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Subjects with Knee Osteoarthritis Exhibit Widespread Hyperalgesia to Pressure and Cold

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Abstract

Hyperalgesia to mechanical and thermal stimuli are characteristics of a range of disorders such as tennis elbow, whiplash and fbromyalgia. This study evaluated the presence of mechanical and thermal hyperalgesia in individuals with knee osteoarthritis (OA), compared to healthy control subjects.

Twenty-three subjects with knee OA and 23 healthy controls, matched for age, gender and BMI, were recruited for the study. Volunteers with any additional chronic pain conditions were excluded. Pain thresholds to pressure (PPT), cold (CPT) and heat (HPT) were tested at the knee, ipsilateral heel and elbow, in randomized order, using standardised methodology. Signifcant between-groups differences for PPT and CPT were found: OA subjects demonstrated signifcantly increased sensitivity to both pressure (p=0.018) and cold (p=0.003), but not to heat (p=0.167) stimuli, compared with controls. A similar pattern of results extended to the pain-free ipsilateral ankle and elbow indicating widespread pressure and cold hyperalgesia. This study found widespread elevated pain thresholds in subjects with painful knee OA, suggesting that altered nociceptive system processing may play a role in ongoing arthritic pain for some patients.

Keywords: Osteoarthritis; Cold hyperalgesia; Mechanical hyperalgesia; Pain thresholds

Introduction

Studies utilizing quantitative sensory testing (QST) data suggest that widespread pressure and cold hyperalgesia are also present in a number of musculoskeletal pain disorders such as tennis elbow [1-3], back pain [4,5], fibromyalgia [6,7] and whiplash associated disorder (WAD) [8,9]. It has been suggested that there is an association between pain severity and chronicity, and the presence of cold hyperalgesia in the immediate period post whiplash injury [10] and based on the findings of a systematic review, the presence of cold hyperalgesia has been identified as an important prognostic factor for long term pain and disability in WAD [11] and tennis elbow [12]. The importance of cold hyperalgesia as a prognostic indicator in other conditions has not been extensively explored.

Osteoarthritis (OA) is and one of the most prevalent musculoskeletal disorders affecting Western society and is associated with joint pain, tenderness and decreased function. It is also often anecdotally associated with exacerbations during adverse weather conditions. Over recent years QST methods have been used to evaluate various aspects of hyperalgesia in this population [13,14]. Most commonly, studies have evaluated pressure pain thresholds and reported widespread mechanical hyperalgesia in subjects with OA of the knee [13,14]. Several studies have reported that mechanical hyperalgesia extends beyond the vicinity of the OA joint indicating relatively widespread changes in nociceptive system function. Imamura et al. [14] reported reduced pressure pain threshold (PPT) and consequent pressure hyperalgesia at a number of lower extremity sites in subjects with knee OA, correlating with higher disability scores. A number of studies have also reported reduced PPT in the upper limb of subjects with knee OA compared with matched controls [13-15].

It has been hypothesised that this widespread mechanical hyperalgesia may be a sign of altered nociceptive system function and reflects centrally augmented nociceptive system processing [16]. Thus it has been proposed that even in an apparently localised musculoskeletal condition such as OA there may be significant central augmentation of nociceptive input [17,18]. This hypothesis is also supported by studies that have reported changes in other centrally mediated pain phenomena in subjects with OA. Bajaj et al. [19] reported that both the area and intensity of secondary hyperalgesia were increased in subjects with knee OA, following hypertonic saline injection into the tibialis anterior muscle. Temporal summation is also significantly facilitated in this patient group [15,17]. Studies have also found conditioned pain modulation processes to be significantly reduced in patients with OA compared with normals [20].

The presence of cold hyperalgesia has also been proposed as a sign of centrally-augmented nociceptive system processing [21]. Whilst animal models of arthritis have demonstrated increased cold hyperalgesia [22] there are few human studies that have investigated the presence of cold hyperalgesia in patients with OA. Wylde et al. [13]

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Cold hyperalgesia

Subject with knee OA also exhibited significantly higher cold pain thresholds compared with matched controls, at the index knee (t=2.25, p=0.03) and also at the ipsilateral elbow (t=2.18, p=0.035) and the ipsilateral heel (t=3.47, p=0.001) (Figure 2). Global CPT values were significantly higher in the subjects with OA compared to the controls (t=3.26, p=0.002).

Heat hyperalgesia

There were no significant differences in heat pain thresholds at the index knee (t=-0.586, p=0.56), ipsilateral elbow (t=0.517, p=0.61) or ipsilateral heel (t=-1.49, p=0.14) (Figure 3). There was also no difference in global HPT values (t=-0.584, p=0.56).

A post hoc power analysis indicated that the study had power of 1-β=0.475 to detect a difference in HPT of 2°C between groups

correlation between Global PPT and total WOMAC score (r=-0.381, p=0.037) but no correlation between total WOMAC score and global CPT (r=0.265, p=0.11).

Discussion

This study compared the mechanical and thermal pain thresholds of subjects with WOMAC-rated mild to moderate knee osteoarthritis with the thresholds of matched healthy controls. The results suggest that both widespread mechanical and cold hyperalgesia may be a feature of the pain experience for patients with OA of the knee.

OA subjects exhibit widespread pressure hyperalgesia

Subjects with knee OA exhibited significantly lower pressure pain thresholds at the index knee compared with their matched healthy counterparts. This increased mechanical hyperalgesia local to an OA joint has been reported in several previous studies [13-15] and is characteristic of localised sensitisation. The current study also found increased mechanical hyperalgesia distally and proximally to the OA joint, at both the ipsilateral ankle and elbow, with OA subjects showing a 20% decrease in pressure pain threshold across all sites. This pattern of widespread mechanical hyperalgesia also reflects the findings of a number of recent studies [13-15]. Imamura et al. [14] reported significantly decreased PPT in the upper limb for subjects with knee OA. Neogi et al. [33] reported significantly increased pain sensitivity across four upper limb sites in subjects with OA of the knee. Arendt-Nielsen et al. [15] found decreased PPT at both the ipsilateral tibialis anterior muscle and extensor carpi radialis longus muscle in the

forearm of subjects with knee OA, although neither were reported as significantly different to control subjects.