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Original experimental

Comparison of spatial summation properties at different body sites

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HIGHLIGHTS

- We compared spatial integration of noxious stimuli among body regions.
- Distance-based and area-based spatial summation did not differ by region.
- Anatomical variance in spatial summation cannot account for spinal pain prevalence.
- Distance-based summation was greatest at 15- and 20-cm separations.

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ABSTRACT

Background and aims: The nociceptive system appears to have evolved a range of protective characteristics that are of great interest in understanding both acute and chronic pain. Spatial summation is one important characteristic, whereby increasing area of a stimulus, or distance between multiple stimuli, results in more intense pain—not only greater area of pain. One of the mysteries of chronic pain is why spinal pain is so prevalent relative to pain at other sites. Since pathological tissue models have failed to fully explain spinal pain, we theorized that body region specific differences in sensory processing—such as a greater propensity for spatial summation—may help to explain its vulnerability. We aimed to examine this by comparing the properties of summation at different body parts: the dorsal forearm, neck, and back.

Methods: Spatial summation of pain was investigated using noxious intra-dermal electrical stimuli in healthy pain-free adults (14 males, 6 females), and the perceived pain intensity was rated on a 0–100 pain scale. Area-based stimulation was investigated by doubling the stimulation area with the addition of a second electrode placed adjacent to the first. Distance-based summation was investigated by randomly varying the separation distance between paired noxious electrical stimuli at separations of 0, 10, 15, and 20 cm.

Results: This study demonstrated that the properties of area- and distance-based summation are uniform across the neck, back, and forearm in healthy adults. Spatial summation of pain was also found to be greatest at 15- and 20-cm paired separations for all body regions tested, confirming that noxious information can be integrated over an extensive anatomical area.

Conclusion: Data from this investigation refutes the thesis that spatial summation of pain may be a contributing factor for the reported difference in chronicity rates between spinal and peripheral sites. It remains, however, a potentially important mechanism by which noxious inputs from multi-level pathology might integrate and contribute to pain.

Implications: While data from this project suggest that there are no regional differences in the properties of spatial summation of noxious stimuli, regional differences in other characteristics of the nociceptive system may yet provide insight into why some spinal pain is so highly prevalent; nociceptive distance-based summation may be highly relevant where two or more conditions co-exist in close proximity.

1. Introduction

Chronic low back pain effects 16.3% of general [1] and 25.4–49% of older populations [2,3]. Similarly, neck pain reportedly affects 22% of females and 16% of males [4,5]. In contrast, the incidence

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of chronic arm and hand pain is only 4.1% [6]. Decades of research attempting to explain the greater prevalence of spinal pain with respect to pathological tissue models have not provided a convincing explanation. For example, degenerative disc changes are not a risk factor for neck pain [7] and tissue abnormalities often blamed for pain occur at similar rates in people without pain [8,9]. Notwithstanding the limitations of imaging techniques, tissue factors at best provide an incomplete picture of the cause of ongoing neck pain [10].

There is therefore interest in other factors that might explain the high rates of spinal pain. One possibility that has received little attention, is that the properties of the nociceptive system governing the spine, are different to those that governing regions less vulnerable to chronic pain. Reid et al. [11] found that SS of paired noxious stimuli on the arm occurs at separations of up to 10 cm, with the maximum magnitude at 5 cm, and decreasing in magnitude at 20 cm. Quevedo and Coghill [12] also found distance-based summation of pain to be most pronounced at 5- and 10-cm separations, however, also found evidence that spatial summation (SS) can occur up to 40 cm separations using heat stimuli. However, not all of the data are consistent, with other studies showing spatial summation occurs at 30-cm separations, but is abolished at 40-cm separations [13]. We aimed to examine whether there are differences in the spatial integration of noxious sensory information between different body areas, and more specifically, between peripheral sites such as the arm (where persistent pain problems are rare) and spinal regions (where persistent pain problems are in epidemic proportions). It was hypothesized that the maximum distance at which two noxious stimuli summate at the dorsal arm will be less compared to spinal areas. Further, it was hypothesized that the magnitude of area and distance-based summation would be greater at spinal sites relative to the arm.

2. Materials and methods

2.1. Participants

Subjects were recruited via a purposive sampling method; through the use of posters and fliers advertised around Griffith University Gold Coast campus. Exclusion criteria included individuals suffering from chronic or acute pain conditions, a history of arm, neck, or back pain requiring treatment in the preceding six months, systemic diseases such as diabetes, peripheral nervous system disorders, mental illnesses including somatoform disorder and conversion disorders, and individuals who take narcotic pain medications. The sample size was chosen to ensure adequate (80%) power to detect a small to medium effect ($F = 0.25$) for the main analysis [3(Region: Back vs. Neck vs. Hand) $\times$ 5(Stimulus separation: 0, 10, 15, 20 RM ANOVA)]. These values were selected based on a previous investigation into nociceptive SS which used noxious electrical stimuli in humans, with an a priori power calculation for a repeated measures experimental design with power equal to 80% and a moderate effect size [11]. Twenty healthy, pain-free individuals (6 females, mean age = 23.3 years, SD = 4.46) volunteered.

2.2. Stimulus material

Two DS7A High Voltage Constant Current Stimulators (Digitimer Ltd, Welwyn Garden City, UK) were used to produce paired electrical stimuli. Spatial summation of pain was assessed using paired stimuli of equal intensity to skin overlying the cervical and lumbar spine, and dorsal right forearm, at separations of 0, 10, 15, and 20 cm (Fig. 1). Participants were asked to rate pain intensity using a 0–100 numeric rating scale (NRS); where 0 = "no pain sensation" and 100 = "worst pain sensation imaginable" after each administered transcutaneous electrical stimulus (TES). The spatial configuration of the electrodes was counterbalanced within each region to control for any proximal-distal gradients in nociceptive distribution. Custom made intra-dermal electrodes were used for application of painful electrical stimuli. The design was based on the intradermal electrodes employed by Inui and Kakigi [14]. The electrode employs a 10 mm gold cup EEG electrode (Genuine Grass®, USA) with a modified Ambu® Neuroline stainless steel monopolar needle electrode positioned in the center, to act as the anode. The resulting configuration is a concentric bipolar electrode with a distance of 5 mm between anode and cathode, that result is a focused activation of free nerve endings in the superficial skin, and thus a relatively nociceptive-specific stimulation. The custom electrode was authorized for research after a Risk Assessment evaluation at the University of South Australia.

2.3. Protocol

Informed consent was obtained from all participants subsequent to screening and explanation. Subjects then filled out a demographic questionnaire and the pain catastrophizing scale (PCS). Participants were not informed about the experimental stimuli contingencies or the hypotheses. To ensure that subjects were naïve to the hypotheses of the study, they were informed that the study was investigating properties of pain perception and that this would involve rating how painful a series of stimulations are on their neck, back, and arm. The experiment was considered to be of minimal risk to participants, and subjects were compensated with a $20 gift voucher for their involvement. Moreover, participants were informed they could withdraw from the study at any time with no penalty, and would still receive payment for their time; one participant withdrew and their data were discarded.

2.4. Experimental environment

Subject testing was carried out in a quiet laboratory with a maintained internal temperature ($22 \pm 2\,^{\circ}C$), lighting, and personnel throughout testing. Participants were placed in the prone position for spinal measurements (neck and lower back) and supine position when assessing the dorsal forearm.

2.5. Pretest assessment

Prior to the assessment of SS, the stimulus intensity required to elicit a pain response rated as 50 on the 100-point NRS was determined, using increasing stimulus intensities. Using the most proximal or caudal electrodes, with initial stimulation intensity of 4.0 mA and pulse duration of 200-μs, stimulation intensity was increased in 4.0 mA increments until the participant indicated that stimulation was moderately painful, experiencing pain that is equivalent to 50 out of 100 of the NRS; this scale is anchored at 0 – indicating no pain sensation and 100 – which indicates the worst pain imaginable. The strength of the single TES for all locations was individually calibrated such that it was based on the subject's perceived pain (50/100) as opposed to the magnitude of the electrical current. This acted to account for differences in sensitivity across each region.

2.6. General procedure

A within-subjects deign was used for this study. All participants had SS measurements recorded from the three testing sites. Following the thresholding procedure, participants received 15 suprathreshold TES (12 paired stimuli and 3 single stimulus) in randomized order at each body region. The order of body region was also randomized. The experimenter stood alongside the participant