The association between reduced knee joint proprioception and medial meniscal abnormalities using MRI in knee osteoarthritis: results from the Amsterdam Osteoarthritis cohort

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Abstract

Background. Osteoarthritis (OA) of the knee is characterized by pain and activity limitations. In knee OA, proprioceptive accuracy is reduced and might be associated with pain and activity limitations. Although causes of reduced proprioceptive accuracy are divergent, medial meniscal abnormalities, which are highly prevalent in knee OA, have been suggested to play an important role. No study has focussed on the association between proprioceptive accuracy and meniscal abnormalities in knee OA.

Objective. To explore the association between reduced proprioceptive accuracy and medial meniscal abnormalities in a clinical sample of knee OA subjects.

Methods. Cross-sectional study in 105 subjects with knee OA. Knee proprioceptive accuracy was assessed by determining the joint motion detection threshold in the knee extension direction. The knee was imaged with a 3.0 Tesla MR scanner. Number of regions with medial meniscal abnormalities and the extent of abnormality in the anterior and posterior horn and body were scored according to the BLOKS method. Multiple regression analyses were used to examine whether reduced proprioceptive accuracy was associated with medial meniscal abnormalities in knee OA subjects.

Results. Mean proprioceptive accuracy was $2.9^{o} \pm 1.9^{o}$. MRI-detected medial meniscal abnormalities were found in the anterior horn (78%), body (80%) and posterior horn (90%). Reduced proprioceptive accuracy was associated with both the number of regions with meniscal abnormalities ($p<.01$) and the extent of abnormality ($p=.02$). These associations were not confounded by muscle strength, joint laxity, pain, age, gender, BMI and duration of knee complaints.

Conclusion.

This is the first study showing that reduced proprioceptive accuracy is associated with medial meniscal abnormalities in knee osteoarthritis. The study highlights the importance of meniscal abnormalities in understanding reduced proprioceptive accuracy in persons with knee OA.

(word count 279)

Key words. Osteoarthritis, Proprioception, Meniscus, Magnetic resonance imaging, Knee.

Introduction

Osteoarthritis (OA) of the knee involves many tissues, such as cartilage, bone, menisci and the synovial membrane (1-4). Clinical characteristics of the disease are joint pain and activity limitations (5). Reduced joint proprioceptive accuracy might be associated with pain and activity limitations (6-10). Although causes of reduced joint proprioceptive accuracy are divergent, meniscal abnormalities have been suggested to play an important role (11-13). As far as we are aware, the direct association between reduced knee joint proprioceptive accuracy and meniscal abnormalities has not yet been demonstrated in persons with knee OA.

Proprioceptive accuracy in knee OA is reduced and not well understood (9,10). Key factors that may affect proprioceptive accuracy in knee OA are: impaired articular mechanoreceptors, muscle weakness through reduced γ-motor neuron activation with reduced muscle spindle sensitivity, OA-related inflammation and effusion, and concomitant abnormalities to the anterior cruciate ligament or meniscus (9,10).

Meniscal abnormalities (i.e. tears or maceration) have been found in up to 80% of knees with OA (2-4). Meniscal abnormalities affect the load transmission of the knee in at least two ways: (i) through alteration of the morphology and anatomical structure of the meniscus, and (ii) by impairing the mechanoreceptors of the knee (2,12). Studies focusing on the mechanical properties of the menisci have found that the most substantive strains and the highest load (70%) are in the medial meniscus (14-16). In the medial meniscus, the mechanoreceptors are located in the outer rim, which is firmly attached to the capsule and the coronary (collateral) ligaments, where mechanoreceptors are also found (17,18). In contrast, the lateral meniscus is only attached to the coronary ligaments, not to the capsule and contains less mechanoreceptors (19). Therefore, it could be expected that a medial meniscal abnormality might reduce the number of mechanoreceptors, as well as impair mechanoreceptor function, thereby affecting proprioceptive accuracy. This effect may be bidirectional. Reduced proprioceptive accuracy may lead to meniscal damage due to impaired neuromuscular control and thereby knee instability. Instability may increase the strains and load on the medial meniscus with a high risk for damage, leading to a self-perpetuating cycle (20). The first step in studying this self-perpetuating cycle is by examining the relationship between proprioceptive accuracy and meniscal abnormality, which will improve knowledge regarding reduced proprioceptive accuracy. Therefore, the aim of this study was to explore the association between reduced proprioceptive accuracy and medial meniscal abnormality in a clinical sample of persons with knee OA.

Methods

Subjects. For the present study, participants were recruited from a randomized controlled trial (STABILITY-trial) from January 2010 to August 2011(21,22). This trial was embedded in the Amsterdam osteoarthritis (AMS-OA) cohort, a cohort of subjects with OA of the knee and/or hip who are referred to a specialized clinic (Reade, centre for rehabilitation and rheumatology, Amsterdam, the Netherlands) (21,22). Inclusion criteria were clinical knee OA diagnosis according to the American College of Rheumatology criteria (23), age between 40 and 75 years, biomechanically assessed and/or self-reported knee instability and written informed consent (21,22). Exclusion criteria were total knee arthroplasty, any form of arthritis other than OA, comorbidities affecting daily functioning, severe knee pain (NRS>8) and contra-indication for MRI (e.g. pacemaker, claustrophobia). The study was approved by the Slotervaart Hospital/ Reade, institutional review board. All measurements were scheduled prior to the start of an exercise program.

Knee joint proprioception. Proprioception was assessed in a knee joint motion detection task, expressed as the joint motion detection threshold. A device was used that provided knee angular displacement in extension and precise measurement of the angular displacement with a resolution of 0.1^{o} (figure 1). This method of assessment has been described in previous studies (6,24). The angular displacement between the starting position and the position at the instant of pushing a stop button was recorded. The threshold for detection of knee joint movement was defined as the difference, in degrees, between the actual onset of motion and the subject's detection of knee joint position change or motion. High joint motion detection threshold meant a great difference between the actual onset of motion and the subject's detection and expressed poor proprioceptive accuracy. The mean joint motion detection threshold from three measurements was used for analyses. ICCs for intra-rater reliability for the assessment of participants with and without OA by a single experienced tester were 0.91 and 0.86, respectively (24). The intra-rater SEM and MDD were 2.26^{o} and 6.26^{o}, respectively, in subjects with knee OA (24).

-Insert Figure 1-

MR imaging. MRI scans were performed of the knee that was clinically diagnosed with knee OA (in unilateral knee OA) or of the knee with most severely affected daily activities (in bilateral knee OA). Knees were imaged by a 3 Tesla whole body magnetic resonance scanner (General Electric Medical Systems, Milwaukee, WI) using a phased array knee coil. The MRI examination included five sequences. The first sequence was a sagittal proton density-weighted turbo spin-echo with fat suppression (slice thickness 3 mm; interslice gap 0.3 mm; repetition time (TR) 3480 ms; echo time (TE) 42 ms; turbo factor 8; matrix 384x256). The second sequence was a sagittal T1-weighted turbo spin-echo (slice thickness 3 mm; interslice gap 0.3 mm; TR 760 ms; TE 14 ms; turbofactor 2; matrix 384x256). The third sequence was a coronal T2-weighted turbo spin-echo with fat suppression (slice thickness 3mm; interslice gap 0.3 mm; TR 5800 ms; TE 85 ms; turbo factor 15; matrix 384x256). The fourth sequence was a sagittal combined multi-echo gradient echo (MERGE; thickness 3.5 mm; interslice gap 0.3 mm; TR 973 ms; excitation angle 20 degrees; matrix 352x224). The last sequence was a coronal combined multi-echo gradient echo (MERGE; thickness 3.0 mm; interslice gap 0.5 mm; TR 854 ms; excitation angle 20 degrees; matrix 352x224). For meniscal scoring, all five sequences were used, particularly the second and third sequences.

MRI medial meniscal abnormality was assessed following a commonly used scoring method, the Boston-Leeds Osteoarthritis Knee Score (BLOKS) (25,26), by a radiologist (JPK) with 27 years of musculoskeletal radiology expertise who was blinded to the participants clinical characteristics. Intra-observer reliability was found to be good in 15 participants (ICC=0.82).

The medial meniscus was divided into three regions: anterior horn, body and posterior horn. The extent of meniscal abnormality was scored as follows: normal, signal only, vertical tear, horizontal tear, complex tear, root tear, and maceration. A signal only was indicated as a signal within the meniscus which did not extend to an articular surface. A tear was indicated as high signal intensity within the meniscus that extended to two meniscal surfaces. Maceration indicated loss of overall normal morphological appearance of the meniscus as well as an associated increased diffuse signal in the meniscal tissue.

Two meniscal abnormality scores were used in statistical analyses. First, the number of regions (ranging from 0 to 3 regions) of the medial meniscus with an abnormality was scored. Second, meniscal abnormality extent was scored as follows: 0= no abnormality, 1 = signal only, 2 = tear (including vertical, horizontal, complex or root tear) and 3 = maceration. The highest score of meniscal abnormality extent of the three regions was used in analyses.

Muscle strength. Muscle strength of the left and right leg was measured isokinetically (EnKnee, Enraf-Nonius, Rotterdam, Netherlands) at 60^{o}/second (6,27). The mean muscle torque (i.e. extension and flexion) per leg was calculated to obtain a measure of overall leg muscle strength (Nm). For the analyses, individual mean muscle strength was divided by the subject's body weight for a normalized measure (Nm/kg).

Knee joint laxity. Joint varus-valgus laxity was measured as the total movement in the frontal plane during varus-valgus load in a non-weight bearing position (27). The mean of three measurements (degrees) was calculated for each knee.

Pain. Knee pain over the past week was assessed by an 11 point numeric rating scale (0 -10), with higher scores representing more pain. Subjects were asked: What was your pain rating on average over the past week?

Radiography. Radiographs of the knee were scored in a blinded fashion by an experienced radiologist. The grading scale proposed by Kellgren & Lawrence (K/L) was used to determine Radiographic Osteoarthritis (ROA) (28). Weight-bearing, anterior-posterior radiographs of the knee joints were obtained following the Buckland-Wright protocol (29).

Demographics. A series of demographic variables were obtained including age, gender, height, weight, Body Mass Index (BMI) and duration of complaints. For the analyses, age, BMI and duration of complaints were used as continuous variables.

Statistical analysis. Data of knee-specific variables were used from the index knee, which was the knee of which MRI had been obtained (i.e. knee diagnosed with clinical OA in unilateral knee OA or participant-reported knee most severely affecting daily activities in bilateral knee OA). First, descriptive statistics (mean ± SD or n, %) of the index knee were obtained. Second, analysis of variance was used to check for linearity of the associations between proprioceptive acuity and the MRI detected number of regions with meniscal abnormality and the extent of meniscal abnormality. Third, in order to assess the relationship between proprioceptive accuracy (joint motion detection) and MRI meniscal abnormality in knee OA two simple linear regression analyses were performed. The dependent variable was proprioceptive accuracy in degrees. The independent variable was the meniscal abnormality score, which was in model 1: number of regions with an abnormality (ranging from 0-3 regions); or 2) and in model 2: abnormality extent (ranging from 0-3, with 0=none; 1= signal only; 2=meniscal tear; 3= macerated meniscus). Results of the regression analyses are expressed as unstandardized (B) regression coefficients that represent the associations between proprioceptive accuracy and the number of regions with a meniscal abnormality and the extent of meniscal abnormality. Fourth, in multiple regression analyses, the dependent variable was proprioception in degrees and the independent variables were the meniscal abnormalities (model 1: number of regions with an abnormality, model 2: extent of abnormality). In both models muscle strength, joint laxity, pain, age, gender, Body Mass Index (BMI) and duration of complaints were included as covariates. Background knowledge identified muscle strength, joint laxity, pain, age, gender, Body Mass Index (BMI) and duration of complaints as potentional confounders, according to the confounder selection by Greenland (30). When with stepwise addition of covariates the regression coefficient of the number of regions with an abnormality or the regression coefficient of the extent of abnormality was not changed by 10%, these covariates were deemed insignificant to the outcome and were excluded from the final model.

All analyses were performed using SPSS software, version 19.0 (SPSS, Chicago, IL, USA).

Results

From a total of 112 potential candidates that participated a randomized controlled trial (21) from January 2010, 7 persons were excluded (reason: MRI could not be scheduled before start of trial).

Table 1 shows the characteristics of participants.

- Insert Table 1 -

The number of regions with a medial meniscal abnormality and the extent of abnormality are shown in Table 2. In 77% of the knees, an abnormality was found in the medial meniscus, with overall the highest prevalence of abnormalities in the posterior horn (89%). Maceration was present mostly in the body of the meniscus (44%). Tears were found most frequently in the posterior horn (29%) and signal only most frequently in the anterior horn (47%).

- Insert Table 2 -

In Table 3 it is shown that the proprioceptive accuracy decreased when the number of regions with a medial meniscus abnormality increased. For those with three regions of the meniscus affected, the proprioceptive accuracy was reduced by 3.2 degrees. It is also shown that the proprioceptive accuracy reduced when the extent of a meniscal abnormality increased. For those with a macerated medial meniscus the proprioceptive accuracy was reduced by 3.2 degrees.

- Insert Table 3 -

To identify cases that were outlying with respect to their values we used Cook's distance and leverage values to assess the influence on the regression model (31). We identified one case as an outlier with extreme proprioceptive inaccuracy and high laxity values and that case was excluded from further regression analyses.

Linear regression analyses (Table 4) showed that the number of regions with a meniscal abnormality was significantly associated with proprioceptive accuracy. This association was not confounded by any of the covariates (muscle strength, joint laxity, pain, duration of complaints and demographic factors). The presentation of the regression coefficient (B) indicates that with every increase in the number of regions with an abnormality in the medial meniscus, the accuracy of proprioception decreased by 0.48 degrees. Linear regression analyses also showed that the extent of meniscal abnormality was also significantly associated with proprioceptive accuracy (Table 4). This association was not substantively confounded by the covariates. The presentation of the regression coefficient (B) indicates that any unit of increase in extent of abnormality in the medial meniscus, ranging from normal to maceration, decreased the accuracy of proprioception by 0.39 degrees.

Discussion

In a cross-sectional study of persons with established knee OA, we explored the association between reduced proprioceptive accuracy and medial meniscal abnormalities. Abnormalities were present in the anterior horn (78%), body (80%) and posterior horn (90%) of the medial meniscus. A significant association was found between reduced proprioceptive accuracy and the number of regions with an abnormal medial meniscus, as well as with the extent of medial meniscus abnormality. Our results confirm the hypothesis that proprioceptive accuracy and meniscal abnormality are associated (2,3). A meniscal abnormality may predispose to reduced proprioceptive accuracy. Alternatively, reduced proprioceptive accuracy might itself add to an overloading of the medial meniscus through its reduced neuromuscular reflex responses, leading to knee joint instability and therefore to a self-perpetuating cycle. The cause and effect relationship need to be confirmed in longitudinal studies.

In proprioception, different active and passive key factors of the knee are integrated and related to each other (9,10). Via neuromuscular reflex responses, proprioception controls muscle activity and as a result protects the knee from excessive and possible injurious loads (9). In cases of injurious loads, meniscal abnormality is indirectly the result of reduced proprioceptive accuracy, but conversely, the meniscal abnormality will alter proprioceptive accuracy. Reduced proprioceptive accuracy, next to muscle weakness, is an important factor of the neuromuscular reflex system in the facilitation of joint stabilization. Knee instability is a highly prevalent characteristic in knee OA subjects (20,21,32-34). Therefore, our results suggest that persons with knee OA with reduced proprioceptive accuracy and meniscal abnormality will suffer from more knee instability. Future studies are needed to explore the associations between knee joint instability, reduced proprioceptive accuracy and meniscal abnormality. Consequently, reduced proprioceptive accuracy and meniscal abnormality necessitate a change in exercise regimes. Neuromuscular exercises might be of great importance in persons with reduced proprioceptive accuracy and meniscal abnormality with the aim to affect the self-perpetuating cycle and improve knee joint stability.

Several scoring methods have been developed over the last few years (25,26,35). We used the scoring of meniscal abnormality as has been described by the BLOKS (25,26). This scoring method provided the radiologist with a clear method to identify and classify the abnormal features of the medial meniscus. An MRI detected meniscal abnormality was defined as a loss of overall normal morphological appearance of the medial meniscus and scored as signal only, vertical tear, horizontal tear, complex tear, root tear or maceration of the anterior horn, body or posterior horn (25). Maceration of the meniscus was highly prevalent, which has also been found in other studies (2,11), indicating that our sample had severe knee OA. Tears were less frequently present (range from 4.7% to 28.6%) when compared to other studies (36-40). In those studies, more than 50% of subjects with knee OA showed tears, particularly in the early stages of knee OA.

Meniscal signal only, can be presumed as the first MRI meniscal feature showing an abnormal integrity of the meniscus (13). Some authors suggest that a signal is an MRI feature indicating normal integrity, while other authors define it as the first feature of a loss of integrity and therefore as an abnormality (13). We scored signal only as a non-severe abnormality, which we interpreted as the first characteristic of the medial meniscus in knee OA with a loss of integrity. A further reason to classify a meniscal signal as an abnormality is to be able to distinguish more precisely between normal morphology of the meniscus and the presence of a tear in the meniscus with high signal.

Several limitations to our study bear attention. Firstly, no control-group was included in the study. It is necessary to control for meniscal abnormalities in a ‘healthy’ population of comparable age and gender. It has been shown that meniscal abnormality is highly prevalent in healthy older subjects (2,3) and that proprioceptive accuracy decreases in the elderly (7,9). The present study is the first exploratory study that has shown an association between proprioceptive accuracy and meniscal abnormality in persons with established knee OA. This needs to be replicated in future studies, including early and severe knee OA, matched with healthy controls. Secondly, we assessed maceration as a severe extent of a meniscal abnormality. Maceration could be the result of destruction of the meniscus as part of the osteoarthritic process, but also the result of a former resection of the meniscus. In scoring MRI features, it is difficult to distinguish between maceration due to destruction or to a resection of the meniscus. History-taking could give additional information about the cause behind maceration. Thirdly, the BLOKS scoring system does not provide a scoring of tears in the 'red' zone, i.e. in the high-vascularization region of the insertional ligaments of the meniscus, while this region is of particular interest as it contains a higher density of mechanoreceptors. Future studies on the relation between meniscal damage and proprioceptive accuracy may need to focus on this particular region. Fourthly, subjects were included when biomechanically assessed and/or self-reported knee instability was present. Therefore, our results cannot be generalized to all subjects with knee OA. Finally, this study confirms former speculations about the relationship between proprioceptive accuracy and meniscal abnormality (2,3), however, it does not prove a causal relationship. Future studies need to focus on MRI detected meniscal features and proprioception in a longitudinal design, to clarify the interaction between meniscal abnormality and reduced proprioceptive accuracy in a self-perpetuating cycle.

To conclude, this is the first study showing that reduced proprioceptive accuracy is associated with medial meniscal abnormality in knee osteoarthritis. The study highlights the importance of meniscal abnormality in understanding reduced proprioceptive accuracy in persons with knee OA.

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Conflict of interest

The authors declare no competing financial interests.

Author contributions

Conception and design: van der Esch, Knoop, van der Leeden, Roorda and Dekker.

Acquisition of data or analysis and interpretation of data: van der Esch, Knoop, Hunter, Klein, van der Leeden, Voorneman, Gerritsen, Reiding, Knol, Lems, Roorda and Dekker.

Drafting the article or revising it critically for important intellectual content van der Esch, Hunter, Klein, Knoop, van der Leeden, Voorneman, Gerritsen, Lems, Roorda and Dekker.

Final approval of the version published: van der Esch, Knoop, Hunter, Klein, van der Leeden, Voorneman, Gerritsen, Knol, Lems, Roorda and Dekker

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Table 1. Characteristics of participants (n =105)

	Value
Age, mean ± SD years	61.4 ± 6.9
Women, no. (%)	73 (70%)
Body mass index, mean ± SD kg/m^2	29.1 ± 4.7
Duration of complaints, mean ± SD years	11.3 ± 9.2
Joint proprioception, mean ± SD degrees	2.93 ± 1.86
Joint laxity, mean ± SD degrees	6.9 ± 2.8
Isokinetic muscle strength (extension), mean ± SD Nm/kg	0.89 ± 0.47
NRS for pain intensity during the past week, mean ± SD (range 0-10)	5.1±2.1
K/L knee score, no. (%)	
0	1 (1%)
1	31 (29%)
2	28 (27%)
3	26 (25%)
4	19 (18%)

Table 2. Prevalence of MRI medial meniscal abnormality* by region, one option per region (n =105)

		Anterior horn	Body	Posterior horn
0	Normal (no signal or tear)	23 (21.9%)	21 (20.0%)	11 (10.5%)
1	Signal	49 (46.7%)	24 (22.9%)	26 (24.7%)
2	Tears	5 (4.8%)	13 (12.5%)	30 (28.6%)
3	Maceration	28 (26.7%)	47 (44.8%)	38 (36.2%)

***** Meniscal abnormalities were scored using the Boston-Leeds Osteoarthritis Knee Score (BLOKS) meniscus score.

Table 3. Distribution of proprioceptive accuracy in degrees over the number of regions with an abnormality and the extent of abnormality of the medial meniscus (n=105)

Number of regions with an abnormality	Proprioceptive accuracy (mean ± SD)	Extent of abnormality	Proprioceptive accuracy (mean ± SD)
0. no region	1.83 (1.06)	0. no abnormality	1.83 (1.06)
1. one region	2.09 (0.79)	1. signal	2.70 (1.74)
2. two regions	2.57 (0.93)	2. tears	2.85 (1.83)
3. three regions	3.20 (2.02)	3. maceration	3.19 (1.80)

Table 4 Results of the regression analyses of the number of regions of the medial meniscus with a MRI abnormality and the extent of MRI abnormality in the medial meniscus on knee joint proprioception

	Model 1: Number of regions			Model 2: Extent of abnormality		
	B	*p*	95% CI	B	*p*	95% CI
Unadjusted*	0.45	.009	0.12 - 0.79	0.37	.023	0.05 - 0.69
Adjusted**	0.48	.006	0.14 - 0.83	0.39	.023	0.05 - 0.72

B unstandardized regression coefficient
CI confidence interval
* simple regression: unadjusted
**multiple regression: adjusted for muscle strength, joint laxity, NRS pain, age, gender, Body Mass Index (BMI) and duration of complaints.

Figure 1. Experimental setup for the assessment of knee joint proprioception, showing the measurement chair control mechanism, handheld button, air splints, and footrest (the moving component of the apparatus).