The Effect of the Menstrual Cycle on Pain Regulation

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Introduction

Research suggests pain perception varies by menstrual cycle phase, with pain being enhanced during the luteal phase relative to follicular. While the mechanisms contributing to this effect are poorly understood, one potential mechanism is phase-related changes in pain regulation. For example, a failure to inhibit pain, or overactive pain facilitatory mechanisms, could contribute to greater pain during the luteal phase. Our laboratory has developed reliable procedures to study one method of pain regulation - emotional regulation of pain. Standardized emotionally-charged pictures are presented to evoke emotional reactions, during which noxious electrocutaneous stimuli are delivered to evoke pain reactions. Using these methods, we have shown that negative emotions enhance pain and physiological pain processes, whereas positive emotions inhibit pain and physiological pain processes. To assess menstrual cycle-related changes in emotional modulation of pain, 15 regularly-cycling, female participants attended two laboratory sessions during the follicular and luteal phases of their menstrual cycle. Given research suggesting sex differences exist in modulation of pain, this study may have important implications in how chronic pain is developed and maintained in women.

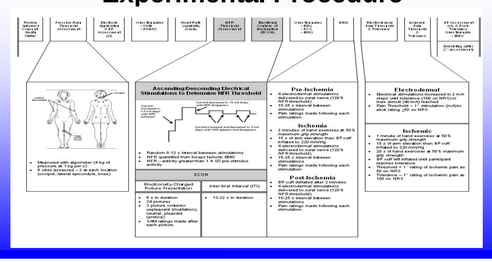
Objective

- To determine if menstrual cycle phase-related changes exist in emotional modulation of pain and physiological pain responses (i.e., NFR, SCR, HR), as well as emotional reactions to affective stimuli

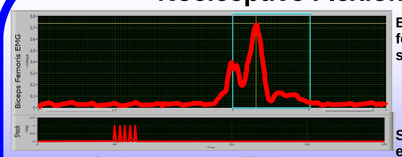
Participants

- **15 Healthy Female Participants**
  - Participant Characteristics: White, non-Hispanic (86.7%), single (53.3%), employed full-time (53.3%), average age = 31.6 yrs (*SD* = 10.10)
- **Exclusion Criteria:**
  - <18 years of age
  - Failure to regularly cycle within 2 months of study inclusion
  - Use of hormone preparations within past 6 months
  - Pregnant within past 6 months
  - Menopausal or post-menopausal
  - Current acute illness
  - Cardiovascular, neurological, circulatory and/or hearing problems
  - Chronic pain condition (e.g., back pain)
  - Recent use of analgesic medication
  - Current use of anxiolytic and/or antihypertensive medication
  - Recent psychological trauma

Experimental Procedure

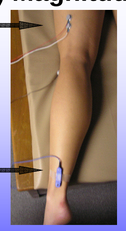


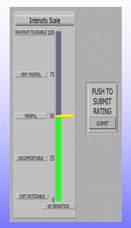
Nociceptive Flexion Reflex (NFR) Magnitude



Biceps femoris EMG sensors

Stimulating electrode over sural nerve





- NFR is a spinally-mediated protective withdrawal reflex elicited by Aδ fiber activation, and NFR magnitude correlates with pain ratings
- **NFR magnitude** = mean of biceps femoris EMG in 90-150 ms post-stimulus interval minus mean of 60 ms pre-stimulus interval, divided by the pooled standard deviation (Cohen's *d* value)
- **Pain Ratings made following each stimulation**

Picture-Viewing: Emotion Induction

The International Affective Picture System
(IAPS; Center for the Study of Emotion and Attention, 2006)

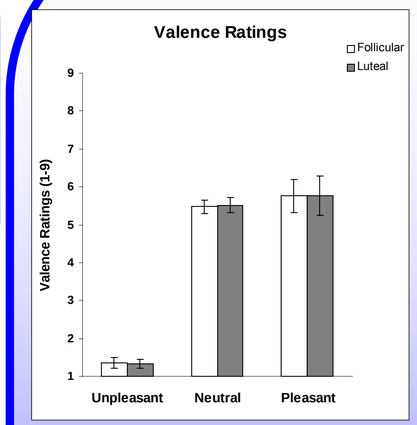
Unpleasant (Mutilation)

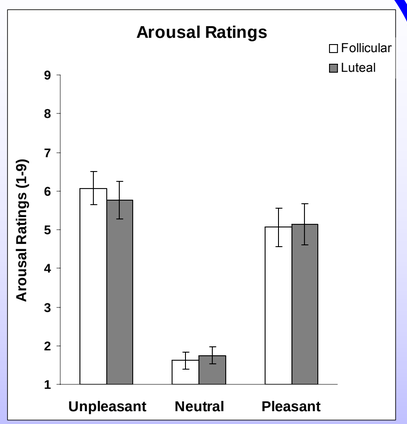
Neutral

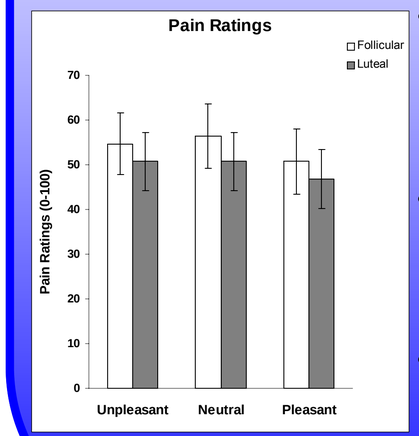
Pleasant (Erotic)

- **24 pictures presented in pseudorandom order**
  - 8 pictures per valence (unpleasant, neutral, pleasant)
  - Pictures presented for 6 s, 11-21 s inter-picture interval
  - Subjective emotional reactions (valence and arousal) assessed on Self-Assessment Manikin following presentation of each picture

Results: Subjective Ratings

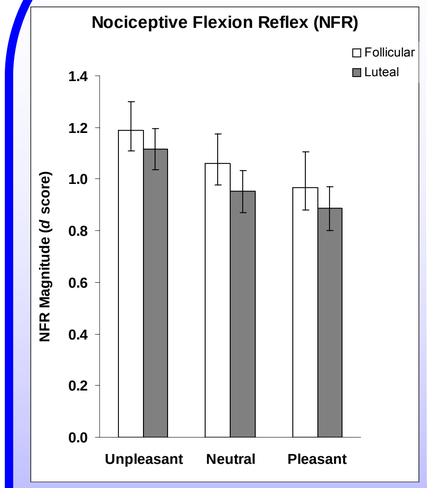


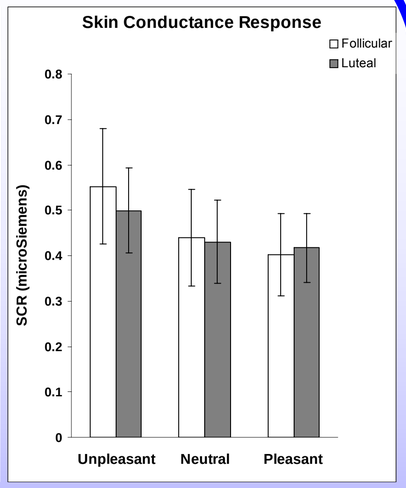


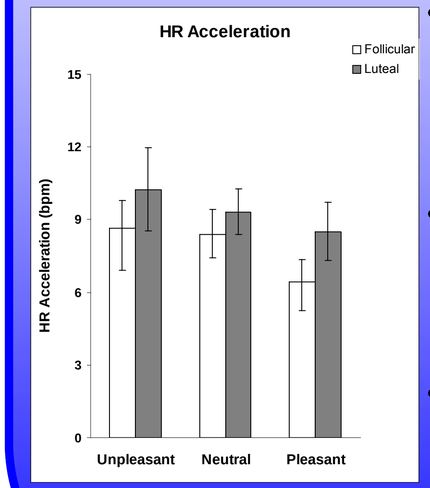


- **Valence Ratings:** The main effect of Picture Content ($F[2, 28] = 74.71$, $p < .001$, $\eta^2 = .84$, $\varepsilon = .01$) was significant for valence ratings; however, the Picture Content x Group interaction was not significant ($F[2, 28] = .04$, $p = .96$, $\eta^2 = .003$, $\varepsilon = .001$)
  - Planned simple effects tests did not indicate differences between groups in valence ratings
- **Arousal Ratings:** The main effect of Picture Content ($F[2, 28] = 47.62$, $p < .001$, $\eta^2 = .77$) was significant for arousal ratings; however, the Picture Content x Group interaction was not significant ($F[2, 28] = 1.16$, $p = .33$, $\eta^2 = .08$)
  - Planned simple effects tests did not indicate differences between groups in arousal ratings
- **Pain Ratings:** The main effect of Picture Content ($F[2, 28] = 4.61$, $p < .05$, $\eta^2 = .25$) was significant for pain ratings; however, the Picture Content x Group interaction was not significant ($F[2, 28] = .29$, $p = .75$, $\eta^2 = .02$)
  - Planned simple effects tests did not Indicate differences between groups in pain ratings

Results: Physiological Pain Responses







- **NFR:** The main effect of Picture Content ($F[2, 28] = 18.10$, $p < .001$, $\eta^2 = .56$, $\varepsilon = .69$) was significant for NFR magnitude; however, the Picture Content x Group interaction was not significant ($F[2, 28] = .09$, $p = .92$, $\eta^2 = .18$)
  - Planned simple effects tests did not indicate differences between groups in NFR magnitude
- **SCR:** The main effect of Picture Content ($F[2, 28] = 6.50$, $p < .01$, $\eta^2 = .32$) was significant for SCR; however, the Picture Content x Group interaction was not significant ($F[2, 28] = .71$, $p = .50$, $\eta^2 = .05$)
  - Planned simple effects tests did not indicate differences between groups in SCR
- **HR Acceleration:** The main effect of Picture Content ($F[2, 28] = 2.17$, $p = .13$, $\eta^2 = .13$), and the Picture Content x Group interaction, ($F[2, 28] = .26$, $p = .77$, $\eta^2 = .02$) were not significant for HR acceleration
  - Planned simple effects tests did not indicate differences between groups in HR acceleration

Conclusions

- Results suggest there were no menstrual phase-dependent changes in emotional reactions to the pictures
- Results also indicated there were no phase-dependent changes in emotional regulation of pain and physiological pain responses
- This suggests supraspinal modulation does not vary with the menstrual cycle to modify central nervous system nociceptive processing