Neurophysiological Correlates of Affective State Across the Menstrual Cycle

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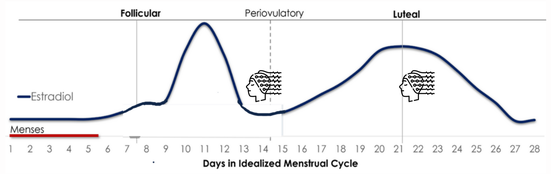
Introduction

- During the pubertal transition:
  - intense reproductive hormone fluctuations
  - refinement of frontal neural networks
- Starting at puberty, female adolescents are 3X more likely to develop depression compared to males. This disparity persists through adulthood, peaking during periods of rapid estrogen and progesterone flux
- Estrogen is a powerful neuroregulator
  - helps metabolize neurotransmitters: norepinephrine, dopamine, and serotonin [1]
  - synthesized in the brain, where there are densely packed receptors
  - regulates neuroplasticity, neural circuit activity, and the HPA Axis. [1]
- Estrogen flux, specifically withdrawal, is associated with depressive symptoms. [2]



Objective

Determine the relationship between depressive symptoms and electrophysiological markers of emotional processing, and whether this relationship is stronger during the premenstrual phase of the menstrual cycle.

Methods

Enrollment

- 22 female adolescents 11-14 years old
- within 1-year post-menarche
- no severe psychiatric or medical disorders

Menstrual Cycle

- 2 lab sessions per participant:
  - 1st follicular lab: estrogen peak at ovulation
  - 2nd luteal lab: estrogen withdrawal
- weekly self-report Mood measures

Electroencephalography Data

Participants completed implicit viewing tasks, where they were shown happy, fearful, and calm facial expressions and asked to attend to a facial feature other than emotional display. Beta oscillations were collected at the parietal lobe (Pz) electrode to measure event-related desynchronization (ERD).

Self-Report Affective State Measures

Positive and Negative Affect Schedule: scored 1-5, Higher Negative Affect (NA) subscore indicates more emotional distress, and feelings of fear, sadness, anger, and guilt. Higher Positive Affect (PA) subscore indicates increased frequency of positive mood.

Brief Irritability Test: scored 1-5, with higher scores indicating increased irritability.

Inventory of Depressive and Anxious Symptoms: scored 1-5 with a minimum of 45 and a maximum of 80. Higher scores indicate severe depression and anxiety symptoms

Results

Estrogen withdrawal is associated with limbic hyperreactivity, causing heightened threat reactivity. This further predicts depressive symptoms.

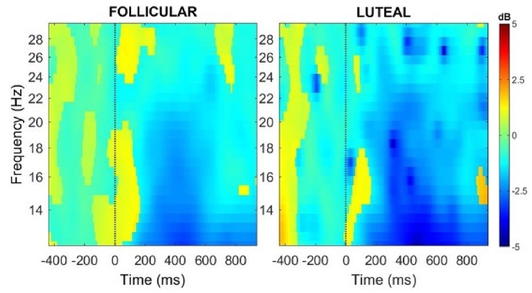


Figure 1. Time-frequency spectrograms depict average parietal beta (12-30 Hz) ERSP (event-related spectral perturbation, dB) for fearful stimuli during the follicular and luteal phase.

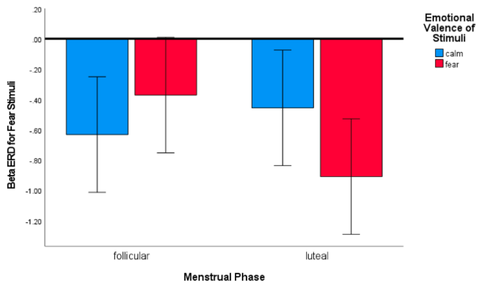


Figure 2. A Univariate General Linear model for ERSP values comparing valence of emotional stimuli across the menstrual phase. 95% CI.

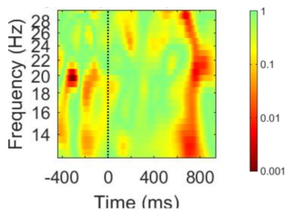


Figure 3. Topographical plot depicting time ranges and beta frequency ranges with the greater significance (p-values).

Figure 4. Facial stimuli in Implicit Viewing Task, depicting calm, fearful, and happy expressions.

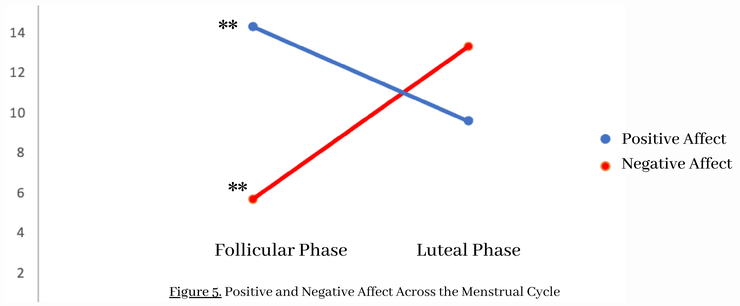


Figure 5. Positive and Negative Affect Across the Menstrual Cycle

	Follicular Phase: Mean (SD)	Luteal Phase: Mean (SD)
Brief Irritability Test	2.0 (0.5)*	1.7 (0.5)*
Inventory of Depression and Anxiety Symptoms	59.7 (11.54)	

*statistically significant; p<0.05. **; p<0.005

Paired-samples t-tests were conducted to compare positive affect, negative affect, and irritability in the follicular and luteal phase.

These questionnaires were administered at the beginning of both EEG lab sessions to assess participant's affect over the past week.

Discussion

- The premenstrual phase predicted increased event-related desynchronization (ERD) towards fearful stimuli and decreased ERD towards calm stimuli. This is indicative of limbic, particularly, amygdala hyperreactivity to fearful stimuli that occurs during estrogen withdrawal, causing heightened threat reactivity.
- Cognitive dysregulation of threat reactivity also coincides with greater negative affect and lower positive affect during the premenstrual phase.
- Estrogen may influence the refinement of frontal-limbic connectivity and associated emotional processing during the pubertal transition, a period of reproductive endocrine instability.

Acknowledgements

1. Schiller, C. E., Johnson, S. L., Abate, A. C., Schmidt, P. J., & Rubinow, D. R. (2016). Reproductive Steroid Regulation of Mood and Behavior. In R. Terjung (Ed.), Comprehensive Physiology (1st ed., pp. 1135–1160). Wiley. https://doi.org/10.1002/cphy.c150014
2. Bloch, M. (2000). Effects of Gonadal Steroids in Women With a History of Postpartum Depression. American Journal of Psychiatry, 157(6), 924–930. https://doi.org/10.1176/appi.ajp.157.6.924