BJA

British Journal of Anaesthesia, 2015, 1–8

doi: 10.1093/bja/aev170
Clinical Investigation

CLINICAL INVESTIGATION

Referred pain and cutaneous responses from deep tissue electrical pain stimulation in the groin

E. K. Aasvang[1,*], M. U. Werner[1,2] and H. Kehlet[1]

[1]Section for Surgical Pathophysiology, and [2]Multidisciplinary Pain Centre, Copenhagen University, Rigshospitalet, Copenhagen, Denmark

*Corresponding author. E-mail: eske.aas@gmail.com

Abstract

Background: Persistent postherniotomy pain is located around the scar and external inguinal ring and is often described as deep rather than cutaneous, with frequent complaints of pain in adjacent areas. Whether this pain is due to local pathology or referred/projected pain is unknown, hindering mechanism-based treatment.

Methods: Deep tissue electrical pain stimulation by needle electrodes in the right groin (rectus muscle, ilioinguinal/iliohypogastric nerve and perispermatic cord) was combined with assessment of referred/projected pain and the cutaneous heat pain threshold (HPT) at three prespecified areas (both groins and the lower right arm) in 19 healthy subjects. The assessment was repeated 10 days later to assess the reproducibility of individual responses.

Results: Deep electrical stimulation elicited pain at the stimulation site in all subjects, and in 15 subjects, pain from areas outside the stimulation area was reported, with 90–100% having the same response on both days, depending on the location. Deep pain stimulation significantly increased the cutaneous HPT ($P<0.014$). Individual HPT responses before and during deep electrical pain stimulation were significantly correlated ($\rho>0.474$, $P\leq0.040$) at the two test days for the majority of test areas.

Conclusion: Our results corroborate a systematic relationship between deep pain and changes in cutaneous nociception. The individual referred/projected pain patterns and cutaneous responses are variable, but reproducible, supporting individual differences in anatomy and sensory processing. Future studies investigating the responses to deep tissue electrical stimulation in persistent postherniotomy pain patients may advance our understanding of underlying pathophysiological mechanisms and strategies for treatment and prevention.

Trial registry numbers: ClinicalTrials.gov (NCT01701427).

Key words: deep tissue; groin; pain; sensory function

Persistent postherniotomy pain is reported around the surgical scar and the external inguinal ring. However, a subset of patients also complain of pain in areas outside the scar located in the abdomen, flank, genitals, or thigh, and in most cases described as deep rather than cutaneous pain.[1] Whether this pain is caused by referral (a central nervous mechanism) or projection (along the innervation area of a specific nerve) from the surgical site due to nerve injury (i.e. local inflammation from tissue trauma, the inserted mesh, or direct nerve injury from entrapment or lesion) or whether the pain is related to other specific local pathology at the area where the pain is perceived is unknown.

Deep tissue hyperalgesia, assessed by pressure algometry, is a frequent finding in postherniotomy pain occurring in ~70% of patients,[1] as well as in other postsurgical pain syndromes.[2] In contrast, the cutaneous sensory dysfunction is characterized by heterogeneity with increased detection and pain thresholds (hypoesthesia/-algesia) to dynamic and static thermal stimulation, increased tactile detection thresholds, or cutaneous hyperalgesia

Accepted: March 6, 2015

Editor's key points

- Persistent pain after hernia surgery is common, although the pathophysiology is not fully understood.
- Effects of deep electrical groin stimulation on superficial thermal sensation was assessed in volunteers.
- Painful deep stimulation was correlated with increases in heat pain thresholds on the skin.
- A link between deep and superficial pain in the groin was demonstrated in volunteers.
- Further studies are needed to explore this relationship in persistent postsurgical pain.

to pinprick stimulation.[1 3] However, the relationship between deep tissue and cutaneous hyperalgesia in persistent postoperative pain has not been clarified, leaving the question unanswered of whether these findings are two independent synchronous pain syndromes or if there is a causal relationship.

Consequently, there is a need to understand if persistent pain after groin hernia surgery follows a referred/projected pattern or originates directly from the tissues where the maximum pain is reported. This information could have direct consequences for diagnosis and treatment, since interventions targeted at the referred/projected pain area alone, and not the actual tissue with ongoing pathology (e.g. inflammation, nerve entrapment), would potentially result in treatment failure.[4] Thus we designed a protocol to investigate if deep tissue pain induced by invasive electrical stimulation was associated with the development of pain outside the stimulation area (projected/referred pain) and if deep tissue pain stimulation altered the cutaneous heat pain threshold (HPT) locally, regionally, or generally, in order to clarify the relationships between deep tissue pain stimulation and referred/projected pain and cutaneous nociception.

Methods

Subjects

Healthy male volunteers ≥18 yr of age were included in the study after written and verbal informed consent were obtained. Reasons for exclusion were previous groin surgery/trauma, acute or chronic pain at the time of the investigation, use of analgesics, known sensory dysfunction (e.g. diabetic polyneuropathy, multiple sclerosis, post-stroke), dermatological disease in the groin, signs of groin hernia, or fear of needles. Subjects were given 1100 DKK (€150) for each session and were paid regardless of whether they completed the session. The herein described study is the second part of a previously published study.[5] The studies were approved by the local ethics committee (ID number H-1-2012-035) and data-protecting agency. The study was conducted in accordance with the Declaration of Helsinki and submitted to ClinicalTrials.gov (NCT01701427).

Sensory testing

Two identical test sequences were conducted on each subject separated by 7–14 days. The test sequence and an anatomical illustration including stimulated areas are depicted in Fig. 1 and were described in detail in a previous paper.[5] Sensory testing was performed with the subject in a semi-reclined position with the abdomen and lower arms exposed. Before stimulations, the test sequence was explained and the equipment demonstrated—except for the electrical needle stimulation—on the left lower arm so the subject would be well acquainted and comfortable with the sequence. The sensory testing was done in the following order and locations:

1. Assessment of HPTs in both groins (starting with the right groin) and the volar side of the lower right arm.
2. Deep electrical detection and pain thresholds.
3. Deep tissue electrical pain stimulation (in the following order: abdominal rectus muscle, ilioinguinal/iliohypogastric nerve, perispermatic cord stimulation).

Cutaneous thermal stimulation

A thermal stimulus (Modular Sensory Analyzer, Somedic, Hörby, Sweden) was used to assess the HPT. A Peltier-based thermode with an area of 12.5 cm^2 was applied to the skin at a constant pressure. The testing sequence started from a baseline temperature of 32°C with a ramp rate of +1°C s^{-1}, a 52°C cut-off limit, and a randomized interstimulus interval of 4–6 s. The HPT was defined as the temperature when the stimulus became painful and was recorded by the subject by pressing a button. The mean value of three stimulations defined the HPT. The HPT was assessed before any other stimulation and during deep tissue electrical pain stimulation. Heat pain was chosen as the singular sensory modality due to less interindividual variance compared with cold or mechanical pain.[1] We refrained from additional sensory testing since this would require more stimulation sequences, with the risk of both subject fatigue and potential sensory disturbances (habituation or sensitizing responses).

Deep electrical pain stimulation

Electrical stimulation, delivered via two disposable needle electrodes acting as anode and cathode, respectively [Dantec, Alpine Biomed, Skovlunde, Denmark; 30 mm length, 2.0 mm uninsulated tip, inner diameter 0.35 mm (28G)] was controlled via a Dantec Keypoint EMG stimulation apparatus (Alpine Biomed). The interelectrode distance was 5 mm and was held constant by inserting the needles into a small plastic block with two 0.37 mm (inner diameter) holes drilled at a 75° angle with respect to the base of the block. The angle facilitated visualisation of the needles by use of ultrasound. Ultrasound visualisation (Venue 40, GE Healthcare, Waukesha, WI, USA) was used to ensure that the needles were inserted into the correct tissue (Fig. 2). After placement of the stimulation needles in the abdominal rectus muscle, rectangular impulses of 0.4 ms were delivered at a rate of 10 Hz, starting from 0.02 mA and increased until a sustained pain score of 6/10 NRS (0=no pain, 10=maximum pain) was reported. A maximum of 45 mA was chosen for safety reasons, although higher intensities (energy/time) have been used previously without reports of side effects.[6] The stimulation protocol was chosen because the initial attempt to use a 150% electrical pain threshold (EPT) did not produce sustainable and intense constant pain in the test subjects (unpublished data). A pain intensity score of 6/10 was chosen because previous studies in other body regions have shown this to induce referred pain and changes in cutaneous sensory thresholds.[7]

Once the electrical stimulus intensity had been established, a >30 s resting period was interpolated while the thermode was placed in the right groin. The electrical stimulation was once more delivered until 6/10 NRS pain points were reported. Meanwhile the subjects reported the HPT, as described later. Thereafter the HPT for the left groin and right arm was assessed. The needle electrodes were then replaced around the ilioinguinal/iliohypogastric nerve—visualized by ultrasound—and the HPT was assessed in both groins and the arm. Finally, the electrodes