Conditioned modulation of pain and NFR in trauma exposed adults

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Introduction

Trauma exposure is associated with hyperalgesia and chronic pain, but it is unknown if descending modulation of spinal nociception is involved. Descending modulation of pain occurs as activation of supraspinal structures modulates pain signaling at the spinal level. One way to measure this form of modulation is through conditioned pain modulation (CPM), a paradigm that measures changes in the nociceptive flexion reflex (NFR) and pain in response to phasic electric stimuli before, during, and after the presentation of tonic, painfully cold water. The current study examined CPM in 194 healthy, pain-free participants that varied in their trauma exposure.

Life Events Checklist and Trauma Demographics

- Participants completed the Life Events Checklist (LEC) for the DSM-IV-TR Questionnaire.
- 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.
- Items were summed based on the events happening to the participant personally.
- Groups were created based on number of traumatic exposures (none [0], low [1], medium [2], high [≥3]).

Objective

To examine the dose-response relationship of trauma exposure on endogenous modulation of pain.

Participants

- Sample Characteristics:
  - Average age = 28.52 yrs (SD = 12.30)
  - White/Caucasian non-Hispanic (50.0%); Native American (44.3%)
  - Male (49.5%)
  - Single (73.1%)
  - Average amount of education = Partial College (50.0%)
  - Employed full time (24.2%)

- 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 anxiolytic, antidepressant, anxiolytic, antihypertensive medications

Procedure

- Overview, Informed Consent & Eligibility Determination (Health Status Screening):
  - Participants were recruited for a study to examine pain risk in Native Americans.
  - Two testing sessions were completed on separate days.
  - Testing session and tasks within days were counterbalanced or randomized.
  - Participants provided informed consent after the procedures were explained.

- Life Events Checklist Administered:
  - Self-report measure that indicated the number of traumatic events an individual has experienced in their lifetime.

- 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.
  - Conditioning stimulus = painful 10° C cold water

Outcome: Measurement of NFR

- Nociceptive Flexion Reflex (NFR): A spinally-mediated protective withdrawal reflex elicited by all fiber activation.
- NFR change: Biceps femoris EMG activity in the 90-150 ms post-stimulus window - NFR change calculated by the following formula (with values <0 represented as 0):
  \[
  \text{NFR change} = \frac{\text{NFR post} - \text{NFR baseline}}{\text{NFR baseline}}
  \]

Outcome: Conditioned Pain Modulation (CPM)

- Participants were exposed to modified one-step M-estimator according to Wilcox.
- Participants trials with NFR baselines higher than 3.0 µV were excluded from analyses due to questionable data validity.

Data Analysis

- Outliers on all variables were addressed through the use of modified one-step M-estimator according to Wilcox.
- Participants with NFR baselines higher than 3.0 µV were excluded from analyses due to questionable data validity.
- Two Multilevel Models (MLM) for the CPM models with Group and CPM phase as the IVs, and pain ratings and NFR change as the DVs.

Conclusions

- Individuals with a high degree of exposure to trauma showed significantly higher pain ratings during the baseline and water immersion suggesting generalized hyperalgesia as well as a delayed return to baseline.
- These results survived even after controlling for sex or catastrophizing.
- Multiple trauma exposures may alter descending modulation of spinal nociception and chronic pain.
- Future research is needed to determine the mediators (e.g., underactivity of the parasympathetic nervous system) of the relationship between trauma exposure and disrupted modulation (e.g., allostatic load) so that interventions can be developed to prevent maladaptive sequelae.

Funding Source:

This work was funded by an award (R01MD007807) from the National Institute On Minority Health and Health Disparities of the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.