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Review

Proprioception in knee osteoarthritis: a narrative review

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SUMMARY

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 osteoarthritis (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

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need of further research, including the need for systematic reviews on specific topics.

Our review will focus on seven 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 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 4133 hits. The search terms used are described in Table I. 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 seven 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 seven study questions and reviewed in a narrative way.

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 II 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 proprioception 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 two 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

Table I
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.

Table II
Proprioceptive receptors of the knee

Receptor	Location	Stimulus specificity
Musculotendinous mechanoreceptors:		
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
Articular mechanoreceptors:		
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)
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].

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, two 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 12 measurement protocols in knee OA patients (studies in which $n \geq 10$) is presented in Table III (position sense) and Table IV (motion sense). The majority of these protocols have acceptable intra-rater reliability, as indicated by an intraclass coefficient (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 two studies presented the intra-rater agreement (absolute measurement error) of the measurement protocol[19,50]. The inter-study differences presented in Tables III and IV 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[6,19,24,29,31,35] 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 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 (3682 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

Table III
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	Intra-rater reliability (ICC)	Intra-rater agreement (S.E.M.)
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; five trials each session	1 week 4 weeks	ICC = 0.43 ICC = 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; two trials each session	1 week	–	S.E.M. = 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; two trials each session	1 week	–	S.E.M. = 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; four trials each session (first trial omitted)	1 week	ICC = 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; six trials each session	1 week	ICC = 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; ten trials each session	10 weeks	ICC = 0.72	–
Bayramoglu *et al.*, 2007[3]	12 knee OA patients and eight healthy subjects	Sitting position, from 90° to 45° knee flexion (towards extension), passive (re)positioning;	Inter-session; five trials each session (first trial omitted)	2 days	ICC = 0.62	–
		Sitting position, from 0° to 45° knee flexion (towards flexion), passive (re)positioning	Inter-session; five trials each session (first trial omitted)	2 days	ICC = 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; two trials each session	1 day	ICC = 0.84	–

CI = confidence interval; S.E.M. = standard error of measurement.

Table IV
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	Intra-rater reliability (ICC)	Intra-rater agreement (S.E.M.)
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°/s	Intra-session; 10 trials each knee (in random order) per session	Consecutive	ICC = 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°/s	Inter-session; three trials each knee (in random order) per session	2 weeks	ICC = 0.91	S.E.M. = 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°/s	Intra-session; three trials each knee (in random order) per session	Consecutive	ICC = 0.88	–

CI = confidence interval; S.E.M. = standard error of measurement.

found four 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 four (small) cross-sectional studies in a total of 146 knee OA patients[3,21,35,46], while only one 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, one 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 anterior cruciate ligament (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 two 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 ROA. 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 2243 persons with or at high risk for knee OA[5]. In a study by Segal *et al.* in 1390 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 5637 knee OA patients)[5,16,18,44–46], while five 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 2000 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 2243 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, nine studies showed a significant association in a total of 2499 knee OA patients[5,16,18,35,40–42,48,55], while five 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 (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)-function) at 2.5 years follow-up (in 2243 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 (both position and motion sense), as well as pain and activity limitations. This has been shown in eight 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 two 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 have an effect on 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 might 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 cannot 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 relevant).

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 ROA, while eight other studies did not. An explanation for this conflicting evidence could be that the eight 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 pre-clinical 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 magnetic resonance imaging (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, two 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 cannot 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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Author contributions

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Conflict of interest

The authors have no conflict of interest to disclose.

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