Adverse Life Events are Associated with Impaired Descending Inhibition of Spinal Nociception

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Introduction

Adverse life events (ALEs) are a significant risk factor for the development of chronic pain. While previous research indicates that ALEs may disrupt important physiological pathways related to pain processing, the specific

Objective

This study sought to elucidate the relationship between ALEs and chronic pain risk by examining the role of ALEs in conditioned pain modulation (CPM), an experimental pain paradigm frequently used to assess descending inhibition of spinal nociception.

Eligibility & Participants

- All participants provided informed consent prior to any study procedures

Exclusion criteria:

- < 18 years of age
- BMI > 35
- Current acute illness, psychotic symptoms, chronic pain condition, or inability to speak/read English
- Cardiovascular, neurological, and/or circulatory problems
- Recent use of analgesic, antidepressant, anxiolytic, stimulant, or antihypertensive medications

Sample Characteristics:

- Average age = 28.92 years (SD = 12.77)
- White/Caucasian non-Hispanic (51.0%); Native American (49.0%)
- Male (47.4%)
- Single (69.6%)
- Average amount of education = Partial College (48.2%)

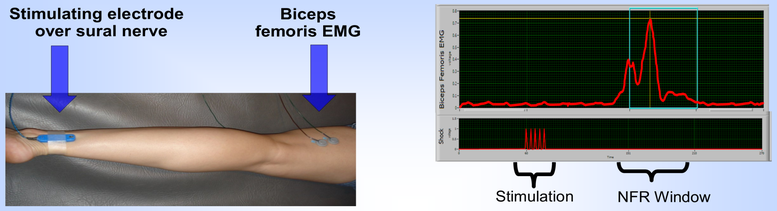
Procedure

- Two testing sessions were completed on separate days
- **Life Events Checklist Administered**
- **NFR Threshold Testing**
  — Sensors and stimulating electrode applied to the left ankle over the sural nerve
  — Electric stimulations delivered to sural nerve at ankle to determine stimulation intensity that elicits reflex
- **Conditioned Pain Modulation (CPM)**
  — Test stimulus = electric stimulations at an intensity that was individually calibrated for each participant

Adverse Life Events

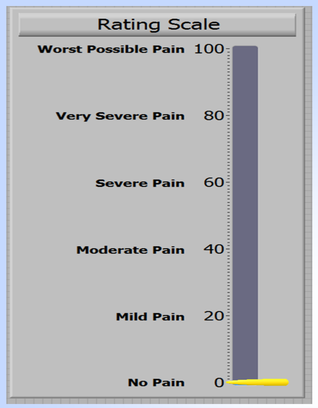
- Participants completed the Life Events Checklist (LEC) for the DSM-IV
- 17-item self-report measure assessing the number of potentially traumatic events to which a participant has been exposed
- Multiple items can be endorsed by the same participant.
- Scored by summing the items that participants reported as "happened to

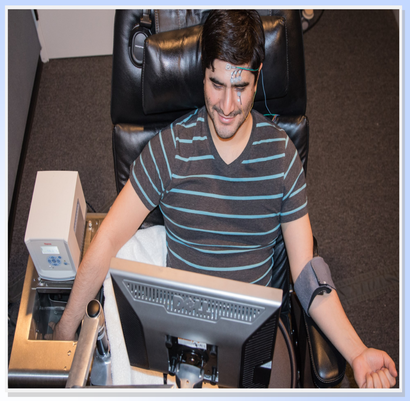
NFR Measurement



- **Nociceptive Flexion Reflex (NFR):** A spinally-mediated protective withdrawal reflex elicited by Aδ fiber activation
- **NFR magnitude:** Biceps femoris EMG activity in the 90-150 ms post-stimulus window
- **NFR d** was used to determine whether an NFR occurred. Calculated by subtracting mean baseline EMG (-60 to 0ms) from mean post-stimulus EMG

Conditioned Pain Modulation (CPM)





Phase	Conditioned Pain Modulation (CPM)
Pre	5 stimulations
	2 min break
Conditioning	5 stimulations with hand in cold water [10 °C]

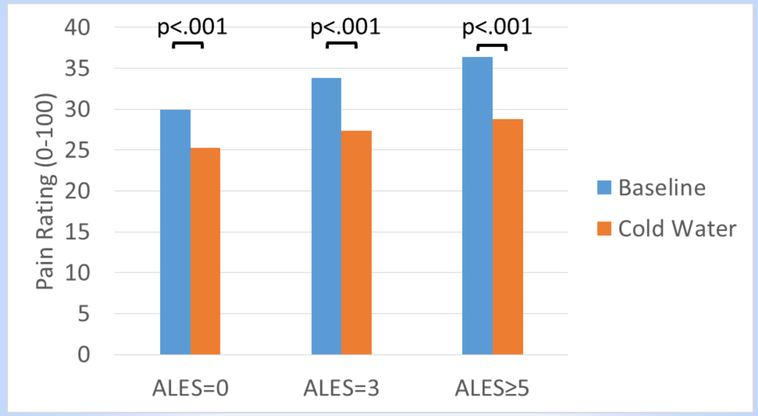
CPM Stimulus Intensity

- **120% NFR Threshold:** Biceps femoris EMG activity in the 90-150 ms post -stimulus window (stimulus intensity required to reliably elicit NFR)
- **Pain30:** An NRS rating ≥ 30 during NFR threshold testing
- **120% 3-Pulse Threshold:** 3-pulse trains of stimulations and biceps femoris EMG activity in the 90-150 ms post-stimulus window of the third stimulus (stimulus intensity required to elicit NFR in response to the third stimulation of the train)

Data Analysis

- Multilevel modeling (2 levels) was used in order to account for variance attributable to nesting effects during CPM
- >5 ALEs on the LEC were winsorized to 5 ALEs
- Control variables were: stimulus number, stimulus intensity, age, sex, BMI, race, mean arterial pressure, perceived stress (PSS), psychological distress (GSI of the SCL-90), general health (General Health Scale of the SF-36)
- Outliers were identified using Wilcox's MAD-median procedure and were winsorized to the nearest non-outlier value

Results: CPM of Pain



- Significant main effect of CPM phase ($p < .001$); average pain ratings were lower during the conditioning phase of CPM
- Significant main effect of psychological distress ($p < .042$); greater psychological distress predicted greater subjective pain during CPM
- **No significant interaction between ALEs and CPM phase on subjective pain ratings ($p = .336$); ALEs did not moderate subjective pain ratings across CPM phases**

CPM of NFR

Conclusions

The current study found that ALEs were associated with impaired NFR modulation but not with subjective pain ratings during CPM. That is, people with more ALEs demonstrated a dose-dependent disruption in their ability to inhibit nociceptive signals at the spinal level, but exposure to ALEs did not affect participants' subjective experience of pain. Taken together, these findings indicate that an impairment in descending inhibitory processes may underlie the relationship between ALEs and the

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