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Emotional Modulation of Pain and Spinal Nociception in Sexual Assault Survivors

Natalie Hellman, B.A., Bethany L. Kuhn, M.A., Edward W. Lannon, M.A., Michael F. Payne, B.S., Cassandra A. Sturycz, M.A., Shreela Palit, M.A., Joanna O. Shadlow, Ph.D, and Jamie L. Rhudy, Ph.D

Department of Psychology, The University of Tulsa, Tulsa OK

Abstract

Objective—Sexual assault (SA) is associated with an increased risk for chronic pain and affective distress. Given that emotional processes modulate pain (e.g., negative emotions enhance pain, positive emotions inhibit pain), increased pain risk in SA survivors could stem from a disruption of emotional modulation processes.

Methods—A well-validated affective picture-viewing paradigm was used to study emotional modulation of pain in 33 healthy, pain-free SA survivors and a control group of 33 healthy, pain-free individuals with no reported history of SA (matched on age, sex, race, and number of non-SA traumas). Unpleasant (mutilation), neutral, and pleasant (erotica) pictures were presented while painful electrocutaneous stimulations were delivered at the ankle. Pain intensity ratings and nociceptive flexion reflex magnitudes (NFR; a physiologic measure of spinal nociception) were recorded in response to electric stimuli. Multilevel models were used to analyze the data with Group (SA vs. no-SA) and Content (mutilation, neutral, erotica) as IVs.

Results—Both groups demonstrated similar emotional modulation of pain [$F_{\text{Group} \times \text{Content}}(2,646.52)=0.44, p=.65$], but a main effect of group [$F_{\text{Group}}(1,65.42)=4.24, p=.043$] indicated the SA group experienced more overall pain from electric stimuli (hyperalgesia). A significant Group X Content interaction for NFR ($p=.035$) indicated that emotional modulation of NFR was present for the no-SA group [$F_{\text{ContentSimpleEffect}}(2,684.55)=12.43, p<.001$], but not the SA group [$F_{\text{ContentSimpleEffect}}(2,683.38)=1.71, p=.18$].

Conclusions—These findings suggest SA survivors have difficulty emotionally engaging brain-to-spinal cord mechanisms to modulate spinal nociception. A disruption of descending inhibition plus hyperalgesia could contribute to comorbidity between sexual trauma and chronic pain.

Keywords

emotional controls of nociception; sexual assault; nociceptive flexion reflex; trauma; pain; affective pictures

Corresponding Author: Jamie Rhudy, PhD. Address: The University of Tulsa, Department of Psychology, 800 S Tucker Drive, Tulsa, OK 74104, Phone: 918-631-2839, Fax: 918-631-2833, jamie-rhudy@utulsa.edu.

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Introduction

Sexual assault (SA) is any form of sexual contact that occurs without the explicit consent of the recipient(1) and ranges from unwanted touch to rape. Estimates suggest that 1-in-4 women and 1-in-100 men are SA survivors(2). Although SA is a physical violation of integrity and an act of sexual violence, only 28% of documented SA survivors report an injury from the assault(3). Despite this low injury rate, 53% of SA survivors report pain in 4 or more body regions within 72 hours of SA, including regions not injured during the assault(4). Thus, SA may promote pain. This notion is consistent with research showing survivors of physical and/or sexual assault show augmented responses to experimental pain stimuli(5,6).

Further, many persons with chronic pain report experiencing SA during their lifetime(7–12), with estimates ranging from 7%-91% and varying by disorder(8). Given that the majority of SA survivors do not report an injury from the assault (but many develop acute or chronic pain), it does not appear that injuries after SA are the primary pathway to chronic pain development.

One factor that may increase pain risk is the disruption of pain modulation mechanisms. SA survivors often report affective distress following the assault(13) and in one study affective distress mediated the relationship between abuse and pain(13). This suggests emotional modulation of pain could be a mechanism linking SA and chronic pain. Indeed, emotions are psychological processes known to modulate pain(14,15). Moreover, animal and human studies suggest supraspinal structures involved with emotion processing are part of a descending circuit (e.g., amygdala, hippocampus, periaqueductal grey, rostral ventromedial medulla) that can inhibit or amplify pain signaling at the spinal level(16,17). Thus, emotions can modulate pain signals very early in the CNS.

To study emotional modulation of pain, our lab developed the Emotional Control of Nociception (ECON) paradigm(18). ECON involves the presentation of emotionally-charged (pleasant, neutral, unpleasant) pictures while painful electric stimuli are delivered. ECON studies of healthy humans find that electric stimuli evoke less pain during erotic pictures and more pain during mutilation pictures(19–22). Furthermore, ECON assesses modulation of the nociceptive flexion reflex (NFR). The NFR is a spinal reflex associated with limb withdrawal (e.g., leg) from a noxious stimulus and is evoked by peripheral (Aδ) pain fibers(18,23–25). Studies show that NFR threshold is correlated with pain threshold and that NFR size/magnitude is correlated with stimulus intensity and pain perception(23,26). In the laboratory, NFR is quantified from electromyogram (EMG) of the biceps femoris (hamstring) muscle following electric stimulation at the ankle, and it is used to assess pain signaling at the spinal level (i.e., spinal nociception)(24). Although the reflex arc does not involve supraspinal regions (Fig 1), it can be modulated by supraspinal circuitry and thus provides a means of assessing descending circuits(27). For example, studies have shown NFR can be inhibited by hypnotic suggestions of analgesia(28) and extreme stress(29), whereas distraction(30) can increase NFR. By contrast, pain catastrophizing has no effect on NFR(31).

ECON studies reliably demonstrate that erotic pictures inhibit NFR and mutilation pictures enhance NFR; thus, NFR is typically modulated in parallel with pain(18). However, emotional modulation of pain and NFR can be dissociated, suggesting their modulation is mediated by separate processes(20–22,32). Indeed, evidence suggests ECON activates separate circuits involved with pain modulation versus NFR modulation (Fig 1)(27).

ECON research has also shown that those at risk for chronic pain and affective distress (fibromyalgia, major depressive disorder, sleep disturbance) show disrupted emotional modulation of pain(20–22,33). Specifically, these individuals failed to inhibit or facilitate pain during emotional pictures. Interestingly, emotional modulation of NFR was intact. This led us to speculate that an inability to regulate nociceptive signals once they reach the brain is a chronic pain risk factor(21). A similar risk may be present in SA survivors. Supporting this, SA is associated with abnormal neural activation in areas associated with emotional modulation of pain (e.g., hippocampus, amygdala)(34).

The present study assessed ECON in a diverse sample of healthy, pain-free individuals with or without a history of SA. Groups were matched on age, sex, and race, as well as non-SA traumas to rule out that any observed group differences were due to trauma exposure more generally. By assessing healthy, *pain-free* individuals our findings may help determine if disruptions exist before chronic pain onset, thus lending support that disrupted pain modulation is a precursor to chronic pain. We predicted SA survivors would fail to emotionally modulate pain, but display intact NFR modulation.

Methods

Study Participants

Participants were recruited as part of a larger study investigating risk factors for chronic pain in Native Americans. Exclusion criteria included: 1) <18 years old, 2) history of cardiovascular, neuroendocrine, musculoskeletal, neurological disorders, 3) chronic pain, 4) BMI ≥ 35 (due to difficulties obtaining NFR), 5) use of anti-depressants, anxiolytic, analgesic, stimulant, and anti-hypertensive medication, 6) current psychotic symptoms (assessed by Psychosis Screening Questionnaire(35)) or substance use problems, and/or 7) an inability to read/speak English. Data collection occurred between March 2014 and February 2017. Testing was completed over 2 days, with each day lasting 4–6 hours. 224 participants began the first testing session, but 34 quit prior to ECON, thus 190 participants were available for analysis. 33 participants reported history of SA ($n=28$ female) based on the Life Events Checklist (described below). Of the 157 participants without SA, 33 ($n=28$ female) were selected who were matched on age, sex, race, and mean number of non-SA traumas (see Table 1). Frequency matching procedure were used for age and mean number of non-SAs, whereas case-by-case matching was used for sex and race. Of the SA group, 25 (76%) experienced at least one non-SA trauma (e.g., physical assault, environmental disaster) and 28 (85%) of the non-SA group experienced at least one non-SA trauma.

The study was approved by Institutional Review Boards of The University of Tulsa, Cherokee Nation, and the Oklahoma City Area Indian Health Service. Participants were given an overview of all procedures and told they could withdraw at any time. All

participants provided verbal and written informed consent prior to enrollment and received a \$100 honorarium for the completion of each testing day (or \$10/hour of non-completed days).

Effect size estimates from prior research assessing group differences in ECON ranged from $d=.87$ to $d=1.50$ (20). A power analysis with 3 within-subject levels (picture contents), 2 between-subject levels (SA vs. non-SA), $\alpha=.05$, power=.80, and the lowest effect size ($d=.87$) suggested a minimum sample size of 15; thus, our sample of 66 should be adequate.

Testing Apparatus

The study was controlled by a computer with dual monitors, analog-to-digital board (USB-6212 BNC; National Instruments, Austin, TX, USA), and LabVIEW software (National Instruments). Participants used one monitor to complete electronic questionnaires and make pain ratings, whereas the experimenter (located in an adjacent room) used the second monitor to monitor physiology. Testing was conducted in a sound attenuated and electrically shielded room. Participants were monitored throughout testing via a video camera and participants wore sound-attenuating headphones to hear the experimenter and pre-recorded instructions.

A stimulator (Digitimer DS7A; Hertfordshire, England) and a bipolar electrode (Nicolet, Model#019–40400, Madison, WI) delivered electric stimuli to the left ankle over the retromalleolar pathway of the sural nerve. Each electric stimulation was a train of five 1-ms rectangular wave pulses at 250-Hz. Timing of electric stimuli was computer-controlled. For safety, maximum intensity was set to 50-mA.

Two active Ag-AgCl electrodes applied over the left biceps femoris muscle approximately 10-cm superior to the popliteal fossa were used for NFR EMG. The signal was collected, filtered (10-Hz to 300-Hz), and amplified ($\times 10,000$) using a Grass Technologies (West Warwick, RI) Model 15LT amplifier (with AC Module 15A54). A common reference electrode was placed over the lateral epicondyle of the femur. To achieve impedances $<5k\Omega$ for EMG and stimulating electrodes, the skin was cleaned with alcohol and exfoliated (Nuprep gel; Weaver and Company, Aurora, CO). EMG was sampled at 1000-Hz. Electrodes/sensors were filled with conductive gel (EC60; Grass Technologies).

Questionnaires

Participants completed a custom-built demographics and health status questionnaire to assess background information and inclusion/exclusion criteria. SA history was assessed from the Life Events Checklist (LEC), which has been shown to have convergent validity with measures of traumatic event exposure(36). A person was assigned to the SA group if they endorsed “happened to me” for either of the two SA items(36). The other 14-items that were answered “happened to me” were summed to indicate the number of non-SA traumas (for matching purposes).

Additional questionnaires were administered to assess group differences in psychological characteristics known to affect pain(37,38). The Symptom Checklist-90-Revised (SCL-90-R) assesses various psychological symptoms(39). The Global Severity Index (GSI) of the

SCL-90-R was used to assess overall psychological distress (higher scores=greater distress) and the depression subscale was used to assess depressive symptoms (higher scores=greater depression). The Pain Catastrophizing Scale assesses catastrophic thoughts (rumination, magnification, helplessness) associated with pain (higher scores=greater catastrophizing) (40). The State-Trait Anxiety Inventory (STAI) was used to assess the severity of state anxiety (higher scores=greater anxiety)(41). The Positive and Negative Affect Schedule (PANAS) assesses current positive and negative affect(42) using two subscales (higher scores=greater positive and negative affect, respectively). The Perceived Stress Scale (PSS) assesses psychological stress within the past month (higher scores=more perceived stress) (43). The Anxiety Sensitivity Index-Revised (ASI-R) assesses a person's fear of anxiety-related symptoms (higher scores=greater fear)(44). The Life-Orientation Test-Revised (LOT-R) assesses perceived optimism (higher scores=greater optimism)(45).

Determination of Stimulus Intensity used during ECON

The stimulus intensity (in mA) used during ECON was set at the highest of: 1.2x the intensity of NFR threshold, 1x PAIN30, or 1.2x the intensity of 3-stimulus threshold. This ensures that stimuli were painful and reliably evoked NFRs; therefore, these procedures (described below) were all assessed prior to ECON. Pain rating instructions were the same for all tasks. Following each electric stimulus, participants were instructed to rate their pain intensity on a computer-presented visual analog scale (VAS, described below) that ranged from “no pain sensation” to “the most intense pain sensation imaginable”(25,46).

Nociceptive Flexion Reflex (NFR) Threshold—NFR threshold was determined from 3 ascending-descending staircases of stimulations(24). The first staircase began at 0-mA and increased in 2-mA increments until a reflex was observed. Once obtained, the stimulus intensity decreased in 1-mA steps until a reflex was not observed. The second and third ascending-descending staircases implemented 1-mA step increments. The interval between electric stimuli varied randomly (8 to 12-s) to minimize predictability and reflex habituation. NFR was determined present if the mean rectified biceps femoris EMG in the 90 to 150-ms post-stimulus interval exceeded the mean rectified biceps femoris EMG activity during the 60-ms pre-stimulus baseline interval by at least 1.4 SD of the baseline EMG activity(24). NFR threshold was defined as the average stimulus intensity (mA) of the two peaks and two troughs of the last 2 ascending-descending staircases.

PAIN30—Pain30 was only assessed if the participant's NFR threshold did not evoke a VAS rating 30 (mildly painful). If assessed, the computer started the stimulus intensity at the intensity of NFR threshold and then increased in 2 mA increments until a rating 30 was obtained.

3-stimulus threshold—This procedure assessed NFRs in reaction to a 3-stimulus series (stimulus=train of five 1-ms pulses at 250-Hz) with a 0.5-s interval between each stimulus. The first series started at 0-mA then the 3-stimulus series was increased by 2-mA until an NFR was evoked by the 3rd stimulus in the series (3-stimulus threshold).

Emotional Control of Nociception (ECON)

ECON is a validated picture-viewing paradigm used to assess emotional modulation of pain and NFR(18,25). Twenty-four pictures were selected from the International Affective Picture Systems (IAPS)(47): 8 mutilation, 8 neutral, 8 erotic. These contents were chosen because mutilation are the only unpleasant pictures, and erotic are the only pleasant pictures, that modulate both pain and NFR(19). During pictures, painful electric stimuli were administered to evoke pain and NFR. A total of 18 electric stimulations were delivered: 12 during 50% of the pictures (equally dispersed across contents) and 6 during inter-picture intervals (to reduce predictability). Stimulations were delivered 3 to 5-s after picture onset (randomly determined). Pictures were presented in a pseudorandomized order, with the limitation that the same content was not shown twice in a row. Each picture was presented for 6-s with a 12 to 22-s inter-picture interval (randomly determined). Immediately following a picture, scales to assess valence, arousal, and pain (if a stimulation occurred) were presented on a single computer screen and participants were instructed to rate their emotional reactions to the pictures and their pain intensity.

Picture ratings—A computerized version of the Self-Assessment Manikin (SAM)(48) was used to assess emotional appraisals of the pictures. This 2-item questionnaire assesses valence/pleasure (1=unpleasant to 9=pleasant) and arousal (1=calm to 9=excited) ratings by moving an indicator on or between any of the 5 manikins for each scale.

Pain ratings—Pain intensity ratings were made using a computer-presented visual analog scale (VAS). The VAS ranged from “no pain sensation” to “the most intense pain sensation imaginable,” and participants made their ratings by dragging an indicator along the line. Ratings were converted to values that ranged from 0 to 100 (higher score=higher intensity).

Nociceptive flexion reflex (NFR) magnitudes—NFR magnitude is used to assess within-subject changes in spinal nociception(23). NFR magnitude was calculated in Cohen’s d units [d =(mean rectified EMG of 90 to 150-ms post-stimulation interval minus the mean rectified EMG of –60 to 0-ms pre-stimulation interval) divided by (the average SD of rectified EMG from –60 to 0-ms pre-stimulation and SD of 90 to 150-ms post-stimulation intervals)]. The d -score method has been shown to produce a stronger correlation with pain report than other scoring methods and produces a more normal distribution(49).

Testing Procedures

Figure 2 presents the tasks on the ECON testing day. On the other testing day, tasks assessed temporal summation of heat, as well as pain thresholds/tolerances for electric, ischemic, cold, heat, and pressure stimuli. Day order was randomized across participants, but stratified based on participant race and sex. Prior to pain tasks on the first testing day, participants completed the demographic questionnaire, LEC, PCS, PANAS, and STAI. During 10- and 20-min breaks (Fig 2), participants completed several questionnaires, including LOT-R, SCL-90-R, PSS, and ASI-R (order randomized). The ASI-R was administered on the day 2, all others were on day 1.

Statistical Analyses

Group differences in background variables were assessed with chi-square analyses (nominal variables) or independent-samples *t*-tests (continuous variables), using group (SA vs. no-SA) as the IV.

Primary outcomes (valence, arousal, pain ratings, NFR magnitude) were analyzed using multilevel models (MLM)(MIXED procedure, SPSS 20.0, IBM, Armonk, NY). Analyses of valence and arousal ratings had 24 rows of data per participant, corresponding to the 24 pictures. Analyses of pain and NFR included 12 rows of data per participant, corresponding to the 12 stimulations delivered during pictures. In MLM models, Level 1 units were responses to pictures (valence/arousal) or responses to electric stimulations (pain/NFR), depending on the analyses. Level 2 units were participants, identified by their subject ID number. All models included a random intercept to model Level 2 variance. The SPSS MIXED procedure implements Satterthwaite estimation procedures to produce non-integer denominator degrees of freedom that vary from analysis to analysis. IVs in MLMs were Group (SA vs. non-SA) and Picture Content (mutilation [Mut], neutral [Neu], and erotica [Ero]). A variable called Stimulus Order (which coded for the order of the electrical stimulations during ECON) was entered as a continuous predictor into MLMs for pain/NFR to model any habituation/sensitization effects unrelated to emotional modulation(50). This improves statistical power and the validity of models(50). Fisher's LSD was used for follow-up tests to significant *F*-tests. All data were tested for normality and within-cell outliers were identified using Wilcox's MAD-median approach(51) and winsorized. Significance was $\alpha=.05$ (2-tailed).

Results

Background variables (Table 1) and missing data

Groups were successfully matched. The groups did not differ on any background variable, including NFR and 3-stimulus thresholds. Importantly, the average electric stimulation intensity administered during ECON did not differ by group, eliminating this as a potential confound.

One non-SA participant only completed the first day of testing thus had no ASI-R data ($n=32$). The stimulating electrode lost contact with the skin for one participant in the SA group, so this person's last 6 pain ratings/NFRs were lost (1 neutral, 3 mutilation, 2 erotic).

Emotional reactions to pictures (Fig 3)

Analysis of valence ratings indicated a significant main effect of picture content [$F(2, 1393.25)=1283.54, p<.001$], but no main effect for group [$F(1, 66)=1.03, p=.31$] or Group x Content interaction [$F(2, 1393.24)=1.53, p=.22$]. For all participants (regardless of SA history), mutilation pictures were more unpleasant than neutral and erotica pictures, and erotica was more pleasant than neutral.

For arousal ratings, there was not a main effect of group [$F(1, 66)=1.94, p=.17$], but there was a main effect of content [$F(2, 1395.45)=500.66, p<.001$] that was qualified by a

significant Group X Content interaction [$F(2, 1395.43)=3.70, p=.035$]. For both groups, mutilation and erotic pictures were rated as more arousing than neutral pictures, but not significantly different from one another. However, erotic pictures elicited slightly more arousal in the SA group ($M_{SA}= 5.74$ vs. $M_{non-SA}= 5.18; p=.035, d=0.33$). There were no other group differences.

Emotional modulation of pain/NFR (Fig 4)

Although groups did not receive significantly different stimulus intensities, the average intensity administered was higher in the SA group so it was entered as a covariate to ensure pain rating analyses were not confounded. Results revealed a significant main effect of content [$F(2, 645.75)=59.10, p<.001$] and a significant main effect of group [$F(1, 65.42)=4.24, p=.043$], but no significant interaction [$F(2, 646.52)=0.44, p=.65$]. In general, pain ratings were higher during mutilation pictures than neutral and positive pictures, and lower during erotic pictures than neutral pictures. Further, the SA group reported significantly higher pain overall than the non-SA group ($p=.043, d=0.50$).

Analysis of NFR revealed a significant main effect of content [$F(2, 686.05)=10.56, p<.001$], such that NFRs were larger during mutilation pictures than neutral ($p=.031$) and erotic pictures ($p<.001$), and smaller during erotic pictures than neutral pictures ($p=.015$). Although no significant main effect of group was observed [$F(1, 63.73)=3.13, p=.082$], a significant Group x Content interaction [$F(2, 686.15)=3.38, p=.035$] indicated the non-SA group emotionally modulated NFR [$F(2, 684.55)=12.43, p<.001$], whereas the SA group did not [$F(2, 683.38)=1.71, p=.18$]. Specifically, NFR magnitudes were not statistically different across picture contents in the SA group, whereas the non-SA group displayed significantly smaller NFR magnitudes during erotic pictures compared to both mutilation and neutral pictures (Fig 4).

To determine whether these pain/NFR findings were explained by individual differences in emotional appraisals of the pictures, the above analyses were rerun after entering valence and arousal ratings as covariates. All conclusions were the same.

Exploratory analyses

To determine whether groups may have differed in attentional modulation of pain/NFR, responses to stimulations delivered during inter-picture intervals (IPIs) were compared to neutral pictures using MLMs similar to those above. For pain ratings, both groups experienced less pain during neutral pictures than IPIs ($M_{Neu}=38.74, SD=24.68$ vs. $M_{IPI}=41.14, SD=24.56; p=.002$), but this effect did not interact with group [$F(1, 495.15)=0.01, p=.92$]. For NFR, there was no effect of attention [$F(1, 532.51)=.78, p=.38$], nor an interaction with group [$F(1, 531.56)=.017, p=.90$]. Together, these results suggest that distraction cannot explain our results.

Discussion

We hypothesized SA survivors would fail to emotionally modulate pain but have intact modulation of NFR(20–22). Surprisingly, the opposite was found. SA survivors failed to modulate NFR, but showed intact pain modulation. Although pain was effectively modulated

by both groups, electric stimulations elicited more pain (i.e., hyperalgesia), but not larger NFRs, in the SA survivors.

Importantly, these results cannot be explained by group differences in electric stimulus intensity or emotional responding. Pictures elicited similar responses in both groups. Mutilation pictures evoked displeasure and arousal, whereas erotic pictures evoked pleasure and arousal. The only minor difference was SA survivors found erotic pictures slightly more arousing, but this could not explain why they failed to emotionally modulate NFR or experienced more pain. Exploratory analyses that controlled for emotion ratings confirmed this. Further, our results cannot be explained by pictures engaging distraction in the no-SA group.

SA and Chronic Pain Risk

There is a strong link between SA and chronic pain(7–12). SA survivors are more likely to report back pain(9) and poorer physical functioning(52), and SA is prevalent in persons with chronic back pain(53), chronic abdominal pain(7), chronic pelvic pain(10), somatization disorder(54), and fibromyalgia(8,55). Despite this, studies examining the mechanisms are lacking.

Hyperalgesia is a risk factor for chronic pain. Many chronic pain conditions are associated with hyperalgesia(56) and prospective studies find that hyperalgesia prior to surgery predicts chronic post-surgical pain(57). Thus, sexual trauma could promote hyperalgesia, which in turn increases the risk for chronic pain. Consistent with this, early life stress is associated with later hyperalgesia(58) and studies find that trauma exposure is associated with enhanced laboratory pain(5,53). Interestingly, a study of chronic back pain sufferers with and without a trauma history observed generalized hyperalgesia in trauma-exposed patients only(53).

To our knowledge, our study is the first to demonstrate that SA, rather than trauma-exposure more generally, is linked to hyperalgesia in healthy, pain-free individuals. Moreover, we found that emotional modulation of NFR was absent in this group. Given that NFR modulation involves descending brain-to-spinal cord circuitry, this implies these circuits are disrupted in SA survivors. A failure of descending circuits (especially inhibitory) may allow more incoming nociceptive signals to reach the brain, thus promoting hyperalgesia. Interestingly, NFR threshold and 3-stimulus threshold, which were assessed in the absence of emotional stimuli, did not significantly differ between the groups, indicating that spinal neurons were not generally sensitized. Thus, SA appears to be associated with a failure of emotion to engage descending circuits, especially inhibitory mechanisms(Fig 1).

Of note, the pain signal was modulated once it reached the supraspinal level, because emotional modulation of pain was intact in both groups. This suggests the supraspinal modulation loop in Fig 1 is intact in both groups. Interestingly, Fig 4 shows that the lowest pain the SA group experienced (i.e., during erotica) was similar to the highest pain the non-SA group experienced (i.e., during mutilation). This suggests that emotional pain inhibition by erotica was not able to overcome the general hyperalgesia the SA group experienced.

Thus, cognitive-emotional interventions to inhibit pain may not help to reverse the effects of hyperalgesia in SA survivors.

This chronic pain risk is different than that observed in persons with major depressive disorder, fibromyalgia, and sleep disturbance who display an intact ability to emotionally modulate NFR, but fail to modulate pain(20–22). Previous research identified a different brain circuit involved with emotional modulation of NFR (e.g., thalamus, amygdala, prefrontal cortex) than that involved with emotional modulation of pain (e.g., insula)(27). Thus, it is possible that amygdala-thalamic circuits are disrupted in SA survivors. Notably, dysregulation of the amygdala-thalamic circuitry is implicated in chronic pain conditions(59) and PTSD(60), both of which have high prevalence rates in SA survivors(61).

Although we argue here that a failure of descending circuits may be one pathway linking SA to chronic pain risk, there are likely other pathways. For example some SA survivors may develop chronic pain following exposure to intense or sustained nociceptive input, rather than exposure to SA specifically(59).

Neurodevelopmental Impact on SA and Chronic Pain

Animal models examining early life stress suggest it leads to altered pain processing in later life(58,62). In humans, repeated SA in childhood is related to reduced hippocampal volume, whereas SA in adolescence is related to reduced prefrontal cortex volume(63). Findings like these imply the developmental age at which SA occurs is important.

Indeed, a recent meta-analysis concluded that age of a trauma (including but not limited to SA) was a moderator of the relationship between biological risk (e.g., elevated heart rate, higher cortisol levels in younger samples) and the development of PTSD symptoms(64). Another meta-analysis suggested childhood abuse is related to greater pain symptoms in adulthood and a higher prevalence of chronic pain(65). Because brain maturation occurs throughout the first 3 decades of human life, trauma exposure in childhood and adolescence may be especially detrimental(64). Unfortunately, our study did not measure the age that SA occurred, so we are unable to draw inferences about developmental processes. Future studies should examine this, because our findings may be stronger for those that experienced SA in childhood and/or the pattern of modulation could be different based on age of exposure.

Limitations

The present study had multiple strengths, as it measured physiologic and subjective outcomes, implemented a well-validated emotional modulation paradigm, used powerful MLM statistical models, and had a well-matched control group. Moreover, samples were ethnically-diverse male and female participants, thus improving generalizability of the findings(2). However, some limitations should be considered.

First, by excluding participants with pain it is possible we hindered our ability to observe important group differences. However, studying pain-free individuals is necessary to rule out that group differences are due to differences in disease severity and/or treatment disparities. Second, although we exceeded the sample size suggested by power analysis, the size was relatively small (n=33 per group). This precluded us from looking at within-group

differences that could be important (e.g., ethnic differences, effects of comorbid trauma, sex differences). Third, we could not assess the severity or the frequency of SA because these are not measured by the LEC. Fourth, we did not assess for PTSD or other psychiatric diagnoses, so we cannot determine if they affected our results. However, our groups did not differ in psychological distress, which would be expected if groups differed in psychiatric diagnoses. Fifth, the partial use of case-by-case matching may have created dependency between the samples that may not have been fully accounted for by the statistical models. Sixth, we used erotic and mutilation pictures because only they reliably modulate pain and NFR, but because of this we cannot determine whether our findings are specific to these contents. Finally, participants agreed to participate after being informed of the picture contents; therefore, it is possible that self-selection bias could limit the generalizability.

Summary

This study found SA survivors were hyperalgesic and had disrupted emotional modulation of NFR. Nonetheless, they emotionally modulated pain. This implies a disruption of descending inhibition that promotes pain amplification. This in turn could contribute to the future development of chronic pain in SA survivors. Interestingly, these deficits are different than those noted in other groups with high pain risk, indicating SA may have a unique pathophysiology for chronic pain development.

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Glossary

SA	Sexual Assault
CNS	Central Nervous System
ECON	Emotional Control of Nociception
NFR	Nociceptive Flexion Reflex
EMG	Electromyogram
BMI	Body Mass Index
LEC	Life Events Checklist
SCL-90-R	Symptom Checklist-90-Revised
GSI	Global Severity Index
STAI	State Trait Anxiety Index
PANAS	Positive and Negative Affect Schedule

PSS	Perceived Stress Scale
ASI	Anxiety Sensitivity Index
LOT-R	Life-Orientation Test-Revised
VAS	Visual Analog Scale
IAPS	International Affect Picture Systems
SAM	Self-Assessment Manikin
IV	Independent Variable
MLM	Multilevel Modeling
LSD	Least Significant Difference
PTSD	Posttraumatic Stress Disorder
mA	milliAmperes
Hz	Hertz
Ag-AgCl	silver/silver chloride

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Figure 1.

Proposed mechanisms engaged by Emotional Controls of Nociception (ECON). Emotional pictures trigger two modulatory circuits. One involves supraspinal communication with the spinal cord and allows modulation of spinal nociception and NFR. The other is purely supraspinal (e.g., cortico-cortical) and can modulate pain independent of spinal nociception. These separate circuits allow emotional modulation of pain and NFR to be dissociated.

Figure 2.

Experimental procedures for the Emotional Controls of Nociception (ECON) testing day.

Note: *indicates the questionnaire was administered on the first day of testing **indicates the questionnaire was administered on the second day of testing.

Figure 3.

Emotional reactions to pictures. Valence (left graph) and arousal ratings (right graph) by mutilation (Mut), neutral (Neu), and erotic (Ero) pictures in sexual assault (SA) survivors and matched non-sexual assault (No SA) controls. Both groups showed similar emotional reactions to the pictures on valence (how pleasant or unpleasant the picture was), and on arousal. However, the SA group rated the erotic pictures as slightly more arousing than the non-SA group. Means $\pm$ SEM.

Figure 4.

Emotional modulation of pain intensity (left graph) and the nociceptive flexion reflex (NFR, right graph) by mutilation (Mut), neutral (Neu), and erotic (Ero) pictures in sexual assault (SA) survivors and matched non-sexual assault (No SA) controls. Both groups showed similar emotional modulation of pain, but the SA group experienced greater overall pain in response to the painful electric stimulations. By contrast, only the No SA group showed emotional modulation of the NFR. Means $\pm$ SEM.

Table 1

Participant characteristics by group

Characteristic	No SA group (n=33)		SA group (n=33)		X ²	p
	n	%	n	%		
Sex (female)*	28	84.8%	28	84.8%		
Race/Ethnicity*						
non-Hispanic white	10	16.7%	10	16.7%	-	-
Native American	22	33.4%	22	33.4%	-	-
Other	1	1.5%	1	1.5%	-	-
Employment (employed full time)	11	34.4%	6	18.2%	4.34	.23
	M	SD	M	SD	t-value	p
Cohen's d [95% CI for d]						
Age (years)*	31.30	12.83	31.12	12.50	-	.01 [-.47, .50]
Number of non-SA traumas (LEC, 0–17)*	2.21	1.65	2.42	2.00	-	-.11 [-.60, .37]
Body mass index (kg/m ²)	25.92	5.42	26.13	4.45	-1.17	.86 [-.52, .44]
Psychological Distress (GSI, 0–4)	1.29	.45	1.39	.34	-1.12	.27 [-.76, .21]
Depression (SCL-90-R, 0–4)	.52	.58	.66	.50	-1.04	.30 [-.74, .23]
State Anxiety (STAI; 20–80)	33.21	7.14	34.91	6.42	-1.01	.31 [-.73, .24]
Pain Catastrophizing Scale (0–52)	9.15	9.50	12.27	9.44	-1.34	.19 [-.81, .16]
Negative Affect Scale (PANAS, 10–50)	2.39	2.84	3.24	2.97	-1.19	.24 [-.78, .19]
Positive Affect Scale (PANAS, 10–50)	16.82	7.92	17.67	9.16	-.40	.69 [-.58, .38]
Perceived Stress Scale (0–40)	13.48	7.89	16.15	5.18	-1.62	.11 [-.88, .09]
Anxiety Sensitivity Index (0–40)	.96	.75	1.06	.73	-.58	.56 [-.63, .34]
Optimism (LOT-R, 0–40)	15.64	3.61	15.73	3.78	-.10	.92 [-.51, .46]
NFR Threshold (0–50 mA)	16.95	10.65	19.57	10.68	-1.00	.32 [-.73, .24]
3-Stimulus Threshold (0–50 mA)	13.03	6.58	15.76	8.91	-1.41	.16 [-.83, .14]
Stimulus Intensity (0–50 mA)	22.23	10.83	27.10	12.91	-1.64	.11 [-.89, .09]

* Denotes a matching variable, therefore no inferential statistics are reported. SA = sexual assault. LEC=Life Events Checklist. GSI = Global Severity Index of the Symptom Checklist 90. SCL-90 = Symptom Checklist 90. STAI = State Trait Anxiety Inventory. PANAS = Positive and Negative Affect Schedule. LOT-R = Life Orientation Test-Revised.