EFFECT OF AGE AND OSTEOARTHRITIS ON KNEE PROPRIOCEPTION

PAI, YI-CHUNG; RYMER, W. ZEV; CHANG, ROWLAND W.; SHARMA, LEENA

Objective. To test the hypotheses that 1) knee position sense declines with age; 2) patients with osteoarthritis (OA) have worse knee position sense than elderly controls; and 3) knee position sense is correlated with functional status.

Methods. The threshold for detection of knee joint displacement was measured in 30 patients with bilateral knee OA (Kellgren/Lawrence grade >=2 in both knees), 29 elderly controls (who met clinical and radiographic criteria for exclusion of OA), and 25 young controls. Range of motion, laxity, radiographic severity, and functional status were also assessed.

Results. A moderate correlation was found between joint displacement detection threshold and age ($r = 0.598$ and $r = 0.501$ for the right knee and the left knee, respectively). The threshold was substantially and significantly different between the OA patients and the elderly controls. Proprioceptive impairment was associated with worse disease-specific functional status.
Conclusion. Proprioception declines with age, and is further impaired in elderly patients with knee OA. Poor proprioception may contribute to functional impairment in knee OA.

Osteoarthritis (OA) is the most common form of arthritis in humans, affecting 15.8 million Americans (1). The knee is the site of involvement most commonly associated with disability (2,3). The prevalence of knee OA increases with age (3). Several factors appear to be related to the variable rate of progression in knee OA. Pathogenetic factors in knee OA progression are likely to exert their effects by 1) increasing the regional load across the articular cartilage, and/or 2) affecting the material properties and the remodeling process of the cartilage, and thereby its ability to withstand load.

In daily activity, a moving knee often encounters impulsive loading repetitively-a condition that requires great stability to protect the joint (4). During normal functional activities, this stability is primarily provided by bony geometry and active muscle contraction (5-7), whereas passive structures such as ligaments and joint capsule provide stabilizing forces largely at the extremes of joint motion. Disturbances of peripheral sensation (e.g., diabetic neuropathy) do not inevitably result in joint abnormality. Nevertheless, knee mechanoreceptors may play a role in promoting stability by providing sensory feedback, which allows modulation of the activation of agonist muscles, or even the coactivation of antagonist muscles (8-12).

The breakdown of such protective, stabilizing mechanisms may initiate or contribute to arthritic changes in a joint. This process is demonstrated in studies of animals after sensory denervation (13). In the canine model, findings after dorsal root ganglionectomy (14) or articular nerve transection (15) demonstrated the importance of afferent pathways in the protection of an anterior cruciate ligament (ACL) transected joint, even though such ipsilateral sensation may not be equally important for a structurally stable joint.

Neuropathic arthropathy, in which one of several processes disrupting afferent input is accompanied by a destructive form of OA, may represent an extreme condition in which both neurologic and joint pathologies are clearly observable. Clinically, sensory deficits are typically not obvious in primary knee OA, although careful cross-sectional studies show that proprioception may be impaired in older subjects with knee OA in comparison with age-matched controls (16,17).
Proprioception in general may decline with age, and there appears to be a specific correlation between increased age and decreased knee position sense in asymptomatic subjects (17-19). However, in previous studies, clinical and/or radiographic criteria to exclude the presence of subclinical knee OA were either not applied or not reported (17-19). In the elderly, the prevalence of asymptomatic OA may be high (3). Therefore, the previously reported correlation between age and decline in proprioception may reflect only the correlation between age and subclinical knee OA (with impairment in proprioception occurring secondarily to changes in the joint tissues).

During the initial phase of a prospective study aimed at investigating the relationship between joint-protective mechanisms and the progression of knee OA, we tested 3 hypotheses: 1) that knee position sense declines with age, even after clinical exam and radiographic criteria are applied to exclude the presence of subclinical knee OA; 2) that patients with knee OA have worse knee position sense than elderly controls; and 3) that knee position sense impairment and self-reported disease-specific functional status are correlated. Our findings with regard to these hypotheses are reported herein.

PATIENTS AND METHODS

Subjects. Thirty patients with bilateral knee OA were recruited from a registry of 320 patients. Registry patients originate from referrals from several departments at Northwestern University, press releases, advertisements in local newspapers, and publications targeting senior citizens, nursing homes residents, and senior community center attendees.

For study inclusion, subjects with knee OA were required to meet criteria for classification into radiographic grade >=2 (i.e., presence of definite osteophytes) in both knees, by the Kellgren/Lawrence scale (K/L) (20). Exclusion criteria consisted of neurologic disease or, in either knee, neuropathic, septic, or inflammatory arthritis, or steroid injection within 2 months.

Twenty-nine elderly control subjects were recruited from the Aging Research Registry of the Buehler Center on Aging, Northwestern University. Exclusion criteria included neurologic disease or, in either knee, symptoms or history of arthritis, physical findings of knee flexion <=125°, effusion, warmth, ligamentous laxity, or any radiographic features of knee OA (osteophytes, decreased joint space, sclerosis, cysts, or bony deformity).

Twenty-five young control subjects were recruited from among the students, faculty, and staff of Northwestern University Medical School. These individuals had no history or symptom of neurologic or musculoskeletal disease.
All OA patients and control subjects lived independently in the community. The absence of symptoms in the unaffected knee of the OA subjects and in both knees of controls was defined as a "no" response to the question, "Are you having any trouble, that is, any pain, swelling, stiffness, or other symptoms in the knee(s)?

The study was approved by the Institutional Review Board of Northwestern University. Each subject gave written informed consent prior to participation.

Threshold for detection of knee displacement. The methods of assessing proprioception were similar to those described in previous studies of subjects with ACL insufficiency, knee OA, or total knee replacement (16,21,22). Proprioception was measured as the threshold for detection of knee joint displacement. An apparatus was constructed, consisting of a stepper motor, transmission and linkage system, seating adjustment components, and angular displacement and force transducers. This provided computer-controlled knee angular motion and a precise measurement of angular displacement with a resolution of 0.1°, while eliminating or minimizing visual, auditory, vibration (as monitored by the force transducers), cutaneous tension, and pressure cues to limb motion.

Subjects were seated in a semi-reclining position with the back supported and the knee hanging over the edge of the apparatus, which was 5 cm proximal to the popliteal fossa. The knees were placed in 90° flexion and the hips in 70° flexion. Foot/ankle air splints (Svend Anderson Plastic Industry, Haarlev, Denmark) were applied and inflated to 20 mm Hg to reduce multisensory afferent discharge at the foot-machine interface, to further reduce sensory cues. The air splints were attached to the foot rest, which is a moving component of the apparatus.

Each subject was given standard instructions informing them which leg was to be tested, that a random delay would occur before motion onset (to reduce the likelihood of guessing the onset of movement), and that a handheld button should be pushed after definite detection of knee joint position change. Each subject underwent several practice trials. The order of the leg testing was randomly chosen. In each trial, both legs were moved to a starting position of 45° knee flexion. After a random delay, computer-controlled constant angular motion of 1 knee was initiated at 0.3°/second. The angular displacement between the starting position and the position at the instant the button was pushed by the subject was computed from the position sensor recording. The threshold for detection of knee joint displacement was defined as the difference, in degrees, between the actual onset of motion and the subject's detection of knee joint position change.

Radiographic assessment. All OA patients and elderly controls had standing anteroposterior radiographs obtained with both knees in full extension. One trained reader (LS) performed all radiographic measurements. Prior to proprioception testing, the subjects had been screened for eligibility for placement in the OA or control group.
Radiographs were assessed using the K/L grading system to score tibiofemoral radiographic severity, in which 0 = normal; 1 = possible osteophytic lipping; 2 = definite osteophytes and possible joint space narrowing; 3 = moderate multiple osteophytes, definite joint space narrowing, some sclerosis, and possible deformity of bone contour; and 4 = large osteophytes, marked joint space narrowing, severe sclerosis, and definite deformity of bone contour (20). The K/L grade was assigned using the following individual feature grades: osteophytes were graded on a 0-4 scale (definite presence represented by grade 2); sclerosis on a 0-2 scale; joint space narrowing on a 0-3 scale; bone cysts were recorded as either present or absent; and bone contour deformity was recorded as absent, possible, or definitely present. The reader was not aware of proprioception test results at the time of radiographic grading.

Other clinical variables. Body mass index was measured as the mass (kg)/height (m$^2$). Other variables were measured to characterize subjects in the knee OA group and the elderly control group. Pain was recorded for each knee on separate 0-10-cm visual analog scales. Physical functional status was assessed using a disease-specific measure, the Western Ontario and McMaster University Osteoarthritis Index physical function scale (WOMAC). This self-administered 17-item questionnaire is valid and reliable for use in the study of knee OA (23,24). Laxity was measured as the sum of medial and lateral joint line opening, in mm, with valgus and varus stress, respectively. Passive range of motion (PROM) for knee flexion/extension was also measured, using a long-arm goniometer.

It is also noteworthy that all OA patients were taking some over-the-counter or prescription analgesic or nonsteroidal antiinflammatory drug as needed for pain. Patients were not required to change their medication regimens since we sought to make all measurements and assessments under conditions that matched typical daily conditions for the patient. Given the variety of medications and regimens being used, we could not consider this analytically. For all these reasons, we chose to examine pain rather than medication use. In addition, all assessments were performed in the same settings (i.e., one setting for the clinical measurements and one laboratory setting for the proprioception measurements).

Statistical analysis. The angular displacement between the initial and final positions for each trial was computed from the transducer recording. The mean result from 10 proprioception trials performed for each knee was used for subsequent analyses. Analysis of variance was conducted to evaluate the group mean differences in threshold for right and left knee displacement detection (i.e., bilateral knee OA group versus elderly control group versus young control group). The correlation coefficient between selected clinical/functional measures (radiographic severity, pain, PROM, joint laxity, and physical functional status) and the detection threshold, and the corresponding $P$ value for the correlation, were also computed for the knee OA group.

RESULTS
Group characteristics. Characteristics of the patients with knee OA and the elderly control subjects are shown in Tables 1 and 2. Mean age did not differ significantly between these 2 groups. Radiographic studies (Table 2) in the 30 knee OA patients revealed K/L grade 2 in both knees in 10, K/L grade 3 in both knees, or grade 3 in one knee and grade 2 in the other knee in 13, and K/L grade 4 in at least one knee in 7. The K/L score was 0 for both knees in all elderly controls. The 2 groups were also distinct with regard to functional status, as demonstrated by the magnitude of the difference in the WOMAC physical function score. Elderly controls reported close-to-perfect knee-specific function (Table 2).

<table>
<thead>
<tr>
<th></th>
<th>Bilateral knee OA (n = 30)</th>
<th>Elderly controls (n = 29)</th>
<th>Young controls (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD years</td>
<td>68.2 ± 8.3</td>
<td>71.3 ± 8.3</td>
<td>30.8 ± 6.9*</td>
</tr>
<tr>
<td>Body mass index, mean ± SD kg/m²</td>
<td>28.6 ± 4.1</td>
<td>24.9 ± 3.9</td>
<td>23.7 ± 4.9</td>
</tr>
<tr>
<td>No. male/no. female</td>
<td>8/22</td>
<td>12/17</td>
<td>6/19</td>
</tr>
</tbody>
</table>

* P < 0.01 versus other 2 groups.

Table 1. Characteristics of the knee osteoarthritis (OA) and control groups
Table 2. Examination results and distribution of the radiographic findings in the knee osteoarthritis (OA) and elderly control groups

| Age and joint position sense. Proprioception data from the young subjects and elderly subjects whose knees were disease-free are plotted in Figure 1. The correlation coefficients between age and the subjects' threshold for detection of joint displacement were 0.598 (P < 0.001) for the right knee and 0.501 (P < 0.001) for the left knee. This

| WOMAC†       | 20.0 ± 12.0‡ | 0.7 ± 1.5 |
| Passive range of motion, in degrees | 127 ± 14/127 ± 16‡ | 135 ± 4/136 ± 4 |
| Knee laxity, in mm | 2.4 ± 1.8/2.2 ± 1.8§ | 1.1 ± 1.0/0.8 ± 1.2 |
| Pain, in cm¶ | 3.3 ± 2.5/3.4 ± 3.0 | 0/0 |
| Symptom duration, in years | 9.0 ± 10.0/7.7 ± 5.7 | 0/0 |
| K/L grade (no. of subjects in each) | 0 | 0 | 29 |
| 1 | 0 | 0 |
| 2 (2/2) | 10 | 0 |
| 3 (2/3, 3/2, or 3/3) | 13 | 0 |
| 4 (2/4, 3/4, 4/2, 4/3, or 4/4) | 7 | 0 |

* Except where otherwise indicated, values are the mean ± SD. Values for passive range of motion, knee laxity, pain, and symptom duration are for the right knee/left knee. K/L grade = Kellgren/Lawrence grade. † Western Ontario and McMaster University Osteoarthritis Index physical function scale score (higher score indicates greater functional impairment; possible scores range between 0 and 68). ‡ P < 0.01 versus elderly controls. § P < 0.05 for the right knee; P < 0.01 for the left knee, versus elderly controls. ¶ Pain in each knee during the past week, assessed using a 10-cm visual analog scale with 0 representing no pain and 10 representing extreme pain.

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Age and joint position sense. Proprioception data from the young subjects and elderly subjects whose knees were disease-free are plotted in Figure 1. The correlation coefficients between age and the subjects' threshold for detection of joint displacement were 0.598 (P < 0.001) for the right knee and 0.501 (P < 0.001) for the left knee. This
indicates that proprioceptive accuracy declines with age.

Figure 1. Age-related changes in the threshold for joint displacement detection in the right and left knees in 25 young and 29 elderly control subjects. Solid and broken lines show linear best-fit models.

OA and joint position sense. As seen in Table 3, there was a significant group effect with regard to the threshold for detection of knee joint displacement \( F[2,81] = 14.18, P < 0.001 \) for the right knee; \( F[2,81] = 12.66, P < 0.001 \) for the left knee). Subsequent analysis revealed a significant difference between the group with bilateral knee OA and the elderly control group \( F[1,57] = 9.12, P = 0.0038 \) for the right knee; and \( F[1,57] = 8.22, P = 0.0097 \) for the left knee), which indicates that proprioceptive accuracy is decreased in the OA knees when compared with the knees of age-matched controls.
Table 3. Threshold of knee displacement detection (in degrees) for the knee osteoarthritis (OA) and control groups.

<table>
<thead>
<tr>
<th></th>
<th>Right knee</th>
<th>Left knee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral knee OA (n = 30)</td>
<td>5.5 ± 4.9</td>
<td>4.5 ± 3.9</td>
</tr>
<tr>
<td>Elderly controls (n = 29)</td>
<td>2.6 ± 1.2</td>
<td>2.4 ± 1.6</td>
</tr>
<tr>
<td>Young controls (n = 25)</td>
<td>1.2 ± 0.9</td>
<td>1.1 ± 0.8</td>
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* Values are the mean ± SD.

Joint position sense and functional status. There was a modest correlation between the average value of the knee displacement detection threshold for the left and right knee and WOMAC physical function score. The positive correlation coefficient of 0.397 ($P = 0.030$) indicated that patients who had greater disease-related functional limitation also had worse joint position sense. The correlation coefficients for the correlation between detection threshold and pain were 0.367 ($P = 0.046$) for the right knee and 0.436 ($P = 0.016$) for the left knee.

We also explored the relationships between measures of disease severity and knee displacement detection threshold, recognizing that the study did not have sufficient power to test hypotheses related to subgroups within the OA sample. For the relationship between K/L grade and detection threshold, correlation coefficients were 0.339 ($P = 0.067$) for the right knee and only 0.075 ($P = 0.695$) for the left knee.

Range of motion restriction and joint laxity may be consequences of disease in knee OA. Knee OA patients had decreased range of motion and slightly greater mediolateral laxity than elderly controls. For patients with knee OA, the correlation between range of motion and the laxity measurement was weak and in a negative direction ($r = -0.349$, $P = 0.059$ for the right knee, $r = -0.338$, $P = 0.067$ for the left knee). In other words, more restricted range of motion was associated with more side-to-side laxity. Neither range of motion nor laxity, however, correlated with the threshold for knee displacement detection.

DISCUSSION

This study provides evidence that knee proprioception declines with age in subjects without OA. Furthermore, joint position sense is worse in subjects with knee OA as compared with elderly controls. Proprioceptive impairment and disease-specific functional status are modestly correlated in knee OA patients.
The findings of a decline in proprioception with age, and of further impairment in proprioception among patients with knee OA, are consistent with the results of previous studies using similar (18) or alternative (17,19,25,26) methods to those used here. In the present study, explicit symptom, physical examination, and radiographic criteria were used to select elderly controls without subclinical knee OA. Application of these criteria was not necessary in the young controls, a population in whom asymptomatic OA is very unusual.

Previous reports describing a relationship between age and proprioception did not address the possibility that age-related decline in position sense might be the consequence of subclinical OA in older subjects. After excluding OA in our elderly control subjects, we were able to demonstrate a strong correlation between proprioceptive accuracy and age. These findings suggest that age-related declines in proprioception may precede the development of knee OA and, perhaps, predispose toward its development.

In studying the impact of age versus disease on proprioception, a cross-sectional study can provide only limited information. Longitudinal studies will better elucidate the directions of the relationships between age, disease, and further decline in proprioception. For example, it is possible that the decline in joint proprioception associated with healthy aging predisposes elderly individuals to develop knee OA (Figure 2). Subgroups of elderly subjects may have less accurate knee proprioception, adversely affecting neuromuscular joint-protective mechanisms, and resulting in the development and progression of disease (pathway A in Figure 2). Alternatively, a decline in knee position sense may result from OA-related mechanoreceptor damage or dysfunction in the capsule, ligaments, and surrounding muscles (pathway B in Figure 2). These 2 pathways are clearly not mutually exclusive, and it is quite likely that they coexist. In a concurrent study (27), we found no difference in proprioceptive accuracy between the knees of patients with unilateral knee OA, but did find a difference between OA and control subjects when either limb was considered. This suggests that the proprioceptive impairment of knee OA cannot be exclusively a local result of disease.
Figure 2. A postulated causal relationship between age-related degradation in proprioception and knee osteoarthritis (OA). Those with a greater age-related decline in proprioception may be at higher risk of having sensory functional impairment (broken line with arrow) that may cause the development or hastened progression of knee OA (pathway A) (thin line with arrow). It might also be possible that knee OA causes further deterioration of the knee proprioception (pathway B) (thick line with arrow).

The present study has inherent limitations. Though the sample size was comparable with or larger than those of several previous studies (18,21,22,25,26), subgroup sizes were small, and it is likely that there was insufficient power to detect a relationship between proprioceptive accuracy and measures of disease severity. Furthermore, no observed assessment of physical function was included. Our findings do suggest, however, that accuracy in knee position sense has some bearing on the (self-reported) ability to perform knee-specific tasks. Future studies should longitudinally examine the impact of proprioceptive inaccuracy on specific performance measures.

Although the threshold for detection of knee displacement may provide a reasonable overall measure of joint proprioception, it does not differentiate the source of sensation. The sensation of position and movement of joints is thought to be derived primarily from the discharge of subsets of peripheral receptors located in muscles and tendons, with contributions from joint capsular and ligamentous structures, and subcutaneous and cutaneous afferents. We did...
not detect a strong correlation between an impaired threshold for detection of knee displacement and pathology of ligaments and capsule (as reflected by restricted range of flexion and extension and increased joint valgus-varus laxity). This may suggest that mechanoreceptors located in these structures contribute little to proprioception in the osteoarthritic joint.

The prospect that the deterioration in knee joint position sense may contribute to rapid progression of knee OA has important implications for the care of patients with this disease. To date, rehabilitation strategies for these patients have not been designed to address these problems, and commonly applied neurotherapeutic physical rehabilitation approaches that facilitate improved sensorimotor integration have not been consistently applied in this patient population (28,29). There have been no coherent efforts to emphasize motor behavior modification and retraining aimed at facilitating neuromuscular joint-protective mechanisms. If a decline in proprioception predisposes to the development of knee OA in the high-risk elderly, there may be a role for preventive therapies that enhance proprioception and neuromuscular joint protection.

In summary, the present results confirm that proprioception declines with age, and that this decline is not simply the consequence of subclinical OA in the elderly. Patients with knee OA have worse knee joint position sense than elderly controls. Knee proprioception appears to be correlated with disease-specific functional status, and may contribute to functional status outcome. Longitudinal studies are needed to determine the impact of impaired proprioception on the development, radiographic progression, and functional decline of knee OA.

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REFERENCES


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