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Original Reports

Dysfunctional Pain Modulation in Torture Survivors: The Mediating Effect of PTSD

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Abstract: **Trauma survivors, and particularly torture survivors, suffer from high rates of chronic pain and posttraumatic stress disorder (PTSD) for years afterward, along with alterations in the function of the pain system. On the basis of longitudinal data on PTSD symptomatology, we tested whether exposure to torture, PTSD or PTSD trajectories accounted for chronic pain and altered pain perception. Participants were 59 torture survivors and 44 age-matched healthy control subjects. Chronic pain was characterized. Pain threshold, pain tolerance, conditioned pain modulation (CPM), and temporal summation of pain were measured. Three PTSD trajectories were identified among torture survivors; chronic, delayed, and resilient. Lack of CPM and more intense chronic pain was found among the chronic and delayed groups compared with the resilient and healthy control groups. Temporal summation of pain was strongest among the chronic group. PTSD trajectories mediated the relationship between torture and CPM. It appears that the duration and severity of posttraumatic distress, rather than the exposure to trauma, are crucial factors that mediate the association between trauma and chronic pain. Because PTSD and its resultant distress are measurable, their evaluation seems particularly important in the management of pain among trauma survivors. The results may be generalized to other instances in which chronic pain persists after traumatic events.**

Perspective: ***This article presents the mediation effect of PTSD trajectory on pain modulation among trauma survivors suggesting that it is the duration and severity of PTSD/distress, rather than the exposure to trauma per se, that influence the perception and modulation of pain.***

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Key words: *Posttraumatic stress disorder trajectories, chronic pain, pain modulation, trauma, torture.*

Survivors of traumatic events are known to suffer from the coexistence of chronic pain and posttraumatic stress disorder (PTSD), the mechanism of which is still not clear (for review see Asmundson and Katz,[6] and Moeller-Bertram et al[37]). War captivity, which usually entails deliberate human cruelty through the infliction of physical and psychological torture, is one of the most severe traumatic experiences. Physical torture in captivity may include severe beating, burning, penetrating injuries, suspension, and electric shocks directed toward vulnerable body parts. Psychological torture may include isolation, humiliation, and mock executions. Torture survivors are thus at an increased risk for physical and mental distress and dysfunction.[21]

Although the immediate suffering in captivity is evident, the long-term effect of torture on the body in general, and on the pain system in particular, has received limited scientific attention. High rates of chronic pain among torture survivors, ranging from 60% to 94%, have been reported.[3,9,43,71,74,75] Clinical and psychophysical testing on the feet of torture survivors who underwent foot beating (falanga) revealed thermal and tactile hypo- or hyperesthesia and mechanical allodynia.[52-54,71] Psychophysical testing in intact body regions of torture survivors revealed abilities poorer than control subjects to modulate pain manifested in abolished conditioned pain modulation

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(CPM) and enhanced temporal summation of pain (TSP), that correlated with their chronic pain intensity.[12]

The effects of torture are unfortunately not limited to the pain system. Captivity and torture have been implicated in PTSD,[23,42,64,76] the most common psychiatric sequelae among trauma survivors, which entails considerable distress, impaired functioning, and disability.[25] Apart from the association of PTSD and chronic pain,[5,61] PTSD among trauma survivors has also been associated with altered pain perception including changes in the sensitivity and reactivity to painful stimuli.[14,16,20,26,32] Thus, the presence or absence of PTSD among torture survivors may mediate the alterations observed in their pain system.

Importantly, PTSD symptoms tend to wax and wane over time. Prospective studies assessing the longitudinal course of PTSD among trauma survivors have characterized 4 main trajectories: 1) chronic PTSD: clinical/subclinical PTSD levels present continuously since the trauma; 2) delayed onset PTSD: an initial asymptomatic period that is followed by PTSD emergence; 3) recovery: initial clinical/subclinical PTSD levels followed by a lack of PTSD; and 4) resilience: lack of clinical/subclinical PTSD since the exposure.[64]

Given the complex interrelationship of trauma, chronic pain, and PTSD, it is yet unclear whether the mere exposure to trauma, its psychological sequelae (PTSD), or PTSD trajectory account for the alterations in the pain system. The aims were, therefore, to examine the implication of torture-induced PTSD and PTSD trajectories on the pain system of torture survivors. Specifically, we hypothesize that torture survivors with chronic PTSD will exhibit more enhanced chronic and experimental pain and more dysfunctional pain modulation than those with delayed-onset PTSD or PTSD-resilient individuals.

Methods

Participants

The study sample included 103 men; 59 torture survivor ex-prisoners of war (POWs; mean age = 57.8 ± 3 years) and 44 comparable veterans (mean age = 58.8 ± 4 years), who fought in the same battles as the ex-POWs but were not imprisoned and therefore were not tortured. This study was part of a large scale longitudinal study of war captivity related to the "1973 war" consisting of 3 waves of assessments (for full details, see Solomon et al[64]). To address potential sources of bias, ex-POWs and control subjects were initially matched on sociodemographic and military variables. Examination of sociodemographic variables revealed that age, ethnic background, marital status, and educational background were similar in the 2 groups. The mean age of the participants during the war was 22 years (range = 18–26 years). Twenty-six percent of the participants were married during the war, and 70% had completed high school. The sample in the present study was randomly selected from participants of the third assessment wave conducted in 2008.

The recruitment process for the present study included sending a letter of invitation to participate in the study, followed by a phone call 2 weeks later. Those who agreed to participate in the study were scheduled for a single testing session, according to their preference. Each participant signed an informed consent after receiving a detailed explanation on the study aims and procedures. The experiment was approved by the institutional review board of Tel-Aviv University.

The ex-POWs were severely tortured during captivity, which lasted either 6 weeks (43 of 59 of the present sample) or 9 months (16 of 59) in the years 1973-1974. They were held in solitary confinement, at times handcuffed and blindfolded, and were subject to harsh physical and psychological torture. Torture included, but was not restricted to, severe beatings, penetrating injuries, suspension, positional torture, electric shock to sensitive organs, burns, and systematic deprivation of food and water. Ex-POWs were also subjected to various forms of oppression and humiliation, including not being permitted to use the toilet, verbal abuse such as curses and threats, demoralizing misinformation about their loved ones, and mock executions. Since their release from captivity, the torture survivors have been receiving medical and psychiatric care according to demand and need.

Testing took place in a quiet room. Temperature in the room was maintained at 22 ± 2°C. The participants sat in a comfortable armchair with their arms supported by holders. All of the participants were trained in the sensory testing before the actual data collection. The participants were reimbursed for travel expenses.

Equipment

Thermal Stimulator

Thermal stimuli were delivered using a Peltier-based computerized thermal stimulator (TSA 2001; Medoc Ltd, Ramat-Ishay, Israel), with a 3 × 3 cm contact probe. A passage of current through the Peltier element produces temperature changes at rates determined by an active feedback system. As soon as the target temperature is attained, the probe temperature actively reverts to a preset adaptation temperature by passage of an inverse current. The adaptation (baseline) temperature was set to 32°C.

Water Bath

Hot stimuli were administered with a water bath apparatus (Chillsafe 8/30 Scanvac SHC 2000; Labotal, Abu Gosh, Israel). This temperature-controlled water tank has a maximum temperature variance of ± .5°C. Water flow is maintained at a constant temperature throughout the water bath by way of a whirlpool and is constantly reticulated to prevent local warming or cooling. The temperature of the water was kept constant at 45°C. Participants were instructed to insert their hand inside the bath up to their wrist line.

Visual Analog Scale

Perceived pain intensity was evaluated using a visual analog scale (VAS).[51] The VAS consists of a 15-cm plastic ruler with a slider in the middle. Moving the slider exposes a horizontal red bar (the visual side) to the

participant while the side facing the experimenter displays an analogue scale with values between 0 and 10. The end points are set as "no pain sensation" = 0 and "the most intense pain sensation imaginable" = 10.

Sensory Testing

General Procedure

Each participant partook in a single testing session that lasted approximately 2.5 hours. The measurements started after participants underwent a training session. The results obtained during training were discarded. Sensory testing was conducted consecutively with an approximate 5- to 10-minute break between each test. Participants sat in a comfortable armchair throughout the experiment. The test included the measurement of heat-pain threshold and heat-pain tolerance limit, stimulus response function, CPM, and windup pain. The order of the tests was random. In addition to the sensory testing, the participants also completed the PTSD questionnaire. Half of the participants completed the PTSD questionnaire before the sensory testing and half after its termination. This was the third time that these participants completed this questionnaire as explained in the Evaluation of PTSD section. The participants were also asked if they suffered from chronic pain (lasting >6 months) and if they did, they were asked to rate the amount of their chronic pain at its least and at its worst on a 0 to 5 scale in which 0 denotes no pain and 5 denotes the most intense pain.

Pain and Intolerance Thresholds

Heat-pain threshold and heat-pain tolerance limit were measured to evaluate the sensitivity of the pain system. The thresholds were measured with the method of limits using the thermal stimulator. The contact probe of the stimulator was attached to the skin of the participants' forearm using a Velcro band. For heat-pain threshold measurement, participants received 4 successive ramps of gradually increasing temperature, starting from a baseline temperature of 35°C, at a rate of 2°C per second. Thermal stimuli were applied at 25-second intervals to minimize tissue damage. During each stimulus, the participant was asked to press a switch when the first pain sensation was perceived, thus defining heat-pain threshold. Pressing the switch resulted in an automatic recording of the threshold temperature and a reset of the probe temperature to baseline values. Heat-pain threshold was computed by averaging the readings of 4 successive trials. For the heat-pain tolerance limit we repeated the same protocol except the instruction to the participant was to press the switch when the pain could no longer be endured.[13]

Stimulus Response Function

The method of direct scaling was used to search for the stimulation intensities to be used for CPM and TSP. Subjects received a series of thermal stimuli with the thermal stimulator and were asked to rate their pain at the end of each stimulus on the VAS. The stimulus intensities, presented in an ascending manner, rose from a baseline temperature of 35°C (rate of rise = 2°C per second), to a destination temperature ranging between 38°C to the intensity eliciting 6 on the VAS, at which it remained for 1 second and then returned to baseline. An interstimulus interval of 45 seconds was maintained to avoid any changes in skin sensitivity and to allow for adequate VAS scoring. The individual temperatures eliciting a value of 5 in the VAS for each subject were extracted from the stimulus-response functions.[17]

CPM

CPM was measured as an indicator of the inhibitory pain processing capacity.[72,78] CPM was measured in a parallel design, by administering a noxious contact-heat stimulus on the volar aspect of one forearm ("test stimulus") and evaluating its perceived pain intensity when administered alone and in the presence of another noxious heat stimulus applied to the contralateral hand ("conditioning stimulus"). The test stimulus was noxious heat equivalent to an intensity of 5 on the VAS (individually adjusted according to the stimulus-response function) applied with the thermal stimulator at its destination temperature for the duration of 10 seconds. The conditioning stimulus was the immersion of the hand into hot bath water, at 45°C, for the duration of 20 seconds. The rating of the test stimulus in the presence of the conditioning stimulus was performed after 20 seconds of immersion time. CPM was present if the test stimulus produced less pain in the presence of the conditioning stimulus than in its absence. The difference between these 2 ratings was the amount of CPM.[17]

TSP

TSP was measured as an indicator of hyperexcitability and hyper-reactivity of the pain system.[50,67] TSP was measured with a Semmes-Weinstein Monofilaments no. 6.65 (300 g). The examiner applied the filament 4 consecutive times to the surface of the middle finger (palmar surface) at 2 different rates: every 3 seconds and every 10 seconds (.3 and .1 Hz, respectively), the latter of which was used as a control. The participant was asked to rate the intensity of the pain after the first and fourth stimulus on a VAS. The first stimulus of the series produced no pain or minimal pain sensation. If the fourth stimulus administered at a rate of .3 Hz evoked a considerable pain whereas that of .1 Hz did not, then an exaggerated TSP was determined. The amount of TSP pain was calculated by subtracting the intensity of the first stimulus from that of the fourth.[14]

Evaluation of Chronic Pain

Participants who suffered from chronic pain (persisting >6 months) completed the McGill pain questionnaire (MPQ).[35] Four quantitative parameters were derived from the MPQ: the pain rating index (PRI)—on the basis of summing the values of the pain descriptors chosen by the participant from a list; the number of words chosen from that list; pain intensity at its least (on a numerical scale of 0–5); and pain intensity at its worst (Pmost; on a numerical scale of 0–5).

Evaluation of PTSD

PTSD symptoms were measured in 3 assessment waves that took place over 17 years using the PTSD Inventory.[66] The first and second assessment waves were in 1991 and 2003. The third assessment wave was in 2008, the time of the data collection for the present study. The PTSD Inventory is a self-report scale consisting of 17 statements corresponding to the 17 PTSD symptoms of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision diagnosis for PTSD.[2] Participants were asked to indicate whether or not they had the symptom in the past month, on a 4-point scale ranging from 1 ("not at all") to 4 ("I usually did"). For each participant, an answer of ≥3 (ie, "often" or "I usually did") was considered a positive endorsement of a symptom. The PTSD Inventory has good psychometric properties in terms of high test-retest reliability and concurrent validity compared with clinical diagnosis.[66] Reliability values for total and subscale scores were high at all assessments (Cronbach α ranging from .78 to .96).

Because dissociation interacts with pain perception among trauma survivors, dissociation was evaluated in the third assessment wave using the Dissociation Experiences Scale-II.[10] This scale consists of 28 questions about dissociative experiences. Participants were asked to rate the frequency of each experience. The total score is calculated by averaging the sum of the scores. The Reliability of the Dissociation Experiences Scale-II was high (Cronbach α = .95). In addition, we also evaluated the perceived magnitude of torture to evaluate the trauma load among the torture survivors. Subjects were asked to rate their physical and psychological suffering as well as their level of perceived humiliation during captivity on a 5-point scale ranging from 1 ("I did not suffer at all") to 5 ("I suffered extremely").

Data Analysis

Data were processed with IBM SPSS Statistics 21 statistics software (SPSS (Hong Kong) Ltd, Quarry Bay, Hong Kong). Parametric and nonparametric models were used to test the effect of group (chronic PTSD, delayed PTSD, PTSD-resilient, healthy control subjects) on the independent variables: chronic pain intensity and extent according to the MPQ, pain threshold, pain tolerance, magnitude of CPM, and magnitude of TSP (continuous variables, described as mean ± SD). The models included main effects and interactions as well as corrected post hoc pairwise comparisons; *P* values < .05 were considered to be statistically significant.

To examine the possible mediation role of PTSD trajectories in the association between captivity (ex-POW vs control subjects) and pain measures we used a bootstrapping method with 1,000 bootstrap resamples.[48] Bootstrapping is a nonparametric approach to effect-size estimation and hypothesis testing that makes no assumptions about the shape of the distributions of the variables or the sampling distribution of the statistic. This approach has been suggested by others as a way of circumventing the power problem introduced by asymmetries and other forms of non-normality in the sampling distribution of *ab*.[63] It also produces a test that is not on the basis of large-sample theory, meaning it can be applied to small samples with more confidence.[49] Bootstrapping generates an estimate of the indirect effect, including a 95% confidence interval (CI). When 0 is not in the 95% CI, one can conclude that the indirect effect is significantly different from 0 at $P < .05$ (2-tailed) and, thus, that the effect of the independent variable (captivity) on the dependent variables (pain measures) is mediated by the proposed mediating variable (PTSD trajectories).

Results

PTSD Trajectories

Using data from the 3 waves of assessment, we classified the ex-POWs into 3 trajectories of PTSD (Table 1): 1) chronic PTSD group—ex-POWs who had PTSD at all 3 assessment waves (n = 12, 20%), 2) delayed PTSD group—ex-POWs who did not have PTSD in the first assessment wave but had PTSD at the second and/or third waves (n = 33, 55%), and 3) PTSD-resilient group—ex-POWs who did not have PTSD at any of the 3 assessment waves (n = 14, 23.3%). We did not include data from ex-POWs in the recovery group because there were none identified as such. The magnitude of PTSD (number of symptoms) among the chronic PTSD groups was significantly higher than that in the delayed PTSD and PTSD-resilient groups along the 3 waves of assessment. The PTSD-resilient group was similar to the control group along the 3 waves of assessment.

There were no significant differences between the 3 PTSD trajectory groups in the level of dissociation ($F_{3,97}$ = .59, P = .62). In addition, the PTSD trajectory groups did not differ in the level of physical suffering ($F_{2,33}$ = .64, P = .54), level of psychological suffering ($F_{2,32}$ = .04, P = .96), nor the level of humiliation ($F_{2,32}$ = .64, P = .54) during captivity. As a result, these variables were not included in the subsequent analyses.

Chronic Pain

Overall, 52 torture survivors (88.13%) and 29 control subjects (65.9%, $P < .01$) reported suffering from

Table 1. Means and SDs of PTSD Severity in Each of the 3 Waves of Assessments According to Group and PTSD Trajectories

	1993		*2001*		*2008*	
Group	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Control group (n = 44)	.68[a]	1.01	1.70[a]	3.25	2.05[a]	3.71
Ex-POW groups						
Chronic PTSD (n = 12)	7.08[b]	2.68	12.25[c]	2.96	12.58[b]	2.46
Delayed PTSD (n = 33)	.58[a]	1.01	10.06[b]	3.77	11.89[b]	3.11
PTSD-resilient (n = 14)	.57[a]	.85	3.29[a]	2.30	2.93[a]	1.72

NOTE. Within the same column, means with different letters are significantly different at $P < .0$.

chronic pain. A significant group effect was found on chronic pain intensity manifested in the indices of the MPQ; number of words chosen ($F_{3,90}$ = 8.25, $P < .01$), PRI ($F_{3,90}$ = 10.16, $P < .01$), and Pmost ($F_{3,90}$ = 3.26, $P < .05$). Post hoc tests revealed that the levels of all of these indices were higher among the chronic and delayed PTSD groups compared with the resilient group and healthy control subjects (Table 2). In addition, the number of painful body regions was significantly higher among the chronic and delayed PTSD groups compared with the resilient and the healthy control groups. The most frequent painful body regions among torture survivors were, in descending order, the back, the nape and neck region, the shoulder region, and feet. The most frequent painful body regions among the controls were the lower back, shoulders, and knees.

Participants of all 3 PTSD trajectories reported taking analgesic medications and/or psychiatric medications with potential analgesic effects, as follows: 10 (83.3%), 22 (66.6%), and 9 (64.3%) of the chronic PTSD, delayed PTSD, and PTSD resilient groups, respectively. Thirty-three healthy control subjects (75%) also reported taking such medications. There were no significant differences in the rate of medication usage between the groups.

Sensory Testing

Table 3 summarizes the differences between the groups in all the variables tested (chronic pain characteristics and pain perception profile) and the trend of the differences. The table shows that the PTSD-resilient group is similar to the control group in most of the variables tested whereas the delayed and chronic PTSD groups are distinctive. In addition, the table presents the gradual worsening of the variables tested with the increase in the severity/chronicity of PTSD. The details of the observed between-group differences are presented in the following sections of the results.

Table 2. Means and SDs of Chronic Pain Indices According to Group and PTSD Trajectories

		ex-POW Group		
	Control Group	PTSD-Resilient	Delayed PTSD	Chronic PTSD
Number of words chosen				
Mean	5.96[a]	6.42[a]	10.06[b]	11.70[b]
SD	3.60	3.78	4.60	3.40
PRI				
Mean	11.88[a]	13.91[a]	22.32[b]	24.00[b]
SD	7.56	8.22	9.54	6.46
Pain at its worst				
Mean	3.8[a]	3.6[a]	4.2[a]	4.7[b]
SD	.9	1.0	.9	.8
Number of pain areas				
Mean	.59[a]	2.01[a]	2.48[b]	2.83[b]
SD	.4	.9	1.6	.8

NOTE. Means within the same row with different letters were significantly different at $P < .05$.

Table 3. Summary of Effects of Torture/PTSD on Chronic Pain and Pain Perception Indices

		ex-POW Group		
	Control Group	PTSD-Resilient	Delayed PTSD	Chronic PTSD
Number of words chosen	→	→	↑↑	↑↑
PRI	→	→	↑↑	↑↑
Pmost	→	↑	↑	↑↑
Number of pain areas	→	→	↑↑	↑↑
Heat pain threshold	→	→	→	→
Heat pain tolerance	→	→	→	→
CPM	→	↓	↓↓	↓↓
TSP	→	→	↑	↑↑

NOTE. → indicates normal (or similar to controls), ↑/↓ indicates moderately enhanced/reduced, and ↑↑/↓↓ indicates severely enhanced/reduced.

Pain Thresholds

The effect of group on pain threshold (df = 3, f = .16, $P = .92$) and on pain tolerance (df = 3, f = 1.01, $P = .82$) was not significant, suggesting that the chronic PTSD and delayed PTSD groups did not differ from the PTSD-resilient and control groups.

CPM

Fig 1 presents the magnitude of CPM for each of the 4 groups. A significant group effect was found for CPM magnitude (df = 3, f = 5.58, $P < .01$). Post hoc analysis revealed that the chronic PTSD and delayed PTSD groups exhibited lack of CPM, as evident by the slight increase in pain intensity (from 5.2 ± 1.8 to 5.6 ± 2.0 VAS units, delta of .37 ± .9, and from 5.7 ± 1.6 to 6.4 ± 2.1 VAS units, delta of .66 ± 1, respectively). In contrast, the PTSD-resilient and healthy control groups had CPM as evident by the decrease in pain intensity (from 5.6 ± 1.9 to 4.7 ± 1.6 VAS units, delta of −.88 ± 1.1, and from 5.4 ± 2.1 to 3.8 ± 1.7 VAS units, delta of −1.6 ± 2, respectively) that was significantly larger

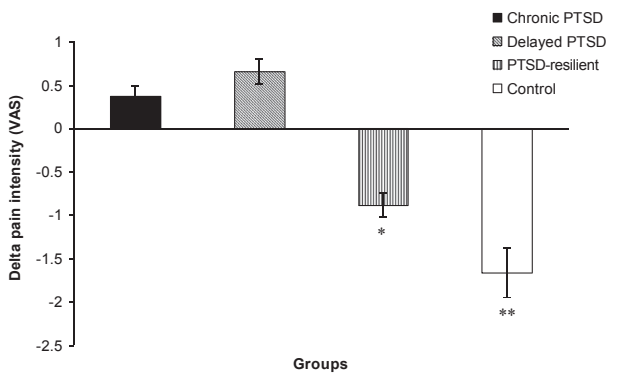

Figure 1. The chronic PTSD and delayed PTSD groups exhibit lack of CPM evident by the increase in pain intensity in the presence of the conditioning stimulus whereas the PTSD-resilient and healthy control groups exhibit CPM evident by the significant decrease in pain intensity (*$P < .05$, **$P < .01$), that of control subjects being significantly better than that of PTSD-resilient subjects. Bars denote mean ± SD.

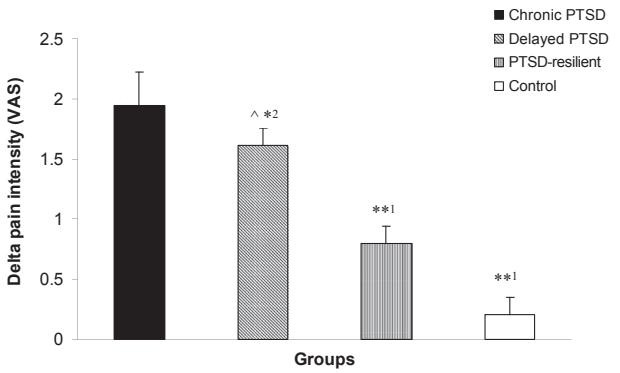

Figure 2. The chronic PTSD group exhibits more pronounced TSP than all other groups; (delayed PTSD: ^ P = .05, PTSD-resilient and healthy control subjects: **1 P < .01, each) and the delayed PTSD group had larger TSP than the PTSD-resilient and healthy control groups (*2 P < .05). Bars denote mean ± SD.

than the chronic PTSD and delayed PTSD groups (P < .05, P < .01, respectively).

TSP

Fig 2 presents the magnitude of TSP for each of the 4 groups. A significant group effect was found for TSP magnitude (df = 3, f = 4.57, P < .01). Post hoc comparisons revealed that the magnitude of TSP exhibited by the chronic PTSD group (an increase from 1.9 ± 1.5 to 3.9 ± 2.5 VAS units, delta of 1.94 ± 2) was more enhanced than that of all other groups; the delayed PTSD group (from 2.4 ± 1.9 to 4.0 ± 2.2 VAS units, delta of 1.61 ± 1, P = .05), the PTSD-resilient group (from 2.2 ± 1.9 to 3.1 ± 1.6 VAS units, delta of .8 ± 1, P < .01), and the healthy control group (from 2.21 ± 1.9 to 2.5 ± 2.0 VAS units, delta of .29 ± 1, P < .01). The delayed PTSD group had larger TSP than the PTSD-resilient and healthy control groups (P < .05 each; Fig 2).

Mediation Effect of PTSD Trajectories

The mediated roles of PTSD trajectories in the relationship between captivity and chronic pain variables were nonsignificant; PRI (mediated effect = 6.83, standard error [SE] = 4.38, 95% CI = −1.94 to 15.12), pain intensity at its least (mediated effect = .62, SE = .40, 95% CI = −.20 to 1.33), Pmost (mediated effect = .11, SE = .32, 95% CI = −.52 to .71), and number of pain areas (mediated effect = .58, SE = .47, 95% CI = −.31 to 1.55). The mediating role of PTSD trajectories in the relationship between captivity and TSP was also nonsignificant (mediated effect = .14, SE = .65, 95% CI = −1.12 to 1.50).

However, significant accelerated corrected-bias bootstrap analyses indicated that PTSD trajectories significantly mediated the relationship between captivity and CPM (mediated effect = 1.90, SE = .76, 95% CI = .56–3.55, Sobel z = 2.36, P < .05; Fig 3). The variance in CPM was accounted for by captivity, whereas PTSD trajectory regression was significant (β = −3.59, SE = .89, t_{93} = −4.02, P < .001). Hence, the relationship between captivity and CPM was partially mediated by PTSD trajectories—exposure to captivity increased the risk for chronic PTSD—which in turn was related to lower CPM.

Discussion

Reduced CPM, enhanced TSP, and chronic pain were significantly more pronounced among torture survivors with chronic/delayed PTSD than resilient participants and control subjects. PTSD mediated the relationship between captivity/torture and CPM.

The Effect of Trauma

Pain thresholds were similar across groups indicating that neither captivity/torture nor PTSD were associated with changes in pain sensitivity. Others have documented mechanical hyperalgesia and thermal hypoesthesia in the feet of falanga victims.[52-54,71] However, this was found in painful, previously tortured body regions, whereas we tested pain-free body regions not subjected to torture. Inconsistencies regarding pain threshold were also found among subjects with PTSD after other traumatic events, being higher,[14,16,20,26,40,68] lower,[18] or similar[58] to control subjects and also after psychological trauma without full-blown PTSD.[70] These inconsistencies may stem from the high between- and within-subjects' variability in pain threshold, the trauma inducing the PTSD and the sensory modality used.

Despite normal pain sensitivity, torture survivors exhibited abnormal CPM and TSP, suggesting their ability to inhibit and modulate noxious stimuli is significantly reduced. Although we could not find comparable studies on torture survivors, studies on PTSD participants have shown increased TSP[38] and increased pain ratings compared with control subjects.[14,16] Furthermore,

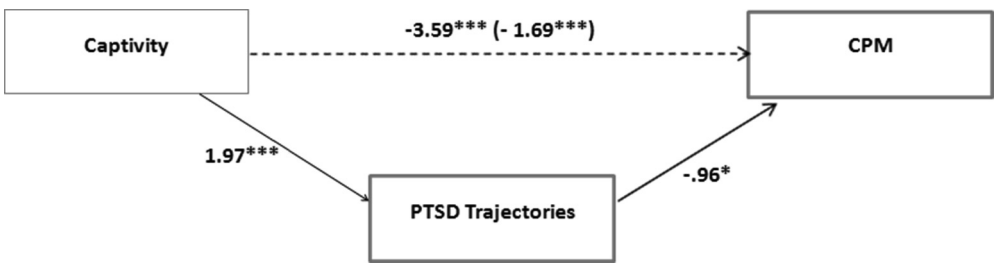

Figure 3. PTSD trajectories as mediator in the relationship between captivity and CPM. All coefficients represent unstandardized regression coefficients. Solid lines represent significant predictions. Dashed lines represent nonsignificant predictions. The value in the parentheses represents coefficient before entering PTSD trajectories to the model (*P < .05, ***P < .001).

higher pain ratings were correlated with anxiety level and PTSD symptomatology.[16] Further evidence is the reduced pain modulation among participants with posttraumatic headache with high PTSD levels.[15] These findings support the association between PTSD and reduced pain modulation.

Interestingly, PTSD trajectory did not affect pain or intolerance thresholds but did affect pain modulation. Pain thresholds measure the sensitivity to pain in a particular moment in time, whereas CPM and TSP evaluate traits of the pain system.[4] Thus, CPM and TSP are more likely to be affected by trauma, exhibiting long-term changes. Furthermore, testing on intact body regions may reflect intact pain thresholds in these regions whereas CPM and TSP, which reflect general processing, may be affected regardless. Remarkably, under induction of negative emotions PTSD participants exhibited increased pain inhibition,[18,28] which may seem to counteract the current findings. However, our findings reflect the baseline status of PTSD participants, which may not predict responses to acute stress.

The Role of PTSD Trajectories

The alteration in CPM and TSP among torture survivors showed a gradient according to PTSD trajectories; the most in torture survivors with chronic PTSD, less so in the delayed PTSD group and the least in the PTSD-resilient group. The former 2 groups had more intense chronic pain occupying more body regions than the latter group. Interestingly, the PTSD trajectories subgroups did not differ in the physical or psychological suffering during captivity, suggesting that the trauma load was similar across groups. Thus, exposure to trauma per se (ie, captivity/torture), or its magnitude, may not be the only factor responsible for the alterations in pain perception. Dissociation level also does not appear to play a role. Conversely, posttraumatic distress and PTSD trajectory seem to have an important role in pain modulation and reactivity.

Indeed, the mediation analysis suggested that PTSD trajectory not only predicted dysfunctional pain modulation but may also underlie its mechanism. Namely, dysfunctional pain modulation may develop among trauma survivors with longer and more severe PTSD. In contrast, the pain system of PTSD-resilient survivors was far less affected despite having shared the same traumas. Exposure to trauma is thus not sufficient to produce alterations in pain modulation, rather it is the PTSD and its duration/intensity that influences responses to experimental and clinical pain. Furthermore, torture survivors underwent multiple event trauma exposure, which induces stronger effects than a single event trauma,[21] possibly further contributing to the differences observed in this study.

Interestingly, individuals with early childhood abuse/neglect and PTSD were at a significantly increased risk of pain,[55] supporting the possibility that PTSD is more crucial than the trauma itself in pain-related pathologies. A gradual increase in the prevalence of chronic pain among torture survivors over 10 years[43] and worsening posttraumatic headache over time among people with PTSD[56] may have resulted from longitudinal changes in PTSD trajectories.

It is important to note that because PTSD is a complex disorder characteristic of significant distress and negative mood (eg, depression, fear, and anxiety),[5,61] it is difficult to indicate whether the PTSD trajectories herein reflect a specific, unique feature above and beyond distress or negative mood trajectories. In the present study, individuals with chronic- and delayed PTSD exhibited PTSD symptoms at the time of pain testing, however, they differed in the duration of the disorder and thus in their social and psychological resources. For example, veterans who presented with more adaptive emotional coping, were more likely to have delayed PTSD[24] and lower pain severity and interference.[1,39] It is therefore possible that the alterations in pain among our participants grew in magnitude and extent according to the duration of PTSD and its consequences. A follow-up study on the development of PTSD and pain among injured accident survivors showed that within the first 6 months a mutual effect of pain and PTSD symptoms was observed, whereas at 12 months the pain intensity was significantly influenced by PTSD symptoms but not vice versa.[22] Thus, chronic pain and dysfunctional pain modulation among torture survivors, years after release from captivity, were probably influenced by the prolonged presence of PTSD and/or the resultant distress and not vice versa.

Torture survivors in our study were exposed to trauma during early adulthood. Therefore, the emergence of PTSD at a younger age and the continuing and intensifying symptoms over time took a greater toll on those with chronic PTSD. Those with delayed and chronic PTSD were found to have significantly more difficulties in social functioning and fewer social resources.[65] However, those with chronic PTSD were less able to develop meaningful relationships and satisfying careers, and hence had significantly lower psychological and social adjustment.[65] Studies suggest that negative emotions are related to increased levels of experimental and clinical pain.[8,29,45,47,69,73] This study contributes further evidence that the longer the exposure to negative emotions and prolonged distress the lesser the coping resources, the higher the risk for chronic pain and dysfunctional pain modulation.

To the best of our knowledge this study is the first to assess the implications of PTSD trajectories in pain perception among torture survivors. Future studies are encouraged to include a more comprehensive assessment of distress and indicators of mood to discern their specific influences on pain perception in the wake of trauma. The possible unique contribution of PTSD in the present study thus remains speculative although previous studies provide some supportive evidence. For example, PTSD individuals were found to exhibit different pain perception profile[14,40] and neuroimaging data[19] than those with anxiety disorders. Neither chronic pain intensity nor pain perception correlated with anxiety or depression levels among PTSD veterans[14] or torture survivors.[54] In the

present study, specific indicators of torture-related distress (physical and mental suffering in captivity) were similar across the PTSD trajectories subgroups. Overall, we may conclude that more intense and prolonged posttraumatic distress/affective disturbance is associated with more altered pain modulation among trauma survivors.

Possible Mechanisms

The mechanism by which PTSD and its resultant distress induce alterations in the pain system is not fully understood. Bottom-up and top-down influences may play a role. Bottom-up influences are related to tissue damage inflicted during torture. Tissue injury generates a chain of events leading to nociceptive inputs followed by pathological changes (eg, sensitization) in the peripheral and central levels of the pain system.[11,77,79] Alterations in the pain processing brain regions may occur months after tissue injury and coincide with the development of pain behavior.[33] Thus, tissue injury may induce long-term alterations in pain perception and modulation leading to chronic pain.

Regarding top-down influences, imaging studies show that induction of negative mood and anxiety increases pain-evoked activation in a number of cortical regions, such as the prefrontal and anterior cingulate cortices.[8,31,46,47,59,73] Frontoperiaqueductal gray circuitry is likely involved in pain modulation,[34,73] specifically in CPM and TSP.[44] Alterations in this circuitry may be partly responsible for intense chronic pain and reduced pain modulation, perhaps more so among especially vulnerable subjects (eg, those with chronic-PTSD in our study). The amygdala is linked to the caudate nucleus[27,60] and to brain stem structures that exert descending pain inhibition.[41,44] Deactivation of the amygdala, observed in distress-related conditions as in PTSD,[20,26,36,62] may thus render painful stimuli to be perceived as more intense, and may also be involved in the reduced pain modulation seen in our study. Interestingly, amygdala deactivation has been associated with the opposite phenomenon, of decreased pain sensitivity in those with borderline personality disorder,[57] suggesting that it may differentially affect pain modulation depending, perhaps, on the disorder.

Conclusions

PTSD trajectories were assessed longitudinally, however, it is uncertain whether the dysfunctional pain modulation among the chronic or delayed PTSD groups preceded or resulted from chronic pain, or whether both developed simultaneously. Studies assessing the interaction between pain modulation and posttraumatic distress in a longitudinal manner may further clarify this issue. Additionally, the sensory profile may have been influenced by medications that may have affected CPM or pain threshold.[7,30] This possibility, however, seems unlikely considering the similar rate of participants of all 4 subgroups using such medications.

Overall, it appears that the magnitude and duration of PTSD and its resultant distress, rather than exposure to trauma, are implicated in the association between trauma and altered pain perception/modulation; the stronger the magnitude and the longer the duration of PTSD/distress, the higher the risk for chronic and perhaps irreversible changes in the pain system.

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