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BRIEF REPORT

The Nerve of Osteoarthritis Pain

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Objective. **Cumulative data suggest that central sensitization may contribute to pain in osteoarthritis (OA) and present with symptoms typically associated with neuropathic pain (NP). We evaluated the responses from focus group participants on the knee OA pain experience for pain descriptions that suggest NP.**

Methods. **Focus group transcripts were analyzed by 2 independent assessors for unprompted use of pain descriptors that suggested NP. Items from validated NP symptom-based questionnaires were used to guide the analysis. Data on sociodemographic factors, duration of knee OA, and OA disease and pain severity (using the Western Ontario and McMaster Universities Osteoarthritis Index and a numerical rating scale) were obtained from questionnaires administered after focus group completion. These factors were compared among participants who did and did not use descriptors that suggested NP.**

Results. **Transcripts from 80 knee OA participants were analyzed. A range of NP descriptors was used to characterize their knee symptoms, including burning, tingling, numbness, and pins and needles. The proportion of participants who used NP descriptors was 0.34 (95% confidence interval 0.24–0.45). Those who used NP descriptors were younger ($P = 0.003$) and, although not statistically different, more likely to be women, with higher pain intensity and OA severity and longer OA duration, than those who did not use NP descriptors.**

Conclusion. **During focus groups, a subset of adults with chronic, symptomatic knee OA used pain quality descriptors that were suggestive of NP. Elicitation of NP descriptors in people with OA may help identify those who could benefit from further evaluation and perhaps treatment for NP.**

Introduction

Pain is the most common disabling symptom for people with osteoarthritis (OA) (1). The management paradigm for pain in OA has changed little over many decades. However, recent studies have shown that long-term use of standard treatments, including acetaminophen and nonsteroidal antiinflammatory drugs, fails to reduce mean pain levels beyond minimal clinically important thresholds (2,3). One potential explanation for suboptimal pain control in OA is a mismatch between the medications used and the underlying pain mechanism(s). Historically, pain associated with OA has been attributed to local tissue injury, causing "nociceptive pain."

Cumulative data suggest that people with OA can experience pain due to both nociceptive and neuropathic mechanisms to varying degrees (4–6). The likely neuropathic mechanism in OA is central sensitization (CS), which may arise from chronic nociceptor stimulation and subsequent modification of central pain-transmitting neurons (7). CS in OA may present with clinical features that are characteristic of neuropathic pain (NP) conditions. The diagnosis of NP is clinical, based on history, physical examination, and sometimes ancillary tests (8). The characteristic verbal descriptors include: burning, prickling, itching, electric shock like, heat, cold, pins and needles, numbness, tingling, and sensitivity to heat, cold, touch, or pressure (9). Questionnaires have been developed based on these descriptors and validated to distinguish nociceptive pain from NP in other chronic pain conditions, e.g., chronic back pain (9). The identification of NP features in people with OA would provide a rationale for an alternative treatment strategy that employs therapies targeted to NP.

However, there is a paucity of data on the presence of NP symptoms in OA. Importantly, it is symptoms that alert physicians to possible underlying neuropathic mecha-

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nisms and the need for further evaluation and/or treatment of NP.

A recent focus group study on the hip/knee OA pain experience identified that participants used a broad range of descriptors to characterize their pain. The quality or characteristics of the pain were important in determining the degree to which they found their OA pain distressing (10). The current study extended these findings, focusing specifically on pain quality descriptions, including unprompted use of typical NP terms by knee OA participants. The primary aim was to determine whether people with chronic, symptomatic knee OA use pain descriptors that are suggestive of underlying NP. If so, NP questionnaires may help identify people with OA who could benefit from alternative mechanism-based treatment strategies.

Patients and Methods

Study participants. Focus groups were conducted in 6 centers: Toronto, Ontario, and Vancouver, British Columbia, Canada; North Carolina and Texas, US; Bristol, UK; and Sydney, Australia. Recruitment sources included the community, clinical practices of study investigators, and existing OA cohorts run by study investigators. Eligible participants were English-speaking adults ages ≥40 years with knee OA (confirmed on radiographs) who had "aching, discomfort, pain and/or stiffness in or around a knee on most days of at least one month during the past year." There was approximately equal representation of: men and women; mild, moderate, and severe pain levels; educational levels (less than or equal to high school and postsecondary education); and ages 40 to ≥75 years.

Recruitment details are published elsewhere (10). The investigators obtained ethics approval from the institutional research ethics review boards at each center. All of the participants gave informed written consent to participate. The study was conducted in compliance with the Helsinki Declaration.

Focus groups. The same standardized method was used to conduct focus groups at each study center. Participants were initially asked broad, open-ended questions, followed by focused questions to obtain detailed descriptions of their pain using a "funnel-approach." Focus group discussions were audio taped and transcribed verbatim. At least two researchers independently reviewed each set of transcripts to identify distinct themes, which were subsequently compared to reach consensus. The themes were entered into N6 (QST N6 full version, release 6.0; QSR International). Details of the content analysis are published elsewhere (10).

After focus group completion, the participants completed a self-administered questionnaire on sociodemographic factors (age, sex, ethnicity, and education level), duration of knee symptoms, knee OA severity (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC]), and pain intensity, using a 10-point numerical rating scale (NRS). The questionnaire data were entered into an Access database (Microsoft). Double data entry and logic checks were used to ensure data quality.

Statistical analysis. Qualitative analysis was performed on focus group transcripts. To inform this analysis, a list of NP descriptors was compiled from shared items on 5 existing, validated questionnaires designed to distinguish nociceptive pain from NP in people with other chronic pain conditions: the PainDETECT, the Leeds Assessment of Neuropathic Symptoms and Signs pain scale with a self-report version, the Neuropathic Pain Diagnostic Questionnaire, ID Pain, and the Neuropathic Pain Questionnaire (9). Compared with expert physician diagnosis of NP versus non-NP, the sensitivity, specificity, and positive predictive values of these measures range from 66.6–85%, 74–90%, and 71.4–86%, respectively (9).

N6 software (QSR International) was used to search the transcripts for text within previously identified themes, including pain and symptom characteristics and triggers. Texts within these themes were independently reviewed by two assessors and coded for symptom descriptions suggestive of NP, including typical NP descriptors: burning, heat, shooting, pins or needles, numbness, tingling, and sensitivity to light touch, pressure, cold, or heat (or similar language). The results for each participant were compared by the two assessors. Where there were discrepancies, the transcripts were reviewed a second time to obtain agreement.

A secondary quantitative analysis was then performed. Participants were categorized into two groups according to their use of descriptions that suggested NP (yes/no). The groups were compared for differences in sociodemographic factors, duration of knee OA pain, pain intensity (NRS), and OA severity (WOMAC total and pain subscale scores). Continuous variables with normal and nonnormal distributions were compared using the Student's *t*-test and Wilcoxon's rank sum test, respectively. The chi-square or Fisher's exact test was used to compare categorical variables, where appropriate. These statistical analyses were performed using SAS software, version 9.1 (SAS Institute). Significance was based on 2-tailed tests. Using the Bonferroni correction for multiple comparisons, a *P*

Table 1. Demographic and clinical features of all of the participants (n = 80)*

Characteristic	Value
Sociodemographic factors	
Age, years	69.6 ± 10.4
Women, no. (%)	57 (71.3)
White, no. (%)	77 (96.3)
Education above high school, no. (%)	56 (83.6)†
OA factors	
Duration of OA, median (range) years	12.0 (1.0–58.0)†
Pain intensity (range 0–10), median (range)	6.0 (1.0–10.0)
WOMAC total (range 0–96)	41.1 ± 20.0
WOMAC pain (range 0–20)	8.1 ± 4.2
WOMAC function (range 0–68)	29.1 ± 15.0

* Values are the mean ± SD unless otherwise indicated. OA = osteoarthritis; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.
† N = 67.

Table 2. Neuropathic pain subthemes identified among the knee osteoarthritis focus group participants (n = 80)

Subtheme	Descriptor(s) within the subtheme
Heat	"very hot," "mine is searing. . .that hot," "a hotness to it"
Sensitivity to light touch	"very tender," "even the skin gets tender"
Pins and needles	"like pins and needles," "felt like there was a pin in there"
Shooting	"this sharp pain comes shooting through my knee"
Burning	"I can feel a burning, aching in my knees"
Numbness	"just sort of a numb feeling"
Sensitivity to heat or cold	"but if you have that cold air blowing across your knees is what hurts"
Sensitivity to pressure	"even putting pressure on it could almost bring you to your knees"
Tingling	"it can go from a tingling to a numbness"

value threshold of 0.007 (0.05/7) was used to indicate statistical significance.

Results

Sample characteristics. Twenty focus groups were conducted in 91 participants with symptomatic knee OA. Eighty participants had sufficient transcript data for inclusion, i.e., descriptions of pain quality within searched themes. Characteristics of the study participants are summarized in Table 1. Their mean ± SD age was 69.6 ± 10.4 years. The majority were women (71.3%) and white (96.3%), with an above high school level of education. The participants had a long median duration of OA (12 years, range 1.0–58.0 years). WOMAC and NRS scores were well distributed across the range of possible values. The mean ± SD WOMAC total (range 0–96) and pain (range 0–20) subscale scores were 41.1 ± 20.0 (range 0.0–75.3) and 8.1 ± 4.2 (range 0.0–17.0), respectively. The median pain intensity score was 6.0 (range 1.0–10.0).

NP descriptors. The participants used a range of descriptors to characterize the quality of their knee OA pain, including descriptors suggestive of spontaneous (e.g., burning, tingling) and evoked (e.g., pain on light touch) NP symptoms (Table 2). For example, some of the participants described spontaneous NP symptoms: "sort of a burning pain" and "I literally felt like there was a pin in there." Others described evoked NP symptoms: "even the weight of a bed sheet bothers." Some participants described both spontaneous and evoked NP symptoms: "It's different kinds of pain. . .a lot of time it's a burning pain. . .and I find the weight of the blanket—I can't have weight on me." Participants also described having more than one type of pain, using descriptors suggestive of mixed neuropathic and nociceptive mechanisms: "I seem to get the whole gamut from tingling and numbness to dullness. . .and even putting pressure on it could almost bring you to your knees" and "It can go from a tingling to a numbness, and a dull ache to sharp pains. . .not just inside the joint itself, but it can also be in the area around."

The proportion of participants who used NP descriptors to characterize their pain was 0.34 (95% confidence interval 0.24–0.45). These participants were younger (mean ± SD age 64.8 ± 9.7 years versus 72.0 ± 10.0 years; P = 0.003), had a longer mean duration of OA, higher pain intensity, and greater OA severity, and were more likely to be women than those who did not use NP descriptors, although only the age difference reached statistical significance (Table 3).

Discussion

Guided by existing NP questionnaires, this study assessed whether adults with knee OA use pain quality descriptors that are suggestive of NP. The underlying premise here is that individual pain descriptors provide clues to underlying pain mechanisms. For example, spontaneous paroxysms of pain, including electric shock–like sensations and

Table 3. Comparison of study participant characteristics by use of one or more NP descriptors (yes/no)*

	With NP descriptor (n = 27)	Without NP descriptor (n = 53)	*P*
Age, years	64.8 ± 9.7	72.0 ± 10.0	0.003†
Women, %	81.5	66.0	NS‡
White, %	96.3	96.2	NS§
Education above high school, %	87.0/23¶	81.8/44¶	NS‡
Duration of OA, median (range) years	14.5/20 (1.0–58.0)¶	12.0/47 (1.0–53.0)¶	NS#
Pain intensity (range 0–10), median (range)	6.0 (2.0–9.0)	5.0 (1.0–10.0)	NS#
WOMAC total (range 0–96)	45.0 ± 20.2	39.1 ± 19.8	NS†
WOMAC pain (range 0–20)	9.1 ± 4.2	7.6 ± 4.1	NS†

* Values are the mean ± SD unless otherwise indicated. NP = neuropathic pain; NS = nonsignificant; OA = osteoarthritis; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.
† By Student's *t*-test.
‡ By chi-square test.
§ By Fisher's exact test.
¶ Sample size is shown as the denominator if it is less than 100% of the sample.
# By Wilcoxon's rank sum test.

burning pain, have been thought to arise from spontaneous firing in peripheral nociceptive afferents, whereas evoked sensitivity to light touch and/or cold is thought to arise from CS (11).

A cluster of symptoms on 5 validated NP questionnaires has been shown to facilitate the discrimination of NP from nociceptive pain when compared with expert physician diagnosis (9). This study found that 34% of knee OA focus group participants used pain quality descriptions suggestive of NP. A subset of adults with chronic, symptomatic knee OA may, therefore, have neuropathic mechanisms contributing to their pain experience. The use of both neuropathic and nociceptive descriptors by some of the participants suggests that OA can be associated with a mixture of pain mechanisms. This fits with the notion that prolonged nociceptive input may lead to CS and features of NP in OA (7). The descriptions of evoked NP-like sensations (e.g., sensitivity to light touch and pressure) suggest that people with OA may have hyperalgesia (reduced pain threshold) or allodynia (pain in response to a nonnoxious stimulus), which are physical examination signs that aid the diagnosis of NP (8).

However, further study using an NP questionnaire is needed to definitively assess whether a subset of people with chronic OA pain have a symptom profile that has been associated with a diagnosis of NP in other chronic pain populations. Attribution of these symptoms to OA will require exclusion of people with alternative conditions that might explain these symptoms. However, from a clinical perspective, concomitant medical/pain conditions are common in the older OA population and may importantly contribute to the OA pain experience. Targeting treatment to symptoms of NP in people with OA could lead to benefit regardless of whether it is the OA or another condition that predominately drives these symptoms.

Interestingly, focus group participants whose pain descriptions were suggestive of NP were younger than those who did not use NP descriptors. One could hypothesize that advanced age is associated with a greater propensity for NP as a proxy for longer disease duration and more prolonged barrage of the nociceptive system. Alternatively, aging may be associated with desensitization of the central nervous system and, therefore, a lower likelihood of developing CS and NP. Neither theory has been consistently supported in the literature, where advanced age has variably been associated with NP symptoms (12,13). Further study is warranted to understand the role of age in the development of NP among people with chronic pain conditions.

Although not statistically different, focus group participants with pain descriptors that suggested NP were more likely to be women, with greater pain intensity and OA severity and a longer OA duration, compared with participants who did not use NP descriptors. In questionnaire-based studies of other chronic pain populations (e.g., chronic low back pain, pain of any cause), an association has been found between pain intensity and NP symptoms (12,14). More severe symptomatic OA may be associated with more peripheral input to the central nociceptive system, leading to a greater degree of CS and NP (7). Alternatively, NP mechanisms may be synergistically or independently induced by other factors that amplify the perception of the nociceptive stimulus; these factors may be reflected in higher scores on OA severity/pain intensity measures. With respect to the duration of OA, more prolonged nociceptive input may also lead to more alterations in central pain processing and increase the likelihood of developing NP. More research is needed to understand how these factors may influence the development of NP in association with OA.

A strength of this study is that the majority of focus group participants were recruited from the community or community-based OA cohorts, minimizing selection bias. The assessment of unprompted use of NP descriptors could also be considered a strength, enabling responses that are not influenced by or restricted to a predefined list of items. However, there are also some study limitations. First, this study was designed to qualitatively assess the OA pain experience. Therefore, the proportion of people with symptoms of NP requires further assessment in a quantitative study using a validated NP symptom-based questionnaire. Second, information was not obtained on comorbid medical or neurologic conditions that may contribute to NP symptoms, although people with other chronic pain conditions were excluded. Third, the small sample size limited the study's power to detect significant differences between participants who did and did not use pain descriptors suggestive of NP. Despite these limitations, this study's findings provide a rationale for further clinical studies on this population that incorporate validated NP questionnaires.

Further elucidation of the role of NP in OA may lead to improved mechanism-based pharmacologic treatment, which will result in reduced pain and disability and improved quality of life for people with OA.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Hochman had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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