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Evidence of generalised mechanical hyperalgesia in patients with advanced knee osteoarthritis undergoing total knee arthroplasty

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ABSTRACT

Background and objective: Persistent pain is reported in up to 34% of patients following total knee arthroplasty (TKA) for management of knee osteoarthritis (KOA). Persistent pain in this group is thought to be at least partly reflective of pain sensory hypersensitivity. The objective of this study was to evaluate sensory hypersensitivity, using mechanical and thermal quantitative sensory testing, in patients about to undergo TKA.

Design and methods: Pressure pain thresholds (PPT) and cold pain thresholds (CPT) were recorded from 30 participants prior to their TKA, and compared with recordings taken from 30 healthy control participants of similar age and gender. Thresholds were recorded locally and remotely (other knee, deltoid) to the operative knee. Group comparisons (KOA, control, groups) were made using a general linear mixed models approach with age, gender, and body mass index (BMI) included as covariates. Pairwise comparisons were conducted with Bonferonni correction for multiple comparisons.

Results: Significantly lower PPTs were at all measured sites in the KOA group compared to the control group ($P < 0.001$ at all sites, except the deltoid $P = 0.004$). Males demonstrated higher pain threshold compared to females, averaged over all sites, $P = 0.02$. There were no observed between-group differences in CPT ($P = 0.122$).

Conclusions: This study suggested that some individuals about to undergo TKA for their advanced KOA demonstrated widespread mechanical sensory hypersensitivity. These findings have potentially important clinical implications regarding perioperative and longer-term pain management in these patients.

1. Introduction

In 2014, 54,227 total knee arthroplasty (TKA) cases were undertaken in Australia primarily for the management of knee osteoarthritis (KOA). This figure represents an 88.3% increase in TKA procedures since 2003 [1]. While generally considered to be ben-

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eficial surgery, persistent pain has been reported in up to 34% of patients following TKA [2]. It is therefore warranted, given the frequency and cost of this procedure, to explore potential risk factors and mechanisms underlying persistent pain in some individuals following TKA.

One potential mechanism underlying persistent pain following TKA is sensitisation of peripheral and central nervous system pathways. Peripheral and central sensitisation may contribute to chronic pain in OA [3]. A recent systematic review and meta-analysis [4] found evidence, using quantitative sensory tests (QST), of nervous system (peripheral and central) sensitisation in patients with KOA compared to healthy individuals. However, studies in this meta-analysis included heterogeneous patient groups and inconsistent quantitative measures. For example, radiographic OA severity of participants ranged from mild to severe, and symptoms were of varying severity [5–11]. Pain sensitivity was also studied with regard to its relationship with variable outcome measures such as knee function, instability [10], and inflammatory markers [5]. Furthermore, confounding factors that can affect QST, like age and body mass index (BMI), were inconsistently reported [6,10]. Of most relevance, however, is that few studies have specifically evaluated QST in patients with advanced KOA of a severity great enough to prompt them to undergo a TKA.

There is some evidence that patients with KOA awaiting TKA have thermal and tactile hypoaesthesia [6] and mechanical hyperalgesia [6,9,11]. However, no studies have investigated QST in individuals with advanced KOA immediately prior to their TKA against a strictly controlled comparator group. An investigation of sensory hypersensitivity in this patient group may be extremely informative for their clinical management, particularly with regard to their preoperative and postoperative pain management. In addition, potentially confounding variables such as characteristics of the control group (especially avoiding less clinically overt KOA), as well as other health-related factors such as comorbidities, age, gender, and BMI, need to be accounted for during these investigations, as they may influence QST comparison.

The purpose of this study was to compare QST in patients about to undergo TKA for their advanced KOA to a strictly controlled healthy comparator group with no evidence of KOA. It was hypothesised that patients with advanced KOA would display lower sensory pain thresholds compared to the healthy control subjects, suggestive of sensory hypersensitivity. To explore if any observed sensory hypersensitivity in the advanced KOA group was specific or generalised to the affected knee, measures were recorded locally and remotely to the affected knee. It was anticipated that the findings of the study would further inform understanding of potential mechanisms underlying persistent pain in some patients following TKA.

2. Material and methods

2.1. Participants

Thirty people with advanced KOA (16 females) and scheduled for TKA in the following 2 weeks were recruited by advertising in participating hospitals, local orthopaedic surgeons' private rooms, and within the local community. Participants in this KOA group were excluded if they reported prior major knee surgery (femoral or tibial osteotomies or fracture fixation), or concomitant pathology of the spine, hip, or ankle, due to the potential for these conditions to alter knee pain and function.

Thirty asymptomatic control participants (15 females) were also recruited from the general community. Participants in the control group were included if there was no clinical evidence (no radiographic imaging were used for the control group) of KOA or other musculoskeletal disorders of the lower limbs. Specifically, they were excluded if any of the following factors were present: current or past knee pain after leisure walking, ascending or descending stairs, or walking on uneven ground; previous knee operations, including arthroscopy; attendance at a health professional (i.e., doctor, physiotherapist) for a knee complaint in the last five years; using any analgesia due to a knee complaint; or using any walking aids or supportive bracing for the knee.

This study received approval from the Institutional Human Research Ethics Committee (WMSBHSD Protocol 25-9 and GPH HREC Protocol 12/27) and all participants provided written informed consent prior to participating.

2.2. Measurements and study procedure

The timing of the experimental session for the KOA group was intentionally not more than two weeks prior to their scheduled TKA; this was to ensure constancy of recordings across the group with respect to time until surgery. Participants first provided demographic information and completed the Knee Society Score (2011). The functional component of this score comprised four activity domains arranged in increasing challenge from essential to advanced, including: walking and standing (maximum 30 points), standard activities (maximum 30 points), advanced activities (maximum 25 points), and discretionary/recreational activities (maximum 15 points). Domain scores were summed for a total score out of a maximum of 100 points for a functional score, with a larger score representing better function of the knee [12]. Participants then underwent the quantitative sensory testing using a standardised protocol [13], and all measurement sessions were conducted by one investigator (KJ).

2.2.1. Cold pain thresholds

Cold pain thresholds (CPT) were evaluated with an MSA Thermotest Unit (Somedic, Farsta, Sweden) using a 25 mm × 50 mm thermode that was pre-set to a baseline temperature of 30 °C and cooled at a rate of one degree Celsius per second. Recordings were taken over the medial and lateral (mid-joint line) aspect of both knees, as well as the lateral surface of the deltoid muscle (surgical side in KOA group and the left side in control group). These testing sites were identical to those used for the pressure pain threshold (PPT) recordings (with the exception of the anterior patella) as demonstrated in Figure 1. A, C and D. Participants were instructed to depress a patient-controlled switch when the progressively increasing feeling of cold was first perceived as

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