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Original Article

Hylonome

# Movement detection impaired in patients with knee osteoarthritis compared to healthy controls: A cross-sectional case-control study

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**Abstract**

The purpose of this study was to clarify whether osteoarthritis (OA) patients have a localized or a generalized reduction in proprioception. Twenty one women with knee OA (mean age [SD]: 57.1 [12.0] years) and 29 healthy women (mean age [SD]: 55.3 [10.1] years) had their joint position sense (JPS) and threshold to detection of a passive movement (TDPM) measured in both knees and elbows. JPS was measured as the participant's ability to actively reproduce the position of the elbow and knee joints. TDPM was measured as the participant's ability to recognize a passive motion of the elbow and knee joints. The absolute error (AE) for JPS (i.e., absolute difference in degrees between target and estimated position) and for TDPM (i.e., the difference in degrees at movement start and response when recognizing the movement) was calculated. For TDPM a higher AE (mean [SE]) was found in the involved knees in patients than in the matched knees of healthy participants (AE: 2.41° [0.20°] versus 1.47° [0.14], $p=0.001$). The same held true for the non-involved knees between OA and healthy subjects (AE: 2.20° [0.20°] versus 1.57° [0.14°], $p=0.016$). Furthermore TDPM was higher in OA patients' right elbows compared to healthy participants' right elbows (AE: 2.15° [0.20°] versus 1.45° [0.15°], $p=0.011$). No significant difference between healthy women and OA patients regarding the left elbow for TDPM, or JPS was observed. The present age-controlled, cross-sectional study suggests that there is an increase in threshold to detection of a passive motion in knees and elbows for patients with knee OA. This indicates that OA may be associated with a generalized defect in proprioception with possible implications for the pathogenesis of the joint degeneration.

**Keywords:** Osteoarthritis, Proprioception, Elbow, Females, Joint Position Sense

## Introduction

There are indications that knee osteoarthritis (OA) may develop and/or progress due to an increased joint load[1]. Joint load and the shock absorption (e.g., during walking) may be moderated by muscle activity around the joint[2]. To achieve the optimal use of muscle activity, a normal sensory input is necessary[3]. Poor proprioception may lead to poor control and greater mechanical load on the joint, which in turn may lead to an increased risk of development and/or progression of OA[4-6].

Compared to healthy participants, patients with knee OA have a poorer sense of joint position and a higher threshold for detection of a passive movement, i.e., a reduced proprioceptive function across the affected joint[7-10]. The decrease in proprioception may increase load on the knee joint when walking, increase laxity of the joint and lead to a higher energy demand during walking, thereby reducing the walking speed[11-13]. Finally poor proprioception could lead to decreased postural control, which increases the risk of falling[14,15].

A decreased proprioception may be due to alterations in the joint mechanoreceptors caused by the osteoarthritic changes in and around the joint (e.g., osteophytes, inflammation, joint effu-

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| | OA | Control | p-value* |
|---|---|---|---|
| N | 21 | 29 | |
| Age (years, mean [SD]) | 57.1 (12.0) | 55.3 (10.1) | 0.565 |
| Height (cm, mean [SD]) | 164.5 (5.4) | 166.8 (7.4) | 0.266 |
| Weight (kg, mean [SD]) | 75.2 (19.0) | 65.2 (10.9) | 0.071 |
| Body Mass Index (BMI, mean [SD]) | 28.5 (7.4) | 23.3 (3.1) | 0.025 |
| Unilateral knee OA (left, n [%]) | 8 (38%) | - | - |
| Unilateral knee OA (right, n [%]) | 5 (24%) | - | - |
| Bilateral knee OA (n [%]) | 8 (38%) | - | - |
| WOMAC function [range: 0-4] | 1.00 (0.53) | 0.04 (0.2) | $p<0.001$ |
| WOMAC pain [range: 0-4] | 1.25 (0.84) | 0.00 (0.00) | $p<0.001$ |
| WOMAC stiffness [range: 0-4] | 1.33 (0.79) | 0.21 (0.61) | $p<0.001$ |
| Lequesne [range: 1-26] | 9.6 (2.9) | 0 (0) | 0.005 |
| Use of NSAID, n (%) | 5 (24%) | 0 (0%) | - |
| Use of Glucosamine, n (%) | 7 (33%) | 0 (0%) | - |
| Antihypertensive, n (%) | 6 (29%) | 0 (0%) | - |
| Use of other medication, n (%) | 6 (29%) | 0 (0%) | - |

*$p$-values for unpaired t-test

**Table 1.** Characteristics of the participants.

sion, etc.)[16]. However another possibility might be that poor proprioception is a risk factor *per se* concerning the development and progression of knee OA. A reduction in shock absorption would exacerbate the OA as a result of poor proprioception across the knee joint when walking[5,6,17]. Some studies have shown poor proprioception across both knees, despite only one knee being affected with OA[8-10,18,19]. One explanation for the contralateral effect of the proprioception might be an overload of the non-affected joint. Poor proprioception could thus be related to knee OA in at least two different ways, either as a local effect of OA in the knee or as a general reason for development or progression of the disease. Whether poor proprioception is local or general in these patients can be evaluated by measuring the proprioception across both knees and a healthy joint unrelated to weight-bearing joints. The elbow joint is rarely affected by OA[20] and may as such serve as a control joint. The aim of the present study was to investigate whether OA patients have a local or general reduction in proprioception. This was examined by testing the proprioception across both knees and elbows in patients with knee OA, compared to the same joints of a healthy control group. Tests for sense of joint position and threshold for detection of a passive movement were chosen because they are the most frequently used methods to measure aspects of proprioception and both have been used to detect abnormalities in patients with knee OA.

## Materials and methods

### Participants

Twenty-one women diagnosed with osteoarthritis - in one or both knees - volunteered to participate (mean age [SD]: 57.1 [12.0] years) (Table 1). The patients were recruited in the outpatient clinic and were all otherwise healthy, without signs of medical diseases (e.g., diabetes mellitus, earlier neurological disease, etc.), neck or back pains, or signs of disease in the elbow joints (e.g., arthritis, tennis elbow, etc.). None of the participants had daily intake of alcohol. All patients fulfilled the ACR criteria for knee OA[21], including both clinical and radiographic signs of OA, and all patients' diagnosis of knee OA had been made from 2 to 10 years before participating in this study; 13 were diagnosed with primary knee OA, and 8 were diagnosed with secondary knee OA. Of the 21 subjects, eight complained of bilateral osteoarthritis, 5 had osteoarthritis in the right knee and 8 in the left knee. The patients had mild to moderate OA, as indicated by both the Western Ontario and McMaster Universities' OA index (WOMAC)[22] and the Lequesne algofunctional indices for the hip and knee[23] (Table 1). The WOMAC scores, which range from 0 to 4 are presented as the mean of the possible scores for each of the three subscales (i.e., function, pain, and stiffness).The Lequesne index is presented as a total score between 1 and 26 (Table 1) with higher scores indicating greater severity. The patients were either on no medication or on stable medication not expected to influence the sensory afferent function, and none had been injected or received other invasive therapies in their joints during the preceding 3 months. The patients' use of other medication is given in Table 1. Weight and height were measured during baseline measurements and body mass index (BMI) was calculated using the formula: weight [kg] / height$^2$ [m$^2$]).

The control group consisted of 29 healthy women volunteers (mean age: 55.3 [10.1] years) (Table 1) recruited among staff, acquaintances and via advertisements in the local press. A clinical examination showed that no volunteers had any signs or symptoms of OA in knees or elbows, and none had had pain in the upper or lower extremities during the previous six months. Weight and height was measured during baseline

measurements and BMI was calculated as noted above.

None of the participants was allowed to use alcohol, analgesics and/or sleeping medicine in the 24 hours before measurement. The Scientific Ethics Committee for Copenhagen and Frederiksberg (J.nr. KF 01-077/02) approved the experimental protocol and each participant signed an informed consent before participating in the study.

## Procedure

Joint position sense (JPS) was defined as the participant's ability to actively reproduce a certain position in either the elbow or the knee. Threshold to detection of a passive movement (TDPM) was defined as the participant's ability to recognize when the calf or forearm was moved passively. Elbow and knee measurements for JPS and TDPM were performed on both left and right sides, each side being measured separately. For JPS each test was repeated three times and for TDPM six times. JPS was measured first followed by TDPM and each measurement lasted 45-50 minutes, meaning that the total measuring time was about 2 hours, all included. Both JPS and TDPM were measured on the same day.

JPS and TDPM were sampled with a frequency of 1000 Hz, a 0.2 second pre-trigger and with no interval between each sweep. JPS was sampled with a sweep length of 5 seconds, and TDPM with a sweep length of 10 seconds. The rest interval between measurements of each joint was approximately 3-4 minutes, and 5-8 minutes between TDPM and JPS. In both JPS and TDPM measurements the joints were tested in the same order to optimize standardization of the test procedure: right elbow, left elbow, right knee and left knee.

Before each JPS measurement the biaxial electrogoniometer (type XM65, Megaelectronics Ltd., Kuopio, Finland) was carefully checked in 0°, 60°, and 90° of elbow flexion and 0, 60° and 90° of knee extension. The goniometer was connected to an A/D converter (National Instruments, Inc.), which was interfaced to a computer with software for data collection (Data Acquisition Software, Pacquire Pro, vers. 1.11, K. Larsen, Aalborg, Denmark). The resulting voltage data was saved in the Pacquire-software program, transferred to MATLAB software program (Math Works, Inc., Copyright 1984-2002, ver. 6.5.0.180913a, June 18, 2002, Release 13), converted to degrees and transferred to Excel (Microsoft Excel 2000, 9.0.6926 SP-3). The reliability/precision of the electrogoniometer has been estimated to ±1.5° measured over 90° from the neutral position, with decreasing precision in movements over ±60° from neutral position.

When analyzing JPS the absolute difference (in degrees) between target angle and the subject's estimated angle, called Absolute Error (AE) was calculated. The AE for TDPM was the calculated difference between the joint start angle and the joint angle at response, when the participant perceived the movement.

Before and after each test session participants were asked to rate their present pain level on a Visual Analogue Scale (VAS: 0-100 mm). Additionally, after each test session participants were asked to rate their level of pain, concentration, stress, exhaustion and boredom during the test. The participants were tested unilaterally and blindfolded during both JPS and TDPM test sessions. Before each test session detailed instructions were given and two trial runs were performed. Furthermore, during TDPM the subjects wore foam earplugs and a hearing protector to exclude any sound from the motor.

## JPS of the elbow (Figure 1A)

JPS of the elbow was measured with the subject sitting, the hips and knees flexed in about 90° and the back supported (Figure 1A). The semi-pronated forearm was supported on an adjustable foamed forearm support. The electrogoniometer was attached on the lateral side of the elbow joint with the point of rotation of the elbow joint corresponding to the middle of the electrogoniometer. During all tests the subject was ordered to keep the thumb pointing upwards.

After attachment of the electrogoniometer an initial calibration procedure was run consisting of two tests performed with the elbow in full extension (0°) and at 90° flexion. Following is a brief explanation of the joint positioning and commands given during the JPS testing:

1. Baseline position. The elbow was placed in a relaxed position in about 0° (full extension), measured with a protractor. Hereafter the tests began and the commands from the test leader were:
   Target position. 'Slowly, flex your arm, until I say stop. Stop, hold and remember this position for 5 seconds.' After 5 seconds the test leader said:
2. Baseline position. 'Please return your arm to your resting position and stay there'. After 5 seconds the test leader said:
   Estimated position. 'Now return to the same position as before, and keep that position for the next 5 seconds'.
   During all tests for estimated positions the subject was allowed to flex and extend the elbow until the subject perceived the estimated position to be found. After 5 seconds the test leader said:
3. Baseline position. 'Now return your arm to your resting position again'.

Hereafter, the procedure was repeated twice, meaning a test session for each elbow consisted of three target positions (around 45°, 60° and 75° of elbow flexion), and three subject estimated positions.

A separate reliability test was performed of this setup with 26 healthy participants (mean age 35 years, range 19-57 years). A significant correlation coefficient between test and retest for JPS over the elbow was found to be $r=0.58$ ($p<0.001$) and a corresponding ICC(2.1)=0.59, indicating a fair to good reliability for AE[24].

## JPS of the knee (Figure 1B)

The participant was seated on a chair with no support for the lower legs. The electrogoniometer was placed on the lateral part of the knee with the flexion/extension axis of the knee

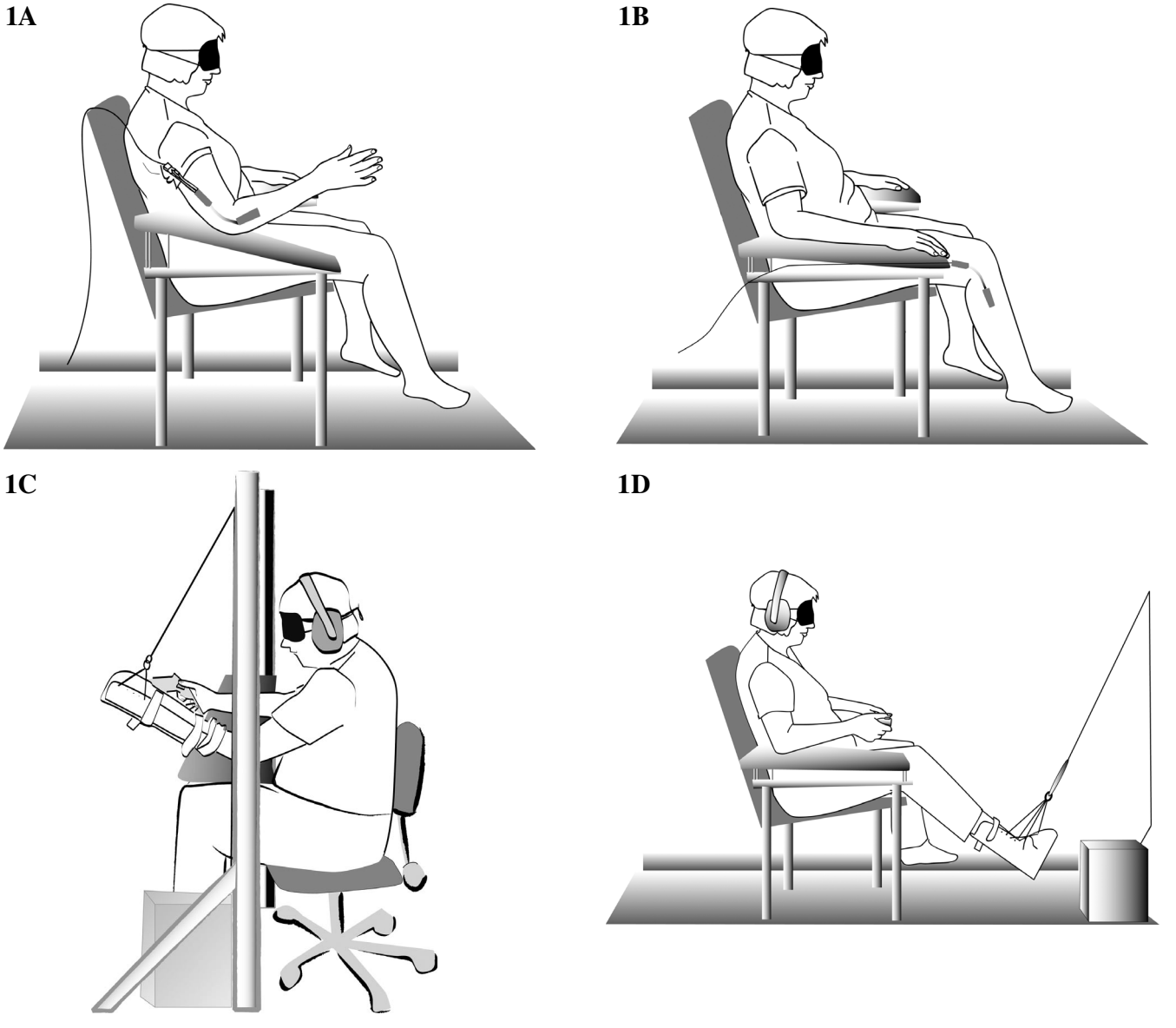


**Figure 1 A-D.** Test setup for the measuring JPS of the elbow (Figure 1A) and knee (Figure 1B). Test setup for measuring TDPM of the elbow (Figure 1C) and knee (Figure 1D).

corresponding to the middle of the electrogoniometer. The initial calibration procedure of the goniometer was two tests performed with the knee in full extension (0˚) and at 90˚ of flexion as measured with a protractor. Finally the knee was placed in a relaxed position of about 80˚ flexion (baseline). The commands used were similar to those described in JPS testing of the elbow. The reliability of knee JPS has previously been tested and found acceptable (ICC[2.1]:0.69)[25].

TDPM of the elbow (Figure 1C) and knee (Figure 1D)

For the elbow a plastic splint with adjustable straps was mounted on the forearm, covering the forearm proximally from about five centimetres from the anterior side of the elbow joint to the distal part of the fingers (Figure 1C). For the knee a plastic splint with adjustable straps was mounted on the leg, covering the calf proximally from about five centimetres below the posterior side of the knee joint to the distal part of the toes (Figure 1D). The forearm/hand and calf/foot were surrounded with an elastic tube sock to make the inputs of pressure from the skin equal. The forearm and calf splints were connected to a wire, which was connected to a motor via two pulleys. By measuring the individual moment arm (i.e., the distance of the forearm/calf from the point of rotation of the elbow/knee joint to a point in the middle of the two attack points of the wires on the splint) perpendicular to the direction of pulling force, and adjusting the motor speed corre-

spondingly, the angular speed of the forearm/calf was adjusted for each individual to be 1˚/sec. TDPM was measured in the elbow/knee with the subject in a sitting position (elbows: height adjustable chair with the shoulder in a relaxed flexed position in about 10˚ flexion, and the elbow flexed in 45˚; knees: in a relaxed position, with no support for the calf, with the hip flexed about 90˚, and the knee flexed about 60˚) and for both the elbow/knee test sessions the back was supported (Figures 1C and 1D). During the test sessions the elbow (starting in 90˚) was flexed 90˚-120˚ and the knee (starting in 60˚) was extended between 60˚-35˚. The subject was asked to detect a passive drive of the calf/forearm and respond manually to this by pressing a button as soon as the movement was detected. Before each test the command of the test leader was: 'Are you ready?' and the subject responded: 'Yes'. Hereafter, the lapse time before engaging the motor was randomised to be between one to eight seconds. Eight tests were performed, including two randomly placed dummy tests (no movements) to assure that the subject was unable to guess when the movement began.

A reliability study was performed to test elbow TDPM with 19 participants (mean age 30 years, range 18-50 years). For TDPM in the elbow there was a significant correlation ($r$=0.69; $p$<0.001) and ICC (2.1)=0.69, indicating a fair to good reliability[24].

A reliability study of knee TDPM was performed before the actual measurements and showed an ICC (2.1) of 0.87, indicating an excellent reliability.

### Data quality control

All procedures were rehearsed by BJK and HL before the actual study began. The JPS measurements were conducted by HL, and the measurements of TDPM were performed by BJK throughout the study.

Whenever the participant did not strictly follow the instructions for the JPS or TDPM measurement or any equipment error was detected (e.g., wire broke, electrogoniometer out of function, computer breakdown etc.), the test was cancelled and repeated. Ten of 200 tests were excluded corresponding to 5.0% of all JPS measurements.

In addition, a TDPM measurement was excluded when the marker was pressed more than once before the motor started and in the event of more than one positive response to a dummy measurement. Eight of 200 tests were excluded corresponding to 4.0% of all TDPM measurements. If there was no response during the measurement, the response time was defined as the maximum within 10 s, which was 9 s. This translates to a maximum TDPM detection error of approximately 9 degrees if there is no response.

## Data analysis

For each elbow and knee joint trial, absolute differences between the target and the estimated position were calculated. The three absolute differences obtained for each joint were then averaged and designated as the JPS Absolute Error (AE) for that joint.

For each elbow and knee joint, eight TDPM measurements were performed; 2 were dummies and were thus not used in the analysis. For each joint the average of the six other measurements was designated AE. Data are presented as mean values ± the standard error (SE) for each elbow and each knee; the primary outcome analysis was based on group mean differences with 95% confidence intervals (95%CI).

Results for the knees are presented as involved and non-involved for participants with knee OA. For participants with bilateral knee OA and for healthy controls the right knee was defined as the "involved knee".

A univariate analysis of covariance (ANCOVA) was performed with TDPM and JPS as dependent variables, respectively, applying group as a fixed factor and age as covariate. Accordingly, these univariate ANCOVA models included the main effect for group and age, with the corresponding interaction term applied: dependent variable, $Y_i=\mu+\alpha_{group,i}+\beta(age_i)+\alpha_{group}\times\beta(age_i)+e_i$. The analysis was conducted stepwise, i.e., if the interaction was non-significant, it was omitted from the final analysis: $Y_i=\mu+\alpha_{group,i}+\beta(age_i)+e_i$. By default, age and group were never excluded from the analysis, as a consequence of the *a priori* hypotheses.

Post hoc: Since a significant difference was observed between the knee OA group and the healthy group for BMI, BMI was also included in the univariate analysis of variance as a covariate, in order to illuminate the participants anthropometric status (e.g., obesity) possibly confounding the results.

A paired t-test was used to compare the JPS and TDPM results for left and right elbow for both subjects with knee OA and healthy participants.

We arbitrarily defined the statistical significance as a risk of making a type I error as 5%; therefore a 2-tailed $p$<0.05 was considered significant. SPSS statistical program (SPSS Inc., 1989-2003, Chicago, IL, version 12.0.1) was used for all the presented analyses.

## Results

Data are presented in Table 2 as mean (SE) values per group, and group mean differences provided with 95% CI.

### Joint Position Sense (JPS)

No significant difference between OA and controls was found for JPS over the knees and elbows (Table 2, Figure 2).

The participants' pain level obtained before measurements, and pain level, concentration difficulties, stress level, exhaustion, and boredom obtained immediately after measurements using a VAS-score showed no significant difference between patients with knee OA and healthy controls. The registration indicates (VAS<10 mm) that these aspects did not have any influence on the measurements (Table 3).

A significant difference of -1.7° (SE:0.6°; $p$=0.014) between left and right elbow was found for participants with knee OA, but no significant difference for healthy participants ($p$=0.93).

| | OA (n=21) Degrees [Mean (SE)] | Healthy (n=29) Degrees [Mean (SE)] | Difference in degrees (95% confidence intervals) | *p*-value | *p*-value (interaction) |
|---|---|---|---|---|---|
| **KNEE** | | | | | |
| **JPS** | | | | | |
| NON-involved | 5.94 (0.83) | 6.50 (0.55) | -0.53 (-1.59 to 1.06) | 0.622 | 0.251 |
| Involved | 5.01 (0.92) | 4.61 (0.61) | 0.40 (-0.77 to 1.57) | 0.733 | 0.314 |
| **TDPM** | | | | | |
| NON-involved | 2.20 (0.20) | 1.57 (0.14) | 0.63 (0.38 to 0.88) | 0.016 | 0.673 |
| Involved | 2.41 (0.20) | 1.47 (0.14) | 0.95 (0.70 to 1.20) | 0.001 | 0.308 |
| **ELBOW** | | | | | |
| **JPS** | | | | | |
| Left | 5.82 (1.50) | 7.55 (0.93) | -1.73 (-3.53 to 0.07) | 0.350 | 0.800 |
| Right | 7.87 (1.61) | 7.52 (1.01) | 0.35 (-1.65 to 2.35) | 0.860 | 0.779 |
| **TDPM** | | | | | |
| Left | 2.12 (0.29) | 1.52 (0.22) | 0.59 (0.20 to 0.98) | 0.135 | 0.016 |
| Right | 2.15 (0.20) | 1.45 (0.15) | 0.71 (0.45 to 0.97) | 0.011 | 0.403 |

**Table 2.** Differences in proprioceptive data for healthy controls and participants with knee osteoarthritis. For patients with bilateral knee OA, the right knee is involved and the left knee is non-involved. For healthy controls, the involved knee is the right knee, and non-involved the left knee.

Threshold to detection of a passive movement (TDPM)

The involved knee of the OA group showed a significant proprioceptive deficit compared to the healthy control group (mean AE of 2.41° (SE:0.20°)) versus 1.47° (SE:0.14°) ($p=0.001$)), respectively. Likewise, the non-involved knee of the OA group showed a significant proprioceptive deficit (AE of 2.20° (SE:0.20°) compared to the control group (1.57° (SE:0.14°)) ($p=0.014$) (Table 2, Figure 2). Additionally, the OA group showed a higher degree of TDPM error over the right elbow compared to the control group: 2.15° (SE:0.20°) vs. 1.45° (SE:0.15°) ($p=0.011$), but no significant difference for the left elbow: 2.12° (SE:0.29°) vs. 1.52° (SE:0.22°), ($p=0.135$) (Table 2, Figure 2).

The participants' pain level obtained before measurements and pain level, concentration difficulties, stress level, exhaustion, and boredom obtained after measurements as a VAS-score showed no significant difference between patients with knee OA and healthy controls. The results indicate (VAS<10 mm) that these aspects do not have any influence on the measurements (Table 3).

| | JPS | TDPM |
|---|---|---|
| **Overall mean** | 3.8 (4.9) | 0.1 (0.2) |
| **Level of pain before test** | 0.7 (1.7) | 0.0 (0.4) |
| **Level of pain after test** | 0.8 (1.9) | 0.0 (0.1) |
| **Difficulties with concentration during test** | 5.0 (10.6) | 0.1 (0.3) |
| **Stress during test** | 0.9 (2.1) | 0.1 (0.3) |
| **Exhaustion during test** | 1.0 (2.8) | 0.1 (0.4) |
| **Boredom during test** | 8.8 (18.5) | 0.1 (0.3) |

**Table 3.** Test condition. Each participant was asked to rate their level of pain before and after the test, and their difficulties with concentration, stress, exhaustion and boredom during the testing using a visual analog scale. Data is presented in millimeters as mean (SD).

No significant differences between left and right elbows for neither healthy participants nor participants with knee OA were observed ($p>0.70$).

BMI was not significant ($p>0.10$) for any of the eight analyses; and were thus omitted from the presented analyses (data not shown).

## Discussion

The results from this study indicate that in patients with knee OA poor proprioception is not limited to the affected osteoarthritic joint but is also found across the elbow joint. Although it is well established that patients with knee OA have decreased proprioception across both the affected knee[7-10,26] and the contralateral knee[8-10,18,27], the present results indicate that these patients have a more generalized proprioceptive problem.

Earlier studies suggest that fatigue and painful muscles give rise to poor proprioception[28-30], but these results indicate a local relationship, not a general one. Long-lasting nociceptic input has been shown to lead to an alteration in the perception of pain, the so-called central sensitization, and a similar picture has been observed in patients with OA[31]. This concept implies that long-lasting pain in one area leads to increased sensibility in another part of the body[31]. Thus it can be speculated that also the mechanoreceptor

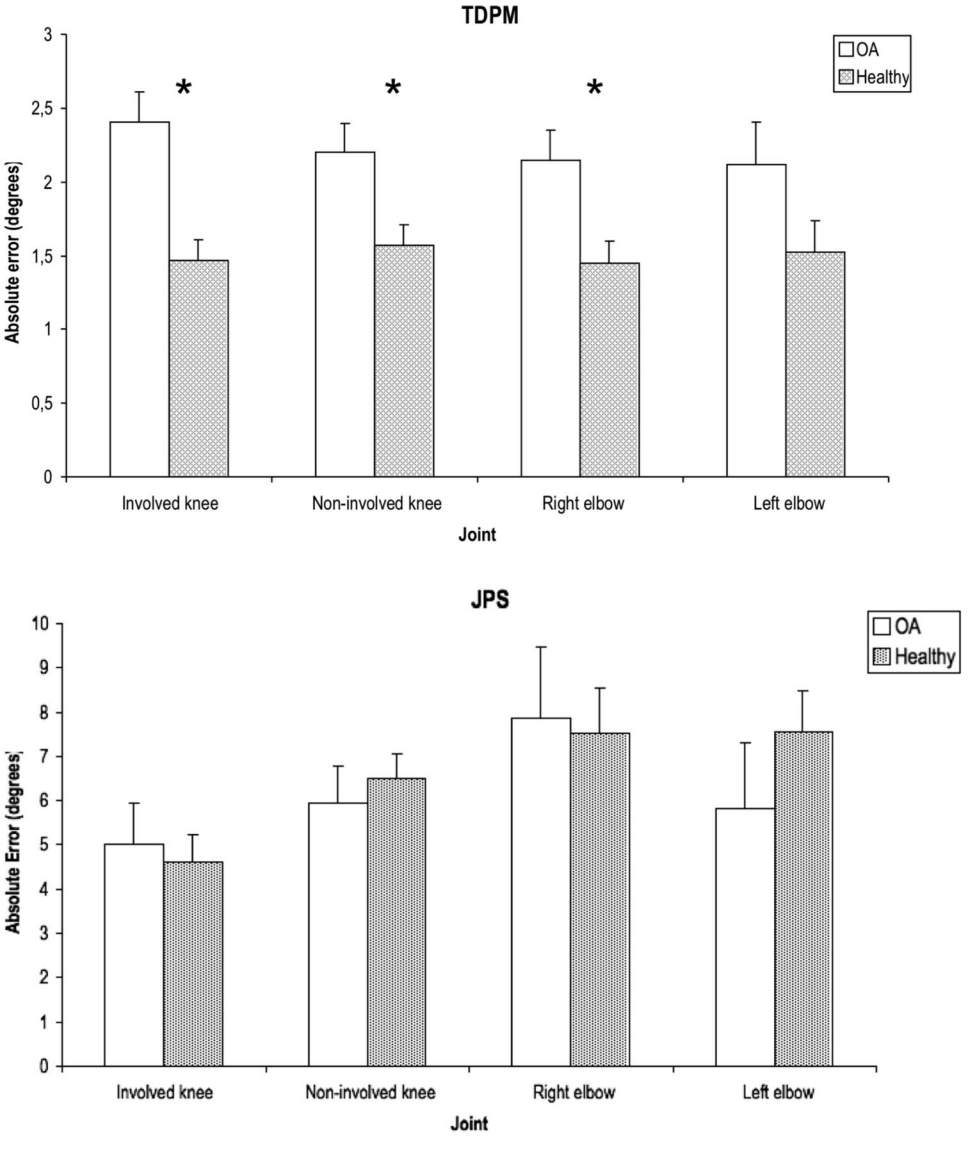


**Figure 2.** Bar graphs depicting the differences between TDPM and JPS across the knees and elbows for patients with knee osteoarthritis (OA) and healthy controls (Mean [SE]). Results for the knees are presented as involved and non-involved for participants with knee OA. * Denotes a significant difference between participants with knee OA and healthy controls.

input could be influenced by the change in the transmission of pain. Conversely, if a sensitization of pain input leads to a lower threshold for transmitting pain higher into the Central Nervous System (CNS)[31,32], a lower threshold of the synapses transmitting mechanoreceptor inputs may also lead to a higher degree of accuracy in proprioception. Another possibility is that the generally increased pain sensory input via the Gate Control[33] results in an overruling of the mechanoreceptor input and a general decrease in proprioception. According to the gate control theory, pain messages encounter "nerve gates" in the spinal cord that open or close at the same time, depending upon a number of factors (e.g., other external inputs at the same time, central inhibitory signals etc.). When the gates open, pain messages "get through" more easily and pain can be intense. When the gates close, pain messages are prevented from reaching the brain and may not even be experienced. However, more data are needed to clarify these issues of possible central mechanisms behind changes in proprioception.

In an earlier study poor proprioception was observed in both the involved knee and the contralateral knee, and it was suggested that poor proprioception could be a contributing factor in the development/progress of knee OA, rather than being secondary to this disease[8]. Studies examining the relationship between lack of afferent input in animal models of severe denervation indicate that this could be the case[4,5]. Nevertheless a

total cut of the afferent nerves was not enough to cause joint damage[34], whereas if the experimental sensory deficit (dorsal root ganglionectomy) was followed by even a minor trauma, the combination resulted in severe joint breakdown[34].

A general dysfunction of neuromuscular control and impairment of the neuromuscular protective reflexes as exemplified by the poor proprioception would lead to greater exposure of the joint to wear and tear (e.g., via diminished shock absorption during walking). However it has also been suggested that poor proprioception could negatively affect other dependent functions such as postural control, which means potentially further exposure of the knee joint to injury[15]. A weakened muscle may lead to higher demands on the passive stabilizing system (ligaments and capsular structure) in turn leading to an increase in the prevailing laxity of the joint[15]. An increased varus or valgus malalignment and/or laxity of the knee joint could lead to both an increased and a poorly distributed rate of load on the knee, which then could worsen the osteoarthritic alterations in the joint[3].

In our study only TDPM showed significant differences across the elbow in patients with knee OA compared to controls. One explanation for the different JPS and TDPM results could be that TDPM and JPS tests do not measure the same proprioceptive property[35]. Combining this with only a fair reliability for JPS over the elbow (ICC: 0.59) it could be concluded that the method used to measure JPS over the elbow was not optimal.

The measurement of both TDPM and JPS demands a high degree of concentration from the patient, and there is a potential risk of one or two lapses in concentration during measurement which can affect the data. If the end result is the mean value of a given number of tests, a higher number of repetitions would diminish the relative influence of a single lapse. With six available trials from TDPM and only three from JPS, a poorer comparative reliability may explain the difference between the TDPM and JPS measures in our study. Finally while both JPS and TDPM depend upon the participant's concentration abilities, only JPS depends upon the participant's memory while performing the test. This might also explain the high degree of error in JPS compared to TDPM. Another explanation for the diverging results between TDPM and JPS could be that the recruited patients in the present study had mild OA, as indicated by the low Lequesne and WOMAC scores (9.6 and 1.19, respectively). A recent study indicates that proprioception measured as a combination of JPS and TDPM showed a decreased proprioception only for participants with severe knee OA[36]. If this is the case, it may indicate that poor proprioception is the result of knee OA and not the cause of knee OA. Studies are needed to investigate this notion further.

Only the right elbow showed a significant decrease in proprioception compared to the healthy control elbow as measured by TDPM. Although there was a similar tendency on the left elbow, the difference did not reach statistical significance. The possibility that arm dominance could affect the results was considered. However when performing a paired t-test for the difference between the left and right elbow on healthy participants and for subjects with knee OA no significant difference was found between the right and left elbow ($p>0.7$). In addition only one participant with knee OA was left handed; accordingly, arm dominance could not be an explanation. Based upon these considerations and the lack of a good explanation we conclude that the poor TDPM was a general problem for participants with knee OA and not an artifact related to arm dominance.

Since eight patients complained of osteoarthritis in both knees defining the right knee as involved could introduce a possible bias to the results. However, an analysis with the left knee defined as involved and the right knee as non-involved for the eight with bilateral knee OA did not change the results. No significant differences for JPS was found and a significant difference for TDPM for both involved and non-involved knee was found with almost the same estimates and differences between patients with knee OA and healthy participants (data not shown).

It could be argued that anti-hypertensive medication may have an influence on the proprioception. However, participants having any kind of dizziness, tiredness (typical side effects to anti-hypertensitives) or lack of concentration due to e.g., menstruation, were not allowed to participate.

In the present study we recruited 21 participants: 13 with primary knee OA and 8 with secondary knee OA. It could be argued that a person with secondary knee OA may not have the same generalized poor proprioception as a person with primary knee OA, since the secondary knee OA is typically due to injuries and/or surgery rather than a generalized problem. However when analysing the secondary knee OA alone the same significant difference between elbows was found between the healthy controls and participants with knee OA ($1.32^{o}$ versus $2.14^{o}$, $p=0.019$)[37]. In addition the improved understanding of osteoarthritis as a multifactorial disease makes the classification into primary and secondary OA irrelevant[38]. This is further supported by the findings that meniscal lesion is often associated with early-stage knee OA[39].

As a significant difference in BMI between the patients with knee OA and the healthy controls was observed (Table 1), BMI could be a possible confounder. A higher BMI might in some cases lead to a lower physical activity level, but since we do not have any data on physical activity level for our participants, we were not able to elaborate more on this. Additionally, our results indicated no relationship between high BMI and poor proprioception.

A VAS-score was obtained for pain before the measurements and for pain, concentration difficulties, stress level, exhaustion, and boredom obtained after measurements in order to evaluate any confounding factors during measurements. A cut-off point of 10.0 mm was regarded as clinically relevant to evaluate the importance of the measured parameters[40]. Only boredom during the JPS measurements was close to the 10 mm (8.8 mm (SD:18.5), Table 3) cut-off point for clinical relevance, but still too low to have any relevance for interpreting the results. Furthermore, 'boredom' was

equally high in both groups and thus could not have biased our results.

An impaired proprioception cannot explain injuries in a knee affected by osteoarthritis, due to the relatively long time it takes for afferent input and motor output to respond to a sudden event[41]. Thus the possible clinical implications of a delayed recognition of a passive movement (TDPM) in both the elbow and knee of patients with knee OA would be that impaired proprioception may eventually lead to changes in the way the person uses the joint during walking and running. It is possible that the impaired proprioception is an indication of less control of the joint's angle during heel strike, poor timing of muscle contractions during heel strike or toe-off, poor co-ordination of the quadriceps and hamstrings and other incoordinations. The possible changes in proprioception in OA support the notion of the importance of extra-articular factors for the onset of joint degradation in knee OA[42]. If this is true, proprioception-promoting exercises may be favorable to the outcome in OA, as has been suggested for both patients with anterior cruciate ligament reconstruction[43] and knee OA[44]. Considering the fact that malalignment across the affected knee could worsen OA[45], exercise for some patients with knee OA should perhaps focus more on the patient's ability to control the knee, rather than simply strengthening the muscles.

## Conclusion

The present age-controlled, cross-sectional study found indications of an increase in threshold to detection of passive motion in the elbows of patients with knee OA. This suggests a generalized defect in movement detection with possible implications for joint degeneration in OA. The possible importance of poor proprioception as both a risk factor and a prognostic factor warrants further investigation. The possibility that subjects developing OA may have a confounder related to poor movement detection, and not OA, should also be investigated in the future using longitudinal cohort studies.

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