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Widespread sensitization in patients with chronic pain after revision total knee arthroplasty

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ABSTRACT

Pain and sensitization are major issues in patients with osteoarthritis both before and after total knee arthroplasty (TKA) and revision TKA (re-TKA). The aim of this study was to assess sensitization in patients with and without chronic pain after re-TKAs. Twenty patients with chronic knee pain and 20 patients without pain after re-TKA participated. Spreading of pain was evaluated as the number of pain sites using a region-divided body chart. The pressure pain threshold (PPT) and pressure pain tolerance (PTT) were assessed by cuff algometry at the lower leg. Temporal summation of pain was assessed by recordings of the pain intensity on a visual analog scale (VAS) during repeated cuff pressure stimulations. Conditioning pain modulation (CPM) was recorded by experimental tonic arm pain by cuff pressure stimulation and assessment of PPTs on the knee, leg, and forearm using handheld pressure algometry. Participants with pain after re-TKA compared to participants without pain demonstrated: (1) significantly more pain sites ($P = .004$), (2) decreased cuff PPTs and PTTs at the lower leg ($P < .001$), (3) facilitated temporal summation ($P < .001$), and (4) impaired CPM ($P < .001$). Additionally, significant correlations between knee pain intensity and cuff PPTs, temporal summation, and CPM and between total duration of knee pain and temporal summation were found ($P < .05$). This study demonstrated widespread sensitization in patients with pain after re-TKA and highlighted the importance of ongoing nociceptive input for the chronification process. This has important implications for future revisions, and precautions should be taken if patients have widespread sensitization.

1. Introduction

The incidence of primary and revision total knee arthroplasty (TKA and re-TKA, ie, when a second surgery is needed to remove, add, or exchange one or more TKA components [13]) has increased since their introduction [18,35], and the numbers are expected to increase in the future as a result of demographic and lifestyle changes [36]. Primary TKA is regarded as an effective and successful treatment for end-stage knee osteoarthritis (OA) [13]. Nevertheless, around 20% of the patients receiving a primary TKA experience small or no improvement in pain or even a worsening of the situation [9] and develop chronic postoperative pain [58]. Pain, aseptic loosening, infection, instability, and stiffness after the primary TKA account for 80% to 90% of all revisions [6,48,55]. However, re-TKA is not as effective as the primary TKA [13], and the risk of repeat revision is 4 to 5 times higher than the risk of revision after the primary TKA [6].

It has been suggested that peripheral and central sensitization in knee OA could be important for the poor pain outcome for some patients after TKA and pharmacological interventions [3,52]. Quantitative sensory testing (QST) has frequently been applied to investigate sensitization in OA, and increased pain sensitivity both locally and distantly from the affected joint has been reported [4,7,26,29,34,38,52,54]. Cuff algometry, a method for investigating deep tissue pain sensitivity and central mechanisms, is less influenced by intertester bias than handheld pressure algometry [45] and has recently been used to assess mechanisms of sensitization in knee OA [26,52].

Temporal summation of pain is the perceptual correlate in humans thought to mimic the initial phase of the windup process in dorsal horn neurons. In chronic musculoskeletal pain such as OA and fibromyalgia, temporal summation to repetitive pressure pain stimulations has been demonstrated to be facilitated compared to healthy controls [4,53] as a result of sensitized central

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mechanisms. In patients with chronic painful knee OA, higher clinical pain intensities and longer pain durations caused relatively more temporal summation of pain compared with patients with shorter duration and less pain [4].

Another important aspect associated with sensitization is the descending inhibitory and facilitatory modulation of the peripheral nociceptive inputs in the dorsal horn neurons [3,57]. Conditioned pain modulation (CPM) is a manifestation of this modulation which can be assessed in patients and is characterized by a changed response to a painful test stimulus when another painful conditioning stimulus is applied [61]. CPM is impaired in chronic pain disorders such as knee and hip OA [4,26,34], temporomandibular joint disorders [33], and fibromyalgia [16,37].

Previous studies have shown that sensitization in knee OA patients is normalized after successful joint replacement [26,34], with no residual pain indicating that the sensitization is maintained by peripheral input [26,34]. However, the state of the nociceptive system after re-TKA with and without pain alleviation is unknown.

The aim of this study was to compare patients with and without pain after re-TKA utilizing a variety of experimental pain techniques for assessing (1) local sensitization, (2) widespread sensitization, (3) temporal summation, and (4) conditioned pain modulation.

2. Methods

2.1. Materials

Patients initially diagnosed with end-stage knee OA who had undergone knee arthroplasty followed by a re-TKA using standard procedures [19] with pain as one of the reasons for the revision surgery were invited to participate in this study. In total, 54 patients were screened and 40 agreed to participate, 20 with pain in the revised knee and 20 without pain in the revised knee. Patients were matched for body mass and reasons for re-TKA (besides pain; loosening, infection, instability, and stiffness). Demographics and clinical characteristics are listed in Table 1. The participants were asked to refrain from using pain medication 24 h before the QST session. The study was conducted in accordance with the Helsinki Declaration and approved by the local ethics committee of the North Denmark Region (N-20100050). Oral and written information were provided to the participants, and written consent was obtained from all participants.

2.2. Protocol and questionnaires

Before the QST, the participants completed a questionnaire on demographics and clinical characteristics including questions on revision knee, reasons for revision other than pain, time between primary arthroplasty and first revision, number of revisions, and total number of surgeries after their primary arthroplasty, duration of pain, and mean pain intensity during daily function in the revised knee before the primary arthroplasty, before the first revision and current knee pain measured on a 100 mm visual analog scale (VAS) with the end point descriptors of "no pain" and "maximal pain," respectively. Furthermore, the participants reported pain sites on a region-divided body chart, completed the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [8], and the Knee Pain Map to evaluate their knee pain location and pattern [56]. The Knee Pain Map identifies areas of the knee that are painful and characterizes knee pain as localized (patellar, superiomedial, inferiomedial, medial joint line, superiolateral, inferiolateral, lateral joint line, or back of knee), regional (medial, lateral, patellar, or back of the knee), or diffuse, defined as unable to identify pain as localized or regional.

The participants rested in a comfortable recumbent position in a quiet, temperature-controlled room during the QST. The participants were carefully instructed in the QST methods before the experiment was initiated to make them familiar with the procedure. The QST procedure consisted of 3 different psychophysical parameters: (1) cuff algometry at the lower leg, (2) temporal summation of cuff-induced pain, and (3) CPM. The procedure was performed bilaterally, and the sequence was randomized. The data were collected by the same examiner (STS).

2.3. Cuff algometry for assessment of pain sensitivity

Pressure pain thresholds (PPT) and pain tolerance thresholds (PTT) were recorded by a computer-controlled cuff algometer (Aalborg University, Denmark) [46]. A 13-cm-wide tourniquet cuff (VBM, Germany) with an equal-size proximal and distal chamber was wrapped around the lower leg at the level of the heads of the gastrocnemius muscle. The pressure was increased with a rate of 1 kPa/s; the maximal pressure limit was 100 kPa. The participants used an electronic VAS to rate their pressure-induced pain intensity and a pushed button to release the pressure. The electronic VAS was sampled at 10 Hz. Zero and 10 cm extremes on the VAS were defined as "no pain" and as "maximal pain," respectively. The participants were instructed to rate the pain intensity continuously on the electronic VAS from when the pressure was defined as pain (PPT) and to press the pressure release button when the pain was intolerable (PTT). The assessments were performed by inflation of the proximal chamber, the distal chamber, and both chambers simultaneously in a randomly generated sequence; each of the 3 conditions was repeated twice, and a mean of the different parameters was applied in the statistical analysis.

Table 1
Demographics and clinical characteristics of 40 study participants.

Demographic variable or clinical characteristic	Pain, mean ± SEM or fractions (n = 20)	No pain, mean ± SEM or fractions (n = 20)	P
Age (y)	61.5 ± 1.8	65.7 ± 1.3	.06
Gender (F/M)	14/6	8/12	.06
Body mass index (kg/m^2)	30.7 ± 1.2	31.5 ± 0.9	.61
Revision knee (right/left)	11/9	6/14	.11
Duration of pain before primary arthroplasty (mo)	66.9 ± 19.0	36.1 ± 9.3	.15
Total duration of knee pain (moths)	167.0 ± 22.6	64.3 ± 11.4	<.001*
Time between primary arthroplasty and first revision (mo)	43.2 ± 11.8	25.4 ± 6.1	.18
Knee pain before primary arthroplasty (mm)	78.3 ± 3.8	81.9 ± 4.2	.53
Knee pain before first revision (mm)	64.6 ± 4.7	55.9 ± 6.8	.30
Current knee pain (mm)	49.7 ± 5.9	0.0 ± 0.0	<.001*
WOMAC total (arbitrary unit)	46.2 ± 4.2	11.2 ± 2.1	<.001*
No. of surgeries after primary arthroplasty (revisions/total)	1.4 ± 0.8/2.9 ± 2.5	1.2 ± 0.7/1.4 ± 1.1	.41/.03*
Total pain sites	5.9 ± 0.6	3.0 ± 0.7	<.001*
Knee pain pattern (localized/regional/diffuse)	2/3/15	0/0/0	.49/.23/<.001*

WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
* Statistically significant difference (P < .05).