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# Explaining very early acute mild traumatic brain injury after motor vehicle collision pain variability: additive value of pain sensitivity questionnaire

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# Abstract

**Introduction and Objectives:** Chronic pain is a common postcollision consequence. Wherein, a clearer understanding of acute pain can help stem the acute-to-chronic pain transition. However, the variability of acute pain is only partially explained by psychophysical pain characteristics as measured by quantitative sensory testing. The Pain Sensitivity Questionnaire (PSQ) may reflect inherent psychocognitive representations of patient's sensitivity and thus may reveal less-explored pain dimensions. In the vein of the biopsychosocial approach, this study aimed to explore whether PSQ holds additive value in explaining head and neck pain reports in very early acute-stage mild traumatic brain injury (mTBI) after collision, above the use of psychophysical assessment. **Methods:** Study cohort (n = 130) consisted of mTBI patients (age range 19–66, 57 F) after accident with area-of-injury pain of at least 20 on the day of testing (mean pain 58.4  $\pm$  21.6, range 20–100 Numerical Pain Scale) who underwent clinical, psychophysical, and pain-related psychological assessment within 72-hour after injury.

**Results:** Pain Sensitivity Questionnaire scores were significantly correlated with acute clinical, psychophysical, and pain-related psychological measures. Regression model ( $R^2 = 0.241$ , P < 0.001) showed that, together, age, sex, high PSQ, enhanced temporal summation, and less-efficient conditioned pain modulation explained head and neck pain variance. This model demonstrated that the strongest contribution to degree of postinjury pain was independently explained by PSQ ( $\beta = 0.32$ ) and then pressure pain threshold-conditioned pain modulation ( $\beta = -0.25$ ).

**Conclusion:** Appraisal of cognitive daily-pain representations, by way of memory and imagination, provides an additional important dispositional facet to explain the variability in the acute mTBI postcollision clinical pain experience, above assessing nociceptive responsiveness to experimentally induced pain.

Keywords: Mild traumatic brain injury, Pain, Quantitative sensory testing, Pain Sensitivity Questionnaire, Motor vehicle collision

# 1. Introduction

According to the pain matrix theory,<sup>25,26</sup> pain results from complex nociceptive processes, which mediates not only the physiological component, but also the emotional or cognitive aspects.<sup>17,30</sup> Furthermore, although there is growing recognition

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of the importance of the biopsychosocial view of pain in various disciplines, the exact interplay of factors, specifically among clinical situations, requires further work.<sup>22</sup> Wherein, a core issue is that only a portion of individuals who experience acute pain resultant from illness or injury will go on to develop chronic pain, and to date, no consistent parameters have been observed to be able to predict the acute-to-chronic pain transition. Pain sensitivity reflects an individual's pain perception and may be, among other variables, a risk factor for chronic pain development.<sup>9</sup>

Quantitative sensory testing (QST) is increasingly wellestablished as a measure of nociception assumed to depict an individual's pain modulation profile (PMP), which ranges between inhibitory (antinociceptive) to facilitatory (pronociceptive).<sup>16</sup> By use of dynamic QST, more specifically conditioned pain modulation (CPM), which reflects descending modulation, and temporal summation (TS), which reflects ascending modulation, individuals can be positioned on the clinical nociceptive spectrum; wherein, pronociceptive individuals express a higher pain phenotype, resultant in higher risk of pain acquisition and/or chronification.<sup>15,16,28,41</sup> Although much dynamic QST research

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explores chronic pain populations,<sup>15,21,29,41</sup> and acute postoperative pain models,<sup>2,10,12</sup> less research has focused on postinjury pain, particularly in the very early phase, which may represent different neuromatrix inner workings. In addition, the current psychophysical PMP model does not adequately explain the variance observed in acute clinical populations and has shown high interindividual variability. As such accompanying tools should be considered which may reveal emotional or cognitive pain components which are not yet comprised within.

The Pain Sensitivity Questionnaire (PSQ) is based on intensity appraisal of imagined, typically painful daily life experiences and has been suggested to be supplemental to experimental pain paradigms which can be time consuming and require the participant to undergo pain.<sup>33</sup> Self-report questionnaires carry the additional advantage of being easily administered and require no advanced training, whereas QST uses a physical stimulus to evoke nociceptive processes, PSQ rests on cognitive representations of previous or expected pain experiences. Among chronic pain patients, PSQ scores were found to be correlated with experimental pain testing performed outside of the clinical pain site<sup>34,35</sup> and clinical pain intensity, <sup>18,35</sup> as well as number of pain sites.<sup>20</sup> and were found to be predictive of acute postoperative pain.<sup>32</sup> As PSQ spans various modalities and body sites, reflecting cross-situational<sup>5</sup> and structural consistency,<sup>24</sup> and has shown good test-retest reliability in healthy controls<sup>33</sup> and chronic pain patients,18 its values may reflect a more stable tendency. Based on previous findings relating to both experimental and clinical pain, it stands to reason that pain sensitivity, as obtained by PSQ, may not only be correlated in acute postinjury pain conditions but also has the potential to expand the psychophysical PMP. This is in light of previous suggestions of developing a more comprehensive view of pain mechanisms by way of incorporating psycho-cognitive factors into QST assessment.31

Mild traumatic brain injury (mTBI) after motor vehicle collision (MVC) represents an excellent clinical model for the study of acute postinjury pain because it embodies a population of otherwise healthy and pain-free individuals whose response to a traumatic event ranges from full recovery to long-term chronic pain and disability. This is important as although oftentimes compared, post-traumatic and post-surgical pain represent 2 distinctive models for the study of acute pain, due in part to the cognitive attributions each may hold. We<sup>19</sup> have recently reported that these patients are psychologically similar to healthy controls in most pain-related psychological characteristics, which bolsters the likelihood that their results are generalizable. Given that most of the work regarding PSQ has been performed in the chronic stage, a preliminary goal was to examine the association between clinical and experimental pain and the PSQ in acute pain patients. Moreover, an additional aim was to explore whether comprehensive QST evaluation together with PSQ assessment, at the very early acute postinjury pain phase before event-related psychological and nociceptive changes occur, can provide additive information to explain the variability of pain reports.

### 2. Materials and methods

### 2.1. Participants

Patients were recruited when visiting the Rambam Health Care Campus emergency department. Inclusion criteria: diagnosis of mTBI injury in road accident up to 24 hours before ER arrival; direct or indirect head and neck injury with complaints of pain, Glasgow coma scale 13 to 15 with no subsequent decline; no traumatic findings in computed tomography if performed; no, or shorter than 30 minutes loss of consciousness and presence of alteration in brain function (eg, confusion and dizziness)<sup>27</sup>; and age 18 to 70 years, both men and women. Exclusion criteria: other major bodily injuries from the accident; previous chronic head/neck pain that requires regular treatment; neurological disease that might affect testing ability or interpretation such as neurodegenerative diseases; any head and neck injury in past year; and any pain condition that requires daily pain medication.

# 2.2. Patient consent forms

The institutional review board of Rambam Health Care Campus approved the study protocol in accordance with The International Helsinki Declaration (No. 0601-14). Written informed consent was obtained from each participant in the presence of a certified physician before any data collection or assessment.

# 2.3. Study design

This is a secondary analysis of cross-sectional data. Patients are part of a larger ongoing study aimed at understanding the trajectory of mTBI with concurrent initial pain, wherein they are recruited in the very early acute postaccident phase and followed for 1 year. A session was scheduled within 72 hours after injury (average days since accident =  $1.7 \pm 0.9$ ) for magnetic resonance imaging (MRI), clinical, psychophysical, pain-related psychological, and neurophysiological assessment. Blood was drawn for genetics. MRI session included: anatomical, fMRI, and DTI scans. Clinical baseline assessment consisted of patients' demographic information, self-reported pain intensity levels, number of postaccident body areas with pain, and use of analgesics.

# 2.4. Pain-related psychological assessment

To attain more insight into several pertinent personality features, previously found to contribute to the pain experience, participants were asked to complete the following questionnaires, using the validated Hebrew version of each, on the day of the psychophysical assessment<sup>3,8,11</sup>:

### 2.4.1. Pain Catastrophizing Scale

Pain Catastrophizing Scale is a self-report 13-item questionnaire providing ratings based on painful life situations. The instrument represents the 3 components of pain catastrophizing: rumination (eg, "I can't seem to keep it out of my mind"), magnification ("I wonder whether something serious may happen"), helplessness ("There is nothing I can do to reduce the intensity of pain"), and can be both situational and dispositional.<sup>37,38</sup> Participants are asked to rate each statement on a 5-point Likert scale ranging from 0 ("not at all") to 4 ("always"). The Pain Catastrophizing Scale provides a total score and 3 subscores. As the main goal was to depict catastrophizing thoughts at the postinjury junction, this questionnaire was completed during the psychophysical assessment as a state/

# 2.4.2. Pain Sensitivity Questionnaire

Pain Sensitivity Questionnaire is a self-report 17-item questionnaire, based on pain intensity ratings of imagined painful daily life situations. The items are rated from 0 ("not painful at all") to 10 ("worst pain imaginable") and span various thermal, chemical, and mechanical pain modalities, noxious intensities, and body sites. Fourteen of the items relate to situations that are painful for most persons and relate to different types of pain (hot, cold, sharp, etc.) (eg, "Imagine you trap your finger in a drawer" and "Imagine you pick up a hot pot by inadvertently grabbing its equally hot handles"). The remaining 3 items (numbers 5, 9, 13) describe normally nonpainful situations (eg, taking a warm shower). The latter are interspersed to serve as nonpainful sensory references for the subjects. The PSQ provides a total, and 2 subscores of minor, which depicts items, which cause a minor amount of pain and moderate, those which cause a moderate amount of pain.

#### 2.4.3. Hospital Anxiety and Depression Scale

Hospital Anxiety and Depression Scale is a self-report 14-item questionnaire devised to be used to measure anxiety and depression in individuals with physical health problems. The questionnaire focuses on nonphysical symptoms, so that it can be used to diagnose depression in people with significant physical ill health.<sup>36</sup> The items are rated from 0 (negative response) to 3 (very positive response). Seven of the items relate to anxiety, and 7 depression, and as such, Hospital Anxiety and Depression Scale provides 2 scores.

# 2.4.4. Perceived Stress Scale

Perceived Stress Scale is a widely used self-report 10-item questionnaire devised to measure the perception of stress. It is a measure of the degree to which situations that occurred within the last month are appraised as stressful. The items are designed to assess how unpredictable ("how often have you been upset because of something that happened unexpectedly"), uncontrollable ("how often have you felt that you were unable to control the important things in your life?"), and overloaded ("how often have you felt that you were on top of things?") the subjects find their lives to be. The items are rated from 0 ("never") to 4 ("very often"), 6 items are worded negative, and 4 are positive. Patients were instructed to include within the month framework the stress related to the accident as well.<sup>6</sup>

### 2.5. Psychophysical assessment

For full-study protocol please see our previous article.<sup>19</sup> It should be noted that the heat pain, cold pain, and pressure pain thresholds (PPTs) were tested within the area of injury (trapezius), whereas all other testing was performed in remote areas (hand or arm).

The following, in short, is the protocol used for mechanical TS (mTS) and PPT-CPM, the measures which were included in the final model.

### 2.5.1. Mechanical TS

Measured using the 256 mN weighted pinprick (DFNS Protocol Issued, Germany). Numerical Pain Scale was obtained after a single application and after the last application in a series of ten 1 Hz repetitive stimuli delivered to the dorsal area of the left hand. Last minus first score was taken as the mTS.

# 2.5.2. Training

Participants were exposed to 3 short pressure stimuli (PPT) and cold water ( $8^{\circ}C-10^{\circ}C$ ) by nondominant hand immersion in the bath for 5 seconds. Participants were asked to rate pain intensity (NPS) at the end of the immersion; if the temperature failed to evoke pain of 20 or greater (0–100 NPS), it was lowered to 4°C to 6°C.

#### 2.5.3. Conditioned pain modulation assessments

The test stimulus comprised 2 types of consecutive stimuli. A combination of 3 PPT stimuli on the trapezius muscle with an inter-stimulus interval of 3 to 5 seconds, followed by a tonic 20 seconds contact heat stimulus on the dominant volar forearm at the Pain50 temperature. The pressure stimuli were delivered with a 1  $\times$  1 cm contact FDN 100 Pressure Algometer (Wagner Instruments, Greenwich, CT) with the experimenter increasing the pressure by 0.5 kg/s (corresponding to 50 kPa/s).

After a 5-minute break, the "conditioning stimulus" is given by 10-second immersion of the nondominant hand in the cold-water bath. Then, the 3 PPT measurements and "thermal test stimulus" were repeated during the immersion. Pain ratings to the conditioning stimulus obtained 10 seconds (preapplication of conditioned stimuli) and 60 seconds (end of immersion) after initiation. The difference between the "test stimuli" (mean PPT value) obtained during the "conditioning stimulus" vs the baseline application was taken as the CPM response.

### 2.6. Statistical analysis

All statistical analyses were performed using JMP version 14 (SAS Institute, Cary, NC). The dependent variables were the intensity of head and neck pain at the very early acute stage (<72 hours). Preliminary analysis determined that both head and neck pain scores were correlated with PSQ scores and QST variables. As such, the scores of mean head and neck pain ratings were averaged to represent area-of-injury pain intensity after accident. The combined score will be referred to as "area-of-injury pain" or "pain."

As this study was aimed at post-mTBI patients with clinically significant acute pain, only those who reported area-of-injury pain of 20 (0–100 NPS) or higher were included in the analyses. As an exact consensus has yet to be reached in the pain community regarding "clinically significant pain" definition, this cutoff was setbased consultation with clinical pain experts and on the accumulative experience found during QST, in which pain reports below 20 were not perceived by subjects as painful, nor able to induce top-down regulation.<sup>1,13,15,40</sup> Eighteen patients (12.2%), out of 148 recruited participants, who reported not clinically significant pain levels (0–19 NPS) on the day of testing, were excluded from the final analysis. All reported values refer only to the 130 included participants.

To elucidate the characteristics of the PSQ as a potential feature involved in the prediction of pain variability, PSQ scores (mild and total) served as independent variables.<sup>34</sup> Distribution of variables was determined to be normal, and as such, correlation of PSQ values (mild and total) and all QST, pain-related personality, and clinical pain (area-of-injury pain and number of painful body areas) measures was performed using Pearson tests.

As both the minor and total PSQ scores were found to be correlated with the other pain-related psychological, clinical, and psychophysical measures, PSQ total score was used for the duration of the analysis. Regression analysis was used to identify the relative contribution of each of the relevant QST and PSQ measures to explain the variability of the clinical pain. Multicollinearity in the regression model was avoided by attention to correlations among predictors, in that the QST measures, which were chosen to be included in the model, were first checked to assure that they were not significantly correlated with the PSQ. Mean and SDs were computed for the various parameters of the study data. Statistical significance was set at P < 0.05.

	e 1	

Values for included psyc	hophysical and pain-rela	ted psychological measures.

Measure	Mean + SD	Range in cohort	Range for questionnaire
Heat pain threshold (HPT) (°C)	45.14 ± 4.77	14.7 to 50.8	
Cold pain threshold (CPT) (°C)	9.26 ± 8.94	0 to 39.9	
Electrical temporal summation (eTS) (NPS)	24.3 ± 21.39	-40 to 80	
mts (NPS)	12.14 ± 16.93	-30 to 70	
Pain50 temperature (°C)	44.99 ± 3.11	35 to 50	
PPT test stimulus (kg)	3.10 ± 1.90	0.1 to 10	
1st cold water (NPS)	45.65 ± 27.20	0 to 100	
PPT-CPM (kg)	0.16 ± 0.89	-2.13 to 3.87	
Heat pain-CPM (Heat-CPM) (NPS)	$-8.94 \pm 20.29$	-75 to 50	
HADS—anxiety	$7.40 \pm 5.08$	0 to 21	0–21
HADS-depression	4.07 ± 3.51	0 to 16	0–21
PSQ minor score	4.01 ± 1.84	0.7 to 9.9	0–10
PSQ total score	5.00 ± 1.71	1.2 to 9.7	0–10
PCS	22.78 ± 10.78	2 to 46	0–52
PSS	15.44 ± 6.26	0 to 26	0–40

CPM, conditioned pain modulation; HADS, Hospital Anxiety and Depression Scale; mTS, mechanical TS; NPS, Numerical Pain Scale; PCS, Pain Catastrophizing Scale; PPT, pressure pain threshold; PSS, Perceived Stress Scale; PSQ, Pain Sensitivity Questionnaire; TS, temporal summation.

## **3. Results**

A total of 130 post-MVC patients with an mTBI were recruited (age  $37.0 \pm 12.0$ , range 19-66, 57 F) who reported an area-ofinjury pain of at least 20 on the day of testing (mean pain  $58.4 \pm 21.6$ , range 20-100 [NPS]) and a mean number of painful body areas of  $3.2 \pm 1.3$  (range 1-7).

Forty-two of 130 patients indicated analgesic consumption in the preceding 24 hours; 39 took paracetamol or a nonsteroidal anti-inflammatory, and 3 participants were given an opioid.

**Table 1** lists the mean and ranges for the included pain-related psychological and psychophysical measures.

As a preliminary, exploratory stage, to examine whether the PSQ is associated with other pain-related psychological and psychophysical measures as obtained in the acute postinjury phase within a painful cohort, simple correlation analysis was performed.

# 3.1. Correlations between pain-related personality characteristics

Positive correlations were found between the minor subscale of the PSQ as well as the total score and the total scores for pain catastrophizing, depression, and perceived stress. For the subscale of anxiety, no significant correlations were found (**Table 2**). That is to say individuals with high total pain sensitivity also reported higher levels of postaccident catastrophizing (r = 0.48, P < 0.001), depression (r = 0.23, P = 0.013), and stress (r = 0.23, P = 0.018).

# 3.2. Correlations between Pain Sensitivity Questionnaire and clinical and experimental pain

Pain sensitivity was found to be significantly correlated with clinical pain measures of area-of-injury pain and total number of painful body areas for both the minor and total scores (**Table 3**).

Numerous significant correlations were found between pain sensitivity scores and the various static and dynamic experimental pain paradigms (**Table 4**). For example, those with higher pain sensitivity also reported lower heat pain (r = -0.30, P = 0.001) and pressure pain (r = -0.25, P = 0.009) thresholds.

In that, individuals with high pain sensitivity, as obtained by PSQ, demonstrated higher levels of postaccident clinical pain, as well as a more psychophysical pronociceptive pain profile.

# 3.3. Regression analysis explaining postaccident area-ofinjury pain variance

To explore whether pronociceptive PMP, as obtained by ascending and descending QST measures as well as pain sensitivity scores, explains enhanced clinical pain, we conducted a regression model. Area-of-injury pain intensity was chosen as the outcome measure to represent clinical pain because it encompasses common post-MVC complaint. As the injury comprised elements of musculoskeletal complaints, mechanical modalities were chosen specifically to represent both ascending and descending pain modulation function, mTS for facilitation, and pressure pain-CPM for inhibition.

#### Table 2

Correlation between pain-related personality factors.

	PCS—total score	PSS—total score	HADS—anxiety	HADS—depression
Minor PSQ Score				
Pearson correlation	0.510	0.227	0.110	0.299
Р	<0.001	0.017	0.247	0.001
Total PSQ Score				
Pearson correlation	0.484	0.226	0.162	0.233
Ρ	< 0.001	0.018	0.088	0.013

HADS, Hospital Anxiety and Depression Scale; PCS, Pain Catastrophizing Scale; PSS, Perceived Stress Scale; PSQ, Pain Sensitivity Questionnaire.

Table 3	
Correlations between PSQ values and clinical pa	ain.

		Minor PSQ score	Total PSQ score
Mean area-of-injury pain Average score of 58.4 $\pm$ 21.6 (NPS)	Pearson correlation P	0.332 <0.001	0.263 0.006
Painful body areas Average number: 3.2 $\pm$ 1.3	Pearson correlation $P$	0.298 0.001	0.280 0.003

NPS, Numerical Pain Scale; PSQ, Pain Sensitivity Questionnaire.

This model ( $R^2 = 0.241$ , P < 0.001) showed that, together, age, sex, high PSQ, enhanced mTS, and less-efficient PPT-CPM explain elevated pain-intensity reports. **Table 5** shows the model, which demonstrates that indicators of the inhibitory pathways, as well as the patients' self-report of inherent pain sensitivity, independently contain additive value in determining the intensity of mTBI after MVC pain. The beta values of the model demonstrate that the strongest contribution to degree of postinjury pain was provided by PSQ ( $\beta = 0.32$ ) and then PPT-CPM ( $\beta = -0.25$ ).

The addition of the other pain-related personality factors did not significantly influence the model (model not included).

### 4. Discussion

This study was conducted to better address whether pain sensitivity, as obtained by the PSQ as a questionnaire, and not through direct noxious stimulation by way of QST, can add to the understanding of the clinical head and neck pain variability reported by acute post-traumatic patients at the very early phase. The main study question aimed to explore whether using the PSQ can add an additional layer to the traditional view of QST-based PMP or "pain hypersensitivity." This move is critical because pain research has seen an upswing of work bringing the psychological components of an individual's experience to the forefront. Accordingly, those with a pronociceptive profile are at higher risk for both pain acquisition and chronification,<sup>14,16,41</sup> putting them at greater need for targeted intervention. The chosen cohort of individuals with acute post-traumatic pain due to MVC offers a unique opportunity to explore pain variability in a setting in which there exists an interplay between clinical pain, contextual psychological factors, and the cognitive processes necessary to interpret and respond to the event. To that end, postinjury individuals with acute pain at the very early phase after injury, who were previously found to be psychologically similar to healthy controls,<sup>19</sup> were investigated.

Our findings of correlations between PSQ and several clinical, experimental, and pain-related psychological components support the notion that cognitive representations of pain can be relevant to address the variability, not only of the chronic, but also the acute pain experience. For example, greater pain sensitivity as obtained by the PSQ was associated with enhanced clinical pain ratings within the area of injury and higher number of painful postaccident body sites, as well as static QST measures of lower heat and cold pain thresholds. These findings expand upon what is already known for remotely performed experimental and clinical parameters among chronic pain patients<sup>20,34,35</sup> and extends the previously found correlations to testing performed within the clinical pain site as well. Although in some cases only mildmoderate, the correlations provided the base, which allowed us to further address the main study question of the additive value of self-report pain sensitivity in discussing the complexity of the postcollision acute pain picture.

Interestingly, although the PSQ was found to be correlated with sensory testing of several modalities, the significant correlations were observed mostly within the static tests, with only heat pain CPM significant among the dynamic tests. This is not unusual as previous literature' found that the PSQ was only weakly correlated with indicators of central sensitization. In addition, it has been stated<sup>33,34</sup> that the PSQ was designed to reflect general pain sensitivity, which is better expressed by static experimental tests and not pain modulation, further reinforcing its place as an independent explanatory factor for clinical pain, even when used in conjunction with a dynamic QST protocol. Indeed, the beta values of the regression model showed that the contribution of reported pain sensitivity is independent of the relative contribution of less-efficient descending pathways activity in explaining acute postinjury pain, and more specifically that cognitive representation of inherent sensitivity is a stronger predictor of postcollision mTBI pain variability than experimental efficacy of the inhibitory pathways as obtained at the area of injury. The emerged picture offers a richer perspective of the nociceptive matrix than is reflected by the traditional psychophysical-only PMP.

Table 4

Correlations between PSQ values and experimental pain.

	Minor PSQ	Total PSQ
Heat pain threshold (HPT) (°C) Pearson correlation <i>P</i>	-0.362 <0.001	-0.304 0.001
Cold pain threshold (CPT) (°C) Pearson correlation P	0.301 0.001	0.243 0.010
mTS (NPS) Pearson correlation P	0.167 0.079	0.153 0.108
Electrical temporal summation (eTS) (NPS) Pearson correlation P	0.169 0.079	0.156 0.105
Pain50 (°C) Pearson correlation P	-0.379 <0.001	-0.358 <0.001
PPT test stimulus (kg) Pearson correlation P	-0.286 0.002	-0.246 0.009
1st cold water (NPS) Pearson correlation <i>P</i>	0.310 0.001	0.288 0.002
PPT-CPM (kg) Pearson correlation P	-0.076 0.427	-0.127 0.186
Heat pain-conditioned pain modulation (Heat- CPM) (NPS) Pearson correlation P	0.259 0.006	0.307 0.001

CPM, conditioned pain modulation; mechanical TS; NPS, Numerical Pain Scale; PPT, pressure pain threshold; TS, temporal summation

Table 5

Outcome measure	Model by model fit	Term	Estimate	Р	Std beta
Area of injury pain at baseline ( $<$ 72 h)	r = 0.49	Intercept	44.51	< 0.001	0
	P< 0.001	Age	-0.19	0.257	0.10
		Sex	3.14	0.122	0.14
		mTS	0.03	0.854	0.02
		PPT-CPM	-6.75	0.005	-0.25
		Pain sensitivity questionnaire (PSQ)—total score	4.57	< 0.001	0.32

CPM, conditioned pain modulation; mechanical TS; PPT, pressure pain threshold; PSQ, Pain Sensitivity Questionnaire; TS, temporal summation.

Although experimental dynamic QST measures are believed to reflect "real-life" modulatory mechanisms of patients when encountered with clinical pain,<sup>16</sup> it should be emphasized that this sensory testing happens in a laboratory setting, where the subjects are asked to provide ratings for their current experience in real-time, which leaves the results time-locked to a specific set and setting, which may explain the high interindividual variability that has been previously noted. Whereas completing the PSQ can happen in any setting independent of the participants' current situation or context because its instructions necessitates using cognitive processes such as imagination, memory, and appraisal for a variety of daily-life situations, addressing a different aspect of the pain experience, and allowing it to be used either independently or in conjunction with other pain-related assessments.

In this vein, previous imaging work on the imagination of pain<sup>30</sup> showed that imagination increased the activity of brain regions involved in the pain-related neural network, suggesting that activations during imagination may be based on the cortical representations of the pain neuromatrix. As such, tools which elucidate pain imagination, such as the PSQ, may be reflecting deeper cortical representations of the pain matrix, without necessitating experimentally induced physical pain to occur, wherein those with higher sensitivity scores hold the potential for a more overall pronociceptive pain profile as well.

In addition, the context of the testing takes on even greater importance among a population of post-trauma individuals because their emotional state is liable to influence their pain perception.<sup>4</sup> Although mild-moderate correlations were found among a number of the pain-related personality factors and the PSQ in our study, it would seem that although inherent pain sensitivity is related to an individual's current emotional state, such as their level of stress, representing features of postcollision distress, and can partially represent them, it cannot be fully explained by linear link with situational characteristics. This is in line with previous work<sup>33</sup> in which PSQ was not found to be correlated with state anxiety and depression; a finding which reinforces that the PSQ is largely context-independent, making it suitable for use even among clinical populations who are post-traumatic.

Although this seems to be the first study to explore the use of PSQ in an acute post-traumatic population, it does have several limitations, which should be acknowledged. First, the crosssectional study design does not allow for the drawing of conclusion regarding causality or whether pain sensitivity as expressed by the PSQ is best described as state or trait, future work might consider a longitudinal component to address this. In addition, it is possible that a selection bias occurred during recruitment because only those individuals who could read and write Hebrew were recruited. Similar to this, it is possible that those who spoke Hebrew, but it was not their mother tongue answered the questionnaires differently than they would have had they been administered not in Hebrew. We only recruited individuals with uncomplicated mTBI concurrent with pain and without other major injuries; as such, it is possible that our results cannot be generalized to mTBI populations, which are nonpainful, complicated, or concurrent with other major accident injuries. Future studies should address this, by recruiting uncomplicated mTBI, complicated mTBI and general trauma patients. Finally, it should be stated that the cutoff for "clinically significant pain" was one based on clinical consensus because there is no clear status quo definition, and we acknowledge that this cutoff may have affected the findings. Future work should consider including both painful and nonpainful patients to confirm our results.

In conclusion, the appraisal of cognitive and imagined daily-life pain situations provides an additional facet to explain the variability in the clinical post-traumatic pain experience above and beyond assessing nociceptive responsiveness to experimentally induced pain alone. This suggests that elements such as recall, imagination, and memory are another layer in the pain matrix and should be explored as part of the biopsychosocial approach to pain. The study findings suggest a broader approach to deal with the complexity of positioning the individual on the spectrum ranging from antinociception to pronociception, which is considered as a key element in understanding of pain variability and the acute-to-chronic pain transition.

#### **Disclosures**

The authors have no conflicts of interest to declare.

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