

Chapter 4

Proprioception in knee osteoarthritis: a narrative review

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Abstract

Objective. To give an overview of the literature on knee proprioception in knee osteoarthritis (OA) patients.

Method. A literature search was performed and reviewed using the narrative approach.

Results. 1) Three presumed functions of knee proprioception have been described in the literature: protection against excessive movements, stabilization during static postures, and coordination of movements. 2) Proprioceptive accuracy can be measured in different ways; correlations between these methods are low. 3) Proprioceptive accuracy in knee OA patients seems to be impaired when compared to age-matched healthy controls. Unilateral knee OA patients may have impaired proprioceptive accuracy in both knees. 4) Causes of impaired proprioceptive accuracy in knee OA remain unknown. 5) There is currently no evidence for a role of impaired proprioceptive accuracy in the onset or progression of radiographic OA (ROA). 6) Impaired proprioceptive accuracy could be a risk factor for progression (but not for onset) of both knee pain and activity limitations in knee OA patients. 7) Exercise therapy seems to be effective in improving proprioceptive accuracy in knee OA patients.

Conclusions. Recent literature has shown that proprioceptive accuracy may play an important role in knee OA. However, this role needs to be further clarified. A new measurement protocol for knee proprioception needs to be developed. Systematic reviews focusing on the relationship between impaired proprioceptive accuracy, knee pain and activity limitations and on the effect of interventions (in particular exercise therapy) on proprioceptive accuracy in knee OA are required. Future studies focusing on causes of impaired proprioceptive accuracy in knee OA patients are also needed, taking into account that also the non-symptomatic knee may have proprioceptive impairments. Such future studies may also provide knowledge of mechanism underlying the impact of impaired proprioceptive accuracy on knee pain and activity limitations.

Introduction

Osteoarthritis (OA) of the knee is the most common form of arthritis and leads to more activity limitations (e.g., disability in walking and stair climbing) than any other disease, especially in the elderly (1). Recently, impaired proprioceptive accuracy of the knee has been proposed as a local factor in the onset and progression of radiographic knee OA (ROA) (2-10). Additionally, proprioceptive impairments could be a cause of knee pain or activity limitations in knee OA patients (11;12).

The most recent review on proprioceptive impairments in knee OA was published in 1999 (10). The last decade has shown a proliferation of studies on proprioception in knee OA, but a general overview is missing. We aim to provide a comprehensive overview of the current state of knowledge on proprioceptive accuracy in knee OA, using the narrative approach. Our review will identify areas in need of further research, including the need for systematic reviews on specific topics.

Our review will focus on 7 questions: 1) what are the functions of knee proprioception? 2) which methods measuring proprioceptive accuracy of the knee in knee OA patients have been described in the literature and are these methods related to each other? 3) do knee OA patients have impaired proprioceptive accuracy compared to healthy controls? 4) what is the cause of impaired proprioceptive accuracy in knee OA? 5) is radiographic knee OA (ROA) caused by impaired proprioceptive accuracy? 6) what is the impact of impaired proprioceptive accuracy on knee pain and activity limitations in knee OA patients? 7) what is the outcome of interventions aiming to improve proprioceptive accuracy in knee OA patients?

Method

A literature search, performed in Pubmed (all publications until September 2010), resulted in 4,133 hits. The search terms used are described in Table 1. A broad search strategy was chosen to minimize the chance of missing relevant articles. Articles were included when they were written in English or German and when they addressed proprioceptive accuracy in knee OA patients, whereby at least one of our 7 study objectives were examined. Studies on knee OA patients after total knee arthroplasty were not included in this review. References of included studies were checked for additional studies meeting the inclusion criteria. A total of 75 studies were found with relevant data on one or more of the study questions. These studies were categorized according to our 7 study questions and reviewed in a narrative way.

Table 1. Search strategy (combination of following search terms)

Key word	Search terms
'knee'	knee
AND	
'osteoarthritis'	osteoarthr* arthrosis degenerative arthritis pain
AND	
'proprioception'	proprio† joint instability joint stability balance coordination position sense motion sense joint motion sense joint reposition sense movement sensation kinesthesia kinaesthesia neuromuscular control sensorimotor changes buckling shifting giving way

* all terms that begin with osteoarthr; † all terms that begin with proprio.

Results

Knee proprioception

There is no single accepted definition of proprioception (3;13). It is mostly defined as a conscious and/or unconscious perception of position and movement of an extremity or a joint in space (6;10;14-16). Knee proprioception derives from the integration of afferent signals from proprioceptive receptors in different structures of the knee (10;17-20) and is also influenced by signals from outside the knee (e.g., from the vestibular organs, visual system, and cutaneous and proprioceptive receptors from other body parts) (10;13). Table 2 gives an overview of proprioceptive receptors of the knee and their location and stimulus specificity. Muscle spindles are thought to be the most important proprioceptive receptors of the knee (10;18;19).

Three presumed functions of knee proprioception have been described in the literature. Firstly, it is hypothesized that proprioceptive information is used to protect the knee against excessive and possible injurious movements via reflex responses (2;3;13;18;21). Secondly, proprioceptive accuracy of the knee is supposed to be needed to stabilize the knee during static posture (22;23). Thirdly, it is hypothesized that knee proprio-

Table 2. Proprioceptive receptors of the knee

Receptor	Location	Stimulus specificity
<i>Musculotendinous mechanoreceptors:</i>		
Muscle spindles	muscles fibres	muscle elongation, velocity, and acceleration (especially at mid-range of knee angle)
Golgi tendon organs	tendons	force developed by the muscle
<i>Articular mechanoreceptors:</i>		
Pacinian corpuscles (quick-adapting receptors)	ligaments, menisci, capsule	small (dynamic) changes in tissue deformation
Ruffini endings (slow-adapting receptors)	ligaments, menisci, capsule	joint angle (especially at extreme knee angles), velocity, intra-articular pressure, and strains
Golgi receptors	ligaments, menisci, capsule	joint angle (especially at extreme knee angles)
<i>Other receptors:</i>		
Bare nerve endings	various tissues in and around knee	(excessive) tissue deformation, pain, inflammation

Based on table of Solomonow and D'Ambrosia (17) and additional literature (10;18-20).

ception is important in coordinating complex movement systems and precise knee joint motions (22;23).

Knee proprioception measurements

Various methods for measuring proprioceptive accuracy of the knee (in the sagittal plane) have been described. The 2 most commonly studied groups of measurement methods are outlined below.

The first group consists of tests measuring knee (re)position sense (position sense tests). In these tests the knee is moved (actively or passively) towards a criterion angle. After a few seconds the knee is returned to the original position. Following this, the subject has to reproduce the perceived angle with the same or contralateral knee, or show the perceived angle on a knee model (2-8;11;16;19;21-47).

The second group consists of tests measuring sensations of passive, slow knee motion (motion sense tests or threshold detection tests). In these tests the knee is slowly and passively moved. The subject is required to detect the start and/or stop of this movement as quickly as possible. Subjects are also sometimes required to name the knee that is moved (8;9;18;24,48-56).

In both position and motion sense tests, visual and if possible other cues (i.e., auditory cues, vibration, cutaneous tension, and pressure) are eliminated.

Different protocols for the measurement of knee proprioception do not correlate well with each other and variations in protocol (e.g., sitting or standing position, passive or active motion, or variation in criterion angle, direction of motion or motion velocity) seem to affect measurement outcome (57-59). Studies in healthy subjects have shown a lack of correlation between the results of knee motion sense and knee position sense tests, and between different position sense tests (14;60). However, 2 of the different motion sense tests correlate significantly with each other (14). Several authors have tried to explain the lack of correlation between motion sense and position sense tests and between different position sense tests. It has been hypothesized that motion sense tests maximally stimulate articular mechanoreceptors with minimal stimulation of muscle spindles, while position sense tests stimulate both receptors (5). It has also been suggested that weightbearing (standing) tests involve more receptors than non-weightbearing (sitting) tests (19;29;61) and that the results from weightbearing tests could be confounded by patients' knee pain (29;61), lack of muscle strength (40;60), and/or lack of balance in standing (61).

The reproducibility (intra-rater reliability and intra-rater agreement) of twelve measurement protocols in knee OA patients (studies in which $n \geq 10$) is presented in Table 3 (position sense) and Table 4 (motion sense). The majority of these protocols have acceptable intra-rater reliability, as indicated by an ICC of 0.7 or higher (62). Motion sense tests seem to be more reliable compared to position sense tests, as indicated by the higher ICC scores. This has been supported by non-knee OA studies (63;64). The weightbearing position sense test (40) showed a lower ICC compared to all non-weightbearing tests indicating lower reliability. This was not supported in another study (61). Only 2 studies presented the intra-rater agreement (absolute measurement error) of the measurement protocol (19;50). The inter-study differences presented in Tables 3 and 4 should be interpreted with caution because of low numbers of subjects and differences in study design and time intervals.

Other methods for measuring knee proprioception (or related aspects of proprioception) have also been described in the literature (e.g., measurement of hamstring reflex contraction latency (65) and quadriceps force accuracy and steadiness (35)). These methods, however, have rarely been studied.

Impaired proprioceptive accuracy in knee OA patients

Proprioceptive accuracy of the knee seems to be impaired in knee OA patients. Eleven studies showed a significant impairment in position sense (6;19;29;31;35) or motion sense (9;18;24;49;51) in a total of 387 knee OA patients, when compared to age-matched healthy controls. Additionally, a study in 21 female knee OA patients found a significant impairment in motion sense, but not in position sense (8). Three other studies, in which 134 knee OA patients were tested, did not find a significant impairment in position sense (3;30) or motion

Table 3. Reproducibility (intra-rater reliability and intra-rater agreement) of knee position sense measurement protocols in knee OA patients ($n \geq 10$)

Author, date (reference)	Study size	Measurement protocol	Study design	Time interval	ICC	SEM
Marks et al, 1993 (40)	10 knee OA patients	standing position (on one leg; weightbearing leg tested), from 0° to angle between 20° and 40° knee flexion (towards flexion), active (re)positioning	inter-session; 5 trials each session	1 week 4 weeks	0.43 0.56	- -
Marks et al, 1993 (19)	10 knee OA patients	standing position (on one leg; weightbearing leg tested), from 0° to angle between 20° and 40° knee flexion (towards flexion), active (re)positioning;	inter-session; 2 trials each session	1 week	-	0.63°
		standing position (on one leg; non-weightbearing leg tested), from 0° to angle between 70° and 90° knee flexion (towards flexion), active (re)positioning	inter-session; 2 trials each session	1 week	-	0.76°
Hassan et al, 2002 (32)	10 knee OA patients and 10 healthy subjects	sitting position, from 90° to angle between 90° and 0° knee flexion (towards extension), passive positioning and active repositioning	inter-session; 4 trials each session (first trial omitted)	1 week	0.89	-
Wada et al, 2002 (21)	10 knee OA patients	sitting position (semi-reclined), from 90° to angle between 50° and 30° knee flexion (towards extension), active (re)positioning	inter-session; 6 trials each session	1 week	0.90	-
Hortobagyi et al, 2004 (35)	12 knee OA patients	sitting position, from 90° to angle between 75° and 15° knee flexion (towards extension), passive positioning and active repositioning	inter-session; 10 trials each session	10 weeks	0.72	-
Bayramoglu et al, 2007 (3)	12 knee OA patients and 8 healthy subjects	sitting position, from 90° to 45° knee flexion (towards extension), passive (re)positioning;	inter-session; 5 trials each session (first trial omitted)	2 days	0.62	-
		sitting position, from 0° to 45° knee flexion (towards flexion), passive (re)positioning	inter-session; 5 trials each session (first trial omitted)	2 days	0.70	-
Lin et al, 2009 (38)	108 knee OA patients	supine position, from 90° to angle between 90° and 0° knee flexion (towards extension), active (re)positioning	inter-session; 2 trials each session	1 day	0.84	-

ICC=intraclass coefficient (for intrarater reliability); CI=confidence interval; SEM=standard error of measurement (for intrarater agreement).

Table 4. Reproducibility (intra-rater reliability and intra-rater agreement) of knee motion sense measurement protocols in knee OA patients ($n \geq 10$)

Author, date (reference)	Study size	Measurement protocol	Study design	Time interval	ICC	SEM
Sharma et al, 1997 (9)	12 subjects with and without knee OA	sitting position (semi-reclined), from 45° knee flexion towards extension with 0.3°/second	intra-session; 10 trials each knee (in random order) per session	consecutive	0.95	-
Hurkmans et al, 2007 (50)	24 subjects with knee OA	sitting position (semi-reclined), from 30° knee flexion towards extension with 0.3°/second	inter-session; 3 trials each knee (in random order) per session	2 weeks	0.91	2.26°
van der Esch et al, 2007 (55)	63 subjects with knee OA	sitting position (semi-reclined), from 30° knee flexion towards extension with 0.3°/second	intra-session; 3 trials each knee (in random order) per session	consecutive	0.88	-

ICC=intraclass coefficient (for intrarater reliability); CI=confidence interval; SEM=standard error of measurement (for intrarater agreement).

sense (52), when compared to age-matched healthy controls. All studies mentioned above compared knee OA patients with age-matched controls. We refrained from summarizing studies not using an age-matched design, as age has been shown to affect proprioceptive accuracy (10;18;48;66-68).

There is some evidence (although conflicting) that knee OA patients with severe ROA have more severely impaired proprioceptive accuracy, when compared to knee OA patients with only doubtful or mild ROA. Two studies showed a significant difference in position sense between Kellgren/Lawrence grade 1 and grade 3 (3) and between grade 2 and grade 4 (45)). On the other hand, eight studies -with predominantly large numbers of subjects (3,682 knee OA patients in total)- showed no significant association between ROA and position sense (5;16;25;30) or motion sense (9;18;48;51).

A striking result in the literature is that proprioceptive accuracy of the non-symptomatic knee (i.e., no clinical or radiographic evidence of OA) in unilateral knee OA patients seems to be impaired as well. We found 4 studies in which proprioceptive accuracy of both knees in unilateral knee OA patients was compared to age-matched healthy controls. Three studies demonstrated an impairment in motion sense (9) or in position sense (29;37) in the non-symptomatic knee, while the other study showed that the non-symptomatic knee was impaired in motion sense, but not in position sense (8).

Causes of impaired proprioceptive accuracy in knee OA

Several (knee OA related) factors have been hypothesized for their possible causal role in impaired proprioceptive accuracy in knee OA patients, in particular impaired mechanoreceptors and muscle weakness. No evidence has been found for any causal role of these factors.

Impaired mechanoreceptors. It has been hypothesized that dysfunctional articular mechanoreceptors, which are prevalent in severe OA knees (69;70), may lead to impaired proprioceptive accuracy (6;71). However, no evidence was found to confirm this hypothesis.

Muscle weakness. Muscle weakness or atrophy may decrease muscle spindle sensitivity, thereby possibly impairing proprioceptive accuracy (6;37;72). However, impaired position sense was not associated with muscle weakness in 4 (small) cross-sectional studies in a total of 146 knee OA patients (3;21;35;46), while only 1 cross-sectional study showed a significant association between muscle weakness and impaired motion sense in 63 knee OA patients (55).

Other potential causes. OA-related inflammation has been hypothesized as a potential cause of proprioceptive impairments in knee OA patients (30;73;74), but this causal relationship has not been studied yet. However, 1 study was found in which (non-inflammatory) fluid was injected in the knee in 20 healthy subjects to study the role of effusion in proprioceptive accuracy. Effusion appeared to have no effect on position sense (73).

Several studies in patients with ACL-deficiency or with meniscal injuries have provided evidence for a role of these injuries in impairing proprioceptive accuracy (10;13;63;75). However, no studies have been found focusing on the role of ACL-deficiency or meniscal injuries in proprioceptive accuracy in knee OA patients.

Impaired proprioceptive accuracy as a cause of radiographic OA

Several authors have suggested that impaired proprioceptive accuracy reduces knee protection during walking, thereby possibly causing degenerative damage of the knee joint (2-10;18;42;72;76;77). One study showed that patients with impaired proprioceptive accuracy have their knees in a more extended position during walking, probably to stabilize the joint, which could lead to more degenerative damage of the knee joint (4). However, there is no evidence that altered walking patterns cause degenerative changes in the knee joint in knee OA patients.

As shown by 2 large longitudinal studies on the same database (5;44), there is currently no evidence that impaired proprioceptive accuracy (position sense) is a causal factor in the onset or progression of radiographic knee OA. Felson et al found no association

between position sense (at baseline) and both onset and progression of radiographic OA at 2.5 years follow-up in 2,243 persons with or at high risk for knee OA (5). In a study by Segal et al in 1,390 persons at high risk for knee OA (without ROA at baseline), position sense at baseline did not play a role in the onset of radiographic OA at 2.5 years follow-up, neither did an interaction between position sense and muscle strength (44).

Knee pain, activity limitations and impaired proprioceptive accuracy

Knee pain and impaired proprioceptive accuracy. Conflicting evidence was found for a cross-sectional relationship between knee pain and proprioceptive accuracy (for both position and motion sense) in knee OA patients. Six studies found a significant association between knee pain and impaired proprioceptive accuracy (in a total of 5,637 knee OA patients) (5;16;18;44-46), while 5 other studies did not find such an association (in a total of 364 knee OA patients) (9;11;30;35;56).

Two large longitudinal studies on the same database (with more than 2,000 subjects per study) showed that impaired position sense at baseline was not associated with onset of pain at 2.5 years follow-up (5;44), nor in interaction with muscle weakness (44) in persons at high risk of knee OA. One of these studies, however, did find a significant association with progression of pain at 2.5 years follow-up (in 2,243 persons with or at high risk of knee OA) (5).

Activity limitations and impaired proprioceptive accuracy. Conflicting evidence was found for a cross-sectional relationship between impaired proprioceptive accuracy (for both position and motion sense) and severity of activity limitations in knee OA patients. Namely, 9 studies showed a significant association in a total of 2,499 knee OA patients (5;16;18;35;40-42;48;55), while 5 studies examining 399 knee OA patients did not (6;11;19;31;49).

Two longitudinal studies provided evidence for a causal role of impaired proprioceptive accuracy (for both position and motion sense) in the progression of activity limitations in knee OA patients (5;53). Felson et al showed an association between impaired position sense at baseline and progression of activity limitations (WOMAC function) at 2.5 years follow-up (in 2,243 persons with or at high risk of knee OA) (5). Sharma et al found in 236 knee OA patients that impaired motion sense at baseline was associated (approaching significance) with a poor outcome on a chair-standing test, but not with a poor outcome on WOMAC-function at 3 years follow-up (53). In that study, poor outcome was defined as having poor function at both baseline and follow-up, or deterioration of function at follow-up compared to baseline.

Interventions aiming at improving proprioceptive accuracy in knee OA patients

Twenty-one studies on the effect of different interventions on proprioceptive accuracy in knee OA patients were found. Evidence for each type of intervention on proprioceptive accuracy, pain and activity limitations is summarized below.

Exercise therapy. Exercise therapy, supervised by physiotherapists, seems to improve proprioceptive accuracy (for both position and motion sense), as well as pain and activity limitations. This has been shown in 8 studies across a total of 582 knee OA patients (7;22;23;27;36;38;47;54). Proprioceptive exercises (both non-weightbearing and weightbearing) (23;27;36;38;47) and weightbearing muscle strengthening exercises (22;23;27) seem to be the most effective exercises in improving proprioceptive accuracy (position sense). Non-weightbearing muscle strengthening exercises, however, do not result in improvements in proprioceptive accuracy (position sense) (22;38). It is unclear whether proprioceptive or muscle strengthening exercises are more effective in improving proprioceptive accuracy and/or pain and activity limitations (23;27;38). A home-based exercise program (without supervision) was not effective in improving position sense in 38 knee OA patients (46). Improvements due to exercise therapy may result from its effect on muscle strength and endurance, thereby possibly increasing muscle spindle sensitivity (38;71), or through stimulation of articular mechanoreceptors (22;23). The suggested importance of weightbearing exercises can be explained by an increase in intra-articular pressure, thereby stimulating Ruffini nerve endings and thus increasing proprioceptive accuracy (22).

Use of knee bandages. We found conflicting evidence regarding the effect of elastic knee bandages on proprioceptive accuracy in knee OA patients. Four studies in 159 knee OA patients showed a significant improvement in position sense when wearing a bandage (2;16;37;45), whereas 2 other studies in 78 knee OA patients found no improvement in position sense (33) or motion sense (49). Furthermore, there is limited evidence that the use of knee bandages can reduce pain (33). It is possible that knee bandages may effect proprioceptive accuracy by stimulating skin receptors around the knee.

Use of knee braces. One study was found investigating the effect of a valgus knee brace on proprioceptive accuracy in 20 varus knee OA patients (26). This study showed a small significant improvement in position sense with the use of a brace, but no improvement in postural control. The authors suggested that braces may only provide subtle proprioceptive cues.

Taping. One study was found examining the effect of patellar taping on proprioceptive accuracy in 87 knee OA patients (34). The application of therapeutic patellar tape for a period of 3 weeks did not improve position sense.

Electrical stimulation. One study was found which examined the effect of electrical stimulation in combination with a knee sleeve on position sense in 38 knee OA patients (16). Electrical stimulation in combination with a sleeve was effective, but electrical stimulation was not more effective when compared to a sleeve-only group. Therefore, no evidence directly attributable to an effect of electrical stimulation on proprioceptive accuracy could be substantiated.

Intra-articular injections. Two studies were found investigating the effect of intra-articular hyaluronan injections on proprioceptive accuracy in knee OA patients (28;43). Diracoglu et al showed a significant, short-term improvement in both position sense, pain and activity limitations in 42 knee OA patients when compared to placebo (28). On the other hand, Payne et al showed no improvement in position sense in 22 knee OA patients (43). Both studies did not find any adverse effects. One study in 68 knee OA patients showed that pain-reducing injections (bupivacaine) resulted in a significant worsening of position sense (32).

Massage. One study on the effect of thigh-muscle massage showed no effect on position sense in 19 knee OA patients (39).

Discussion

In the last decade numerous studies on proprioception in knee OA patients have been published. However, an overview is lacking. We have provided a comprehensive overview of the current state of knowledge on this issue, categorized by study objective.

Knee proprioception is presumed to be required for protection against excessive movements, stabilization during static posture and coordination of movements, and therefore potentially important for joint damage prevention.

Different protocols for the measurement of knee proprioception have been described in the literature. These protocols correlate poorly with each other. Knee position sense and knee motion sense seem to be different aspects of knee proprioception and probably stimulate different receptors. One protocol can not be used to predict results from other protocols (61). Therefore, literature on proprioception may need to be differentiated into studies on position sense and studies on motion sense. Position sense tests are thought to be a measure closer to real life proprioceptive accuracy (5), but motion sense tests seem to be more reliable. We suggest that a new measurement protocol needs to be developed. Ideally, such a new protocol would combine the benefits of both motion sense tests (reliable) and position sense tests (functional relevance).

Multiple studies have shown that knee OA patients may suffer from impaired proprioceptive accuracy (for both position and motion sense). A few studies, however, did

not find an impairment in knee OA patients, possibly due to lack of power (30;52) or an absence of patients with severe knee OA (3). Two studies found an association between impaired proprioceptive accuracy and severity of radiographic knee OA, while 8 other studies did not. An explanation for this conflicting evidence could be that the 8 studies mainly included subjects with mild to moderate ROA, while a more marked contrast in ROA may be required to demonstrate an association with proprioceptive accuracy. Unilateral knee OA patients may have impaired proprioceptive accuracy in both knees. Four explanations for proprioceptive impairments in the non-symptomatic knee have been offered in the literature. Firstly, impaired proprioceptive accuracy could be a generalized problem and not a local phenomenon in knee OA patients. This explanation is supported by Lund et al who demonstrated impaired motion sense of the elbow in knee OA patients (8). Secondly, the non-symptomatic knee may develop symptomatic OA over time and thus show impaired proprioceptive accuracy in a preclinical phase (9;29). Thirdly, impaired proprioceptive accuracy of the non-symptomatic knee may be caused by an overload of this knee (8). Fourthly, a generalized reduction in physical condition of both knees, possibly due to reduced physical activity, has been described as a possible explanation for impaired proprioceptive accuracy in the non-symptomatic knee (9;37). Additional studies on knee OA patients, focusing on proprioceptive accuracy of joints other than the knee to test the hypothesis that proprioceptive accuracy is a systemic factor, are needed.

No OA-related causes of impaired proprioceptive accuracy in knee OA patients have yet been identified. Therefore, more research focusing on possible causes of impaired proprioceptive accuracy (e.g., inflammation) is needed. Such research should also take into account that the non-symptomatic knee may also have proprioceptive impairments. Use of MRI may reveal potential causes in a pre-clinical phase of knee OA.

No evidence for the hypothesized role of impaired proprioceptive accuracy on the onset or progression of ROA could be found. Two large longitudinal studies in knee OA patients showed no association.

Several (large) cross-sectional studies, but not all, have shown a positive significant relationship between knee pain, activity limitations and impaired proprioceptive accuracy in knee OA patients. In the literature, 2 opposite hypotheses on the influence of knee pain on proprioceptive accuracy are mentioned. Firstly, nociceptive input may overrule proprioceptive input, thereby impairing proprioceptive accuracy (8). Secondly, long-lasting nociceptive input may lead to a lower threshold of the synapses transmitting pain signals and possibly other inputs as well (e.g., proprioceptive input), thereby improving proprioceptive accuracy (8). A majority of studies demonstrating a positive relationship between knee pain and impaired proprioceptive accuracy may point to the first hypothesis. Three explanations can be offered for the mixed results on the relationship between knee pain, activity limitations and impaired proprioceptive accuracy in knee OA patients. Firstly, it

is possible that only severe proprioceptive impairments influence pain or activity limitations (5;6;11;22;30). Secondly, knee OA patients may compensate their impaired proprioceptive accuracy with other capacities, for instance greater muscle strength (5;6;19;31;55). This may suggest that impaired proprioceptive accuracy would only affect pain or activity limitations if other (compensatory) factors are also impaired, as shown by van der Esch et al (55). Thirdly, inter-study differences in proprioceptive measurement protocols could explain the conflicting evidence. Because of these mixed results, a systematic review incorporating a meta-analysis is indicated. Longitudinal studies have shown that impaired proprioceptive accuracy could be a risk factor for progression (but not onset) of pain and activity limitations in knee OA patients. It is possible that impaired proprioceptive accuracy affects pain and activity limitations only when the disease is at an advanced stage (i.e., it may contribute to progression of pain and activity limitations), but not at an early stage of the disease (i.e., it may not contribute to onset of pain and activity limitations). Future studies may provide more knowledge of the mechanism underlying the impact of impaired proprioceptive accuracy on pain and activity limitations.

Proprioceptive accuracy seems to be a modifiable factor in knee OA. This is evident from the results of a number of studies in knee OA patients which have shown significant improvements in position sense, as well as in pain and activity limitations, when following a supervised exercise program. Knee braces may also improve position sense, but evidence is scarce. Studies on other interventions have shown conflicting or no evidence for improvement in proprioceptive accuracy. No systematic review on the effectiveness of interventions on proprioceptive accuracy has been performed. Therefore, systematic reviews with meta-analysis are needed to draw definitive conclusions regarding the effect of these interventions, in particular exercise therapy, on proprioceptive accuracy and their clinical relevance (i.e., reduction in pain and activity limitations).

A limitation of this review is its narrative approach. No meta-analysis of the included articles was performed, therefore definitive conclusions can not be drawn. Furthermore, as our search was only conducted in one database, relevant articles may have been missed. Nevertheless, we assume this narrative review presents a comprehensive overview of the current state of knowledge of the role of proprioceptive accuracy in knee OA. Furthermore, it highlights areas in need of future research.

To conclude, recent literature has shown that proprioceptive accuracy may play an important role in knee OA. However, this role needs to be further clarified. A new measurement protocol for knee proprioception needs to be developed. Systematic reviews focusing on the relationship between impaired proprioceptive accuracy, knee pain and activity limitations and on the effect of interventions (in particular exercise therapy) on proprioceptive accuracy in knee OA are required. Future studies focusing on causes of impaired proprioceptive accuracy in knee OA patients are also needed, taking into account

that also the non-symptomatic knee may have proprioceptive impairments. Such future studies may also provide knowledge of the mechanism underlying the impact of impaired proprioceptive accuracy on knee pain and activity limitations.

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References

- (1) Guccione AA, Felson DT, Anderson JJ, Anthony JM, Zhang Y, Wilson PW et al. The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. *Am J Public Health* 1994;84(3):351-358.
- (2) Barrett DS, Cobb AG, Bentley G. Joint proprioception in normal, osteoarthritic and replaced knees. *J Bone Joint Surg Br* 1991;73(1):53-56.
- (3) Bayramoglu M, Toprak R, Sozay S. Effects of osteoarthritis and fatigue on proprioception of the knee joint. *Arch Phys Med Rehabil* 2007;88(3):346-350.
- (4) Bennell KL, Hinman RS, Metcalf BR. Association of sensorimotor function with knee joint kinematics during locomotion in knee osteoarthritis. *Am J Phys Med Rehabil* 2004;83(6):455-463.
- (5) Felson DT, Gross KD, Nevitt MC, Yang M, Lane NE, Torner JC et al. The effects of impaired joint position sense on the development and progression of pain and structural damage in knee osteoarthritis. *Arthritis Rheum* 2009;61(8):1070-1076.
- (6) Hurley MV, Scott DL, Rees J, Newham DJ. Sensorimotor changes and functional performance in patients with knee osteoarthritis. *Ann Rheum Dis* 1997;56(11):641-648.
- (7) Hurley MV, Scott DL. Improvements in quadriceps sensorimotor function and disability of patients with knee osteoarthritis following a clinically practicable exercise regime. *Br J Rheumatol* 1998;37(11):1181-1187.
- (8) Lund H, Juul-Kristensen B, Hansen K, Christensen R, Christensen H, Danneskiold-Samsøe B et al. Movement detection impaired in patients with knee osteoarthritis compared to healthy controls: a cross-sectional case-control study. *J Musculoskelet Neuronal Interact* 2008;8(4):391-400.
- (9) Sharma L, Pai YC, Holtkamp K, Rymer WZ. Is knee joint proprioception worse in the arthritic knee versus the unaffected knee in unilateral knee osteoarthritis? *Arthritis Rheum* 1997; 40(8):1518-1525.
- (10) Sharma L. Proprioceptive impairment in knee osteoarthritis. *Rheum Dis Clin North Am* 1999;25(2):299-314.
- (11) Bennell KL, Hinman RS, Metcalf BR, Crossley KM, Buchbinder R, Smith M et al. Relationship of knee joint proprioception to pain and disability in individuals with knee osteoarthritis. *J Orthop Res* 2003; 21(5):792-797.
- (12) van Dijk GM, Dekker J, Veenhof C, van den Ende CH. Course of functional status and pain in osteoarthritis of the hip or knee: a systematic review of the literature. *Arthritis Rheum* 2006;55(5):779-785.
- (13) Jerosch J, Prymka M. Proprioception and joint stability. *Knee Surg Sports Traumatol Arthrosc* 1996; 4(3):171-179.
- (14) Grob KR, Kuster MS, Higgins SA, Lloyd DG, Yata H. Lack of correlation between different measurements of proprioception in the knee. *J Bone Joint Surg Br* 2002;84(4):614-618.
- (15) Lephart SM, Pincivero DM, Rozzi SL. Proprioception of the ankle and knee. *Sports Med* 1998;25(3):149-155.
- (16) Collins AT, Blackburn JT, Olcott CW, Miles J, Jordan J, Dirschl DR et al. Stochastic resonance electrical stimulation to improve proprioception in knee osteoarthritis. *Knee* 2011;18(5):317-22.
- (17) Solomonow M, D'Ambrosia R. In: Scott WN, ed. *Neural reflex arcs and muscle control of knee stability and motion*. St. Louis: The Knee; 1994:107-120.
- (18) Pai YC, Rymer WZ, Chang RW, Sharma L. Effect of age and osteoarthritis on knee proprioception. *Arthritis Rheum* 1997;40(12):2260-2265.
- (19) Marks R, Quinney HA, Wessel J. Proprioceptive sensibility in women with normal and osteoarthritic knee joints. *Clin Rheumatol* 1993;12(2):170-175.
- (20) Lephart SM, Pincivero DM, Giraldo JL, Fu FH. The role of proprioception in the management and rehabilitation of athletic injuries. *Am J Sports Med* 1997;25(1):130-137.

- (21) Wada M, Kawahara H, Shimada S, Miyazaki T, Baba H. Joint proprioception before and after total knee arthroplasty. *Clin Orthop Relat Res* 2002;(403):161-167.
- (22) Jan MH, Lin CH, Lin YF, Lin JJ, Lin DH. Effects of weightbearing versus nonweightbearing exercise on function, walking speed, and position sense in participants with knee osteoarthritis: a randomized controlled trial. *Arch Phys Med Rehabil* 2009;90(6):897-904.
- (23) Lin DH, Lin YF, Chai HM, Han YC, Jan MH. Comparison of proprioceptive functions between computerized proprioception facilitation exercise and closed kinetic chain exercise in patients with knee osteoarthritis. *Clin Rheumatol* 2007;26(4):520-528.
- (24) Barrack RL, Skinner HB, Cook SD, Haddad RJ, Jr. Effect of articular disease and total knee arthroplasty on knee joint-position sense. *J Neurophysiol* 1983;50(3):684-687.
- (25) Birmingham TB, Kramer JF, Kirkley A, Inglis JT, Spaulding SJ, Vandervoort AA. Association among neuromuscular and anatomic measures for patients with knee osteoarthritis. *Arch Phys Med Rehabil* 2001;82(8):1115-1118.
- (26) Birmingham TB, Kramer JF, Kirkley A, Inglis JT, Spaulding SJ, Vandervoort AA. Knee bracing for medial compartment osteoarthritis: effects on proprioception and postural control. *Rheumatology (Oxford)* 2001;40(3):285-289.
- (27) Diracoglu D, Aydin R, Baskent A, Celik A. Effects of kinesthesia and balance exercises in knee osteoarthritis. *J Clin Rheumatol* 2005;11(6):303-310.
- (28) Diracoglu D, Vural M, Baskent A, Dikici F, Aksoy C. The effect of viscosupplementation on neuromuscular control of the knee in patients with osteoarthritis. *J Back Musculoskelet Rehabil* 2009; 22(1):1-9.
- (29) Garsden LR, Bullock-Saxton JE. Joint reposition sense in subjects with unilateral osteoarthritis of the knee. *Clin Rehabil* 1999;13(2):148-155.
- (30) Hall MC, Mockett SP, Doherty M. Relative impact of radiographic osteoarthritis and pain on quadriceps strength, proprioception, static postural sway and lower limb function. *Ann Rheum Dis* 2006;65(7): 865-870.
- (31) Hassan BS, Mockett S, Doherty M. Static postural sway, proprioception, and maximal voluntary quadriceps contraction in patients with knee osteoarthritis and normal control subjects. *Ann Rheum Dis* 2001;60(6):612-618.
- (32) Hassan BS, Doherty SA, Mockett S, Doherty M. Effect of pain reduction on postural sway, proprioception, and quadriceps strength in subjects with knee osteoarthritis. *Ann Rheum Dis* 2002; 61(5):422-428.
- (33) Hassan BS, Mockett S, Doherty M. Influence of elastic bandage on knee pain, proprioception, and postural sway in subjects with knee osteoarthritis. *Ann Rheum Dis* 2002;61(1):24-28.
- (34) Hinman RS, Crossley KM, McConnell J, Bennell KL. Does the application of tape influence quadriceps sensorimotor function in knee osteoarthritis? *Rheumatology (Oxford)* 2004;43(3):331-336.
- (35) Hortobagyi T, Garry J, Holbert D, DeVita P. Aberrations in the control of quadriceps muscle force in patients with knee osteoarthritis. *Arthritis Rheum* 2004;51(4):562-569.
- (36) Jan MH, Tang PF, Lin JJ, Tseng SC, Lin YF, Lin DH. Efficacy of a target-matching foot-stepping exercise on proprioception and function in patients with knee osteoarthritis. *J Orthop Sports Phys Ther* 2008; 38(1):19-25.
- (37) Jerosch J, Schmidt K, Prymka M. [Modification of proprioceptive ability of knee joints with primary gonarthrosis]. *Unfallchirurg* 1997;100(3):219-224.
- (38) Lin DH, Lin CH, Lin YF, Jan MH. Efficacy of 2 non-weightbearing interventions, proprioception training versus strength training, for patients with knee osteoarthritis: a randomized clinical trial. *J Orthop Sports Phys Ther* 2009;39(6):450-457.

- (39) Lund H, Henriksen M, Bartels EM, Danneskiold-Samsøe B, Bliddal H. Can stimulating massage improve joint repositioning error in patients with knee osteoarthritis? *J Geriatr Phys Ther* 2009;32(3):111-116.
- (40) Marks R, Quinney AH. Reliability and validity of the measurement of position sense in women with osteoarthritis of the knee. *J Rheumatol* 1993;20(11):1919-1924.
- (41) Marks R. An investigation of the influence of age, clinical status, pain and position sense on stair walking in women with osteoarthrosis. *Int J Rehabil Res* 1994;17(2):151-158.
- (42) Marks R. [Correlations between measurements of the sense of knee position and the severity of joint lesions in knee osteoarthritis]. *Rev Rhum Ed Fr* 1994;61(6):423-430.
- (43) Payne MW, Petrella RJ. Viscosupplementation effect on proprioception in the osteoarthritic knee. *Arch Phys Med Rehabil* 2000;81(5):598-603.
- (44) Segal NA, Glass NA, Felson DT, Hurley M, Yang M, Nevitt M et al. The Effect of Quadriceps Strength and Proprioception on Risk for Knee Osteoarthritis. *Med Sci Sports Exerc* 2010;42(11):2081-8.
- (45) Sell S, Zacher J, Lack S. [Disorders of proprioception of the arthrotic knee joint]. *Z Rheumatol* 1993;52(3):150-155.
- (46) Shakoor N, Furmanov S, Nelson DE, Li Y, Block JA. Pain and its relationship with muscle strength and proprioception in knee OA: results of an 8-week home exercise pilot study. *J Musculoskelet Neuronal Interact* 2008;8(1):35-42.
- (47) Tsao JY, Cheng PF, Yang RS. The effects of sensorimotor training on knee proprioception and function for patients with knee osteoarthritis: a preliminary report. *Clin Rehabil* 2008;22(5):448-457.
- (48) Collier MB, McAuley JP, Szuszczewicz ES, Engh GA. Proprioceptive deficits are comparable before unicondylar and total knee arthroplasties, but greater in the more symptomatic knee of the patient. *Clin Orthop Relat Res* 2004;(423):138-143.
- (49) Hewitt BA, Refshauge KM, Kilbreath SL. Kinesthesia at the knee: the effect of osteoarthritis and bandage application. *Arthritis Rheum* 2002;47(5):479-483.
- (50) Hurkmans EJ, van der Esch M, Ostelo RW, Knol D, Dekker J, Steultjens MP. Reproducibility of the measurement of knee joint proprioception in patients with osteoarthritis of the knee. *Arthritis Rheum* 2007;57(8):1398-1403.
- (51) Koralewicz LM, Engh GA. Comparison of proprioception in arthritic and age-matched normal knees. *J Bone Joint Surg Am* 2000;82-A(11):1582-1588.
- (52) Pap G, Machner A, Awiszus F. [Measuring knee joint kinesthesia for determining proprioceptive deficits in varus gonarthrosis]. *Z Rheumatol* 1998;57(1):5-10.
- (53) Sharma L, Cahue S, Song J, Hayes K, Pai YC, Dunlop D. Physical functioning over three years in knee osteoarthritis: role of psychosocial, local mechanical, and neuromuscular factors. *Arthritis Rheum* 2003;48(12):3359-3370.
- (54) Trans T, Aaboe J, Henriksen M, Christensen R, Bliddal H, Lund H. Effect of whole body vibration exercise on muscle strength and proprioception in females with knee osteoarthritis. *Knee* 2009;16(4):256-261.
- (55) van der Esch M, Steultjens M, Harlaar J, Knol D, Lems W, Dekker J. Joint proprioception, muscle strength, and functional ability in patients with osteoarthritis of the knee. *Arthritis Rheum* 2007;57(5):787-793.
- (56) Weiler HT, Pap G, Awiszus F. The role of joint afferents in sensory processing in osteoarthritic knees. *Rheumatology (Oxford)* 2000;39(8):850-856.
- (57) Ageberg E, Flenhagen J, Ljung J. Test-retest reliability of knee kinesthesia in healthy adults. *BMC Musculoskelet Disord* 2007;8:57.
- (58) Boerboom AL, Huizinga MR, Kaan WA, Stewart RE, Hof AL, Bulstra SK et al. Validation of a method to measure the proprioception of the knee. *Gait Posture* 2008;28(4):610-614.

-
- (59) Pincivero DM, Bachmeier B, Coelho AJ. The effects of joint angle and reliability on knee proprioception. *Med Sci Sports Exerc* 2001;33(10):1708-1712.
- (60) Kramer J, Handfield T, Kiefer G, Forwell L, Birmingham T. Comparisons of weightbearing and non-weightbearing tests of knee proprioception performed by patients with patello-femoral pain syndrome and asymptomatic individuals. *Clin J Sport Med* 1997;7(2):113-118.
- (61) Stillman BC, McMeeken JM. The role of weightbearing in the clinical assessment of knee joint position sense. *Aust J Physiother* 2001;47(4):247-253.
- (62) Streiner DL, Norman GR. *Health measurement scales: a practical guide to their development and use*. 3th ed. New York: Oxford University Press, 2003.
- (63) Friden T, Roberts D, Ageberg E, Walden M, Zatterstrom R. Review of knee proprioception and the relation to extremity function after an anterior cruciate ligament rupture. *J Orthop Sports Phys Ther* 2001;31(10):567-576.
- (64) Reider B, Arcand MA, Diehl LH, Mroczek K, Abulencia A, Stroud CC et al. Proprioception of the knee before and after anterior cruciate ligament reconstruction. *Arthroscopy* 2003;19(1):2-12.
- (65) Beard DJ, Kyberd PJ, Fergusson CM, Dodd CA. Proprioception after rupture of the anterior cruciate ligament. An objective indication of the need for surgery? *J Bone Joint Surg Br* 1993;75(2):311-315.
- (66) Kaplan FS, Nixon JE, Reitz M, Rindfleish L, Tucker J. Age-related changes in proprioception and sensation of joint position. *Acta Orthop Scand* 1985;56(1):72-74.
- (67) Skinner HB, Barrack RL, Cook SD. Age-related decline in proprioception. *Clin Orthop Relat Res* 1984;(184):208-211.
- (68) Petrella RJ, Lattanzio PJ, Nelson MG. Effect of age and activity on knee joint proprioception. *Am J Phys Med Rehabil* 1997;76(3):235-241.
- (69) Franchi A, Zaccherotti G, Aglietti P. Neural system of the human posterior cruciate ligament in osteoarthritis. *J Arthroplasty* 1995;10(5):679-682.
- (70) Schultz RA, Miller DC, Kerr CS, Micheli L. Mechanoreceptors in human cruciate ligaments. A histological study. *J Bone Joint Surg Am* 1984;66(7):1072-1076.
- (71) Hurley MV. The effects of joint damage on muscle function, proprioception and rehabilitation. *Man Ther* 1997;2(1):11-17.
- (72) Marks R. Further evidence of impaired position sense in knee osteoarthritis. *Physiother Res Int* 1996; 1(2):127-136.
- (73) McNair PJ, Marshall RN, Maguire K, Brown C. Knee joint effusion and proprioception. *Arch Phys Med Rehabil* 1995;76(6):566-568.
- (74) Sharma L, Pai YC. Impaired proprioception and osteoarthritis. *Curr Opin Rheumatol* 1997;9(3):253-258.
- (75) Jerosch J, Prymka M. [Proprioceptive deficits of the knee joint after rupture of the medial meniscus]. *Unfallchirurg* 1997;100(6):444-448.
- (76) Hurley MV, Rees J, Newham DJ. Quadriceps function, proprioceptive acuity and functional performance in healthy young, middle-aged and elderly subjects. *Age Ageing* 1998;27(1):55-62.
- (77) Radin EL, Martin RB, Burr DB, Caterson B, Boyd RD, Goodwin C. Effects of mechanical loading on the tissues of the rabbit knee. *J Orthop Res* 1984;2(3):221-234.