BDNF genetic polymorphism interacts with menstrual cycle phase to predict rule-plus-exception category learning

Mateja Perović, Janice Hou, Shreeansha Bhattarai, Cathlin J. Han, Yao Chen & Michael Mack

Department of Psychology, University of Toronto

Introduction

Hippocampal structure, function, and cognition change across the menstrual cycle [1,2,3].

Category learning, a core cognitive process strongly associated with hippocampal function, has recently been shown to vary across the menstrual cycle [4].

A potential mechanism for menstrual cycle effects on cognition is through modulating effects of the ovarian hormone estradiol (E2) on brain-derived neurotrophic factor (BDNF) expression [5,6].

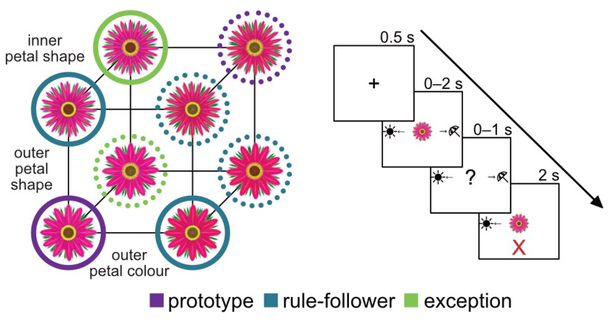
We use BDNF genetic polymorphism as an estimate of participants' baseline BDNF availability and study their performance in the low- and high-E2 phases of the menstrual cycle.

Methods

Participants (N=64; Age: 27.17± 4.77 years; Education: 17.41 ± 2.63 years) came in for two sessions – during the early follicular (EF; low E2; days 3.2 ± 1.2 of cycle) and late follicular (LF; high E2; days 12.0 ± 1.31 of cycle) phase. Phases and task versions were counter-balanced.

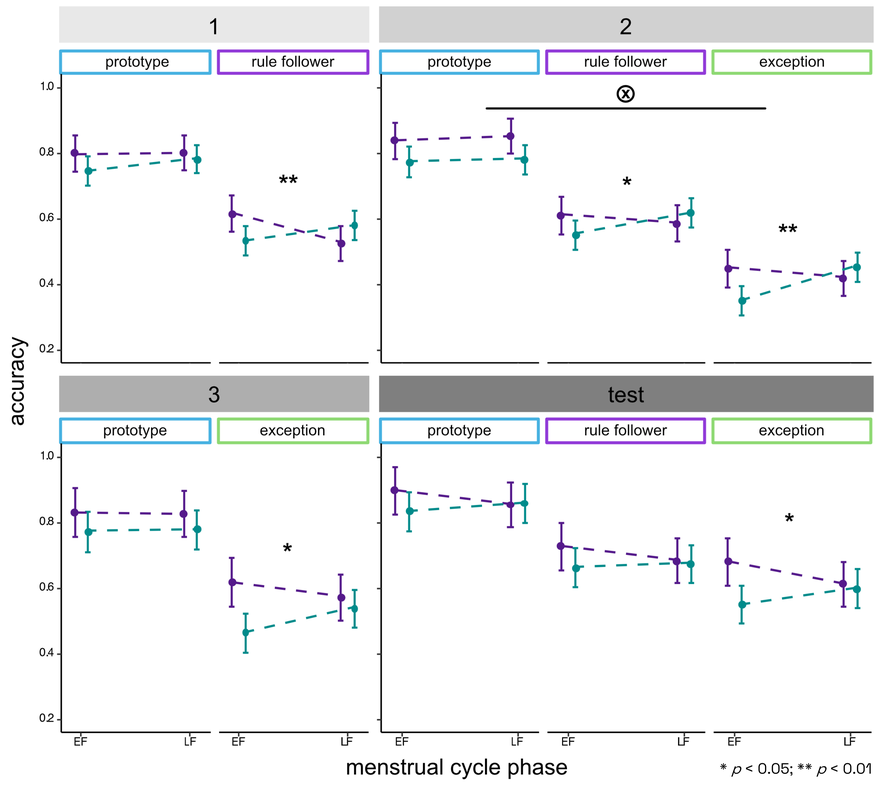
Salivary estradiol (E2) and progesterone (P4) were sampled using the passive drool method; saliva for genotyping was sampled using Genotek OG-500 kits.

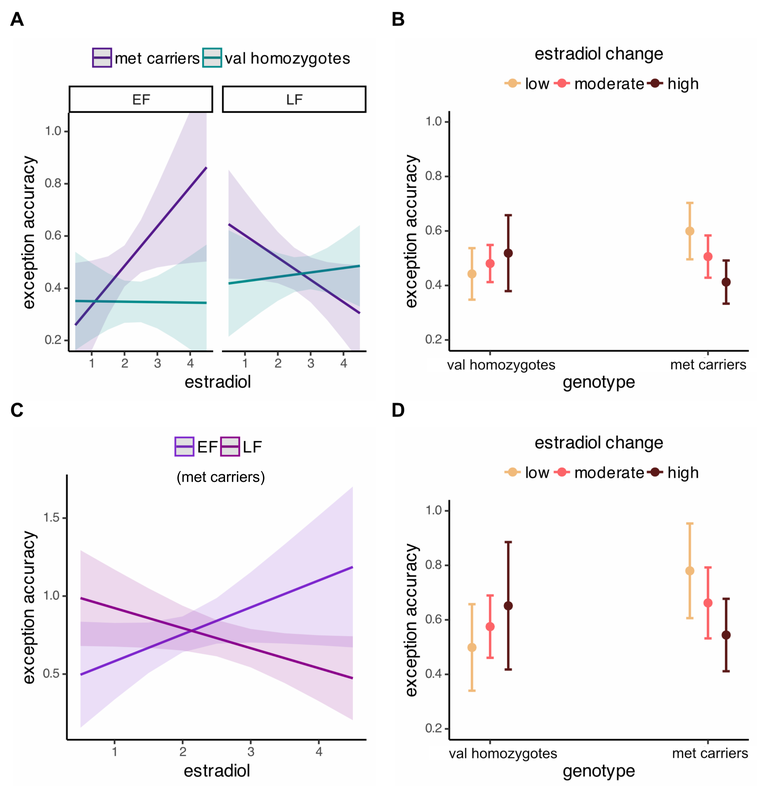
Task design (version 1)



Trial structure

Results





A and B = after exception introduction / block 2, C and D = in test block. All $p < 0.05$

Discussion

BDNF genotype interacts with menstrual cycle phase to predict categorization accuracy. While *met* carriers outperform *val* homozygotes in the early follicular phase, this effect either disappears of reverses by the late follicular phase.

Hormone-based analyses indicate that this is likely due to *met* carriers' increased sensitivity to E2. *Met* carriers benefit from E2 in the low-E2, EF, phase but this reverses in the high-E2, LF, phase. Increases in E2 between phases affect performance of *val* homozygotes positively, but performance of *met* carriers decreases with steeper increases of E2 between phases.

Our results align with research showing that episodic memory performance varies by BDNF genotype[7,8], research on exception categorization across the menstrual cycle[4], and rodent studies indicating genotype-dependent changes in cognition across the estrous cycle[9].

References

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