Does Experimental Pain Sensitivity Vary Across the Menstrual Cycle?

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Introduction
Prior research indicates pain sensitivity varies across the menstrual cycle, with the luteal phase generally associated with enhanced pain and nocice-reactivity. Although the mechanisms underlying the relationship between menstrual phase and pain have yet to be established, cyclical variation in sex hormones may account for changes in pain modulation. However, prior research in this area has suffered from methodological limitations such as small sample size, lack of verification of cycle phase, and inadequate assessment of menstrual cycle regularity. Because of these limitations, ascertaining the relationship between the menstrual cycle and pain processing is challenging. The current study was designed to address some of these limitations by (i) assessing pain outcomes from multiple stimulus modalities, (ii) recruiting a relatively large sample size, (iii) verifying menstrual phase timing by utilizing hormone tests and daily menstrual calendars, (iv) having women monitor their menstrual phases over three menstrual cycles to verify cycle regularity, and (v) using powerful mixed model statistical analyses.

Objective
To determine if menstrual cycle phase-related changes exist in experimental pain sensitivity including electrocutaneous pain threshold/tolerance, physiological pain responses (i.e., NFR), ischemic pain threshold/tolerance, subjective sensory and affective pain, and pressure-pain responses.

Participants
Healthy Female Participants: N = 41
- Participant Characteristics: White, non-Hispanic (71%); married (73%); employed full-time (58%); yrs of education: 13 (SD = 1.72); age: 21 (SD = 3.28); average length of luteal phase = 15 days (SD = 3.48)
- Exclusion Criteria:
  - <10 years of age
  - Failure to regularly cycle within 2 months of study inclusion
  - Use of hormone preparations within past 3 months
  - Menopause or past-menopause
  - Current acute illness
  - Carcinogenic, neurological, circulatory and/or hearing problems
  - Chronic pain condition (i.e., back pain)
  - Recent use of anesthetic medication
  - Recent use of antidepressant or anti-anxiety medication
  - Recent psychological illness

Experimental Procedure
- Pain Sensitivity: Electrocutaneous
  - NFR is a spinal reflex-mediated protective withdrawal reflex elicited by Aβ fiber stimulation of the femoral nerve.
  - NFR threshold correlates highly with pain threshold.
- Pain Threshold: Ascending series of 2 mA electrical stimulation pulses until the participant indicated it as being painful (pain threshold).

- Pain Sensitivity: Ischemic
  - Procedure: 1 min. of hand exercises at 50% maximum grip strength, 15 sec. of arm elevation for exsanguination, blood pressure cuff inflated to 220 mg/Hg, 20 sec. of ischemia for 6 sites assessed—2 at each location (occiput, lateral epicondyle, fatty knee)
  - NFR Threshold: 1st rating of ischemic pain as ≥50 on numerical rating scale
  - Ischemic Pain Tolerance: 1st rating of ischemic pain as ≥100 on numerical rating scale

- Pain Sensitivity: Mechanical Pressure-Pain
  - Mechanical Pressure: Ascending series continued with Fisher’s LSD tests

- Data Analysis
  - Mixed procedure in SPSS 14.02 used
  - Menstrual Phase was entered as a nominal variable
  - Follow-up mean comparisons to significant F-tests were conducted with Fisher’s LSD tests

- Results: Electrocutaneous Subjective Responses
  - Electrocutaneous Threshold: The main effect of Menstrual Phase (F(1, 36) = 4.33, p = .04) was significant for Electrocutaneous Threshold.
  - Electrocutaneous Tolerance: The main effect of Menstrual Phase (F(1, 36) = 4.23, p = .04) was significant for Electrocutaneous Tolerance.
  - NFR Threshold: The main effect of Menstrual Phase (F(1, 31) < .05, p < .37) was not significant for NFR Threshold.

- Results: Ischemic Pain Responses
  - Ischemic Threshold: The main effect of Menstrual Phase (F(1, 36) = .88, p = .36) was not significant for Ischemic Threshold.
  - Ischemic Tolerance: The main effect of Menstrual Phase (F(1, 31) = 11.0, p = .00) was significant for Ischemic Tolerance.

- Results: Mechanical Pressure–Pain
  - Mechanical Pressure: The main effect of Menstrual Phase (F(1, 31) = 21.0, p = .05) was significant for Mechanical Pressure.

Conclusions
- Results indicated there were no phase-dependent changes in NFR threshold, electrocutaneous pain tolerance, ischemic pain threshold/tolerance, mechanical pressure-pain threshold, and MPQ ratings.
- Electrocutaneous pain threshold was the only pain sensitivity measure shown to vary across the menstrual cycle, with lower thresholds found during the late-luteal phase, relative to the mid-follicular phase.
- This suggests the menstrual cycle may exert little influence on pain sensitivity in healthy women.
- Given that women experience more pain-related symptomatology during the late-luteal phase of their menstrual cycle, and have more chronic pain conditions than men (i.e., fibromyalgia, migraine headache), this research is important in further elucidating the pain/hormone relationship and its impact on pain sensitivity in women.