Supraspinal Modulation of Pain and Spinal Nociception Across the Menstrual Cycle

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Introduction
Pain varies across the menstrual cycle, with hyposensitivity generally noted during the follicular phase. Although this phenomenon underpins the relationship between menstrual phase and pain, it has yet to be established. Cyclical variation in sex hormones may account for changes in supraspinal pain modulation. One method to study supraspinal pain modulation is the emotional control of nociception (ECON) paradigm, which uses a standardized set of affectively-charged pictures to evoke emotional reactions, during which nociceptive, electrocutaneous stimuli are delivered. Our laboratory has demonstrated effective picture modulations of pain and nociceptive responses (e.g., NFR), with negative emotions enhancing pain and NFR and positive emotions inhibiting pain and NFR. Another paradigm for studying supraspinal pain modulation is diffuse nociceous inhibitory controls (DNIC), which involves the application of a noxious stimulus to inhibit pain at a distal body site. Therefore, to evaluate menstrual phase-related changes in supraspinal pain modulation, healthy female participants attended testing sessions scheduled during their follicular and luteal phases (with testing order randomized) and ECON and DNIC procedures were assessed at both sessions.

Objective
• To determine if menstrual cycle phase-related changes exist in affective regulation of pain and nociception (e.g., NFR), DNIC modulation, as well as subadditive reactions to emotionally-charged picture stimuli.

Participants
Healthy Female Participants: N = 41
• Participant Characteristics: White, non-Hispanic (71%), married (73%); employed full-time (56%); yrs of education = 15; SD = 1.75; yrs of age = 31 yrs (SD = 8.68); average menstrual cycle length = 29 days (SD = 2.38); average length of luteal phase = 15 days (SD = 2.46).
• Exclusion Criteria: <13 years of age; Failure to regularly cycle within 2 months of study inclusion; Use of hormonal prescriptions within past 6 months; Pregnant within past 6 months; Menopause or premenopause; Current acute illness; Cardiovascular, neurological, circulatory, and/or hearing problems; Chronic pain condition (e.g., back pain); Persons of any age exposed to psychiatric hospitalization; Current use of any antidepressant medications and/or antipsychotic medication; Recent psychological trauma.

Methodology
• Nociceptive Flexion Reflex (NFR) and Pain Ratings
• Picture-Viewing: Emotion Induction
• Data Analysis
• ECON Results: NFR and Subjective Pain
• DNAIC Results: NFR and Subjective Pain

Conclusions
• Results suggested there were no menstrual cycle phase-related changes in subjective reactions to emotionally-charged picture stimuli.
• Results also indicated there were no phase-related changes in affective regulation or DNIC modulation of the NFR.
• However, cyclical changes in subjective pain were observed in emotional modulation of pain, as well as DNIC, with lower pain ratings occurring during the luteal phase of the menstrual cycle. Therefore, menstrual cycle-related changes in the modulation of pain should be considered when designing studies involving menstrual cycle-related variables.

Future Studies
• Future studies should directly assess the relationship between cyclical hormone levels and supraspinal modulation of pain.

Picture-Viewing: Emotion Induction
The International Affective Picture System (IAPS; Center for the Study of Emotion and Attention, 2006).

Data Analysis
A mixed model ANOVA was applied to study menstrual phase-related changes in pain and nociceptive responses. The main effect of Menstrual Phase was not significant for NFR Magnitude (F[1, 83] = 6.70, p = .01). However, cyclical changes in subjective pain were observed in emotional modulation of pain, as well as DNIC, with lower pain ratings occurring during the luteal phase of the menstrual cycle. Therefore, menstrual cycle-related changes in the modulation of pain should be considered when designing studies involving menstrual cycle-related variables.