

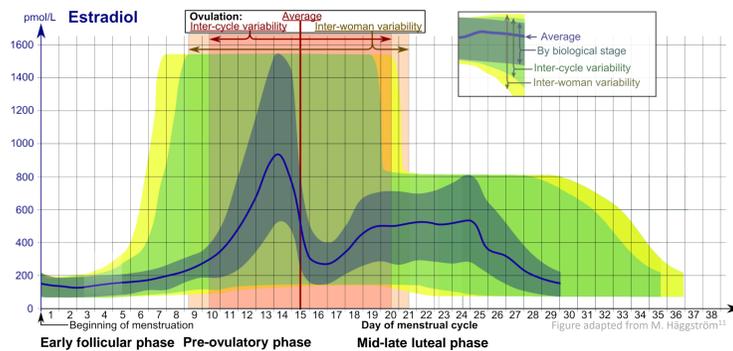
Learning exceptions to category rules varies across the menstrual cycle

Introduction

17 β -estradiol (E2) – the most bioactive estrogen – is strongly associated with hippocampal structure and function, yet its effects on cognition across the menstrual cycle remain understudied^{1,2,3,4}.

Category learning is a hippocampal-dependent core cognitive process likely affected by these E2-driven effects^{5,6,7}.

We hypothesized that E2-mediated changes to hippocampal function across the menstrual cycle would be reflected in cycle-dependent differences in category learning performance, ie. high E2 phase would be associated with better performance.



Methods

Menstrual cycle phases

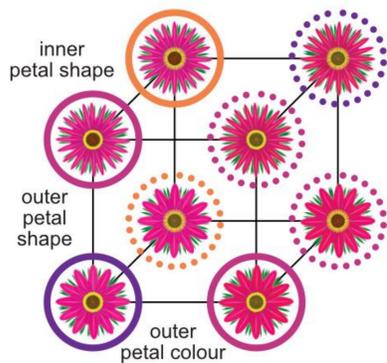
Early follicular (EF; low E2)

Late follicular/pre-ovulatory (PO; high E2)

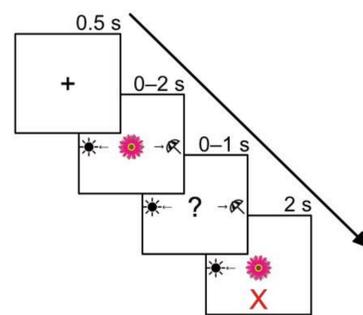
Mid-late luteal (ML; moderate E2)

Participants. N = 171 (Age: 29.59 \pm 5.05 years; Education: 15.89 \pm 3.41 years). There were 39 participants in the EF phase, 40 in the PO phase, 39 in the ML phase, and 53 male participants. Average menstrual cycle length was 27.87 \pm 5.03. Average days of cycle per group were: 4 \pm 3.58 for PO, 13.1 \pm 3.25 for LF/PO, and 21.5 \pm 3.42 for ML.

Task category structure



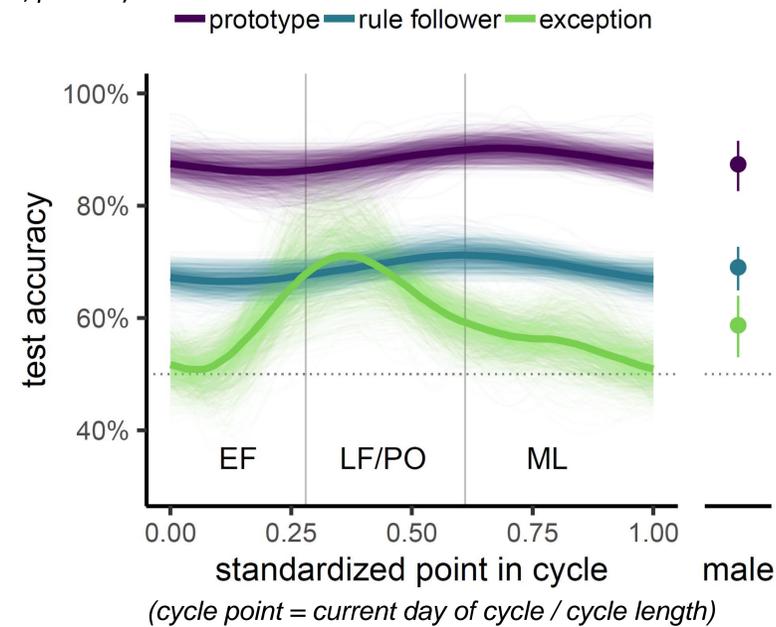
Trial structure



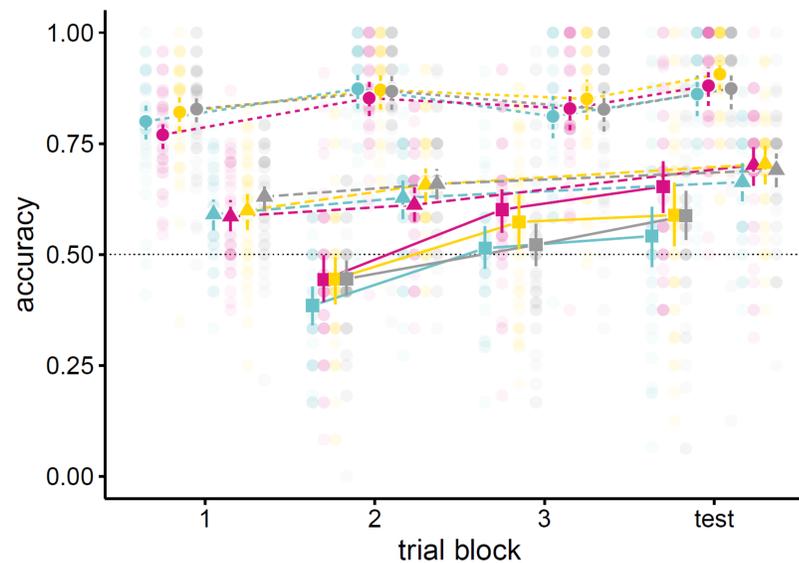
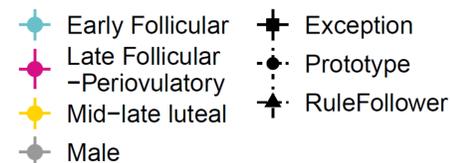
■ prototype ■ rule-follower ■ exception

Results

Test performance. Significant effect of cycle point ($EDF=1.31$, $F(8)=13.13$, $p=.048$) with a distinctly non-linear effect on categorization of exceptions ($EDF=2.93$, $F(8)=85.17$, $p<.001$).



Learning process. EF had lower accuracy for exceptions across learning blocks relative to LF/PO ($\beta=0.07$, $p=0.01$, 95%CI [0.02, 0.12]) and ML ($\beta=0.06$, $p=0.03$, 95%CI [0.01, 0.11]); Categorization accuracy of PO for exceptions improved more quickly than that of the male group ($\beta=-0.09$, $SE=0.04$, $t(164)=-2.19$, $p=0.03$)



Discussion

The menstrual cycle affects learning of exceptions in a distinct way that parallels the typical E2 cycle, and high-E2 participants learn exceptions faster than those in the male group.

This aligns with research showing that E2 supports learning in rodent models⁸ as well as hippocampal-dependent tasks in humans^{9,10}.

The observed effect is likely driven by E2's action on the hippocampal subfields implicated in pattern separation and completion.

Strengths of the current study involve sampling from all stages of the menstrual cycle and the use of non-linear methods to capture nuanced, continuous changes in categorization accuracy across the cycle.

Conclusions

The menstrual cycle affects learning of exceptions to category rules in a way that mirrors the typical estradiol cycle. Participants in the high estradiol phase outperform those in the low estradiol phase and learn exceptions faster than the male group. This suggests that estradiol affects category learning, likely through action on pattern separation and completion pathways in the hippocampus

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