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Deficiency in endogenous modulation of prolonged heat pain in patients with Irritable Bowel Syndrome and Temporomandibular Disorder

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Abstract

Females with Irritable Bowel Syndrome (IBS) and Temporomandibular Disorder (TMD) are characterized by enhanced sensitivity to experimental pain. One possible explanation for this observation is deficiencies in pain modulation systems like Diffuse Noxious Inhibitory Control (DNIC). In a few studies that used brief stimuli, chronic pain patients demonstrate reduced DNIC. The purpose of this study was to compare sensitivity to prolonged heat pain and the efficacy of DNIC in controls to IBS and TMD patients. Heat pain (experimental stimulus; 44.0-49.0°C), which was applied to left palm, was continuously rated during three 30-second trials across three separate testing sessions under the following conditions: without a conditioning stimulus; during concurrent immersion of the right foot in a 23.0°C (control); and during noxious cold immersion in a (DNIC; 8.0-16.0°C) water bath. Compared to controls, IBS and TMD patients reported increased sensitivity to heat pain and failed to demonstrate pain inhibition due to DNIC. Controls showed a significant reduction in pain during the DNIC session. These findings support the idea that chronic pain patients are not only more pain sensitive and demonstrate reduced pain inhibition by pain, possibly because of dysfunction of endogenous pain inhibition systems.

Keywords

Pain modulation; Diffuse noxious inhibitory control; psychophysics; Irritable bowel syndrome; Temporomandibular Disorder; dysfunction; focal heat pain

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Introduction

Pain is a complex phenomenon that is constantly modulated by inhibitory and facilitatory mechanisms. Consequently, extensive research has been focused on the ability of the central nervous system to shape an individual's perception of pain through a number of physiological and psychological factors [23, 33, 35]. A frequently used experimental method that modulates pain via descending inhibition is demonstrated by a "counterstimulation" procedure. Activation of descending inhibitory mechanisms is accomplished by administering a noxious conditioning stimulus at a remote area, which attenuates pain responses to a second focal stimulus, which is known as Diffuse Noxious Inhibitory Control (DNIC) [21, 22, 24, 56]. In healthy pain-free participants, a number of psychophysical studies have demonstrated that a noxious conditioning stimulus significantly reduces the perception of a second experimental stimulus [21, 22, 23, 34, 44, 51, 52, 56, 61, 63, 65].

Dysfunction of CNS pain regulatory systems has been proposed as a significant factor in clinical pain disorders. Psychophysical studies with somatic pain stimuli that examine pain modulation in patients with fibromyalgia [18, 20, 47] and chronic headaches [32, 41] and in older subjects [8, 10, 57] have observed comparable deficits in inhibition of somatic pain using DNIC paradigms. In contrast to somatic processing, several psychophysical studies have shown that Irritable Bowel Syndrome (IBS) [1, 46, 58, 59] patients have reduced capacity to inhibit painful visceral stimulation during cold foot immersion and, therefore, are unable to engage systems believed to underlie DNIC. To the best of our knowledge, no studies have tested the efficacy of inhibition systems on somatic pain in patients with IBS or Temporomandibular Disorder (TMD). A study by Bragdon et al. [2] reported differences in modulation of pain by female patients with temporomandibular disorder (TMD) elicited by a laboratory stressor but not a second painful conditioning stimulus. Overall, reduced endogenous inhibitory capacity is likely to be involved in augmented responses to experimental pain in IBS [30, 40, 54, 55] and TMD [26, 27, 50] patients.

In the present study, we wanted to determine if pain inhibition was diminished in patients with IBS and TMD compared to healthy pain-free controls using a paradigm that has been shown to activate mechanisms underlying DNIC. In contrast to previous DNIC studies, we wanted to compare the usefulness of more prolonged measures of somatic pain sensitivity and its modulation between controls and patients with IBS and TMD. Previous studies have used brief stimuli to examine the efficacy of DNIC in chronic pain groups by evaluating differences in somatic pain thresholds of pressure [17] and electrical [32, 41] stimulation. The hypotheses are that, compared to controls, patients with IBS and TMD will (1) demonstrate a higher baseline sensitivity to prolonged thermal stimulation, indicated by lower temperatures to elicit moderate pain intensity, and (2) fail to suppress heat pain during the immersion with the noxious cold water bath (DNIC session). An additional aim was to determine the temporal profile of prolonged stimulation to reveal the contribution of endogenous systems in the etiology of IBS and TMD.

2. Methods

2.1. Subjects

Twenty-eight female patients with IBS (n = 14) or TMD (n = 14) were recruited from clinics at the University of Florida and the surrounding area. Twenty-eight pain-free female controls were recruited using posted advertisements and word of mouth from the same urban area. No age differences were observed among the three groups as listed in Table 1 ($F = 0.992$, $p = 0.378$).

The inclusion criteria for control subjects included the following: the absence of narcotics or antidepressant use and of conditions or diseases associated with altered pain perception (i.e., neurological or psychiatric disorders, diabetes, or cardiovascular disorders). IBS patients also had to meet the inclusion criteria with the exemption of being diagnosed with irritable bowel syndrome based on ROME III criteria and exclusion of organic disease [25]. All subjects with IBS were examined for fibromyalgia using the 1990 American College of Rheumatology criteria [13] and none of the patients were diagnosed as having fibromyalgia. All patients reported pain longer than 6 months. TMD patients were screened at the Facial Pain Center (F.Wong) in the College of Dentistry. TMD patients had to meet the Research Diagnostic Criteria for TMD (RDC/TMD) for an Axis I Group I diagnosis (myofascial TMD) at the time of evaluation [6], and patients, who reported symptoms of fibromyalgia, were excluded from the study based on the inclusion/exclusion criteria. For both patient cohorts, patients were also excluded if they were currently using antidepressants, anxiolitics, or narcotic pain medications in order to reduce the probability of interfering with the experimental testing paradigm and increasing their risk of thermal injury. The study was approved by the Institutional review Board (IRB) at the University of Florida. Prior to sensory testing and completion of questionnaires, written consent was obtained from each subject. Subjects participated in one training session and three testing sessions.

2.2. Pain measurement

The intensity of experimental pain, which was produced by the contact thermode, was continuously measured during the 30-second trial with an electronic visual analogue scale (eVAS). As described in Rodriques et al. [40], the eVAS consists of a low-friction sliding potentiometer (100mm travel) mounted to a inclined desk. Two anchors were provided for the scale: the left endpoint designated as ‘no pain’ and the right endpoint designated as ‘most intense pain imaginable.’ Subjects were instructed to move the slider in proportion to their pain intensity in real time. The position of the slider (i.e., pain intensity ratings) was automatically converted into a percentage (0-100%). A custom-built computer program collected data related to temperature (set and actual) and pain ratings. At the end of the trial, the slider automatically returned to the left endpoint (‘no pain’). Continuous ratings of heat pain provided a temporal profile of pain intensity over the trial duration.

2.3. Experimental stimulus (painful thermal contact)

Focal thermal stimuli (44.0-49.0°C) were administered to the subject’s palm (thenar eminence) by Peltier-based thermode (23mm × 23mm). Subjects were instructed to rate the pain produced by the thermode with the eVAS. For the each trial, the thermode was brought to a neutral temperature (33.0°C), and then brought into light skin contact with a solenoid. After a short period, the temperature was ramped (1.5°C/s) to the desired temperature. After 30 seconds, the thermode was retracted. Subsequent trials used widely spaced thermal pulses (3-minute inter-stimulus interval) to minimize sensitization.

2.4. Conditioning stimulus (water immersion)

Cold-water immersion was used as the conditioning stimulus. The water bath was cooled by a refrigerated water circulator (Neslab, Portsmouth, NH). Water flow was maintained at a constant temperature throughout the water bath and constantly recirculated to prevent local warming or cooling around the foot. Subjects were instructed to immerse their foot to the ankle in water set at 23.0°C (control session) or a noxious cold temperature (DNIC session; 16.0 to 8.0°C ± 0.1°C). The water level was set at a height of 7 cm in order to keep the stimulated area consistent.

2.5. Testing Protocol

2.5.1. Psychological Questionnaires

State-Trait Anxiety Inventory: State (STAI-S) was used to assess anxiety before each testing session. The STAI-S contains 20 questions to which assess how a person feels "right now, at the present moment." Overall, the STAI has high internal consistency and can discriminate between different levels of anxiety and is sensitive to change [45].

Weekly Clinical Pain: Before each testing session, IBS and TMD patients were asked to use the eVAS to rate the average pain over the past week. The left endpoint was designated as 'no pain' and the right endpoint as 'most intense pain imaginable.'

2.5.2 Training Session—First, all subjects underwent a training session consisting of several 30-second trials applied to the forearm to become familiarized with the experimental apparatus and rating procedure. Then, a second series of 30-second trials was applied to the thenar eminence of the hand to establish an individualized temperature for the subsequent testing sessions. Time between each trial was 3 minutes (ISI). The thermode temperature was gradually increased over the multiple trials from 42.0°C up to a maximum of 49.0°C. Temperatures at which a subject rated pain intensity at greater than 60% were not repeated.

After individualized temperatures were determined for the focal heat stimulus, a similar process was used for the cold water immersions (16.0-8.0°C). Subjects placed their foot into the water bath for 30-second trials, and the time between each trial was 3 minutes (ISI). For each temperature, subjects alternated immersion of their right and left foot until a pain rating range (20-30%) was reached. This strategy was used to prevent subsequent numbing of the subject's foot during repeated immersions. In addition, a towel was provided to warm the subject's foot between foot immersions.

The temperatures of both the focal thermode and the immersion bath were individually tailored to produce a pain rating of 40-50% eVAS and 20-30%, respectively. These temperatures were used for the remaining sensory testing sessions. Individualized temperatures were used to standardize the pain intensity range for all tests and subjects since the same temperatures, which are easily tolerated by healthy individuals, may be intolerable for a chronic pain patient. Because our clinical samples were expected to show increased sensitivity to thermal stimuli, tailoring the stimulus intensity to fit an individual's own unique stimulus-response relationship provided a better method than comparing pain ratings to a standardized painful stimulus between groups [48, 49]. A customized stimulus temperature minimizes the risk of unaccpetbale discomfort for the subjects and reduces potential reporting biases.

2.5.3. Testing Sessions—Subjects participated in three testing sessions on different days following training. Sessions were scheduled on consecutive days. Subjects were queried about their health and medication use, and then they were asked to complete the STAI, rated their clinical pain (IBS and TMD groups). Subsequently, they were allowed to rest for an additional 10-20 minutes before testing began. Each session consisted of three 30-second trials in which the experimental stimulus was presented to the palm alone or in combination with the conditioning stimulus. Sessions were counterbalanced and consisted of a session with: (1) the focal heat stimulus to the left palm only (i.e., *no water bath session*) presented to the left palm; (2) the focal heat stimulus to the left palm during concurrent immersion of the subject's right foot (i.e., *DNIC bath session*; 16.0-8.0°C); and, (3) the focal heat stimulus to the left palm during concurrent with immersion of the subject's right foot into a neutral water bath (i.e., *23.0°C control bath session*).

2.6. Data analysis

The dependent variables were mean peak pain ratings (PPR) and area under the curve (AUC) and were calculated by averaging across the three trials for each session. The highest rating obtained during each 30-second stimulation period was categorized as the peak pain rating for that trial. AUC for each trial was calculated by summing the recorded pain rating for each of the 30 seconds and dividing by thirty. Using the general linear model module of SPSS, a 3×3 mixed model analysis of variance (ANOVA) was used to calculate differences in pain ratings among the three groups. The between subject variable was group (control, IBS, and TMD) and the within subject's variable was session (thermode only, concurrent 23.0°C immersion, and concurrent noxious cold immersion). The model also included anxiety, measured by the state subtotal of the State-Trait Anxiety Inventory, as a covariate. To evaluate hypothesis 2 (i.e., reduced pain for controls during immersion with the noxious cold water bath session but not for patients with IBS or TMD), a paired-samples t-test with a Bonferroni correction was used to test for differences between the 3 sessions within each group.

3. Results

3.1. Baseline pain characteristics

For the contact heat, a one way-ANOVA revealed that temperatures required to produce a pain rating between 40-50 eVAS were significantly different among the three groups (Table 1; $F=9.379$, $P< 0.001$). Bonferroni post-hoc test indicated that control subjects required a higher temperature to produce the targeted pain intensity range compared to IBS or TMD patients. No differences were observed between IBS and TMD patients. These results support the hypothesis that IBS and TMD patients demonstrate increased sensitivity to experimental heat stimuli. However, no significant differences were observed in the individualized foot immersion temperature among the groups ($F=1.531$, $P=0.226$).

3.2. Anxiety

As measured by the STAI-S, anxiety levels (Table 1) were significantly different across testing groups during the no water bath session ($F=9.723$, $P<0.001$), DNIC water bath session ($F=7.361$, $P=0.002$), or 23 °C control bath session ($F=3.194$, $P=0.049$). Bonferroni post-hoc tests revealed that control groups had significantly lower levels of anxiety before pain testing compared to IBS and TMD patients.

3.3. Clinical pain ratings

The average clinical pain ratings for the IBS and TMD patients are presented in Table 1. Six (43%) of the IBS patients and seven (44%) of the TMD patients reported having clinical pain during the week of their testing sessions. Ratings of clinical pain were higher in TMD patients (32.4-37.4) compared to patients with IBS (21.4-25.2).

3.4. Profile of continuous pain ratings

Continuous ratings during 30-second trials for each of the three testing sessions are presented in Figure 1. Across all groups, pain ratings exhibited an early phase of rapid temporal sensitization (0-15 seconds) followed by a phase of adaptation (15-25 seconds) and a second sensitization phase (25-30 seconds).

3.4.1 Continuous pain ratings in control, IBS, and TMD groups—For the control group (Figure 1A), continuous rating of pain intensity was lower during the DNIC water bath session (gray circle) compared to the session without an immersion stimulus (open circle) or the session with a neutral immersion stimlus (closed circle) water bath sessions. A

lower pain rating during the DNIC sessions suggests that concurrent application of a mildly painful water bath inhibited focal heat pain. In contrast to controls, IBS (Figure 1B) and TMD (Figure 1C) patients reported either no change or an increase in pain intensity during the DNIC session, respectively.

3.5. Differences in peak pain ratings

Analysis for PPR (Table 2) by a repeated measures ANOVA revealed a significant group × testing condition interaction ($F = 7.466$, $p>0.001$). However, no main effects of group or testing conditions were observed, which was expected since the thermal stimuli were calibrated to each subject. The mean pain rating for each group by condition is presented in Figure 2. Control subjects reported less pain produced by the heated probe during concurrent immersion with noxious cold (31.9 eVAS±1.7) compared to conditions with no water bath (39.9 eVAS±1.6) and immersion with a neutral temperature (23.0°C control session; 36.7 eVAS±1.6). Reductions in pain ratings in these subjects indicate a significant inhibition of thermal pain by the conditioning stimulus. In contrast, the mean pain intensity ratings during control (37.1 eVAS±2.4) and DNIC (40.5 eVAS±2.5) sessions for IBS patients were not statistically different and comparable to ratings obtained during the session with the thermode (40.0 eVAS±2.3). Patients with TMD reported higher pain intensity scores during the DNIC session (50.2 eVAS±2.3) compared to conditions with the heated probe only (42.3 eVAS±2.1) and the control session (42.3 eVAS±2.1).

3.6. Differences in area under the Curve

Similar to peak ratings, examination of AUC scores (Table 2) by a repeated measures ANOVA revealed a significant group × testing condition interaction ($F = 6.630$, $p>0.001$). No main effects of group or testing conditions were observed. Figure 2 illustrates the mean AUC scores for control, IBS, and TMD subjects across the three testing conditions. The intensity of pain was significantly lower in control subjects during the DNIC session (AUC score of 16.4±1.1) when evaluated against ratings during without the water bath (AUC score of 21.7±1.3) or the control session (AUC score of 20.3±1.1). No differences in AUC scores were observed in patients with IBS among the no foot immersion condition (AUC score of 21.3±1.6), the 23.0°C water bath condition (AUC score of 20.0±1.7), or the noxious water bath condition (AUC score of 23.0±2.0). However, AUC scores of TMD patients were higher, which indicated an increase in pain ratings, during the DNIC condition (AUC score of 27.9±1.4) compared to ratings in the absence of a water bath (AUC score of 23.0±2.0) or immersion into a control water bath (AUC score of 23.9±1.5).

3.7. Other analyses

In supplementary analyses to determine the effect of clinical pain, we tested whether the effects of the noxious water bath differed depending whether the patients (n=13) had clinical pain compared to those without (n=15). Differences scores were calculated for AUC and PPR between: (a) 23.0°C control bath session - DNIC water bath sessions; and, (b) no water bath sessions - DNIC water bath sessions. Although no ANOVAs were statistically significant, effect size ranged from 0.3 to 0.7 SD units, such that patients with current pain reported greater heat pain in the DNIC session than the comparison sessions compared to IBS and TMD patients not reporting pain.

4. Discussion

The aim of the current study was to compare the efficacy of pain inhibition pain in patients with IBS and TMD compared to healthy control subjects using an experimental DNIC paradigm in which a painful conditioning stimulus (foot immersion) was used to moderate pain elicited by a focal thermal stimulus to the hand, our experimental stimulus. In support

of our hypothesis, the patients with IBS and TMD groups: 1) had an increased sensitivity to the prolonged focal thermal stimulus (e.g., a lower temperature that produced a pain rating between 40-50 eVAS); 2) failed to exhibit an inhibitory effect on thermal heat pain when their foot was immersed into the noxious water bath (*DNIC session*). Thus, the results of the study add to previous literature concerning increased sensitivity to experimental pain among participants with IBS [30, 40, 54, 55] and TMD [26, 27, 50]. In addition, the study suggests that individuals with TMD also display a deficit in pain inhibition by a second painful stimulus, which has not been evaluated to the best of our knowledge. This is consistant with reportes of deficiencies in pain modulation in IBS patients [46, 58, 59] that assessed DNIC effects on prolonged visceral pain. Furthermore, use of prolonged focal heat and immersion has not been examined in healthy individuals or in IBS and TMD patients.

4.1. Differences in baseline sensitivity to prolonged heat stimulation

The stimulus temperatures needed to elicit a given amount of pain were lower in IBS and TMD patients compared to healthy individuals. Compared to healthy controls, enhanced sensitivity in IBS patients is often characterized by lower pain thresholds to rectal distention [30, 54, 55] and higher intensity of pain during noxious thermal stimulation with a immersion bath [54, 55] or contact heat [40]. In comparison, TMD patients frequently reported higher pain intensity to experimental pain applied to the face [26, 27]. Taken together, these studies provide evidence a general hyperactivity of central pain processing systems, which is consistent with the hypothesis that alterations in the pain modulation in individuals with chronic pain may limit their capacity to respond appropriately to pain. Since our novel psychophysical testing method supports conclusions consistent with other studies, we are confident our findings are not an anomaly.

4.2. Differences in temporal profile of prolonged heat stimulation

While increased sensitivity to shorter experimental stimuli among chronic pain patients is well established, we used a 30 second focal heat stimulus to induce a pain intensity that was moderate. This strategy was based on the concept that suprathreshold noxious stimuli with a longer duration will demonstrate late onset pain modulation and better resembles the tonic nature of clinical pain [31] where episodes may last for hours or longer at a time. One hypothesis is that pain sensitization has multiple stages depending the stimulus duration and intensity. When a stimulus with a longer duration is used, a period of sensitization is observed during the early phase of noxious stimulation in which pain ratings quickly rises. If the noxious stimulus persists and is sufficiently intense, inhibitory mechanisms are activated leading to a reduction in rating of pain intensity.

Several studies have reported similar phenomenon related to prolonged stimulation of heat [19, 31]. A period of adaptation between 15-20 seconds (i.e., transient drop in pain ratings) was recently reported by Koyama et al. [19] and Naert et al. [31] with prolonged heat stimulation. In the current study, periods of sensitization and adaption during prolonged thermal stimulation were observed in both chronic pain patients and healthy controls during all sessions. This suggests that the internal modulation produced by continuous, intense stimulation utilizes different mechanisms other than DNIC. At the present time, it is unclear what mechanisms are involved in transient decrease in pain. A number of peripheral (i.e., primary afferent fatigue; Aδ activity) [53] and/or central mechanisms (i.e., off-set analgesia; discharge rates of WDR neurons) [5, 16] maybe involved in addition to phenomenon unique to the testing methodology.

4.3. Differences in efficacy of endogenous inhibition of focal heat pain

The study also demonstrated significant group differences in the ability to engage endogenous pain modulation systems during the DNIC session when compared to other

sessions. A heterotopic effect of noxiously cold conditioning stimuli on thermal pain ratings was observed in healthy controls, who report a significant decrease in pain intensity as expected. However, patients with IBS and TMD failed to engage endogenous mechanisms underlying DNIC, which is consistent with a number of studies [18, 20, 32, 41, 47]. While studies like Staud et al. [47] evaluated DNIC with more dynamic pain stimuli, most studies have used brief test stimuli to examine the efficacy of DNIC, which usually consist of thresholds to pressure or electrical pain stimulation. Furthermore, reports of pain modulation in IBS patients using other methodology suggested evidence of altered endogenous inhibition following heterotopic stimulation. To the best of our knowledge, only one study [26] provided evidence that patients with TMD failed to inhibit clinical facial pain during heterotopic stimulation with a procedure previously shown to reduce experimental and acute facial pain [44]. Some patients even reported an increase in facial pain during the ischemic stimulus, which may be comparable to enhanced sensitivity of TMD patients in the current study. This observation might be unique to the current population of patients but other studies have observed pain facilitation during DNIC among older adults [8] and IBS patients [58].

4.5. Mechanisms underlying altered endogenous pain inhibition

A number of potential pathophysiological mechanisms underlying the enhancement of pain processing in IBS and TMD patients have been proposed including a neuronal hyperexcitability of dorsal horn neurons [28, 35, 36, 37, 38, 42, 43], which may be a result of altered central modulation of the nociceptive activity. Neuroplastic changes in the nervous system can result in increased hyperactivity of peripheral nociceptors and dorsal horn and are known as central sensitization [4, 28, 34, 36, 37]. Its physiological correlate is related to a corresponding increase in wide dynamic neurons (WDR) activity in the spinal cord [34, 36], which is reduced during heterotopic application of a conditioning stimulus via descending pathways in animal models [3, 21, 22]. In addition, pain ratings during sensitization paradigms (i.e., temporal summation) are dependent on C-fiber activation, which are reportedly extremely sensitive to inhibition by DNIC under normal conditions [34, 47]. Furthermore, an explanation of reduce endogenous pain inhibition in our cohort of pain patients could be the result of an increase expectation of pain based on the study by Goffaux and collogues [15]. Expectations and other psychological factors (i.e., catastrophizing) have been show to be associated with pain processing and modulation [7, 15], which should be evaluated in future studies in clinical populations.

4.4. Limitations

It is important to note some important limitations to current findings of the study. First, inhibition of experimental pain during concurrent administration of noxious conditioning stimulus is frequently associated with mechanisms of DNIC. However, additional mechanisms could also contribute to these effects including stress-induced analgesia (SIA) [60, 62, 65] or blood pressure [9, 14, 29] or distraction [47]. Second, the direction of causation between DNIC and clinical pain still remains an enigma since it is unclear if a reduced capacity to engage pain modulation systems is a cause or a result of clinical pain [7, 11, 47]. Evidence for both assertions is found in the literature. Individuals with a high sensitivity to experimental pain and an inability to mount endogenous inhibition have an increase likelihood of experience clinical pain [7]. Alternatively, the presence of clinical pain will reduce an individual’s capacity to inhibit pain as demonstrated by a restoration of DNIC responses following hip surgery in patients with osteoarthritis [17]. The duration of clinical pain symptomatology may also influence pain modulation [25, 42]. Third, the duration of clinical symptoms in our current cohort of patients were not assessed, which raises questions about the influence of other physical and emotional symptoms on pain sensitivity. Our group patients, who were recruited in the general community, were fairly

healthy and younger than a typical individual with these chronic pain conditions. Patients were excluded from the study if they were currently using medications (antidepressants, anxioiytics, or narcotics), which may reduce sensitivity and increase risk of blistering or burning. Additionally, these drugs may also have an effect with DNIC [39]. However, our results might be different if we recruited patients from chronic pain clinics. Futures studies could address these issues in patients with IBS and TMD and related associations with DNIC responses and prospective studies may address this problem in contrast to the present cross-sectional design.

4.6. Conclusions

The present investigation demonstrated that the pain inhibition mechanisms underlying DNIC can reduce pain produced by prolonged thermal stimulation in healthy individuals. Patients with IBS and TMD were unsuccessful in engaging endogenous inhibition in which pain ratings of contact heat was unaffected during concurrent administration a noxious water bath. These findings suggest that patients with chronic pain conditions have reduced ability to inhibit pain, possibly because of dysfunction of internal pain inhibition systems.

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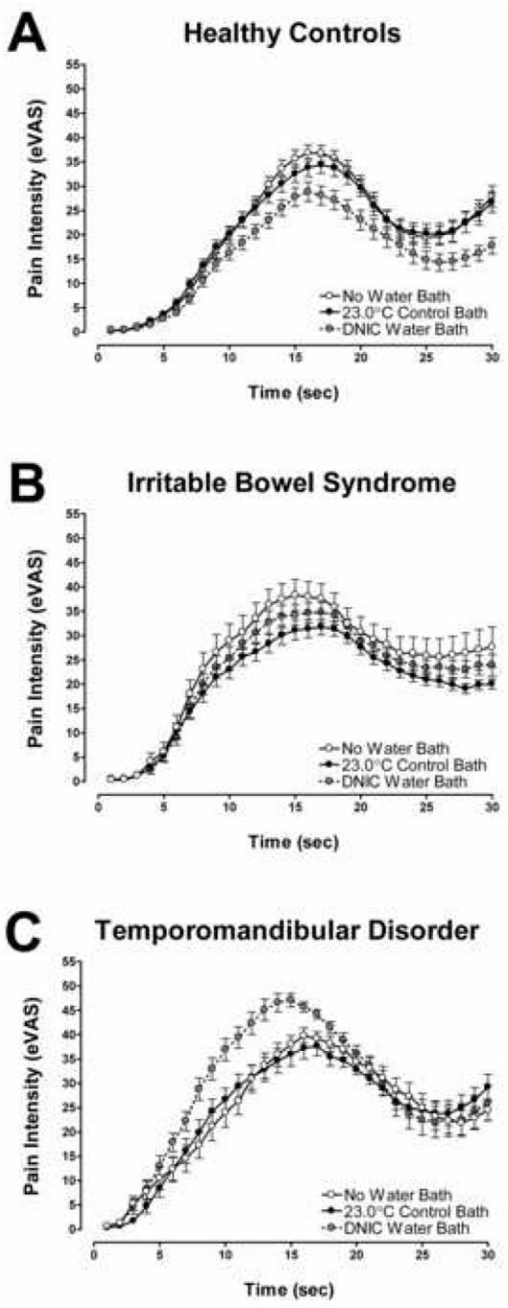

Figure 1.

Average continuous ratings of pain intensity during testing sessions with either no water bath, a 23.0°C water bath, or DNIC water bath for (a) control subjects, (b) IBS patients, and (c) TMD patients. For each group, pain intensity gradually increased during the first 15 seconds followed by a brief decay.

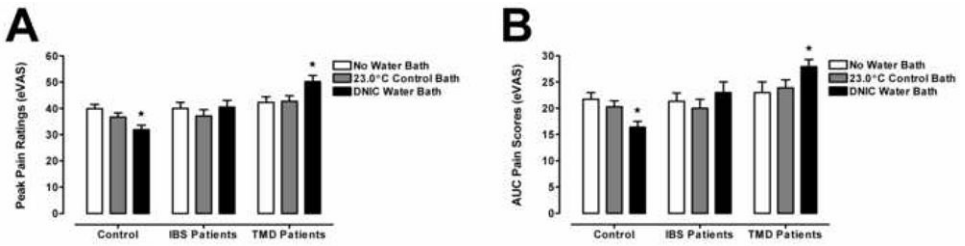

Figure 2.

Average PPR (a) and AUC (b) for control subjects and patients with IBS and TMD during a session with no water bath (open bar), a session with 23.0°C water bath (gray bar), and a session with the DNIC water bath (close bar). PPR and AUC values were obtained during continuous ratings of pain intensity and are represented as means ±SD. * P <0.01 indicates differences between the DNIC session and No bath/23°C sessions. Peak pain ratings (PPR); Area under the curve (AUC); Electronic visual analogue scale (eVAS).

Table 1

Means (SD) of characteristics for control subjects and patients with IBS and TMD.

	Controls N=28	IBS N=14	TMD N=14
Age (mean ± SD)	28.6 (10.8)	26.8 (8.5)	31.0 (10.2)
Experimental pain variables (mean ± SD)			
Average temperature for heat pain (°C)	47.9 (0.7)[a]	46.6 (1.3)	46.8 (1.2)
Average temperature for cold immersion (°C)	11.5 (2.4)	13.2 (3.0)	11.9 (1.9)
Measures from STAI (mean ± SD)			
No bath session	26.8 (6.1)[a]	33.7 (9.9)	31.9 (9.2)
23°C control session	25.1 (4.5)[a]	32.6 (10.2)	31.1 (7.2)
DNIC session	24.9 (6.3)[a]	36.7 (11.0)	32.9 (9.2)
Average weekly pain (0-100; mean ± SD)			
No bath session	---	21.4 (18.5) [#]	35.0 (25.5) [*]
23°C control session	---	24.0 (12.7) [#]	32.4 (19.4) [*]
DNIC session	---	25.2 (22.2) [#]	37.4 (20.6) [*]

Abbreviations: STAI, state trait anxiety inventory; DNIC, diffuse noxious inhibitory control Values with different superscript represent group differences at $p \leq 0.017$ (Bonferroni correction).

[a] controls were significantly different than chronic pain subjects for this variable

[#] For patient samples with n = 6

[*] For patient sample with n = 7

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Table 2

Adjusted PPR and AUC scores for controls, IBS, and TMD with significant within subject effects.

	Controls N=28	**IBS N=28**	**TMD N=28**
Measures for PPR (mean ± SD)			
No bath session	39.9 (1.6)	40.0 (2.3)	42.3 (2.1)
23°C control session	36.7 (1.6)	37.1 (2.4)	42.7 (2.1)
DNIC session	31.9 (1.7)[a]	40.5 (2.5)[b]	50.2 (2.3)[a]
Measures for AUC (mean ± SD)			
No bath session	21.7 (1.3)	21.3 (1.6)	23.0 (2.0)
23°C control session	20.3 (1.1)	20.0 (1.7)	23.9 (1.5)
DNIC session	16.4 (1.1)[a]	23.0 (2.0)[b]	27.9 (1.4)[a]

Abbreviations: PPR, peak pain ratings; AUC, area under the curve; DNIC, diffuse noxious inhibitory control.

[a]Significant differences between the DNIC session and No bath/23°C control sessions.

[b]No differences between sessions.