Conditioned pain modulation of pain and the nociceptive flexion reflex across the menstrual cycle in women with and without premenstrual dysphoric disorder

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Introduction

Premenstrual dysoric disorder (PMDD) is characterized by severe affective and pain-related symptoms during the late-luteal phase of the menstrual cycle. Furthermore, women with PMDD appear to have a disruption of pain processing, in that they evidence hyperalgesia in response to painful stimuli. At this time, it is unclear whether this hyperalgesia is due to a deficiency in descending inhibitory mechanisms and whether these mechanisms are influenced by menstrual phase.

Objective

To examine conditioned pain modulation (CPM; i.e., pain inhibiting pain) of experimentally-induced pain and the nociceptive flexion reflex (NFR, a physiological correlate of spinal nociception) in healthy controls and women with PMDD across phases of the menstrual cycle.

Participants

Healthy controls (n=20); PMDD (n=20)

• PMDD was diagnosed prospectively via daily diaries completed over 3 months
• Average cycle lengths were not significantly different (p=0.71)
• PMDD=29.75; Healthy controls=30.34

Participants did not differ significantly in age, race, sexual orientation, years of education, employment, or marital status.

• Exclusion Criteria:
  - <15 yrs of age
  - Failure to regular cycle within 2 months of study inclusion
  - Use of hormone preparations within past 6 months
  - Menopause or post-menopause
  - Cardiovascular, neurological, or respiratory problems
  - Chronic pain condition (e.g., back pain)
  - Recent use of analgesic medication
  - History of anxiolytic, antidepressant, and/or antihypertensive medication

Procedure

• Tested during three phases: mid-follicular, ovulatory, and late-luteal
• Menstrual phase and ovulation were verified via daily symptom diaries and salivary hormone tests
• Testing order was counterbalanced
• During each testing session:
  - Informed consent obtained. Sensors and stimulating electrode applied
  - NFR threshold and pain threshold assessed by sending electrical stimulations to the left ankle over the sural nerve
  - CPN of pain and NFR administered

Methods: CPM Procedure

Pre-Ischemia (Baseline)
• 4 electrotactile stimulations delivered to sural nerve (120% pain or NFR threshold): 15-25 s interval between stimulations
• Pain ratings and NFR recorded after each stimulation

Ischemia
• 2 minutes of hand exercises (50% maximum grip strength) followed by 15 s of arm elevation then blood pressure cuff inflated to 220 mm/Hg
• 4 electrotactile stimulations delivered to sural nerve (120% pain or NFR threshold): 15-25 s interval between stimulations
• Pain ratings and NFR recorded after each stimulation

Post-Ischemia
• Blood pressure cuff deflated after 2 minutes
• 4 electrotactile stimulations delivered to sural nerve (120% pain or NFR threshold): 15-25 s interval between stimulations
• Pain ratings and NFR recorded after each stimulation

Results: CPM of pain

Main effect of menstrual phase (p<.01), with highest pain ratings during mid-follicular phase and lowest pain ratings during late-luteal phase

Main effect of CPM phase (p<.01), with highest pain ratings during baseline and lowest pain ratings during post-ischemia

Interaction effect for CPM phase by diagnosis (p<.05), such that PMDD=29.75; Healthy controls=30.34

Conclusions

• No differences were observed between PMDD and Healthy Controls in ischemia task ratings or overall pain ratings. Thus, we did not find evidence of hyperalgesia in women with PMDD.

• We did not find evidence that women with PMDD have impaired conditioned modulation of pain for pain or NFR.

• Additionally, conditioned pain modulation of pain and NFR did not differ across phases of the menstrual cycle.

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