Pain catastrophizing is related to temporal summation of pain but not temporal summation of the nociceptive flexion reflex

Jamie L. Rhudy, Satin L. Martin, Ellen L. Terry, Christopher R. France, Emily J. Bartley, Jennifer L. DelVentura, Kara L. Kerr

Abstract

Pain catastrophizing is associated with enhanced temporal summation of pain (TS-Pain). However, because prior studies have found that pain catastrophizing is not associated with a measure of spinal nociception (nociceptive flexion reflex [NFR] threshold), this association may not result from changes in spinal nociceptive processes. The goal of the present study in healthy participants was to examine the relationship between trait (traditional) and state (situation-specific) pain catastrophizing and temporal summation of NFR (TS-NFR) and TS-Pain. A secondary goal was to replicate prior findings concerning relationships between catastrophizing and NFR threshold, electrocutaneous pain threshold, and sensory and affective ratings of electrocutaneous stimuli. All analyses controlled for depression symptoms, pain-related anxiety, and participant sex. As expected, multiple regression analyses indicated that neither trait nor situation-specific catastrophizing was associated with NFR threshold, but that situation-specific catastrophizing was associated with pain ratings. Multilevel linear growth models of TS data indicated that situation-specific catastrophizing was associated with TS-Pain but not TS-NFR. Trait catastrophizing was not related to TS-Pain or TS-NFR. Together, these results confirm prior studies that indicate that catastrophizing enhances pain via supraspinal processes rather than spinal processes. Moreover, because catastrophizing was associated with TS-Pain but not TS-NFR, caution is warranted when using pain ratings to infer temporal summation of spinal nociceptive processes.

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1. Introduction

Pain catastrophizing is a set of cognitive–affective processes associated with enhanced pain [24–26,48]. Recent evidence suggests that the strength of the relationships between catastrophizing and pain outcomes are affected by the way in which catastrophizing is measured. Traditional (trait) measures of pain catastrophizing ask individuals to report on their catastrophic thoughts to painful experiences in general, whereas situation-specific (state) measures of pain catastrophizing ask individuals to report on their catastrophic thoughts immediately after a specific painful event. Although research has shown a relationship between pain and both types of catastrophizing, the relationship between pain and situation-specific catastrophizing is stronger [4,5,9,12,13,38,39].

Studies have also demonstrated that catastrophizing is associated with enhanced temporal summation of pain (TS-Pain) [13,20,22]. TS-Pain occurs when a series of constant-intensity noxious stimuli, with a short interstimulus interval (eg, 2.0 Hz), evoke greater pain on later stimuli in the series relative to the first stimulus [32,34]. The results of previous studies demonstrate that individuals who catastrophize tend to have a greater increase in pain ratings across the stimulus series.

TS-Pain is believed to result from a temporary hyperexcitability of spinal cord neurons (wind-up) [29,30], a process that may contribute to central sensitization [27,52]. However, using pain ratings to make inferences about spinal nociception may be problematic, because modulation of nociception at the supraspinal level can cause pain report to diverge from spinal nociception [7,40,41]. For example, pain catastrophizing correlates with pain report but not the nociceptive flexion reflex (NFR) threshold [16,18,38,39], a physiologically correlate of spinal nociception. This implies that catastrophizing modulates pain at the supraspinal, not spinal, level. As a result, it is unclear whether the association between catastrophizing and enhanced TS-Pain reflects changes in spinal nociception.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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- Pain catastrophizing
- Coping
- Spinal cord
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A series of noxious stimuli can also elicit larger NFRs on the last stimulus than the first, i.e., TS-NFR [3,14,17,23,44]. Given that NFR is a correlate of wind-up that overcomes problems of TS-Pain [23,52]. To our knowledge, only 1 published study has examined the association between catastrophizing and TS-NFR. Neziri et al. [31] found that trait catastrophizing was unrelated to the stimulus intensity that evoked TS-NFR (i.e., TS-NFR threshold). However, this study (1) did not examine whether catastrophizing was related to the change in NFR across the stimulus series, (2) dichotomized the measure of trait catastrophizing, thereby reducing scale variance and potentially statistical power, and (3) examined only the traditional (trait) measure of catastrophizing.

Given the noted gaps in the literature, the present study examined the relationships between catastrophizing (trait and situation-specific) and TS-Pain/TS-NFR using powerful multilevel linear growth analyses. Furthermore, because NFR threshold, electrocutaneous pain threshold, and subjective ratings of electrocutaneous pain were assessed before TS procedures, a secondary goal was to replicate prior relationships between pain catastrophizing and these outcomes. We predicted that catastrophizing would be associated with subjective ratings and TS-Pain, but not NFR threshold or TS-NFR. Moreover, the effects of situation-specific catastrophizing were expected to be stronger than trait catastrophizing.

2. Materials and methods

This is a secondary analysis of data from a study that determined the optimal parameters to elicit TS-NFR and TS-Pain [51]. That study found that a 3-stimulus series delivered at 2.0 Hz worked best; thus, TS-NFR and TS-pain evoked using these parameters were used to test the hypotheses for the present study.

2.1. Participants

Participants for this study were healthy individuals recruited from the University of Tulsa psychology subject pool and the surrounding community. Exclusion criteria were as follows: neurological, cardiovascular, or circulatory problems; chronic pain; recent psychological trauma; use of over-the-counter pain medication within 24 hours, or prescription pain medication within 2 weeks of participation; use of antidepressant, anxiolytic, or high blood pressure medications; having a body mass index of 35 or greater (because of potential difficulties with obtaining an NFR in individuals with high adiposity); and being less than 18 years of age.

A total of 58 individuals were found to be eligible and participated, although 1 participant was excluded from analyses because of reaching pain tolerance before an NFR could be obtained. The 57 participants included in analyses had a mean age of 21 years (SD = 2.8 years), had completed an average of 14 years of education (SD = 1.4), and tended to be female (63%, n = 36), white non-Hispanic (67%, n = 38), and employed fewer than 40 hours per week (53%, n = 30).

2.2. Apparatus

All stimulus presentation and data collection were controlled by a computer, A/D board (PCI-PCI-6071E; National Instruments, Austin, TX), and LabVIEW software (National Instruments). Testing was completed in a sound-attenuated and electrically shielded testing chamber. Participants were monitored from an adjacent control room by video camera. Participants wore sound-attenuating headphones that allowed them to hear the experimenter’s instructions, and could speak to the experimenter via the microphone on the video camera. Electric stimuli were generated by a Digitimer stimulator (DS7; Digitimer Ltd, Hertfordshire, England) and delivered using a bipolar surface stimulating electrode (Nicolet, Madison, WI; 30 mm interelectrode distance) attached to the left leg over the retromalleolar pathway of the sural nerve. The maximum intensity was set at 50 mA.

The NFR was assessed from biceps femoris electromyogram (EMG) recorded from 2 active Ag-AgCl electrodes placed 10 cm superior to the popliteal fossa. A ground electrode was placed over the lateral epicondyle of the femur. Before electrodes were applied, the skin was cleansed with alcohol and exfoliated using an abrasive paste (Nuprep) to reduce impedances below 5 kΩ. All electrodes were then attached with self-adhesive collars after conductive gel (Grass Technologies, West Warwick, RI, EC60) was applied. Bi-ceps femoris EMG was sampled at 1000 Hz and amplified/filtered using Grass Technologies Model 15LT amplifier (with AC Modules 15A54 and DC Modules 15A12).

2.3. Questionnaires

2.3.1. Pain catastrophizing

The Pain Catastrophizing Scale (PCS) was used to measure trait and situation-specific pain catastrophizing. The PCS is a reliable and valid 13-item scale that assesses catastrophic thinking associated with pain [49]. Participants made responses on a 5-point scale that ranged from 0 (not at all) to 4 (all of the time). For the present study, all items were summed to achieve a PCS total score. The PCS was administered before any pain testing using the traditional instructions to assess trait catastrophizing (“Using the following scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.”). In addition, the PCS was administered immediately after electrocutaneous pain threshold testing and midway through temporal summation testing, with instructions to assess situation-specific catastrophizing (“Thinking back to your experience during the electric stimulations, please indicate the degree to which you had these thoughts and feelings.”). In the present study, the internal consistency was adequate for all 3 PCS administrations (traditional, α = 0.88; situation-specific pain threshold, α = 0.88; situation-specific temporal summation, α = 0.95).

2.3.2. Pain-related anxiety

To assess anxiety related to painful electric stimulations, a numerical rating scale was presented that ranged from 0 (not at all anxious) to 100 (extremely anxious). Instructions were to “rate how anxious these electric stimulations make you feel.” Pain-related anxiety was assessed twice, once after the electrocutaneous pain threshold procedure and again midway through temporal summation testing. Pain-related anxiety was used as a predictor in analyses to rule out the possibility that the effects of pain catastrophizing on pain outcomes may be due to negative affect in response to pain.

2.3.3. Center for epidemiological studies—depression scale (CES-D)

The CES-D is a reliable and valid 20-item questionnaire that measures depressive symptoms [35]. Participants responded on a scale that ranged from 0 (rarely or none of the time) to 3 (most or all of the time), with instructions to rate their symptoms during the past week. Items were summed to achieve a total score, with higher scores indicating greater depressive symptomatology. The CES-D was used as a predictor in analyses to rule out that the effects of pain catastrophizing on pain outcomes may be due to depression [47].

2.3.4. McGill pain questionnaire—short form (MPQ-SF)

The MPQ-SF is a reliable and valid measure to assess pain experience [28]. Participants were asked to rate their experience during the electrocutaneous pain threshold phase using 11 sensory (eg,
throbbling, shooting) and 4 affective (eg, sickening, fearful) pain descriptors on a scale from 0 (none) to 3 (severe). Sums of all sensory words and affective words were used to compute sensory and affective pain rating scores, respectively.

2.4. Assessment of nociceptive responses

To assess NFR threshold, pain threshold, and TS-NFR, electric stimuli were delivered over the retromalleolar pathway of the sural nerve. Each electric stimulus consisted of a train of 5 rectangular wave pulses of 1-millisecond duration with an interpulse interval of 3 milliseconds (250 Hz). For NFR threshold and pain threshold testing, a single train of 5 electric stimuli was presented. For temporal summation testing, a series of 5 trains of 5 electric stimuli was presented (but only responses from the first 3 stimuli were used in the present analyses) [51].

2.4.1. Pain ratings

Pain intensity ratings were assessed from a computer-presented scale, with the following anchors: 0 (no pain), 50 (painful), and 100 (the most intense pain imaginable). During NFR and pain threshold testing, a single pain rating scale was presented after each stimulus. During temporal summation, participants were asked to provide 5 separate pain ratings, 1 rating for each train of 5 stimuli.

2.4.2. NFR threshold assessment

NFR threshold was assessed using 3 ascending–descending staircases of electric stimuli. The first ascending–descending staircase case started at 0 mA and increased in 2-mA steps until an NFR was detected. NFR was defined as a mean biceps femoris EMG response in the 90- to 150-millisecond post-stimulus interval that exceeded the mean biceps femoris EMG activity during the 60-millisecond pre-stimulus baseline interval by at least 1.4 standard deviations [19,37]. The 90- to 150-millisecond post-stimulus interval avoids contamination from the nonnociceptive R1 response that can occur before 90 milliseconds and from startle and voluntary responses that can occur after 150 milliseconds [10]. After an NFR was obtained, the current was decreased in 1 mA steps until an NFR was no longer detected. The second and third ascending–descending staircases used 1-mA steps. The interval between electric stimulations varied randomly between 8 and 12 seconds to reduce predictability and habituation. NFR threshold was defined as the average stimulus intensity (mA) of the last 2 peaks and troughs.

2.4.3. Pain threshold assessment

Pain threshold was assessed using 3 ascending–descending staircases of electric stimuli (8–12 seconds varying interstimulus interval). The first ascending–descending staircase started at 0 mA and increased in 4 mA steps until pain threshold was reached (rating ≥50 on pain scale). The current was then decreased in 2-mA steps until the participant rated a stimulus as ≤40 on the pain rating scale. (For the first 12 participants, the criteria used to stop a descending staircase was a rating of ≤25; however, to shorten the length of the assessment the criterion was changed to ≤40.) The second and third ascending–descending staircases continued with 2-mA steps. Pain threshold was defined as the average intensity (mA) of the 4 stimuli immediately above and immediately below a rating of 50 on the last 2 ascending and descending staircases.

2.4.4. Temporal summation of pain and NFR

A total of 25 trains of stimuli, delivered in 5 blocks of 5 stimulus trains, were used to elicit temporal summation in the parent study [51]. The trains varied in their frequency (Hz). Each stimulation frequency was presented only once per block, with order randomized within each block (across participants). Five trains were delivered at 0.33 Hz (3.0-second interstimulus interval [ISI]), 5 at 0.5 Hz (2.0-second ISI), 5 at 1.0 Hz (1.0-second ISI), and 5 at 2 Hz (0.5-second ISI), and 5 trains had a variable frequency (0.5- to 3.0-second ISI). After each train of stimuli, a set of 5 computer-presented pain rating scales were administered. Participants were instructed to rate pain intensity for each of the 5 stimulations in the train individually and then to click a button to submit their answers before the next train was delivered. The interval between trains was at least 8 seconds, but varied based on the time taken for the participant to complete the ratings. Participants were offered short (1- to 2-minute) breaks between blocks. The parent study found that TS-NFR was observed only for the 2.0 Hz stimulation frequency; thus only trains at that stimulation frequency were used in the present analyses [51]. Furthermore, temporal summation of NFR reached an asymptote by the third stimulus in the train of 5 stimuli, and the correlation between TS-NFR and TS-Pain was strongest when temporal summation was defined as the change from the first to the third stimulus [51]. For these reasons, only responses to the first 3 stimuli in the 2.0 Hz trains were used in analyses.

2.5. Study procedures

Verbal and written informed consent was obtained from all participants after the study procedures were fully explained. Participants were explicitly told that they could withdraw at any time. A health status questionnaire and a brief interview were then administered to assess inclusion/exclusion criteria. Next, participants were trained to use the computer-presented pain rating scales, instrumented for NFR testing, and were administered the trait pain catastrophizing questionnaire. Throughout pain testing procedures, participants sat comfortably in a reclining chair with the foot rest extended to maintain a knee angle of approximately 160°. Participants were informed that the experiment contained 2 phases.

Phase 1 assessed subjective and physiological reactions to single electric stimulations (NFR threshold and electrocutaneous pain threshold testing), and lasted approximately 20 to 30 minutes. The order of NFR threshold and pain threshold testing was counterbalanced across participants but was stratified by sex to maintain an equivalent sex distribution across testing order. Immediately after pain threshold testing, the McGill Pain Questionnaire—Short Form, the pain-anxiety scale, and the Pain Catastrophizing Scale (situation-specific) were administered. After the questionnaires were completed, a 5-minute rest break was provided.

Phase 2 assessed reactions to 5 electric stimulations in a series (temporal summation testing) and lasted approximately 20 minutes. The stimulus intensity used during temporal summation testing was set at either NFR threshold or pain threshold, whichever was highest. Midway through temporal summation testing (after the third block of stimulations), situation-specific pain catastrophizing and pain-related anxiety were assessed.

At the completion of the study, participants were debriefed, thanked for their participation, and received either research credit (for undergraduate participants) or a $25.00 honorarium (community participants).

2.6. Data analysis and preliminary data screening

Four separate hierarchical multiple regression analyses were conducted with NFR threshold, pain threshold, MPQ sensory pain ratings, and MPQ affective pain ratings as the dependent variables. These analyses controlled for sex, depressive symptoms, and pain-related negative affect (anxiety) by entering them in Step 1, because these variables may influence pain and/or catastrophizing [1,9,15,47–50]. Trait catastrophizing was entered in Step 2, and situation-specific catastrophizing was entered in Step 3. All tolerance
values were $>0.40$, indicating that there was no problem with multicollinearity [6]. Sex was dummy coded as male = 0 and female = 1.

For all biceps femoris EMG trials during temporal summation, a trained experimenter visually inspected the waveform for errors (e.g., EMG contamination resulting from movement) and judged whether an NFR was present in the 90- to 150-millisecond post-stimulus interval. Three trials were eliminated because of errors in the waveform. If the waveform did not contain errors, then NFR magnitude was calculated in response to each stimulus. NFR magnitude was defined as the mean biceps femoris EMG in the 90- to 150-millisecond post-stimulus interval minus the average biceps femoris EMG in the 60 milliseconds before the first stimulus in each train [51].

Seven participants withdrew during temporal summation testing because they could not tolerate the electrical stimulations, leaving 50 participants available for analysis of temporal summation data. The stimulation intensity setting during temporal summation testing was higher for these 7 individuals because they had a significantly higher NFR threshold (mean = 24.11 mA vs 14.41 mA, $P < .005$). Visual inspection of data determined that NFRs were not reliably elicited during temporal summation trials in 19 of the 50 completers, possibly because the stimulus intensity was set too low as a result of lower NFR and pain thresholds in these participants (stimulus intensity setting: nonresponders = 9.68 mA vs responders = 20.68 mA, $P = .001$). Of these participants, 10 were retested and 7 had adequate NFR responses, resulting in a final sample of 38 participants for temporal summation analyses.

Temporal summation data were analyzed using multilevel growth models using SPSS 17.0 (SPSS Inc., Chicago, IL). Five 3-pulse trains were administered and analyzed; therefore, 15 total stimulations were used as Level 1 units. The Level 1 covariance structure was modeled with a first order autoregressive structure (AR1). Stimulus Number (pulse 1, pulse 2, pulse 3) was entered as a continuous predictor, with the first stimulus coded as zero, thus allowing it to be the intercept. Subject number was entered as a grouping variable to define participants as the Level 2 units. The intercept and slope of the predictor Stimulus Number were allowed to vary across participants by entering them as random effects. Trait catastrophizing and situation-specific catastrophizing were grand-mean centered and entered as predictors, which provided a method of predicting variance in participants’ intercepts (their pain/NFR response to the first stimulus in the 3 stimulus train). The interactions of centered pain catastrophizing variables with Stimulus Number were also entered as predictors to provide a way of predicting variance in the Stimulus Number slopes (the change in pain/NFR over the 3 stimulus train, ie, the degree of temporal summation). These growth model analyses also entered participant sex, CES-D scores, and pain-related anxiety as control variables. Significance level was set at $P < .05$ (2-tailed) for all analyses.

3. Results

Table 1 presents means, SDs, observed ranges, and intercorrelations of relevant study variables.

<table>
<thead>
<tr>
<th>Variable (Possible range)</th>
<th>Mean SD</th>
<th>Observed Min–Max</th>
<th>Dep T-Cat</th>
<th>NFR PTh</th>
<th>MPQ Sens PS SS-Cat</th>
<th>PS Anx TS SS-Cat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression symptoms (0–60 units)</td>
<td>9.67 6.31</td>
<td>0–25</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait catastrophizing (0–52 U)</td>
<td>14.07 8.56</td>
<td>1–33</td>
<td>0.34 1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NFR threshold (0–50 mA)</td>
<td>15.60 8.80</td>
<td>2–39</td>
<td>0.06 0.13 1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electric pain threshold (0–50 mA)</td>
<td>11.68 8.56</td>
<td>1–48</td>
<td>0.10 0.08 0.24 1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MPQ sensory pain ratings (0–33 units)</td>
<td>7.16 5.25</td>
<td>1–21</td>
<td>0.26 0.48 0.12 0.29 1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MPQ affective pain ratings (0–12 U)</td>
<td>1.62 2.22</td>
<td>0–8</td>
<td>0.49 0.38 0.08 0.31 0.72 1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PS situation-spec. cat. (0–52 U)</td>
<td>6.91 8.56</td>
<td>0–37</td>
<td>0.32 0.62 0.16 0.28 0.72 0.64 1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PS pain-related anxiety (0–100 U)</td>
<td>49.34 26.18</td>
<td>0–88</td>
<td>0.31 0.26 0.05 0.17 0.42 0.36 0.60 1.00</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>TS situation-spec. cat. (0–52 U)</td>
<td>13.00 11.81</td>
<td>0–40</td>
<td>0.30 0.50 0.02 0.14 0.57 0.46 0.79 0.56 1.00</td>
<td></td>
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</tr>
<tr>
<td>TS pain-related anxiety (0–100 U)</td>
<td>62.08 23.05</td>
<td>4–100</td>
<td>0.33 0.35 0.01 0.11 0.34 0.25 0.57 0.76 0.70 0.77</td>
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</tr>
</tbody>
</table>

Note: NFR = nociceptive flexion reflex; PTh = electric pain threshold; MPQ Sens PS SS-Cat = pain sensitivity situation-specific catastrophizing; PS Anx = pain sensitivity pain-related anxiety rating; TS SS-Cat = temporal summation situation-specific catastrophizing; $N = 57$ for all variables, except TS is $N = 38$.

Table 2 presents means, standard deviations, observed ranges, and intercorrelations of relevant study variables.

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Step/Predictors</th>
<th>$\beta$</th>
<th>$sr^2$</th>
<th>$R^2$</th>
<th>$AR^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>NFR threshold</td>
<td>Step 1: Sex</td>
<td>-0.21</td>
<td>0.04</td>
<td>0.03</td>
<td>0.03</td>
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<tr>
<td></td>
<td>CES-D</td>
<td>0.02</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anxiety</td>
<td>-0.03</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Step 2: PCS-trait</td>
<td>0.05</td>
<td>0.00</td>
<td>0.05</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Step 3: PCS-SS</td>
<td>0.19</td>
<td>0.02</td>
<td>0.07</td>
<td>0.02</td>
</tr>
<tr>
<td>Pain threshold</td>
<td>Step 1: Sex</td>
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<td>0.01</td>
<td>0.05</td>
<td>0.05</td>
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<tr>
<td></td>
<td>CES-D</td>
<td>0.04</td>
<td>0.00</td>
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<td></td>
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<tr>
<td></td>
<td>Anxiety</td>
<td>-0.05</td>
<td>0.00</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Step 2: PCS-trait</td>
<td>-0.18</td>
<td>0.02</td>
<td>0.05</td>
<td>0.00</td>
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<td>0.06</td>
<td>0.11</td>
<td>0.06</td>
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<td>MPQ-sensory</td>
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<td>0.02</td>
<td>0.25</td>
<td>0.25</td>
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<tr>
<td></td>
<td>CES-D</td>
<td>0.02</td>
<td>0.00</td>
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<tr>
<td></td>
<td>Anxiety</td>
<td>-0.04</td>
<td>0.00</td>
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<tr>
<td></td>
<td>Step 2: PCS-trait</td>
<td>0.03</td>
<td>0.00</td>
<td>0.36</td>
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<td>Step 3: PCS-SS</td>
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<td>0.19</td>
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<td>MPQ-affect</td>
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<td>0.00</td>
<td>0.30</td>
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<tr>
<td></td>
<td>CES-D</td>
<td>0.36</td>
<td>0.04</td>
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<tr>
<td></td>
<td>Anxiety</td>
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<td>0.01</td>
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<td></td>
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<tr>
<td></td>
<td>Step 2: PCS-trait</td>
<td>-0.15</td>
<td>0.01</td>
<td>0.33</td>
<td>0.03</td>
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<tr>
<td></td>
<td>Step 3: PCS-SS</td>
<td>0.69</td>
<td>0.25</td>
<td>0.52</td>
<td>0.19</td>
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</table>

Note: $\beta$ values and squared semipartial correlations are from the final regression model that included all predictors. $NFR = $ nociceptive flexion reflex; MPQ = McGill Pain Questionnaire—Short Form; CES-D = Center for Epidemiological Studies—Depression Scale; Sex (male = 0, female = 1); anxiety = pain-related anxiety; PCS-trait = Pain Catastrophizing Scale—trait instructions; PCS SS-Cat = Pain Catastrophizing Scale—situation-specific instructions. Statistics in boldface type are significant at $P < .05$.
3.1. Associations between catastrophizing and NFR, pain threshold, and pain ratings

Correlation analyses (Pearson’s $r$) revealed significant associations between situation-specific pain catastrophizing and pain threshold ($r = 0.28$), sensory pain ratings ($r = 0.72$), and affective pain ratings ($r = 0.64$), but not with NFR threshold ($r = 0.16$). Trait pain catastrophizing was associated with sensory and affective pain ratings ($r = 0.48$ and $r = 0.38$, respectively), but not with NFR threshold ($r = 0.13$) or pain threshold ($r = 0.08$).

However, examination of the regression beta weights ($\beta$) in Table 2 indicates that only the relationships between situation-specific pain catastrophizing and sensory and affect pain ratings survived in the regression models that controlled for sex, depression, and pain-related anxiety. Notably, according to the squared semi-partial correlations ($sr^2$), situation-specific catastrophizing explained 19% of the unique variance in sensory pain ratings and 25% in affective pain ratings. Trait catastrophizing was not associated with any outcome in the regression models, and the unique variance explained ($sr^2$) ranged from 0% to 2%. However, in the regression predicting sensory pain ratings, trait and situation-specific catastrophizing appear to be competing for variance, because trait catastrophizing significantly explained 11% of the variance above and beyond sex, depression, and pain-related anxiety ($AR^2 = 0.11$) before situation-specific catastrophizing was added to the model. However, once situation-specific catastrophizing was added to the model, trait catastrophizing was no longer a significant predictor.

3.2. Multilevel growth model predicting temporal summation of pain (TS-Pain)

In brief, the multilevel growth model analysis of pain ratings indicated that pain summed across the 3-pulse train and that greater situation-specific catastrophizing, but not trait catastrophizing, was related to greater summation of pain.

Fig. 1 depicts the intraindividual linear growth in pain ratings associated with temporal summation (the 3-stimulation series). As can be seen, there was a general increase in pain across the 3 stimulations, albeit a small growth on average. However, it is noteworthy that there was considerable interindividual variability in intercepts (response to first stimulus) and slopes (change in response across the 3 stimuli).

Results from the multilevel growth model predicting pain ratings indicated that there was significant temporal summation of pain, as indicated by a significant main effect of Stimulus Number (Table 3). After controlling for the other variables in the model, there was a 1.05 average increase in pain ratings with each subsequent stimulus in the 3-stimulus series, with the first stimulus being rated 64.99 on average (the group-level intercept). As predicted, situation-specific catastrophizing was associated with enhanced TS-Pain (ie, a significant Stimulus Number $\times$ Situation-Specific Catastrophizing interaction). Specifically, with each 1-point increase in situation-specific pain catastrophizing score, there was a 0.08 increase in the slope for Stimulus Number (slope more positive). No other predictor was significant in the model (see Fixed Effects in Table 3). Results of random effects indicated that there was still significant unexplained interindividual variability in the intercept and slope of Stimulus Number (ie, TS-Pain). However, the lack of significant covariance between the intercept and slope suggests that the degree of TS-Pain was unrelated to the initial pain level evoked by the first stimulus in the series (eg, less temporal summation of pain was not due to higher pain ratings to the first stimulus). For exploratory purposes, growth models were conducted with trait catastrophizing alone as a predictor and control variables together as the only predictors (depression, pain-related anxiety); none of these variables were significant predictors of TS-Pain. However, it is worth noting that when situation-specific catastrophizing was not included in the model, trait catastrophizing approached significance as a predictor of slope (temporal summation) in pain ($P = .079$).

3.3. Multilevel growth model predicting TS-NFR

In brief, the multilevel growth model analysis of NFR indicated NFR summed across the 3-pulse train, but that neither situation-specific nor trait catastrophizing was related to temporal summation of NFR.

Fig. 2 depicts the intraindividual linear growth in NFR associated with temporal summation (the 3-stimulation series). As with TS-Pain, there was a general increase in NFR across the 3 stimulations. However, there was considerable interindividual variability

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**Table 3**

Results from multilevel linear growth model predicting pain ratings during temporal summation.

<table>
<thead>
<tr>
<th>Fixed effects</th>
<th>Estimate</th>
<th>SE</th>
<th>95% Confidence limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>64.99</td>
<td>2.09</td>
<td>60.76 – 69.22</td>
</tr>
<tr>
<td>Stimulus number</td>
<td>1.05</td>
<td>0.36</td>
<td>0.32 – 1.77</td>
</tr>
<tr>
<td>Trait catastrophizing</td>
<td>0.43</td>
<td>0.34</td>
<td>–0.25 – 1.11</td>
</tr>
<tr>
<td>Situation-specific catastrophizing</td>
<td>–0.31</td>
<td>0.28</td>
<td>–0.87 – 0.26</td>
</tr>
<tr>
<td>Depression symptoms</td>
<td>0.17</td>
<td>0.40</td>
<td>0.00 – 0.48</td>
</tr>
<tr>
<td>Pain-related anxiety</td>
<td>0.15</td>
<td>0.13</td>
<td>–0.11 – 0.41</td>
</tr>
<tr>
<td>Stimulus number $\times$ trait Catas</td>
<td>0.02</td>
<td>0.06</td>
<td>–0.09 – 0.14</td>
</tr>
<tr>
<td>Stimulus number $\times$ situation-specific Catas</td>
<td>0.08</td>
<td>0.04</td>
<td>0.01 – 0.15</td>
</tr>
</tbody>
</table>

**Random effects**

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>SE</th>
<th>95% Confidence limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR1 diagonal</td>
<td>58.72</td>
<td>9.38</td>
<td>42.94 – 80.30</td>
</tr>
<tr>
<td>AR1 rho</td>
<td>0.74</td>
<td>0.04</td>
<td>0.65 – 0.81</td>
</tr>
<tr>
<td>Stimulus number intercept variance</td>
<td>134.65</td>
<td>36.91</td>
<td>78.69 – 230.42</td>
</tr>
<tr>
<td>Intercept and slope covariance</td>
<td>–3.36</td>
<td>4.59</td>
<td>–12.36 – 5.63</td>
</tr>
<tr>
<td>Stimulus number slope variance</td>
<td>3.30</td>
<td>1.09</td>
<td>1.73 – 6.30</td>
</tr>
</tbody>
</table>

Note: Estimates are unstandardized relationships between predictors and dependent variable. Estimates in boldface type are significant at $P < .05$.

SE = standard error of coefficient/estimate; Catas = pain catastrophizing; AR1 = first-order autoregressive structure.
in both intercepts (response to first stimulus) and slopes (change in response across the 3 stimuli).

Results from the multilevel growth model predicting NFR magnitude during temporal summation (Table 4). After controlling for the other variables in the model, there was a 1.54 \( \Delta \mu \text{V} \) peak NFR magnitude (mean change in 90- to 150-millisecond post-stimulus interval minus the average biceps femoris EMG in the 60 milliseconds before the first stimulus in each train [51]).

Table 4

<table>
<thead>
<tr>
<th>Fixed effects</th>
<th>Estimate</th>
<th>SE</th>
<th>95% Confidence limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>2.61</td>
<td>0.62</td>
<td>1.35 - 3.88</td>
</tr>
<tr>
<td>Stimulus number</td>
<td>1.54</td>
<td>0.59</td>
<td>0.35 - 2.74</td>
</tr>
<tr>
<td>Trait catastrophizing</td>
<td>0.13</td>
<td>0.09</td>
<td>-0.07 - 0.32</td>
</tr>
<tr>
<td>Situation-specific catastrophizing</td>
<td>-0.08</td>
<td>0.08</td>
<td>-0.24 - 0.08</td>
</tr>
<tr>
<td>Depression symptoms</td>
<td>0.18</td>
<td>0.12</td>
<td>-0.07 - 0.42</td>
</tr>
<tr>
<td>Pain-related anxiety</td>
<td>0.03</td>
<td>0.04</td>
<td>-0.05 - 0.11</td>
</tr>
<tr>
<td>Stimulus number ( \times ) trait Catas</td>
<td>-0.01</td>
<td>0.09</td>
<td>-0.19 - 0.17</td>
</tr>
<tr>
<td>Stimulus number ( \times ) situation-Specific Catas</td>
<td>0.05</td>
<td>0.06</td>
<td>-0.07 - 0.16</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Random effects</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>AR1 diagonal</td>
<td>10.17</td>
<td>0.86</td>
<td>8.61 - 12.01</td>
</tr>
<tr>
<td>AR1 rho</td>
<td>0.41</td>
<td>0.05</td>
<td>0.30 - 0.51</td>
</tr>
<tr>
<td>Stimulus number intercept variance</td>
<td>12.35</td>
<td>3.36</td>
<td>7.25 - 21.04</td>
</tr>
<tr>
<td>Intercept and slope covariance</td>
<td>1.12</td>
<td>2.24</td>
<td>-3.27 - 5.50</td>
</tr>
<tr>
<td>Stimulus number slope variance</td>
<td>12.21</td>
<td>2.97</td>
<td>7.57 - 19.68</td>
</tr>
</tbody>
</table>

Note: Estimates are nonstandardized relationships between predictors and dependent variable. Estimates in boldface type are significant at \( P < 0.05 \). SE = standard error of coefficient/estimate; Catas = pain catastrophizing; AR1 = first-order autoregressive structure.

in both intercepts (response to first stimulus) and slopes (change in response across the 3 stimuli).

Results from the multilevel growth model predicting NFR magnitude indicated that there was significant temporal summation of NFR, as indicated by a significant main effect of Stimulus Number (Table 4). After controlling for the other variables in the model, there was a 1.54 \( \Delta \mu \text{V} \) increase in NFR magnitude with each subsequent stimulus in the 3-stimulation series, with the first stimulus evoking a 2.61 \( \Delta \mu \text{V} \) NFR magnitude (mean change in 90- to 150-millisecond post-stimulus interval) on average (the group-level intercept). No other predictor was significant in the model (see Fixed Effects in Table 4). Results of random effects indicated there was still significant unexplained interindividual variability in the intercept and slope of Stimulus Number (ie, TS-NFR). However, the lack of significant covariance between the intercept and slope suggests that the degree of TS-NFR was unrelated to the initial NFR magnitude evoked by the first stimulus in the series (eg, less temporal summation of NFR was not due to higher NFRs in response to the first stimulus). For exploratory purposes, growth models were conducted with trait-catastrophizing alone as a predictor, situation-specific catastrophizing alone as a predictor, and control variables together as the only predictors (depression, pain-related anxiety); none of these variables were significant predictors of TS-NFR.

4. Discussion

This study used multilevel linear growth analyses to examine the relationships between pain catastrophizing (trait and situation-specific) and temporal summation of pain (TS-Pain) and nociceptive flexion reflex (TS-NFR). As predicted, situation-specific catastrophizing was associated with enhanced temporal summation of pain, but not temporal summation of NFR. Trait catastrophizing was unrelated to either. Interestingly, there were no main effects of trait or situation-specific catastrophizing in the growth models, indicating that catastrophizing was not associated with pain and NFRs evoked by the first stimulus (no effect on the intercept). Thus, when repeated noxious stimulations are delivered, situation-specific catastrophizing appears to have a stronger effect on the processes involved with summation of pain experience than the response to the first stimulus.

Given that neither trait nor situation-specific pain catastrophizing was associated with the intercept or slope of TS-NFR, pain catastrophizing does not appear to exert its effects by engaging descending cerebrospinal mechanisms to modulate spinal nociception. This notion is consistent with prior studies [16,18,31,38,39] that have noted that pain catastrophizing is associated with subjective responses to noxious stimuli, but not NFR threshold. We replicated these prior findings in our analyses predicting NFR threshold, pain threshold, and sensory and affective ratings of the electrotactile stimuli. We found that trait and situation-specific pain catastrophizing were not associated with NFR threshold or pain threshold in our regression analyses; however, greater situation-specific catastrophizing was associated with higher sensory and affective ratings of the electrotactile stimuli. When considered together with imaging studies noting that catastrophizing correlates with brain activation during painful stimulation [11,21,43], it appears that catastrophic thoughts exert their effects supraspinally to modulate pain experience without altering spinal nociception.

4.1. Implications for studies of temporal summation of pain

Nociceptive processing in healthy individuals involves the activation of peripheral nociceptors that relay the signal to spinal cord neurons, which in turn evoke withdrawal reflexes (eg, NFR). Spinal neurons also relay the signal to supraspinal centers (eg, thalamus, anterior cingulate cortex, insula, somatosensory cortices) that further process the nociceptive message [2,33,36]. Ultimately, pain experience results from this supraspinal processing. Temporal summation of pain is argued to be the psychophysical correlate of wind-up in animals [45], a process dependent on NMDA receptors [8] that results in the temporary hyperexcitability of dorsal horn neurons [45], a process dependent on NMDA receptors [8]. Given that NFR is a spinal reflex that involves dorsal horn neurons in the reflex arc (primary afferent \( \rightarrow \) dorsal horn neurons \( \rightarrow \) motoneuron) [42], then temporal summation of NFR should be affected by wind-up. Supporting this, a study of NFR in rats found a correlation between the activity of dorsal horn neurons and single motor units, both of which increased in re-
sponse to repetitive noxious stimulation [53]. Moreover, there is evidence that temporal summation of NFR in human beings involves NMDA receptors [23]. Ostensibly then, temporal summation of pain is the subjective correlate of these spinal processes after the nociceptive message has been relayed to supraspinal centers [46]. Importantly, the present findings indicate that caution is warranted in using pain ratings to infer hyperexcitability of spinal neurons (ie, wind-up). Specifically, we found that situation-specific pain catastrophizing was related to the degree of temporal summation of pain, but not temporal summation of NFR. Although others have noted a relationship between catastrophizing and temporal summation of pain [13,20,22], the present study and the study by Neziri et al. [31] suggest that catastrophizing is unrelated to temporal summation of NFR. Taken together, it appears that nociceptive signals in response to repetitive noxious stimuli undergo additional processing at supraspinal levels, implying that pain ratings may not accurately reflect temporal summation (or wind-up) of spinal nociception. In further support of this, we have found that only 25% of the variance in temporal summation of NFR is shared with temporal summation of pain [51].

4.2. Trait vs situation-specific pain catastrophizing

Significant zero-order (Pearson's r) correlations were found between trait pain catastrophizing and sensory and affective pain ratings. However, these associations did not survive in the multiple regression models, with situation-specific catastrophizing emerging as the only significant predictor in both models. Thus, our results are also consistent with an emerging literature that suggests that state (situation-specific) catastrophizing is a stronger predictor of experimental pain outcomes than trait catastrophizing. This idea was first noted by Dixon et al. [9], who observed that retrospective ratings of catastrophic thoughts evoked during a cold pressor task were more strongly correlated with cold pressor pain than ratings of pain-related catastrophic thoughts assessed before the cold pressor. These findings were replicated by Edwards et al. [12], and subsequent studies have extended the findings to electrocutaneous pain [38,39], capsaicin pain [5], pressure pain [4], heat pain [4], and temporal summation of heat pain [13]. A recent study by Campbell et al. [5] using a cross-lagged panel analysis suggested that increases in situation-specific catastrophizing precede increases in pain, thus arguing against the notion that the correlation between pain and situation-specific catastrophizing is explained by pain causing situational catastrophic thoughts.

To our knowledge, the present study is the first to examine the relationship between situation-specific catastrophizing and temporal summation of NFR. The study by Neziri et al. found that the catastrophizing subscale of the Coping Strategies Questionnaire was not associated with the stimulation intensity that evoked temporal summation of NFR (ie, temporal summation of NFR threshold) [31]. However, they assessed trait catastrophizing and dichotomized the scale; thus scale variance was reduced, possibly reducing their ability to detect a relationship. Our study extends prior research to demonstrate that situation-specific catastrophizing is also a stronger predictor of temporal summation of pain than trait-catastrophizing, and that the relationship is not better accounted for by depressive symptoms, pain-related anxiety, or sex differences.

4.3. Study strengths and limitations

The present study had a number of strengths, including being one of the few studies to examine temporal summation of pain and catastrophizing, and the only study to examine temporal summation of NFR and situation-specific catastrophizing. Moreover, we used statistically powerful multilevel growth modeling to examine intra- and interindividual variability in temporal summation, and the analyses controlled for other potentially relevant variables (depression, pain-related anxiety, sex). Nonetheless, a few limitations are worth noting.

First, 7 of the 57 participants (12%) dropped out during temporal summation testing. These participants tended to have a higher NFR threshold; therefore, it is possible that this limits the generalizability of our findings. It is noteworthy that these 7 individuals did not differ from those who completed testing in trait or situation-specific pain catastrophizing.

Second, we found that NFRs were not reliably evoked in 19 participants during temporal summation testing. These individuals had lower NFR and pain thresholds; therefore the stimulus intensity used was lower, on average, than in NFR responders. However, the NFR nonresponders did not differ in regard to any other study variable. We were able to contact and retest 10 of these participants and to reliably evoke NFRs in 7 individuals when higher stimulus intensities were used. As a result, we do not believe that this affected the generalizability of our results. It is possible, however, that power was compromised in the multilevel growth models. To examine this possibility, we computed squared zero-order correlations between catastrophizing and temporal summation change scores (TS change = Pulse3–Pulse1). This indicated trait catastrophizing explained 10.7% of the variance in TS-Pain; but, this was reduced to 0.8% of the variance when situation-specific catastrophizing was controlled (squared semi-partial correlation). Furthermore, trait catastrophizing explained only 0.5% of the variance in TS-NFR and situation-specific catastrophizing only explained 2.5% of the variance in TS-NFR. Thus, we do not believe that low power led to our failure to find associations between catastrophizing (state or trait) and TS-NFR. Although power may have limited our ability to resolve an association between trait catastrophizing and TS-Pain, this does not change the conclusion that situation-specific catastrophizing is a better predictor of TS-Pain. Nonetheless, caution is always warranted when interpreting null findings.

Third, because 2.0 Hz (0.5-second interstimulus interval) is the optimal stimulus frequency for evoking temporal summation of NFR, pain ratings to each stimulus had to be made after the last stimulus in the series. This could have introduced response bias, especially for the first 2 stimuli in the series, and may have affected our ability to see a relationship between catastrophizing and pain to the first stimulus in the series (intercept). Although there is no easy way to correct for this problem using the current study paradigm, it is interesting that another study also failed to find a relationship between catastrophizing and the first stimulus when heat pain was assessed and there was ample time to make the rating [20]. Finally, the current study was conducted in healthy participants; therefore, findings may not generalize to clinical populations (eg, chronic pain).

5. Conclusion

This study found that situation-specific catastrophizing was significantly associated with temporal summation of pain, sensory pain ratings, and affective pain ratings, but not temporal summation of NFR or NFR threshold. Together, these results imply that pain catastrophizing enhances pain via supraspinal processes rather than spinal processes. Moreover, because catastrophizing was associated with TS-Pain but not TS-NFR, caution is warranted when using pain ratings to infer temporal summation of spinal nociceptive processes.

Conflict of interest statement

The authors have no conflicts of interest to report.
Acknowledgments

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References


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