Diffuse Noxious Inhibitory Control in Patients with Irritable Bowel Syndrome and Myofascial Pain Disorder

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ABSTRACT

Diffuse noxious inhibitory control (DNIC) is the phenomenon by which the perception of painful stimulus at a local area of the body (test stimulus) is inhibited by a second painful stimulus administered at a distal body site (conditioning stimulus) or, simply, pain is inhibited by pain. Previous DNIC studies have demonstrated that comparable pain modulation between healthy controls and fibromyalgia (FM) patients did not occur and that pain attenuation seen in normal controls is not seen in individuals with FM. Individuals with myofascial pain disorder (MPD) and irritable bowel syndrome (IBS) experience increased sensitivity to pain similar to that of FM. Therefore, it is appropriate to test the DNIC pain modulatory systems of patients with MPD and IBS for a dysfunction of the pain regulatory system found in FM patients. To our knowledge this is the only study that aims to test the effects of DNIC in individuals with IBS and MPD. The subjects were nine female IBS patients, five female MPD patients, one male MPD patient, ten female healthy controls, and eleven male healthy controls. The experimental stimulus was a series of three 30-second thermal stimuli trials administered to the thenar eminence of the palm using the TSAR-2000 thermal contact stimulator. The DNIC conditioning stimulus consisted of immersion of the right foot in a re-circulating cold-water bath. Each subject participated in training sessions and two DNIC sessions where exogenous pain inhibition was measured using both the test stimulus and conditioning stimulus. Pair-wise comparisons, using a repeated measures ANOVA, indicated that the decrease in pain following the DNIC condition was significantly different than the increase in pain experienced by the MPD (p = 0.007) and the IBS (p = 0.037) groups. We interpret our findings as the result of significant differences in pain modulation between normal controls and individuals with IBS and MPD.

INTRODUCTION

Individuals suffering from irritable bowel syndrome (IBS) and myofascial pain disorder (MPD) are more sensitive to pain than healthy individuals. Studies conducted by Maixner et al.\(^1\) and Fillingim et al.\(^2\) report that increased pain sensitivity is not limited only to the painful areas, which suggests an altered central processing of somatosensory inputs in musculoskeletal pain conditions. Furthermore, these localized pain conditions in the musculoskeletal system may spread per continuitatem locally/regionally and may become generalized.\(^3\)
Because of this generalization, individuals with one chronic pain condition are more likely to develop other pain conditions.

One method for engaging pain modulatory systems is referred to as diffuse noxious inhibitory control (DNIC). DNIC is the phenomenon by which the perception of painful stimulus at a local area of the body (test stimulus) is inhibited by a second painful stimulus administered at a distal body site (conditioning stimulus) or, simply, pain inhibition by pain.

In individuals that do not suffer from chronic pain disorders, pain administered by the test stimulus is decreased or inhibited upon introduction of the conditioning stimulus at a distal body site. Evidence suggests that patients with certain chronic pain conditions have minimal pain inhibition following a DNIC manipulation, which suggests a pain regulatory dysfunction may be involved. Fibromyalgia (FM) is a chronic pain condition that shares many clinical manifestations with IBS and MPD patients. Three studies, each using differing pain-induction methods, tested for a diminished response to the DNIC pain inhibitory mechanism in females diagnosed with fibromyalgia. Lautenbacher and Rollman presented evidence that concurrent thermal stimulation produces pain attenuation in healthy control subjects but not in patients with FM. In the same study it was determined that comparable pain modulation between healthy controls and FM patients did not occur. Kosek and Hansson reported that FM patients had increased sensitivity to non-painful cold in the forearm and a tendency toward increased sensitivity in the thigh compared to controls. Staud et al. reported that heat stimuli inhibited wind up of second pain only in normal control males but not in normal control females or female FM patients.

Individuals with myofascial pain disorder (MPD) and irritable bowel syndrome (IBS) experience increased sensitivity to pain similar to that of FM. Therefore, it is appropriate to test the DNIC pain modulatory systems of patients with MPD and IBS for a dysfunction of the pain regulatory system found in FM patients. To our knowledge this is the only study that aims to test the effects of DNIC in individuals with IBS and MPD.

**METHODS**

**Subjects**

Nine female IBS patients, five female MPD patients, one male MPD patient, ten female healthy controls, and eleven male healthy controls participated in the study. MPD patients were recruited in the facial pain clinic at Shands Hospital, where they were screened by the doctors in the clinics. The IBS patients and normal controls were recruited by advertisements and word of mouth throughout the Shands healthcare complex. The average age of the IBS patients, MPD patients, and normal control patients was 27.8 (13.29 SD) years, 40.5 (19.55 SD) years, and 28.38 (13.29 SD) years, respectively.

**Exclusion Criteria**
Exclusion criteria for all groups included being younger than 18 years of age, being unable to adequately communicate and understand informed consent form, being unable to reliably rate pain intensity, having a health condition or taking drugs or substances making it unsafe or illegal to drive a car, current use of narcotics, chronic use of analgesics (3 months of daily use), uncontrollable hypertension, advanced stage of pregnancy, serious systematic diseases (e.g., diabetes, thyroid problems, etc.), neurological problems with significant changes in somatosensory and pain perception at the intended stimulation sites (hand, foot), cardiovascular or pulmonary disease, serious psychological problems (e.g., schizophrenia, bipolar disorder), chronic pain condition other than MPD (lower back pain, postherpetic neuralgia, etc.), and active infectious disease or febrile condition (e.g., sinusitis, influenza).

**Experimental Heat Pain Stimulus**

Thermal heat pain was tested on the thenar eminence of the left hand and was administered using the TSAR-2000 thermal contact stimulator and a Peltier device based on a thermode of 23x23 cm² surface area. A computer program controlled the temperature of the thermode and was responsible for bringing the thermode in and out of contact with the palm.

**Diffuse Noxious Inhibitory Control Stimulus**

The conditioning stimulus was tested by immersion of the right foot in a re-circulating cold-water bath. A re-circulating tank with an external refrigeration unit was used to keep the water at the desired temperature and prevent warming due to the presence of the foot.

**Procedure**

Each subject participated by making continuous pain ratings using a visual analog scale to noxious thermal stimuli applied to the volar palm for 30-second intervals. The DNIC conditioning stimulus was immersion of the foot in a re-circulating cold water bath.

**Training Session**

Each subject participated in a training session which began with a short video that explained the experimental and conditioning stimulus and gave instruction on how to use the pain rating scale. The goal of the training session was to familiarize subjects with the electronic visual analog scale (eVAS), teach them to differentiate between heat and pain and give continuous pain ratings using the eVAS. The eVAS had anchors of 0 (no pain, only heat) and 100 (the most intense pain imaginable). The training session was also the time in which the experimental temperatures were determined for the experimental and conditioning stimulus.

Training consisted of four trials on three different parts of the body. The first four trials were administered to the
left palm. A temperature of 46°C was used as the initial temperature since it was thought to be below the threshold of pain for most individuals. From there the temperature was increased a degree or a degree and a half, depending on the peak ratings of the individual. The temperature for the experimental stimulus was chosen so pain ratings peaked between 30 and 45 on a scale of 0-100. This process was continued until four trials had been completed on both the right forearm and the right palm.

After training with the experimental stimulus was complete, training began with the conditioning stimulus with a five minute break between the two. Three trials were normally used; however, some subjects required additional trials in order to find their test temperature. A base temperature of 14°C was used and the temperature was increased or decreased 2°C until pain ratings peaked between 25 and 30 using the same 0-100 scale during a 30-second trial.

Some subjects were asked to complete a second training session either because it was determined they were not proficient in rating the pain or their experimental temperature for either stimulus could not be accurately determined. During the second training session the experimental stimulus was only applied to the right and left palm. Five trials were used on each and the temperature was determined as mentioned above.

After training was complete, subjects completed two additional sessions that consisted of four 30-second trials each using only the test stimulus on the left volar palm. The only difference between the two sessions was the length of the rest periods between the four trials. This data is not reported here.

**Diffuse Noxious Inhibitory Control Session**

Subjects then participated in a DNIC and control session, the order of which was also randomized among subjects. Both sessions consisted of three trials with 10-minute rest periods between the trials. The temperature of the water differentiated the two trials, one using a control temperature of 23°C and the other using the temperature determined during the training session. During the each trial subjects were instructed to insert their foot into the cold water tank with their foot flat on the floor of the tank (which resulted in the water being slightly above the ankle). After 5 seconds the test stimulus was activated and subjects were asked to differentiate between the pain in their palm and the pain in their foot and to rate continuously only the pain in their palm.

**Statistical Analysis**

The data was analyzed using a repeated measures ANOVA with trial as the within-subjects factor and group as the between-subjects factor.

**RESULTS**
There was a significant main effect for group (F = 5.478, p = 0.008); however, the effect of the DNIC condition did not differ across each of the three trials when collapsed across groups (F = 0.753, p > 0.05) and the group differences were the same across the three trials (F = 0.193, p > 0.05). Pair-wise comparisons indicated that the decrease in pain following the DNIC condition was significantly different than the increase in pain experienced by the MPD (p = 0.007) and the IBS (p = 0.037) groups. There was no difference between the MPD and IBS groups (p > 0.05).

Pain ratings were calculated by taking the area under the curve for each trial and dividing by thirty. The DNIC effect was calculated by subtracting the DNIC pain rating from the control pain rating. Figure 2 shows graphically that IBS and MPD patients experience a negative DNIC effect while normal controls experience a positive DNIC effect.

**DISCUSSION**

This was the first study to investigate endogenous pain mechanisms in individuals with IBS and MPD by comparing their DNIC response to that of normal control individuals. In the present study, significant differences were found between normal controls and individuals with IBS and MPD; however, no difference was found between the IBS and MPD groups, nor was there a difference among trials when examined within groups. Our study revealed that subjects in the IBS and MPD group modulated pain differently from those in the normal control group. Subjects in the MPD and IBS groups did not experience a decrease in pain when the conditioning stimulus was applied, as is seen in normal control individuals. We interpret our findings as the result of significant differences in pain modulation between normal controls and individuals with IBS and MPD. The results in this study are analogous to earlier findings that pain is attenuated in healthy individuals but not in patients with FM.⁴
The results of this study suggest that there are similarities between IBS, MPD and FM patients. IBS and MPD patients are similar to FMS patients in that their pain is not inhibited or attenuated by pain. We propose that a different internal mechanism exists in patients with IBS and MPD, though. the causal effect of this mechanism is not clear.

Compared to previous studies, this study used an electronic visual analog scale (eVAS) in which the pain ratings were continuously measured throughout the duration of the trial. This study also employed the use of heat pain for the test stimulus and cold pain for the conditioning stimulus, which helped to differentiate the two pains. However, precautions were not taken to help prevent distractions from occurring during the differentiation of heat pain and cold pain during DNIC testing sessions.

In summary, patients with IBS and MPD did not experience a decrease in pain from a DNIC effect that is normally seen in healthy individuals. This further links IBS and MPD conditions to that of FM. These results suggest a difference in pain modulation mechanisms between healthy individuals and individuals with MPD and IBS.

REFERENCES


