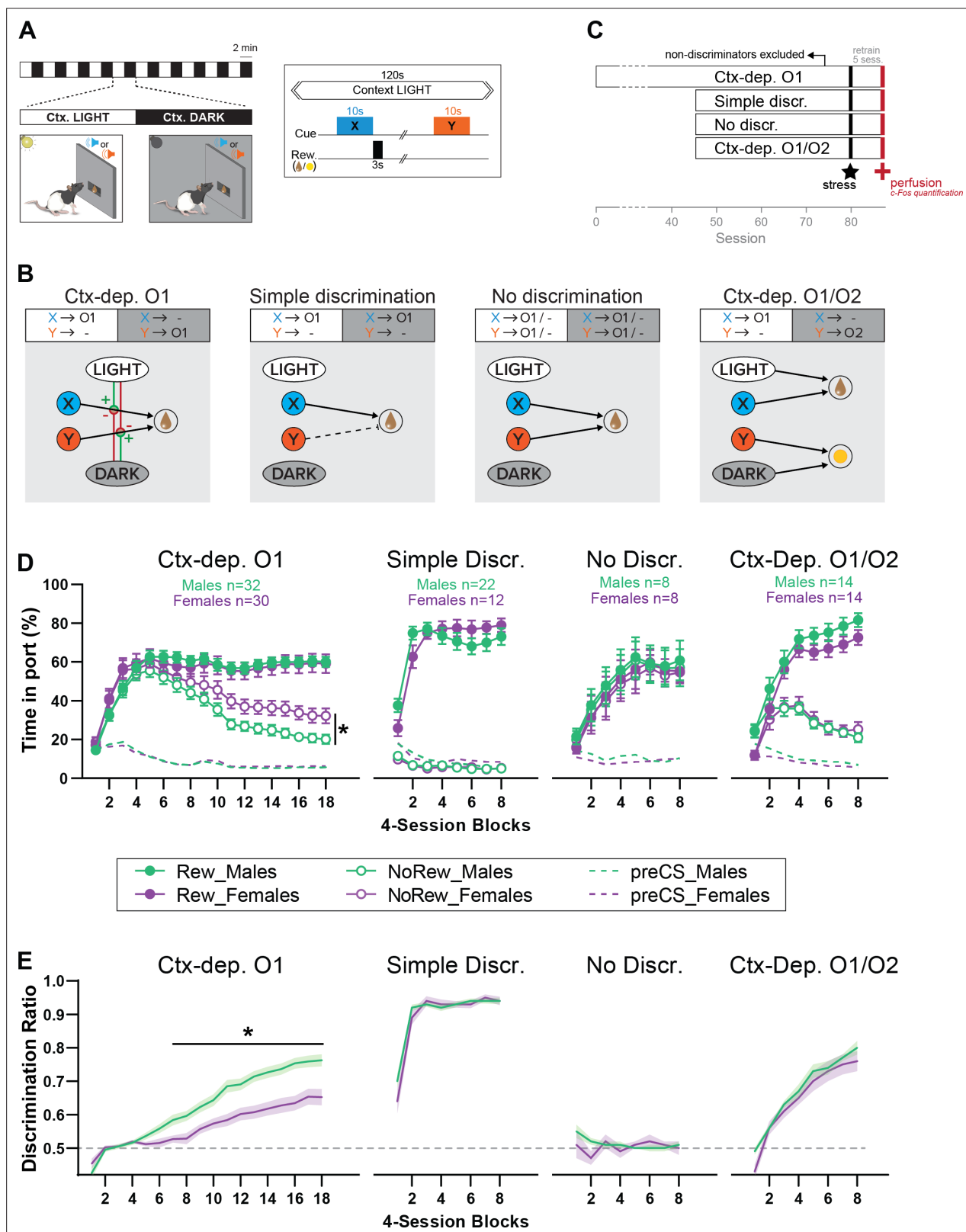


Figure 1. Sex differences in the acquisition of context-gated but not context-independent reward predictions. **(A)** Apparatus and general task design. During each session, the local context alternates every 2 min between a Ctx. LIGHT (house light on) and Ctx. DARK (house light off). Embedded in these context cycles, brief auditory stimuli (X or Y; 10 s) are presented and potentially followed by reward (chocolate milk or banana pellets). **(B)** Reward contingencies and corresponding associative structures for each training condition. Ctx-dep. O1: the local context informs (hierarchically 'gates') the

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predictive status of the ambiguous reward cues X and Y. *Simple discrimination*: reward cues are not ambiguous (only X is rewarded) and the local context is irrelevant. *No Discrimination*: reward cues X and Y are potentially rewarded and the local context is irrelevant. *Ctx-dep. O1/O2*: context-dependent discrimination with differential outcomes; in this case, the local context is relevant but may contribute to context-sensitive performance via simple (nonhierarchical) associations (summation of cue- and context-evoked predictions). **(C)** Experimental timeline. **(D)** Time in port (% cue time) during rewarded and non-rewarded trials across acquisition for male and female rats trained in each task. **(E)** Discrimination ratio across acquisition for male and female rats trained in each task. Error bars and error bands indicate \pm standard error of the mean (s.e.m.). * $p < 0.05$, t-tests.

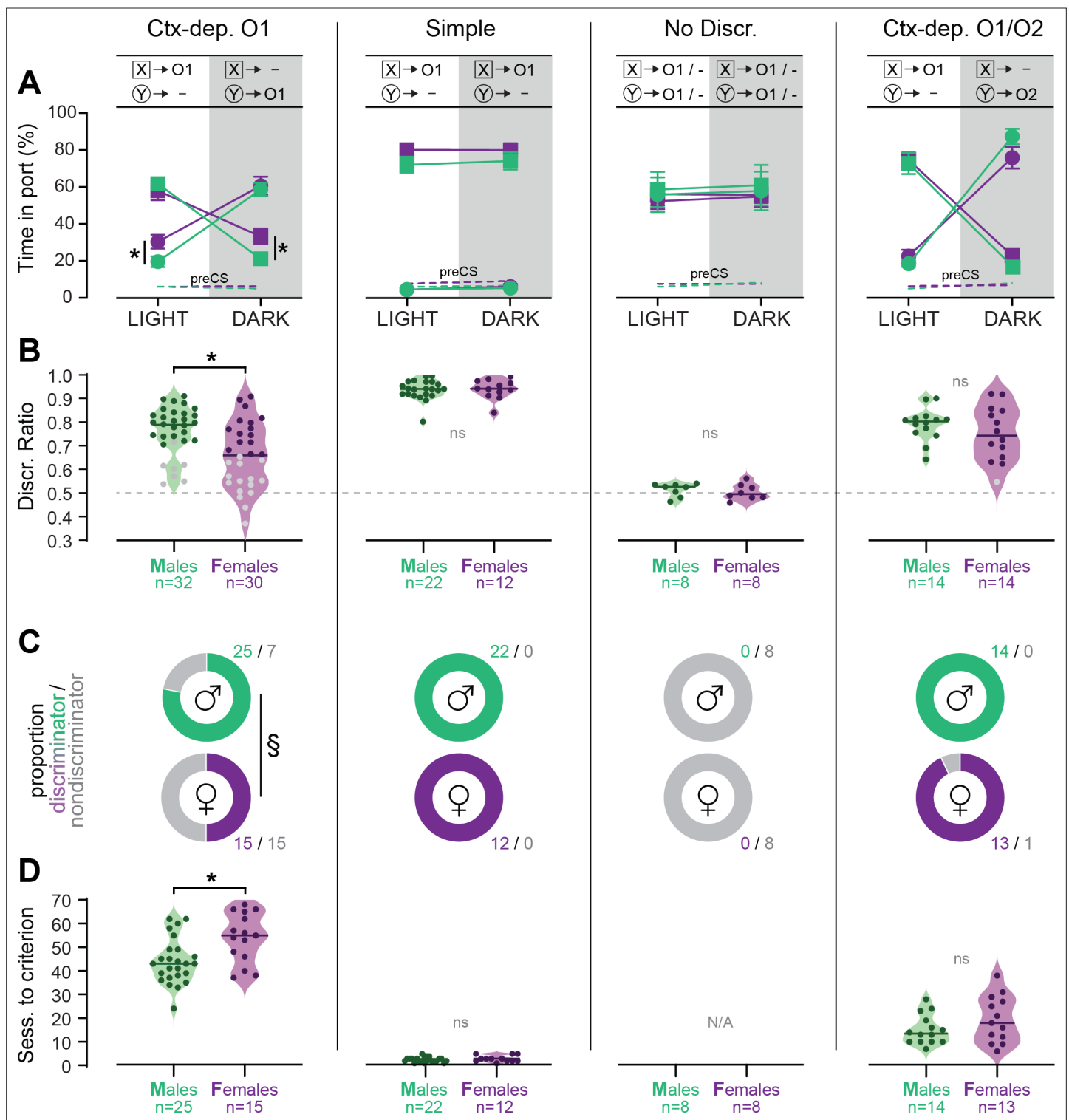


Figure 2. Individual differences in the acquisition of discriminated Pavlovian approach. **(A)** Time in port (% cue time) during the four different trial types (LIGHT: X/DARK: X/LIGHT: Y) at the end of the training period (last 3 days average) for male and female rats trained in each discrimination task. **(B)** Discrimination ratio at the end of the training period (last 3 days average) for male and female rats trained in each discrimination task. Dark symbol: discriminator; gray symbol: non-discriminator. Horizontal bar = group median; dashed horizontal line represents the indifference level (no discrimination). **(C)** Proportion of male and female rats classified as discriminator or non-discriminator in each task. **(D)** Speed of acquisition (sessions to criterion) for discriminator rats, in each task. Horizontal bar = group median. * $p < 0.05$ males vs. females, t -tests; § $p < 0.05$ chi-square test.

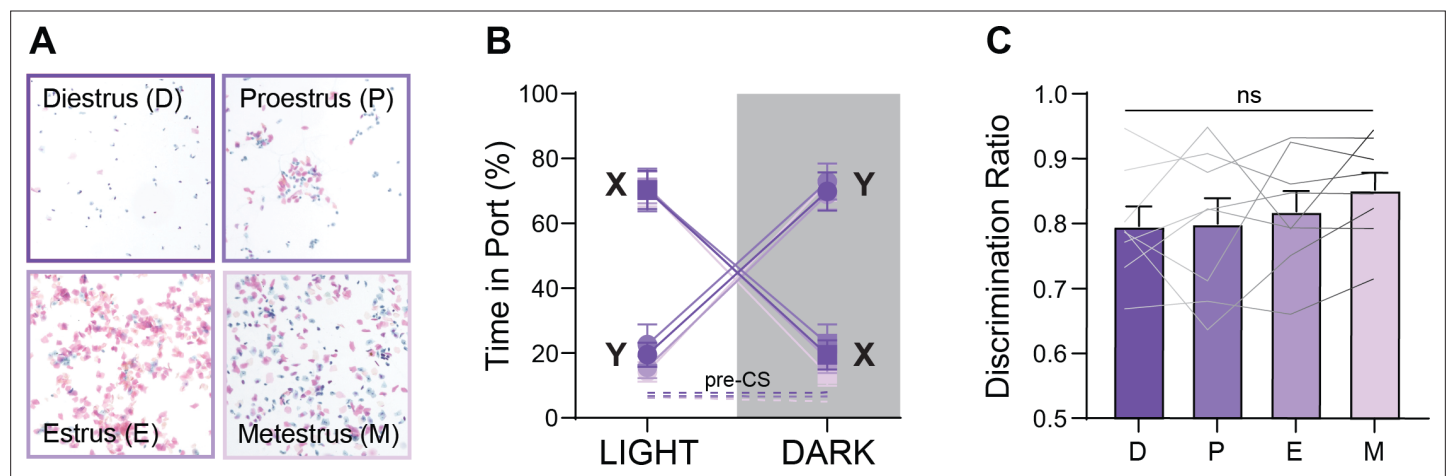


Figure 2—figure supplement 1. Estrus cycle does not influence the expression of context-gated reward seeking. **(A)** Vaginal cytology was used to track the stage of estrous cycle in a subset of female discriminators trained in the *Ctx-dep. O1* task ($n = 8$). **(B)** Time in port during the four trial types (LIGHT: X/DARK: X/LIGHT: Y/DARK: Y) was not influenced by the estrous cycle (Estrous Stage $F(3, 21) = 0.450$; $p = 0.720$; Estrous Stage \times Trial: $F(2.258, 15.808) = 1.293$; $p = 0.305$). **(C)** Discrimination ratio was not influenced by the estrous cycle ($F(3, 21) = 1.601$; $p = 0.219$). Error bars indicate \pm standard error of the mean (s.e.m.).

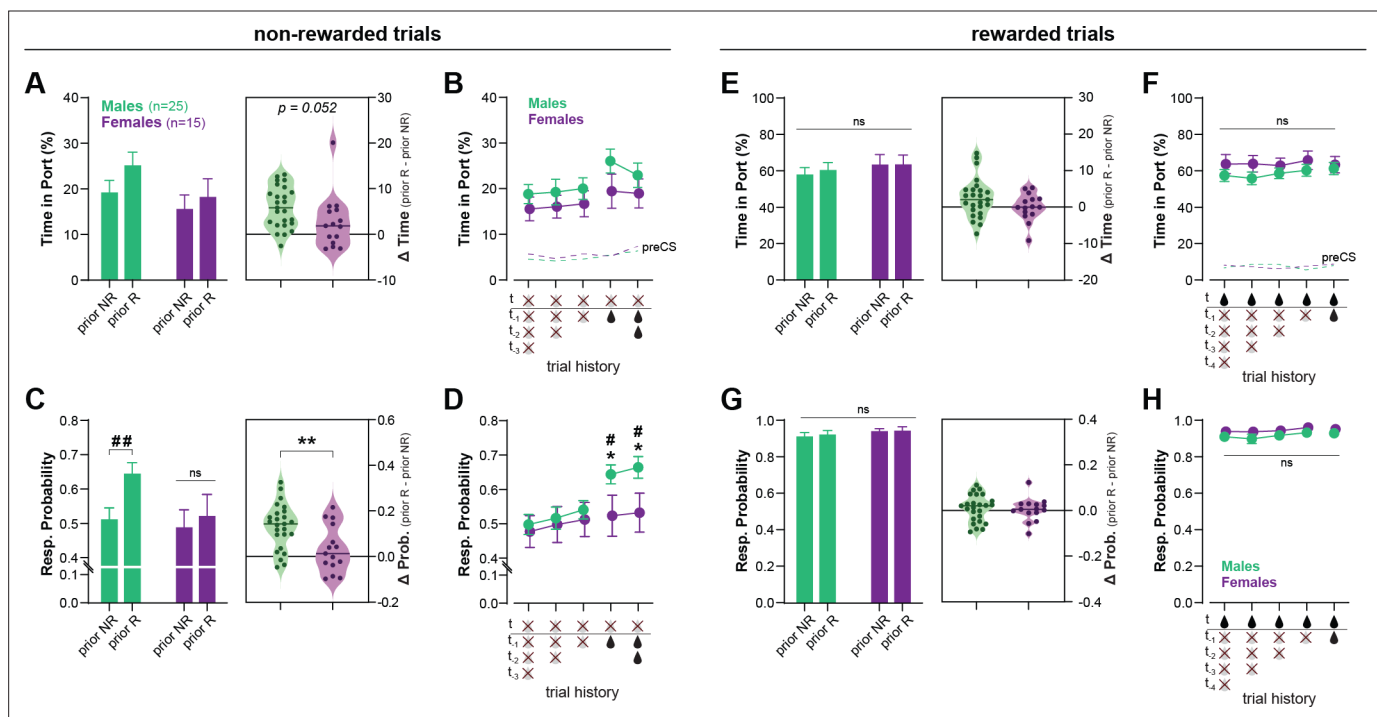


Figure 3. Recent rewards disrupt contextual control of reward seeking in male, but not female, rats. **(A)** Time in port (% cue time) during non-rewarded trials as a function of prior trial (rewarded: prior R, or non-rewarded: prior NR) for male and female rats trained in Ctx-dep. O1 task. Inset: increase in responding caused by prior reward for male and female rats (horizontal bar = median difference score). **(B)** Time in port during non-rewarded trials as a function of prior consecutive non-rewarded or rewarded trials. **(C)** Response probability on non-rewarded trials as a function of prior trial (rewarded: prior R, or non-rewarded: prior NR). Inset: increase in the probability of responding caused by prior reward for male and female rats (horizontal bar = median difference score). **(D)** Response probability on non-rewarded trials as a function of prior consecutive non-rewarded or rewarded trials. **(E)** Time in port (% cue time) during rewarded trials as a function of prior trial (rewarded: prior R, or non-rewarded: prior NR). Inset: difference in responding caused by prior reward for male and female rats. **(F)** Time in port during rewarded trials as a function of prior consecutive non-rewarded or rewarded trials. **(G)** Response probability on rewarded trials as a function of prior trial (rewarded: prior R, or non-rewarded: prior NR). Inset: difference in the probability of responding caused by prior reward for male and female rats. **(H)** Response probability on rewarded trials as a function of prior consecutive non-rewarded or rewarded trials. Error bars indicate \pm standard error of the mean (s.e.m.). * $p < 0.05$; ** $p < 0.01$ males vs. females; # $p < 0.05$; ## $p < 0.01$ prior R vs. prior N; t -tests.

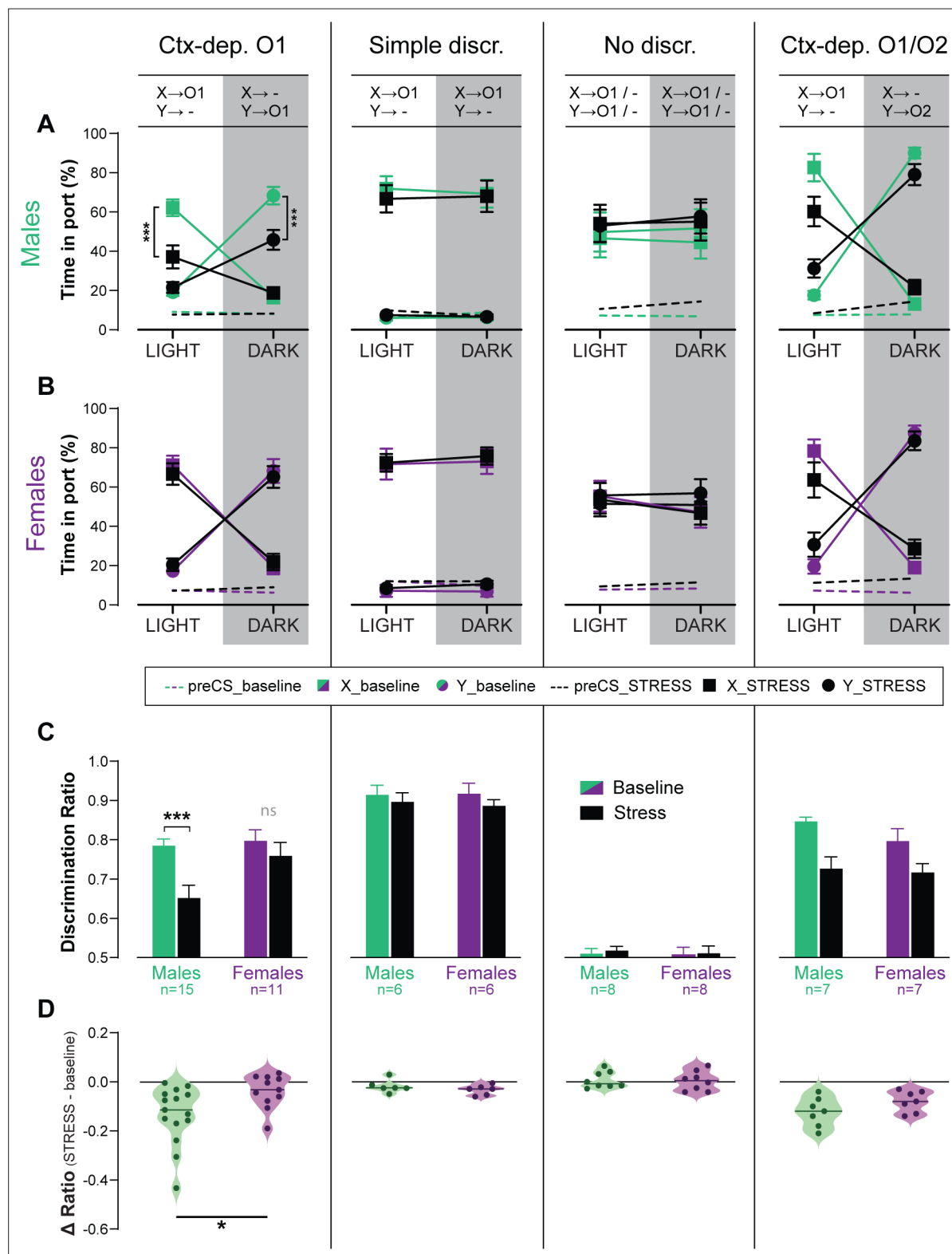


Figure 4. Acute stress disrupts context-gated reward seeking in male but not female rats. Time in port (% cue time) during the four different trial types (LIGHT: X/DARK: X/LIGHT: Y/DARK: Y) at baseline and after acute stress for male (A) and female (B) rats trained in each discrimination task. (C) Discrimination ratio at baseline and after acute stress, for male and female rats trained in each discrimination task. (D) Stress-induced disruption in discrimination performance (stress – baseline) for male and female rats trained in each discrimination task (horizontal bar = median difference score). Error bars indicate \pm standard error of the mean (s.e.m.). * $p < 0.05$; *** $p < 0.001$, t-tests.

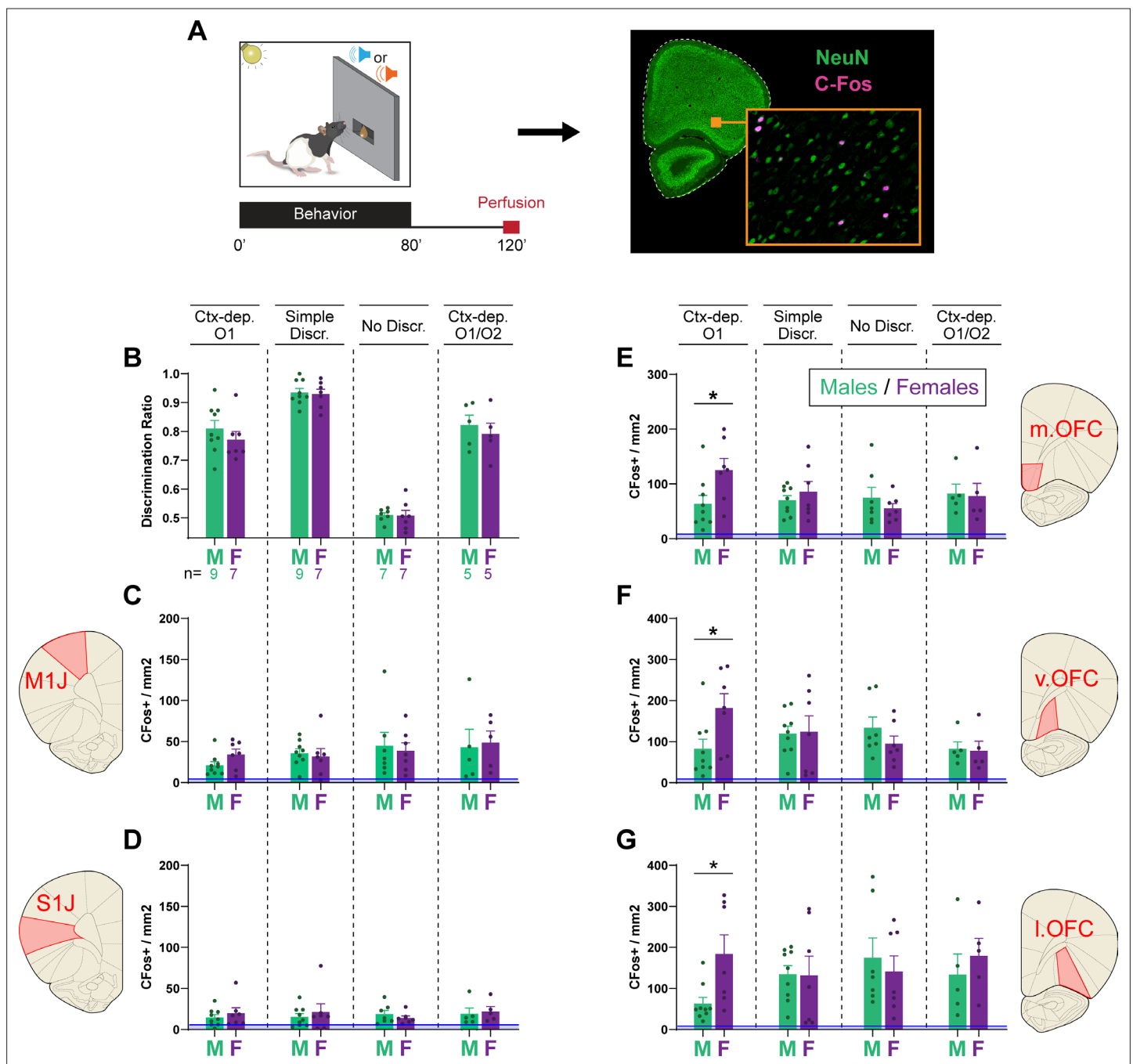


Figure 5. Female rats show higher orbitofrontal engagement during context-gated reward seeking. **(A)** Experimental design. Brains were collected 2 hr after the start of the behavioral session. Brain sections were stained for c-Fos (activity marker) and NeuN (general neuronal marker). **(B)** Discrimination ratios during the final behavioral session, before tissue collection for male and female rats trained in each task. c-Fos+ density in the primary jaw motor cortex **(C)**, primary jaw somatosensory cortex **(D)**, medial orbitofrontal cortex **(E)**, ventral orbitofrontal cortex **(F)**, and lateral orbitofrontal cortex **(G)** for males and females trained in each discrimination task. Error bars indicate \pm standard error of the mean (s.e.m.). Blue lines (close to floor level) indicate average c-fos+ densities for animals who remained in their homecage prior to tissue collection (homecage controls; $n = 5$). * $p < 0.05$ males vs. females, t -tests.