Assessing hyperexcitability of spinal nociceptive processes in humans: Refining methods for temporal summation of the nociceptive flexion reflex

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Introduction

Temporal summation of pain occurs when a series of noxious stimuli with a short stimulation frequency (2.0 Hz to 0.33 Hz) is administered and the last stimulus elicits greater pain than the first. Based on observations from animal studies, this phenomenon is believed to be mediated by hyperexcitability of spinal neurons (i.e., wind-up). Thus, temporal summation paradigms are often used to make inferences about hyperexcitability of spinal nociceptive processes even though pain ratings (a supraspinal response) are generally measured as the outcome. This inference may be problematic, though, given that pain ratings are influenced by factors that do not affect spinal nociceptive processes (e.g., pain catastrophizing). To overcome this problem, some researchers have assessed the nociceptive flexion reflex (NFR), a spinal-mediated withdrawal reflex assessed from electromyogram (EMG) that is used as a physiological correlate of spinal nociception. Yet, there have been relatively few attempts to determine the optimal methods to evoke temporal summation of NFR.

Objective

The present study varied the stimulation frequency (2.0 Hz, 1.0 Hz, 0.5 Hz, 0.33 Hz, and variable), and determine: 1) the stimulation frequency that causes the least EMG contamination (i.e., increased muscle tension in baseline EMG on later stimulations) and 2) the stimulation frequency that elicits the most reliable temporal summation of NFR.

Methods: Temporal Summation of Pain

Participants

- **50 Healthy Individuals**
  - Characteristics: Female (62%, N = 31), White non-Hispanic (94%, N = 47), employed fewer than 40 hours a week (N = 27), average years of education (14 years, SD = 1.4) and average age (21 years, SD = 2.8).

- **Exclusion Criteria:**
  - <18 yrs of age
  - Neurological, cardiovascular, or circulatory problems
  - Chronic pain condition (e.g., back pain)
  - Recent use of anesthetics
  - Use of antidepressants, anxiolytic, or high blood pressure medications
  - Body mass index = 35

Procedure

- **Overview, informed consent, & eligibility determination (health status screening)**
- **Electrode application**
- **Determine stimulus intensity using higher stimulation of either nociceptive flexion reflex (NFR) threshold or pain threshold**
- **Temporal Summation Testing**

Methods: Temporal Summation Testing

- **Stimuli were delivered in 5 Blocks, with short rests between Blocks**
- **Each Block contained 5 series of 5 electric stimulations that differed in the number of series (2.0 Hz, 1.0 Hz, 0.5 Hz, 0.33 Hz, and variable).**
- **Stimulus frequency randomized within Blocks.**

Methods: Temporal Summation of Pain

Results: Baseline Biceps Femoris Electromyogram (EMG)

- **Baseline biceps femoris EMG activity increased regardless of the stimulus frequency, especially for 2.0 Hz.**
- **Thus, EMG prior to stimulus 1 was used to adjust NFR magnitudes.**

Preliminary Data Screening/Scoring

- **Data was scored off-line to visually inspect that NFRs were reliably elicited during temporal summation testing.**
- **NFRs were not reliably elicited in 19 participants (average NFRs elicited was 18%).**
- **Data from these individuals could not be analyzed.**
- **NFR threshold and pain threshold were significantly lower for non-responders than responders (p < .001).**
- **Stimulus intensity used during temporal summation was significantly lower for non-responders (M = 9.52 mA, SD = 4.77) than responders (M = 20.99 mA, SD = 8.43).**
- **There were no other group differences in background or demographic variables (sex, ethnicity, age, and years of education), p > .05.**

Data Analysis

- **Data was analyzed using within-subjects repeated measures ANOVAs**
  - **IV1: Stimulus Number in a series (1-5)**
  - **IV2: Stimulus Frequency (0.33 Hz, 0.5 Hz, 1.0 Hz, 2.0 Hz, and variable Hz)**
  - Bonferroni corrections were made

Results: Temporal Summation of Pain

Conclusions

- **All stimulus frequencies resulted in contamination of baseline EMG activity.**
- **Only series delivered at 2.0 Hz reliably elicited temporal summation of NFR.**
- **Series delivered at 1.0 Hz and 2.0 Hz resulted in temporal summation of pain ratings.**

Implications

- **Care should be taken when using NFR magnitude given the possibility of EMG contamination.**
- **These results indicate that a stimulation frequency of 2.0 Hz should be used because it reliably elicited temporal summation of NFR.**
- **The discrepancy between temporal summation of NFR and pain ratings underscores the problem of using pain ratings to make inferences about hyperexcitability of spinal nociceptive processes (i.e., wind-up).**

Results: Temporal Summation of NFR

![Temporal Summation of NFR](image)

- **There was a significant Stimulus Frequency X Stimulus Number interaction (p = .001).**
- **Only the simple effect of Stimulus Number for 2.0 Hz was significant (p = .024).**
- **Thus, only 2.0 Hz test to temporal summation of NFR.**