Effects of experimentally-induced anterior knee pain on knee joint position sense in healthy individuals

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Abstract

Purpose. The ability to sense the position of limb segments is a highly specialised proprioceptive function important for control of movement. Abnormal knee proprioception has been found in association with several musculoskeletal pathologies but whether nociceptive stimulation can produce these proprioceptive changes is unclear. This study evaluated the effect of experimentally induced knee pain on knee joint position sense (JPS) in healthy individuals.

Study design. Repeated measures, within-subject design.

Methods. Knee JPS was tested in 16 individuals with no history of knee pathology under three experimental conditions: baseline control, a distraction task and knee pain induced by injection of hypertonic saline into the infrapatellar fat pad. Knee JPS was measured using active ipsilateral limb matching responses at 20° and 60° flexion whilst non-weightbearing (NWB) and 20° flexion single leg stance. During the tasks, the subjective perception of distraction and severity of pain were measured using 11-point numerical rating scales.

Results. Knee JPS was not altered by acute knee pain in any of the positions tested. The distraction task resulted in poorer concentration, greater JPS absolute errors at 20° NWB, and greater variability in errors during the WB tests. There were no significant correlations between levels of pain and changes in JPS errors. Changes in JPS with pain and distraction were inversely related to baseline knee JPS variable error in all test positions (r = -0.56 to -0.91) but less related to baseline absolute error.

Conclusion. Knee JPS is reduced by an attention-demanding task but not by experimentally induced pain.

Keywords: Knee joint; Proprioception; Joint position sense; Experimental pain; Hypertonic saline

Introduction

The ability to sense the position and movement of limb segments individually and relative to one another are proprioceptive functions. Abnormal proprioception has been reported in association with a number of knee disorders including knee joint osteoarthritis [14,31], patellofemoral pain syndrome [2] and anterior cruciate instability [3,19]. However, the temporal relationship between abnormal proprioception and development of these clinical conditions is unclear. Proprioceptive deficits could predispose to the condition by altering the control of movement [29]. For example, in knee joint osteoarthritis sensorimotor dysfunction may cause greater impact of the leg at heel strike thereby initiating or perpetuating arthritic damage [28,31]. Since proprioceptive information from knee muscles and joint structures contributes to the overall neuromuscular control, abnormal proprioceptive feedback of knee position.
could contribute to the development of patellofemoral pain syndrome. Alternatively, nociceptive stimulation and pain, may directly interfere with the central processing of proprioceptive input and thus contribute to the abnormal proprioception reported in individuals with clinical knee pain conditions.

However, while pain is a consistent feature in many musculoskeletal knee conditions, it is difficult to isolate the effects of nociceptive and pain stimulation on knee joint proprioception from other features associated with pathology such as inflammation or altered joint and muscle function. Although one study found a correlation between average magnitude of pain and knee joint position sense (JPS) in individuals with osteoarthritic knees [26], this study did not assess pain at the time of JPS assessment. Previous research suggests the hypothesis that pain at the time of JPS testing may interfere with the perception of the position of the painful knee. For example, there is evidence that stimulation of nociceptors may interfere with proprioception at the point of convergence of afferent inputs in the dorsal horn [8]. One suggested mechanism is that a large proportion of free nerve endings are sensitised by peripheral release of pain modulating substances produced during the pain response. Neuroplastic changes in the integration of inputs from group III and IV (pain) and group II (proprioceptive) afferents in the spinal cord may lead to abnormal drive of muscle spindles in the affected region and thus abnormal sense of joint position [13,16,30]. Whether nociceptive stimulation and pain can cause clinical changes in proprioception similar to those identified in these largely animal studies has not been determined.

Using an experimental pain model in healthy volunteers allows controlled investigation of the effects of pain on proprioception. Injection of hypertonic saline is a well-accepted, efficient and safe method to induce pain in the knee joint angles, is one component of proprioception. Active ipsilateral matching is a commonly used and accepted method for measuring JPS [20,32]. It has face validity because muscle receptors are the primary contributors to proprioceptive information. Thus with active testing, in contrast to passive testing, the input from these receptors is maximised. Furthermore, active testing is more functional than passive testing. Our JPS test protocol has published discriminative validity as we have found significant differences in JPS between individuals with and without patellofemoral pain syndrome [2] and between individuals with and without hypermobile knees [33].

Knee JPS was examined using ipsilateral active matching under both non-weightbearing (NWB) and single leg weightbearing (WB) test conditions [2,32]. The NWB position confines JPS testing to the knee joint while the WB position is more functional. Four reflective markers were fixed with double-sided adhesive tape to the skin of the lateral thigh and leg over the apex of the greater trochanter, iliotibial tract level with the posterior crease of the knee when flexed to 80°, neck of the fibula and prominence of the lateral malleolus. These marker positions facilitated computer measurements of videotaped knee joint test and response positions.

Non-weightbearing JPS test

Participants sat with eyes closed on the side of a treatment couch with knees flexed and the supported trunk inclined backwards 25° from the vertical. The investigator lightly grasped the participants' foot and passively extended the relaxed knee at ~10°/s from the initial position (~80° flexion) to one of two target positions, approximately 20° and 60° flexion. The exact test (and response) positions were accurately measured from the videotape images on completion of the assessments. Participants were instructed to hold the knee (isometrically) in each test position for ~5s whilst attempting to identify (sense) the knee position. The investigator then re-supported the foot and returned the relaxed limb to the initial position. Participants were then instructed to extend the knee to the perceived test position and to hold that position for ~5 s. Five tests were performed at each target position.

Single limb weightbearing JPS test

Participants stood in bare feet with fingertip support for balance. The untested lower limb was flexed at the hip and knee so that it did not bear weight. Participants were instructed to close their eyes and flex the weightbearing knee until told to stop when knee was in the test position (≥20° flexion) as judged by the investigator.
asked to identify (sense) this position whilst holding it steadily for ~5 s. The participant then straightened the weightbearing knee before attempting to replicate the previous test position. This test was repeated for five times.

Measurement of knee joint angles

The Peak measurement system (Peak Motus \textsuperscript{v4.3.1}, Peak Performance Technologies Incorporated, Englewood, USA) was used to measure the angle of the knee from videotape records of each test and response position. A segment of videotape showing each position was automatically digitised for 0.32 s at a frequency of 50 Hz; that is 16 consecutive images. The obtained raw data representing the spatial location of the four reference markers were then filtered using a robust non-linear least-squares fourth order (Butterworth) filter (Peak Performance Technologies, 1995). Finally the knee angle was calculated from the filtered data using standard trigonometric formulae.

Three dependent variables were calculated for each knee JPS test: (i) relative error—the mean difference between the five test and response positions at each target (with positive errors representing over-estimation). Relative errors represent accuracy with directional bias; (ii) absolute error—the average signless difference between the five test and response positions at each target. Absolute errors represent accuracy without directional bias; (iii) variable error—the standard deviation from the mean of the five relative errors at each target. Variable errors represent the consistency of the five responses at each target.

The reliability of the chosen method of measuring JPS was established in 15 individuals (age 18–25 years) tested on two occasions one week apart. The results demonstrated good to excellent test-retest reliability with intraclass correlation coefficients (ICC 3,5) ranging from 0.76 to 0.86 with the exception of variable error at 20° NWB where the ICC was lower (0.65).

Pain measurements

During trials with experimentally induced pain, participants were asked to verbally indicate the severity of their pain using an 11-point numerical rating scale marked in 1-cm increments with the descriptors ‘no pain’ and ‘worst pain’ at the scale ends. Pain severity was measured at the start and end of each knee JPS task and the average of these measurements chosen to indicate pain level during each test. The location of pain was assessed in two ways at the conclusion of testing. First, we asked participants to indicate the average size of the area of knee pain felt during testing from a diagram depicting a series of 10 circles increasing in size from 1 to 10 cm in diameter. Second, we asked the participants to shade the region of pain on a body chart.

A McGill pain questionnaire (MPQ) was used to indicate the quality of the experimental pain [25].

Distraction measurements

At the end of each JPS test, participants were asked to verbally indicate their degree of concentration during the test using an 11-point numerical rating scale marked in 1-cm increments with the descriptors ‘no concentration’ and ‘maximal concentration’ at the ends. The measure of distraction was calculated as the concentration level subtracted from 10. We chose to measure distraction in this manner to focus the participant on concentration rather than on distraction.

Procedure

Participants performed the knee joint position sense tests under three experimental conditions: (i) baseline control; (ii) while performing a distraction task and (iii) during knee pain experimentally induced by injection of hypertonic saline. The order of the baseline control and distraction task experimental conditions was randomised but the induced pain condition was always undertaken last. During each of these three experimental conditions, the order of WB and NWB tests was randomised across participants but kept constant within each participant.

Distraction task

The distraction task required participants to count aloud backwards by threes starting at a random number between 500 and 600.

Experimental knee pain induced by injection of hypertonic saline

Sterile hypertonic saline (5%, 0.2–0.25 ml, Astra, Sweden) was injected medially into the infrapatellar fat pad using a 25-gauge needle at an angle of 45° in a superolateral direction (Fig. 1) [4]. The needle was inserted to a depth of approximately 10 mm. Knee JPS testing commenced once the pain was judged to be at least four on the numerical rating scale. If insufficient pain was experienced, a second injection was given. This was necessary in three participants.

Data analysis

Data were processed using the SPSS computer program (Norusis/SPSS Inc., Chicago, IL, USA). Concentration and pain levels were compared between JPS tests in each experimental condition using Freidman’s tests. Wilcoxon tests were then conducted post hoc to locate the source of any significant differences. After an initial examination for normality and homogeneity of variance, comparisons of difference in JPS errors between experimental conditions were made using one way repeated measures analysis of variance (ANOVA). Post hoc Fishers’ tests were conducted to locate the source of any significant differences. There was 80% power to detect a 1.5° difference between baseline and pain experimental conditions with a standard deviation of 1.1°. Relationships were sought between changes in JPS absolute and variable errors with pain and distraction relative to baseline levels and (i) pain levels (ii) baseline JPS errors, using Spearman’s ($r$) correlation coefficients. Correlations with relative error were not sought as they would not be meaningful given the method of calculating relative error.

Results

Experimentally-induced pain

The most common pain descriptors used by participants were ‘aching’ (50%), ‘annoying’ (44%), ‘throbbing’ (38%), ‘nagging’ (38%) and ‘dull’ (32%). Pain was experienced in the inferomedial knee and retropatellar region.
by the majority of participants (Fig. 1). Three participants reported pain proximally into the thigh and lateral hip aspect and one reported pain distal into the calf. The average (SD) self reported diameter of the area of pain was 4.9 (2.0) cm. Average pain levels were similar across the NWB test: 3.8 (2.6) min and WB test: 4.9 (2.7) min, respectively in the time between the JPS tests and the hypertonic saline injection (20° NWB test: 2.7 (1.9) min, 60° NWB test: 3.8 (2.6) min and WB test: 4.9 (2.7) min, p > 0.05). There was no difference in the time between the JPS tests and the hypertonic saline injection (20° NWB test: 2.7 (1.9) min, 60° NWB test: 3.8 (2.6) min and WB test: 4.9 (2.7) min, p > 0.05).

**Distraction levels**

The mean (SD) distraction levels reported by participants during the knee JPS tests in each experimental condition are shown in Table 1. There was a significant difference in distraction levels across the three tests in each experimental condition (all p < 0.001). Participants were more distracted during the distraction and pain conditions than during the baseline condition for most JPS tests (p < 0.01). Distraction was greater in the distraction condition than in the pain condition for both NWB tests (both p < 0.01). Overall the distraction task resulted in more distraction than the other tasks.

**Knee joint position sense**

**Comparison of knee joint position sense across experimental conditions**

The mean (SD) knee JPS errors for each test across experimental conditions are shown in Table 2. Differences in JPS error with pain and distraction compared to baseline are shown in Fig. 2. There was a significant difference in absolute error at 20° NWB across experimental conditions (p = 0.03). Post hoc tests revealed that the JPS absolute errors were greater in the distraction condition than in both the baseline and pain conditions (p < 0.05). There were no differences across experimental conditions for any of the other errors at 20° NWB or 60° NWB. For the WB tests, differences were noted for both absolute (p = 0.05) and variable (p = 0.017) errors. Again, JPS errors were greater during the distraction condition than during the baseline and pain conditions (p < 0.05).

**Relationship between levels of pain and changes in knee joint position sense relative to baseline**

There were no significant relationships between changes in knee JPS errors relative to baseline and levels of pain reported during each of the JPS tests. For 20° NWB, the correlation coefficients ranged from −0.07 to 0.28, for 60° NWB they ranged from −0.28 to 0.35, and for the WB tests, values ranged from −0.08 to 0.34 (all p > 0.05).

**Effect of baseline joint position sense on change in joint position sense with pain or distraction**

Although there was no effect of pain on JPS when group data were analysed, some effects were apparent when data were considered with respect to baseline error (Table 3). The change in variable error in all test positions with pain and distraction was significantly related to corresponding baseline variable errors. Correlation coefficients ranged from −0.56 to −0.91 indicating moderate to strong relationships. However, relationships were less apparent between baseline absolute errors and changes with pain and distraction with significant correlations only noted at 20° NWB (pain r = −0.73) and WB (distraction r = −0.72). Those with less JPS errors at baseline showed the greatest increase in JPS variable errors with pain and distraction.

**Discussion**

We used an experimental pain model to provide nociceptive stimulation of the infrapatellar fat pad thus allowing the effects of pain on knee JPS to be assessed. The results of this study indicate that acute anterior knee pain emanating from the infrapatellar fat pad...
and of a moderate to high intensity does not alter knee JPS consistently in a group of young healthy individuals.

We chose the infrapatellar fat pad as the site of nociceptive stimulation because we were specifically interested in the effects of anterior knee pain. The infrapatellar fat pad has been identified as a highly sensitive structure of the knee and a potential source of pain in a proportion of individuals with patellofemoral pain syndrome. Nerve fibres that are sensitive to substance P (a peptide that activates nociceptors) have been found in the fat pad [37,38] and instrumented arthroscopic palpation of internal components of the human knee without intraarticular anaesthesia has revealed that the fat pad is one of the most pain-sensitive structures [9]. We have recently established that in healthy asymptomatic individuals, hypertonic saline injected into the infrapatellar fat pad replicates the distribution and location of pain in patellofemoral pain syndrome. However, we acknowledge that our experimental pain model does not mimic all features of clinical pain. For example, the perception of pain with this model is reduced with movement and muscle activity unlike pain in patellofemoral pain syndrome [4].

Despite the differences between experimental and clinical pain, this technique allows investigation of the isolated effect of nociceptive stimulation and pain on motor control parameters. Our data indicate that simple nociceptive stimulation of the infrapatellar fat pad does not induce the same deficits in proprioception that are seen in clinical knee populations [2,31]. This suggests that other elements of the condition must be responsible for these reported deficits, including those specific to chronic pain states, the specific pathological changes or the actual source of pain production.

There is the possibility that we may have observed detrimental effects on knee JPS if pain was evoked from nociceptive stimulation of knee musculature rather than from the infrapatellar fat pad because muscle spindles play a key role in signalling proprioceptive information [27]. Although most participants felt pain in the region of the patellar tendon, few felt pain over the quadriceps muscle. Two studies have reported disruption of proprioceptive ability at the ankle [23] and at the elbow [36] when pain was induced in the muscles responsible for moving the test joint. In one study, a close correlation was found between the size of the errors and the level of perceived pain [36] which differed from our...
results where no relationship was apparent. Deficits in elbow proprioception have also been found when painful heat was applied to the skin over the contracting muscles, although the errors were smaller than those produced by experimentally induced muscle pain [36]. Heating skin remote from the elbow flexors had no effect. These studies may indicate a differential effect of pain on proprioception depending on the site of nociceptive stimulation.

Since there is evidence that the distribution of pain may affect proprioception [5,23], it is possible that the size of our pain region was insufficient despite the pain being of moderate to high intensity (average of 6 out of 10). At the ankle joint it has been shown that muscle spindle information from several muscles contributes to ankle proprioception [5]. It has been suggested that a large distribution of pain can interfere with proprioception by disturbing a large number of muscle spindles. With the same intensity pain felt in a smaller area, fewer spindles would be disturbed and the central nervous system may receive sufficient information from synergists, agonists and antagonists for proprioception [23].

Other explanations for our non-significant results may relate to aspects of the methodology. Our method of measuring knee JPS did not control the speed of movement to reach the criterion position and this may have provided different cues during the baseline and pain conditions thus influencing JPS results. Furthermore, the pain condition in our study was undertaken at the end of the trial in all participants. This was necessary to control for any latent effects of the experimental pain protocol and the occasional longer duration of pain (i.e., exceeding 30 min) that we have reported previously [4]. Although we cannot exclude an order effect, it is unlikely to have affected the results systematically as JPS did not differ from baseline values.

Joint position sense is one component of proprioception and we cannot exclude an effect of pain on other components such as movement sense or sense of force. This is supported by the study of Matre et al. [23] who found that pain induced by hypertonic saline injected into the tibialis anterior and soleus, and of similar intensity to that in our study, did not affect ankle joint position sense but did affect ankle movement detection threshold. Weerakkody et al. [36] investigated a torque-matching task in which elbow flexion torque was generated on one side and the task was to replicate that elbow flexion torque in the other limb. They found that muscle pain, and to a lesser extent skin pain, impaired the sense of muscle force.

Since pain demands attention [10], it was hypothesised that pain could affect proprioception by virtue of distraction. The central nervous system has finite cognitive resources and distraction by pain increases reaction time and decreases movement performance [35]. Thus, a distraction task was used to isolate the physiological effects of nociceptive stimulation on JPS from a 'simple' distraction effect. The increase in some JPS variables with distraction is consistent with other studies of JPS [34], reaction time [6] and movement accuracy [15] indicating that distraction interferes with task performance. The fact that the distraction condition but not pain influenced JPS might be because the degree of self-reported distraction during the pain condition was not as great as during the distraction condition. If we had matched the level of distraction in the pain condition to that in the distraction condition (i.e., via increased pain intensity or area), this may have induced a greater decrement in JPS. This is supported by Matre et al. [23] who assessed the relative importance of pain intensity and distribution in proprioceptive acuity. They found that pain of a moderate, but not mild, intensity was associated with changes in movement detection thresholds. They surmised that this might be due to greater spatial summation and/or greater shift of attention during pain [10].

The effects of distraction on JPS differed across the test positions and across the error types. In NWB, distraction only had an effect on absolute error at 20° knee flexion. The fact that relative error was not affected simultaneously indicates that participants did not systematically under- or over-estimate the target position with distraction. Effects may have been seen at 20°, but not at 60° as there is less absolute error and thus, more scope for distraction to decrease JPS. This is consistent with the finding that participants with less baseline absolute error also showed increases in error with pain at this knee angle but not with pain at 60°. Distraction resulted in greater errors in weightbearing and whilst there is additional afferent input available from other joints in this position, the effects of distraction may have been compounded by an influence on balance components of this task. Previous studies have identified changes in postural stability during similar distracting tasks in healthy young adults [21]. Furthermore, differences in results between the NWB and WB test positions may be due to differences in how the criterion position is reached. For the NWB test it is by passive movement of the limb by the researcher while in WB it is by voluntary active movement by the participant. These differences in cues received during movements into the criterion position may affect JPS errors perhaps due to different contributions of muscle afferents.

In some of the JPS test conditions, individuals with small baseline errors had largest increases in error with pain and distraction. This was evident for variable error more so than for absolute error. This dependence of an effect on baseline proprioception is consistent with previous studies whereby the propensity for change in JPS depends on the initial error. Although few studies have investigated whether increases in error may be greater in people with low initial error, several studies have
argued that this group may have reduced potential for improvement. McNair and Heine [24] could only observe a reduction of trunk JPS error with application of a brace in people with large initial errors. They were unable to find improvement in those who were initially very accurate. Similarly, the application of tape to the patella in healthy individuals improved knee JPS only in those with high initial errors [7].

There are numerous methods of measuring JPS described in the literature. We used a reliable method of active ipsilateral matching in both NWB and WB. While it is difficult to compare with other studies due to methodological differences particularly participant age and knee angles tested, our baseline errors appear comparable. Absolute errors in WB of asymptomatic individuals of a similar age have ranged from 2° to 3° [11,18] similar to the 2.1° in the current study. For NWB, the errors have ranged from 0.4° to 3.4° [18,22] which are comparable to our values of 1.5° and 2.7°.

Conclusion

This study suggests that the previously reported decrements in knee proprioception identified in people with clinical knee conditions such as patellofemoral pain syndrome might not be simply explained by the presence of acute nociceptor stimulation and pain. Other factors associated with the clinical condition may contribute. If this is the case, then resolution of pain is unlikely to lead to improvements in JPS. Furthermore, it remains possible that deficits in proprioception precede or even contribute to the development of pain and this cannot be determined from the current study. It is possible that pain from other knee structures may have different effects on knee proprioception to those seen from nociceptive stimulation of the infrapatellar fat pad.

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References


