

Quadriceps Arthrogenic Muscle Inhibition: Neural Mechanisms and Treatment Perspectives

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Objectives: Arthritis, surgery, and traumatic injury of the knee joint are associated with long-lasting inability to fully activate the quadriceps muscle, a process known as arthrogenic muscle inhibition (AMI). The goal of this review is to provide a contemporary view of the neural mechanisms responsible for AMI as well as to highlight therapeutic interventions that may help clinicians overcome AMI.

Methods: An extensive literature search of electronic databases was conducted including AMED, CINAHL, MEDLINE, OVID, SPORTDiscus, and Scopus.

Results: While AMI is ubiquitous across knee joint pathologies, its severity may vary according to the degree of joint damage, time since injury, and knee joint angle. AMI is caused by a change in the discharge of articular sensory receptors due to factors such as swelling, inflammation, joint laxity, and damage to joint afferents. Spinal reflex pathways that likely contribute to AMI include the group I nonreciprocal (Ib) inhibitory pathway, the flexion reflex, and the gamma-loop. Preliminary evidence suggests that supraspinal pathways may also play an important role. Some of the most promising interventions to counter the effects of AMI include cryotherapy, transcutaneous electrical nerve stimulation, and neuromuscular electrical stimulation. Nonsteroidal anti-inflammatory drugs and intra-articular corticosteroids may also be effective when a strong inflammatory component is present with articular pathology.

Conclusions: AMI remains a significant barrier to effective rehabilitation in patients with arthritis and following knee injury and surgery. Gaining a better understanding of AMI's underlying mechanisms will allow the development of improved therapeutic strategies, enhancing the rehabilitation of patients with knee joint pathology.

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Marked weakness of the quadriceps muscles is typically observed following knee injury, after knee surgery and in patients with arthritis. This is partly due to muscle atrophy and partly to ongoing neural inhibition that prevents the quadriceps from being fully activated, a process known as arthrogenic muscle

inhibition (AMI). AMI has been linked to articular swelling, inflammation, pain, joint laxity, and structural damage (1-4). The relative importance of these factors is not clearly understood but it is generally accepted that AMI is caused by a change in the discharge of sensory receptors from the damaged knee joint (1,2,4-8). Anomalous joint afferent discharge may have powerful effects on the central nervous system, influencing the excitability of multiple spinal and supraspinal pathways that combine to limit activation of the quadriceps muscles.

Quadriceps AMI has long been of concern to clinicians as it contributes to muscle atrophy and can delay or even prevent effective strengthening, hindering rehabilitation considerably. While mild AMI does not preclude strength gains (9-11), it is likely to restrict their magnitude as a portion of the muscle cannot be activated. During the first few months after injury or surgery, or when joint damage

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is extensive, AMI may be severe and quadriceps strengthening protocols can be largely ineffective. Despite resistance training, quadriceps strength may remain unchanged or even decline significantly (12-17), an effect attributed to AMI (12,17). As a result, quadriceps strength deficits often remain long after the initial joint trauma (18,19). Persistent quadriceps weakness is clinically important as it may impair dynamic knee stability (14,20), physical function (14,21-23), and quality of life (22), increase the risk of re-injury to the knee joint (24), and contribute to the development and progression of osteoarthritis (OA) (25-27).

The objective of this review is to provide the reader with a deeper understanding of AMI, with a focus on its potential neural mechanisms and therapeutic interventions that may help reduce its impact on rehabilitation. The first section of this article describes the presentation of AMI, including factors that may influence its severity and time course. We then review the sensory innervation of the knee joint and provide an outline of factors that may alter afferent discharge in the presence of knee damage. Thereafter, we examine the spinal reflex pathways that have been implicated in AMI and discuss the potential influence of supraspinal centers on this process. Finally, we present the most promising therapeutic interventions that may help clinicians overcome AMI.

METHODS

To implement the review, an initial search of the literature was undertaken using a variety of sources including experimental papers, review papers, and conference proceedings, as well as a general internet search. From this initial search an extensive keyword list was developed (eg, quadriceps, knee extensors, muscle inhibition, voluntary activation, arthrogenic, arthrogenous, knee injury, knee trauma, OA, gonarthrosis, rheumatoid arthritis, knee surgery, joint receptors, articular receptors, afferent, sensory, neuromuscular, reflex inhibition, interneuron, motoneuron, supraspinal, swelling, effusion, inflammation, pain, instability). An initial check of the keyword list was made again in a number of databases (AMED, CINAHL, MEDLINE, OVID, SPORTDiscus, and Scopus), where appropriate additional keywords were added and modifications to the keyword list were made. This was supplemented with a review of the bibliographies of past review papers on AMI, as well as the personal libraries of the contributing authors. Only peer-reviewed papers published in the English language were included in this review.

RESULTS

The Presentation of AMI

AMI occurs across a wide range of knee joint pathologies, with significant quadriceps activation deficits observed in patients with OA (11,28,29), rheumatoid arthritis (RA)

(9), anterior knee pain (30), patella contusion (31), following anterior cruciate ligament (ACL) rupture (10,32) and reconstruction (33), after meniscal damage (34) and meniscectomy (35,36), and in patients who have undergone knee joint arthroplasty (17,37,38).

AMI has been quantified using electromyography (EMG), interpolated twitch, or burst superimposition. Interpolated twitch and burst superimposition are the most commonly used methods and rely on electrical stimulation augmenting quadriceps force production during maximum effort contractions, thereby revealing incomplete muscle activation. Interpolated twitch superimposes 1 or multiple electrical stimuli on various levels of muscle contraction, calculating activation failure using the formula: $1 - (\text{superimposed twitch force at maximum effort} / \text{superimposed twitch force at rest})$. Burst superimposition superimposes a train of stimuli only during maximum contraction and calculates voluntary activation using the formula: $\text{maximum effort torque} / (\text{maximum effort torque} + \text{superimposed stimulus torque})$. Unfortunately, researchers have used a number of different stimulation parameters (eg, single versus multiple stimuli, different joint angles, estimated versus measured resting twitch force) to quantify AMI, all of which can alter estimates of muscle activation (39). Furthermore, in healthy subjects quadriceps activation has been found to be 8 to 16% higher using burst superimposition compared with interpolated twitch (39), while even interpolated twitch has been suggested to overestimate true activation (40). The heterogeneity and limitations of the methods used to assess AMI make it difficult to compare the absolute magnitude of inhibition across studies and suggest that in many cases the magnitude of AMI may have been underestimated.¹ Nevertheless, repeated measures of interpolated twitch and burst superimposition within single studies (ie, using the same stimulus parameters) provide valuable information concerning the time course of AMI and how its severity may vary across different patient groups.

AMI appears to be most severe in the acute stages of joint damage. To investigate the early progression of AMI, Shakespeare and coworkers (36) asked patients to perform maximum effort isometric quadriceps contractions and compared the amplitude of presurgery quadriceps EMG to that recorded at various times in the first 2 weeks after meniscectomy. These authors found that EMG amplitude was typically reduced by 50 to 70% in the first few hours post surgery. Over the next 24 hours, inhibition tended to become more severe (80-90%) and by 3 to 4 days was still 70 to 80%. After 10 to 15 days inhibition

¹For the purposes of this review, the magnitude of AMI as assessed by burst superimposition and interpolated twitch was calculated under the assumption that full quadriceps activation equals 95%. In studies that used the same stimulus parameters to compare quadriceps activation in healthy controls and patients with joint pathology, the difference between the 2 groups is presented.

had subsided somewhat but was still 30 to 50%. Similarly, AMI is enhanced in the first 3 to 4 weeks after total knee joint arthroplasty (TKA). Using burst superimposition, researchers (17,38) have shown that AMI increases substantially from presurgery values of approximately 10% to almost 30% when assessed 3 to 4 weeks after surgery. During the same time period, quadriceps strength decreased by an average of 60% (range, 30-85%), with multiple linear regression analysis suggesting that AMI contributed almost twice as much as muscle atrophy to the observed weakness (38).

There is evidence that with time the severity of AMI lessens. For instance, Snyder-Mackler and coworkers (41) found that 9 of 12 patients with a subacute, isolated ACL tear (average of 3 months post injury) had significant quadriceps inhibition but that no inhibition was present in patients with a chronic ACL rupture (average of 2 years postinjury). Furthermore, Urbach and coworkers (33) have shown that the magnitude of AMI is reduced in the long term following ACL reconstruction. Before surgery (average of 13 months post injury) patients demonstrated mean quadriceps activation deficits 16% greater than matched controls with no history of knee injury. Eighteen months postsurgery quadriceps activation had improved significantly to be 6% lower than controls. Similarly, 18 months after unicompartmental knee arthroplasty, Machner and coworkers (37) observed a reduction in AMI to 18% from presurgery quadriceps activation deficits that were, on average, 28%. Over a longer time frame, Berth and coworkers (42) found that AMI improved from ~15% presurgery to ~6% by 33 months after TKA.

However, in the medium term (up to 6 months after joint damage) clear reductions in AMI do not always occur with time. Following knee arthroscopy, Suter and coworkers (34) found no significant change in the magnitude of AMI when patients were assessed presurgery and 6 weeks and 6 months postsurgery. More recently, Berth and coworkers (43) compared the recovery from 2 different surgical approaches for TKA (subvastus versus midvastus approach). Across both groups, AMI remained unchanged (15-20%) from presurgery to 3 and 6 months postsurgery.

Thus, based on the available evidence, it appears as if AMI is most severe in the first few days after joint damage before reducing somewhat, plateauing in the medium term (up to 6 months), and then slowly declining in the longer term (18-33 months). However, it is apparent that notable levels of AMI may still be present months and in many cases years after joint damage. To further highlight this point, Becker and coworkers (35) have shown that residual levels of AMI (approximately 8% compared with healthy, age-matched controls) remain a mean of 4 years after arthroscopic meniscectomy, despite no radiological or clinical evidence of further joint degeneration.

Following acute injury, the severity of AMI varies according to the extent of joint damage (2,32,44). Among patients with isolated ACL ruptures, relatively small

quadriceps activation deficits may be seen following injury with AMI ranging from 3 to 8% when tested a mean of 6 weeks to 31 months post injury (10,32,45,46). In contrast, patients with ACL ruptured with additional joint damage (ligamentous, capsular, meniscal, and/or bony) demonstrate AMI of 15 to 41% several months or in some cases years after joint damage (12,32). The relationship between joint damage and AMI is less clear in patients with chronic joint disease. In patients with OA, Pap and coworkers (47) assessed the magnitude of quadriceps AMI in relation to joint damage, scored retrospectively according to the extent of cartilage degeneration observed during articular surgery. Quadriceps activation deficits were found to be higher in subjects with moderate (stage II) joint damage (19%) compared with those with greater (stage IV) deterioration (12%).

In patients with OA, researchers (21,48) have reported a significant relationship between gender and the magnitude of AMI, with inhibition tending to be more severe in women. In contrast, among ACL-injured subjects no such relationship has been found (32,45). There does not appear to be a significant relationship between age and the severity of quadriceps inhibition in patients with ACL injuries or OA (21,32).

Importantly, AMI often occurs bilaterally after unilateral knee trauma or pathology. Bilateral inhibition has been observed in patients with isolated ACL ruptures (10,32,33,45,46), extensive traumatic knee injuries (12,32), OA (11,34,37), anterior knee pain (30), and following ACL reconstruction (33), partial meniscectomy (35), and knee arthroplasty (37). AMI in the contralateral limb is typically less severe than that in the injured limb. However, quadriceps activation deficits as high as 16 to 24% have been documented in the uninjured limb among patients with extensive traumatic knee injuries (12,32), anterior knee pain (30), and after knee arthroplasty (37). Similar to the injured side, contralateral AMI may persist for up to 4 years after joint damage (35). These findings highlight the need to ensure a bilateral approach to rehabilitation and suggest that caution be applied when attempting to quantify quadriceps weakness by comparing the injured to the uninjured limb. Both clinicians and researchers should be aware that in many cases these comparisons may substantially underestimate quadriceps strength deficits associated with knee joint pathology (32).

Sensory Innervation of the Knee Joint

To better understand the mechanisms involved in AMI it is important to appreciate the range of sensory receptors within the knee joint and their function. Sensory receptors within the knee joint can be divided into 2 major classes, those that are innervated by large, myelinated afferent fibers (group II afferents), and those that are innervated by thinly myelinated or unmyelinated afferents (group III and IV afferents) (49). Group II afferents terminate in corpuscular nerve endings that are activated by

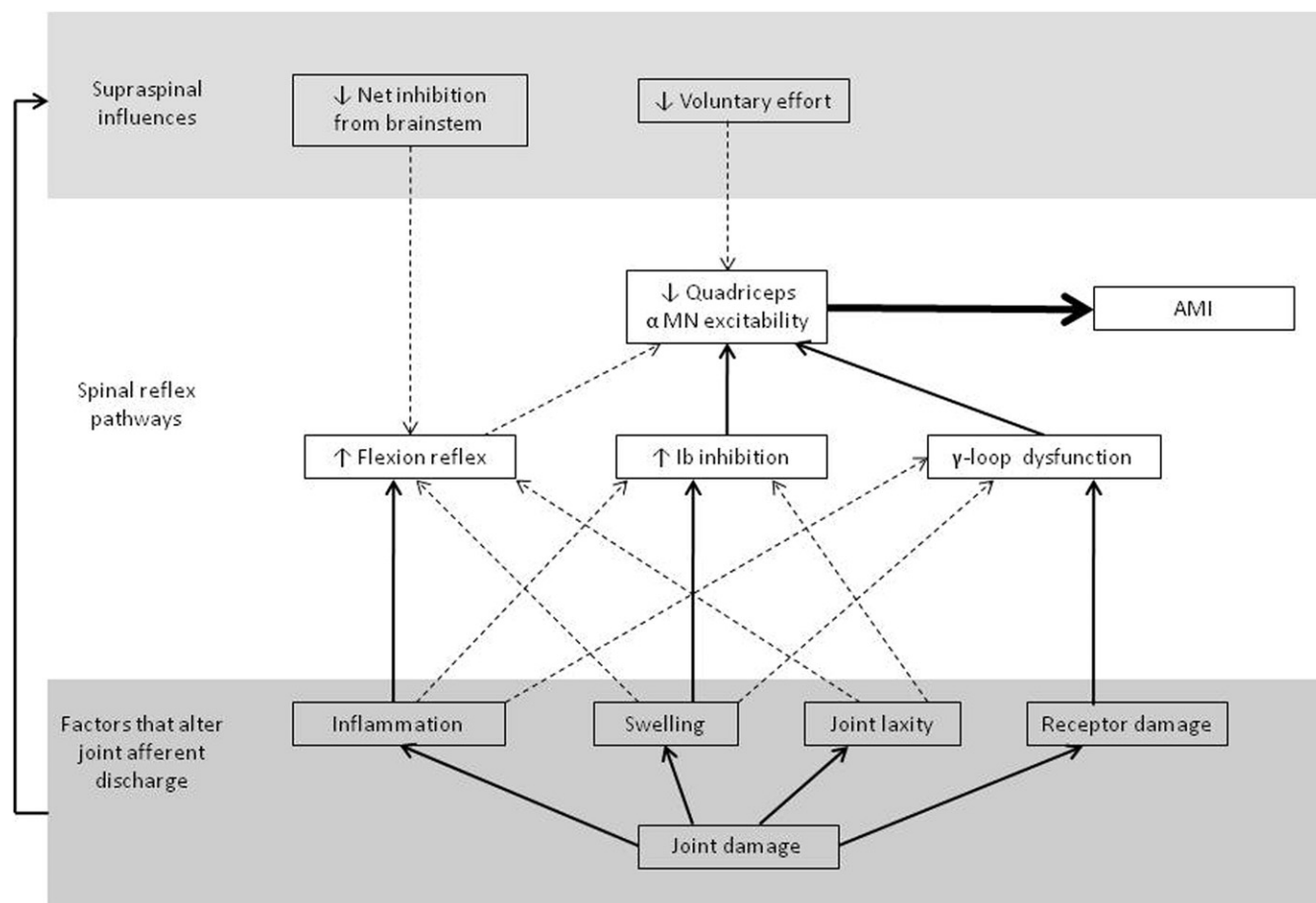


Figure 1 Schematic diagram summarizing the proposed mechanisms contributing to quadriceps arthrogenic muscle inhibition (AMI). Solid lines are mechanisms with stronger evidence to support their existence.

mechanical stimuli such as stretch and pressure (49-51). Most of these nerve endings are highly sensitive, with low firing thresholds, and include Ruffini endings, Pacini-form corpuscles, and Golgi tendon organ-like endings. The proportion of group II afferents in the knee joint is relatively small. While precise data from the human knee are not available, as few as 16% of sensory fibers are thought to be of group II origin in the cat's knee joint (51).

The large majority of afferent fibers innervating the knee joint are high-threshold, lightly myelinated (group III) or unmyelinated (group IV) fibers (49,51,52). In humans, ~70% of fibers in the articular branch of the tibial nerve, the largest articular nerve supplying the knee joint, are reported to be group IV, unmyelinated afferents (52). Group III and IV afferents terminate in free nerve endings, responding to strong mechanical, thermal, and chemical stimuli. Their major function appears to be as nociceptors, signaling actual or potential damage to joint structures. However, it may be that a portion of free nerve endings also function as mechanoreceptors as experiments in the cat have found that approximately 55% of group III and 20% of group IV afferents tested are activated by nonpainful, passive movements and local mechanical stimulation of the knee joint (53,54).

Changes in Afferent Discharge Due to Joint Damage

A number of factors have been identified that may alter afferent discharge from the knee joint in patients with arthritis or following knee injury and surgery (Fig. 1). These include swelling, inflammation, joint laxity, and a loss of output from articular sensory receptors due to structural damage (2-4,53).

Swelling

Swelling is often perennial in arthritic conditions and can also continue long after the acute phase of knee injury and surgery. Despite aspiration of acute hemarthrosis, swelling has been shown to persist for an average of 3 months after ACL rupture and for 12 months following ACL reconstruction (55). Swelling causes significant quadriceps AMI, even in the absence of factors such as inflammation, pain, and structural damage. This has been repeatedly demonstrated by infusing fluid into undamaged knee joints. Direct recordings from articular nerves in animals have shown that swelling significantly increases both the firing frequency and the recruitment of group II afferents (56-60). Moderate levels of joint infusion rarely evoke pain (1,61-64), making it unlikely that a significant

number of group III and IV afferents are stimulated by swelling alone. However, as some of these fibers can be activated by mechanical stimulation (53,54), a portion may increase their discharge in response to swelling, particularly at higher intra-articular pressures or in the presence of inflammation (53,65).

By infusing fluid into human knee joints, researchers have shown that swelling reduces quadriceps EMG activity (1,63,66-69), Hoffmann reflex (H-reflex) amplitude (7,8,61,70-72), and force output (62,64,69,73-75). The potency of swelling's effect is revealed by the finding that as little as 10 mL of fluid may cause notable inhibition (1,64,76), while infusions between 20 and 60 mL are capable of reducing maximum isokinetic quadriceps torque by 30 to 40% (62,64). Several lines of evidence suggest that swelling's inhibitory effect is mediated by joint afferents. Injecting local anesthetic into swollen joints largely abolishes AMI (8,64) and an infusion as large as 300 mL failed to provoke inhibition in a patient with Charcot neuropathy of the knee (1). Astonishingly, a recent case study (77) has reported absolute increases in quadriceps torque of approximately 400% 1 to 2 hours after aspirating 150 mL of synovial fluid from an acutely injured knee joint. From the results presented, this appears to represent almost a 50% (from ~13% to ~60%) increase in the quadriceps strength ratio between the injured and uninjured limbs.

In swollen knee joints particularly, there is a close relationship between intra-articular pressure (IAP) and the discharge of articular afferents. In the presence of swelling, IAP is raised across all joint angles (74,78,79). Even in the resting position, an effusion as small as 5 mL is sufficient to lift IAP above atmospheric pressure (64). In the swollen knee, passive movement of the joint produces a characteristic U-shaped curve, with peaks in IAP occurring in full extension and at end range flexion, with a decrease in mid range (74,78,80,81). The modulation of IAP with joint angle becomes progressively more pronounced with greater volumes of effusion (57,64,74). Similarly, direct recordings from animals have shown that as the knee is moved toward the extremes of motion, in both extension and flexion, joint afferent discharge increases significantly (54,82,83), a pattern that becomes exaggerated in the presence of an effusion (57).

Given the relationships presented above, it is perhaps not surprising that the magnitude of AMI has been found to vary with joint angle. Greater inhibition occurs toward the extremes of joint motion, where IAP and afferent discharge are greatest (74,77,84-87). In acutely injured knee joints, quadriceps inhibition is significantly greater in full extension (87) and toward end range flexion (77) than in mid range. In patients with chronic, perennial effusions, it has been demonstrated that AMI is greater in full extension than in 90° of flexion (84). Even in the absence of a clinically detectable effusion, patients may exhibit more than double the amount of AMI in full

extension when compared with 30 to 40° of knee flexion in the first few days following meniscectomy (85,86).

In summary, swelling raises IAP and increases the discharge of group II afferents from the knee. Swelling has a strong inhibitory effect on the quadriceps and even small, clinically undetectable effusions may cause significant AMI. Thus, clinicians should make every effort to minimize the swelling associated with joint pathology. Furthermore, the magnitude of AMI is modulated according to joint angle and the greater the level of effusion, the stronger the relationship between joint angle and inhibition is likely to be. For these reasons, in the acute stages after injury or surgery, isometric quadriceps exercises should be performed in 30 to 50° of knee flexion, where IAP is lowest (64,74,88). This is likely to maximize activation of the quadriceps, allowing more effective strengthening of the muscle to take place (74,76).

Inflammation

While swelling clearly has the potential to cause severe AMI, it is not solely responsible for this process. In patients with RA, the combination of aspiration and intra-articular corticosteroid injection has been found to increase quadriceps peak torque and EMG amplitude by approximately 30% after 14 days, an effect attributed to a reduction in AMI (89). Torque increased by 8.8 Nm immediately after aspiration but by a much larger 21 Nm 14 days after corticosteroid injection, suggesting that decreased inflammation due to the corticosteroid may have played an important role in reducing AMI. Similarly, Fahrner and coworkers (90) showed that after aspirating OA knee joints, subsequent infusion of local anesthetic led to further increases in quadriceps activation. These findings suggest the involvement of other non-pressure-mediated afferent impulses in the genesis of AMI.

In support of this conjecture, several studies involving animals have examined the effects of inflammation on joint afferent discharge using experimental models of arthritis. These investigations have shown that the induction of inflammation produces potent, long-lasting changes in the sensitivity of articular free nerve endings supplied by group III and IV joint afferents, a process known as peripheral sensitization (53,91,92). The activation threshold of these receptors is lowered so that normal joint movement or nonnoxious mechanical stimulation of articular structures results in notable group III and IV afferent discharge (53,91,92). In addition, these sensory receptors demonstrate increased responsiveness to noxious mechanical stimuli and an augmented spontaneous discharge when the knee joint is held in a static position (53,91,93). Finally, the inflammatory process may activate a number of silent free nerve endings (91,92,94). Usually insensitive to both innocuous and noxious stimuli, the release of inflammatory mediators "awakens" these receptors, substantially lowering their threshold and allowing them to respond to a wide range of mechanical

stimuli (92,95). Collectively, these phenomena greatly enhance the output from group III and IV joint afferents to the central nervous system after joint damage.

As most group III and IV joint afferents are considered to be nociceptive, inflammation can be expected to increase pain in conjunction with afferent discharge (96). However, it is important to remember that AMI can occur in the absence of pain. Furthermore, nociceptive afferent output is modulated at multiple spinal and supraspinal sites, all of which can influence pain perception (97). Thus, consciously perceived pain may not closely reflect the motor effects of nociceptive afferent output (eg, muscle inhibition), which may be largely mediated at the spinal level and are subject to their own modulatory influences.

This is reflected in the literature, where the relationship between pain and AMI is inconsistent. Among subjects with anterior knee pain, those who rated their knee pain higher on a visual analog scale tended to have higher levels of quadriceps AMI (34). Furthermore, reductions in knee pain have been associated with an increase in quadriceps activation post surgery (98) and in patients with RA (89) and OA (99,100). In contrast, other studies have found a weak relationship between pain and AMI (17,21,30,36,38,44,101). After knee surgery, a 15 mL intra-articular injection of local anesthetic was found to significantly reduce both pain and AMI (36,101). However, if only 10 mL of anesthetic was infused, pain was largely eradicated while AMI remained unchanged. Shakespeare and coworkers (36) further demonstrated that in the first 24 hours after meniscectomy, quadriceps activation during a maximum voluntary contraction was typically reduced by 80 to 90% compared with presurgery measures and patients reported severe pain with muscle contraction. However, 3 to 4 days postsurgery pain had decreased to 7/100 on a visual analog scale, yet inhibition was still between 70 and 80%. Two weeks after the operation, when pain was largely absent, AMI was commonly 30 to 50%. Similarly, poor correlations ($r^2 = 0.09-0.22$) have been found between pain and AMI in patients with OA (21) and after TKA (17,38). Finally, in patients with anterior knee pain, nonsteroidal anti-inflammatory drugs (NSAIDs) have been shown to significantly reduce pain compared with placebo but have no effect on the magnitude of AMI (30).

To summarize, the release of inflammatory mediators due to arthritis, injury, or surgery substantially increases joint afferent discharge by sensitizing free nerve endings innervated by group III and IV afferents. In humans, the intra-articular injection of local anesthetic or corticosteroid reduces quadriceps AMI over and above aspiration, probably by silencing some of these sensory endings. Many of the group III and IV joint afferents influenced by peripheral sensitization are involved in nociceptive signaling. While the presence of knee pain may be associated with quadriceps inhibition, it appears to be a poor indicator of the magnitude of AMI. Importantly, substantial

inhibition occurs in the absence of pain and reducing pain does not necessarily lessen the severity of AMI.

Joint Laxity

Joint laxity may alter the activation of sensory receptors in the knee joint. Structural damage or degeneration (eg, to ligaments, capsule) leads to greater translation of the joint surfaces during movement that is likely to increase the activation of mechanoreceptors and nociceptors involved in signaling the limits of joint motion (2). This has been demonstrated in animals by surgically transecting the ACL and directly measuring afferent activity from the major nerves supplying the knee joint. Following ACL transection, Gomez-Barrena and colleagues (102,103) noted significant increases in the transmission of afferent impulses during a range of standardized movements of the knee joint. Immediately after transection, Gomez-Barrena and coworkers (102) surgically reconstructed the ACL and repeated articular nerve recordings. Reconstruction was found to partially reverse these changes, with overall articular discharge decreasing toward baseline values. However, differences in afferent discharge were still noted between normal and ACL reconstructed knee joints. A recent study by the same researchers (104) suggests that despite afferent discharge tending to normalize over time, some differences still persist 9 to 18 months after reconstruction. While direct comparison to humans cannot be made, these studies provide evidence that joint laxity may cause anomalous firing of sensory receptors during joint movement. Surgical stabilization of the knee reduces joint laxity and can perhaps normalize afferent activity to a degree. However, abnormalities in joint afferent discharge may still be apparent compared with the uninjured knee, even in the absence of damage to other joint structures.

Damage to Articular Receptors

Joint damage does not unequivocally lead to increased firing of articular sensory receptors. Trauma to joint structures (eg, ligaments, joint capsule) may simultaneously damage the sensory endings located within these tissues, thus reducing the afferent output from this population of receptors (2,3,44,105). An anomalous increase in joint afferent discharge (as with swelling) is strongly associated with AMI. However, different populations of joint afferents may have opposing effects on motoneuron excitability. Experiments involving cats suggest that background joint afferent discharge has competing excitatory and inhibitory influences on the quadriceps α -motoneuron pool and that in the normal, undamaged knee the net effect may be excitatory (106,107). In support of this premise, Konishi and coworkers (3,108) have shown that injecting undamaged human knee joints with 5 mL of local anesthetic reduces quadriceps force output ($-8.8 \pm 7.3\%$) and integrated EMG ($-17.1 \pm 11\%$) during maximum voluntary isometric contractions. Repeating the

procedure in an ACL-injured population had no such effect, with quadriceps torque and EMG remaining unchanged. These observations led Konishi and coworkers to reiterate previous authors' suggestions (2,44,105) that in some cases AMI may arise due to a loss of sensory output from receptors in the knee joint.

Spinal Reflex Pathways Implicated in AMI

Abnormal afferent discharge from the knee may alter the excitability of reflex pathways within the spinal cord, which in turn reduce the excitability of the quadriceps α -motoneuron pool and prevent supraspinal centers from fully activating the muscle (2-4,7,109). Joint afferents project widely to many classes of spinal neurons (110,111) and thus have the potential to influence quadriceps α -motoneuron excitability via multiple, independent pathways. At this time, 3 spinal pathways have been identified that may contribute to AMI (Fig. 1). These are the following:

- Group I nonreciprocal (Ib) inhibitory pathway
- Flexion reflex
- Gamma (γ)-loop

These pathways should not be thought of as mutually exclusive (4). Instead, it is likely that they are simultaneously affected by joint pathology, with the sum of their actions governing the magnitude of AMI. While other spinal pathways (eg, recurrent inhibition, lumbar propriospinal pathways) may well be involved in AMI, their role has not yet been explored in any detail.

Group I Nonreciprocal (Ib) Inhibition

Group I nonreciprocal (Ib) interneurons are located in lamina VI and VII of the spinal cord (110). Their dominant input is from Ib afferent fibers originating from Golgi tendon organs located near the musculotendinous junction. However, Ib interneurons receive widespread convergent input from a number of peripheral sensory receptors, including joint afferents (112). Lundberg and coworkers (113) investigated the link between joint afferent discharge and Ib interneuron activity by electrically stimulating the posterior articular nerve of the cat knee joint at low stimulus intensities. Ib inhibition of extensor motoneurons was facilitated at 2 distinct latencies, suggesting the existence of both disynaptic and trisynaptic excitatory pathways from group II knee joint afferents to Ib inhibitory interneurons. These findings were later confirmed by Harrison and Jankowska (112) using direct, intracellular recordings from Ib interneurons in the lumbosacral spinal cord of the cat.

As swelling is known to significantly enhance the discharge of group II afferents, joint effusion may contribute to AMI by facilitating Ib inhibition of the quadriceps motoneuron pool. This is supported by the findings of Iles and coworkers (7), who infused uninjured human knee joints with saline and used the spatial facilitation

technique to show that swelling enhances Ib inhibition of the quadriceps H-reflex both at rest and during voluntary muscle contraction. It is unknown whether an increase in group III and IV joint afferent discharge also facilitates the Ib inhibitory pathway. However, this remains a possibility as electrical stimulation of group III and IV joint afferents has been shown to excite Ib interneurons in the cat, probably via polysynaptic pathways (112).

Flexion Reflex

The flexion reflex is a polysynaptic pathway that typically produces a pattern of flexor facilitation and extensor inhibition (114,115). As such, it has been suggested (4,116) that enhanced flexion reflex excitability may be partially responsible for quadriceps AMI. The interneurons involved in the flexion reflex have not yet been clearly identified. However, recent evidence from studies involving animals suggests that wide dynamic range neurons play a major role in mediating the flexion reflex (117,118). These interneurons are predominantly located in lamina V of the dorsal horn and receive convergent input from a number of peripheral afferent sources, including articular receptors (111,119). A consequence of articular inflammation and the resulting barrage of group III and IV afferent input is that wide dynamic range neurons become hyperexcitable (120). This process is known as central sensitization and is characterized by long-lasting plastic changes in synaptic efficacy (for review see (121)). As a result, the activation threshold of wide dynamic range neurons is progressively reduced following the onset of knee joint inflammation and they demonstrate enhanced activity in response to innocuous and noxious stimuli applied to the knee (120). Additionally, as inflammation develops, there is an expansion of their receptive fields, with neurons showing a heightened response to mechanical stimuli from adjacent areas such as the thigh, or even remote, noninflamed tissue as far afield as the contralateral limb (120).

In studies involving animals, the induction of knee arthritis is followed by a corresponding increase in flexion reflex excitability. Flexor (biceps femoris and semitendinosus) motoneurons show significantly enhanced responses to standardized pinching of both the ipsilateral and the contralateral toes, indicating an enhanced central excitability of the flexion reflex pathway (122). Remarkably, at the peak of knee joint inflammation the amplitude of the electrically induced flexion reflex has been reported to increase by an average of 545% (SEM \pm 174%) (109), while the number of flexor motoneurons responding to local pressure and/or gentle flexion and extension of the knee increased from 14 to 41%, suggesting a parallel reduction in flexion reflex threshold (65). Ferrell and coworkers (109) demonstrated that injecting a local anesthetic into the inflamed knee returned reflex intensity back to control values, confirming the role of articular sensory receptors in this response.

While evidence from studies involving humans is less cogent, it is highly probable that the flexion reflex contributes to quadriceps AMI. Leroux and coworkers (123) examined the relationship between knee joint pathology and flexion reflex excitability. Compared with healthy controls, significantly lower flexion reflex thresholds were found in patients with anterior knee pain, probably inferring an amplified excitability of this pathway. Importantly, these authors showed that activation of the flexion reflex produced concomitant inhibition of the quadriceps during isometric contraction of the knee extensors. Recently, it has been shown that flexion reflex thresholds are lower in patients with knee OA compared with age- and gender-matched controls (124). However, no significant relationship was found between flexion reflex threshold and the magnitude of AMI, assessed using burst superimposition. This may be partly due to the insensitivity of burst superimposition to lower levels of inhibition as surprisingly only 4 of 20 subjects with OA were found to have quadriceps activation deficits in this study. Further research is warranted.

Gamma (γ)-Loop

The γ -loop is a spinal reflex circuit formed when γ -motoneurons innervate primary muscle spindles that in turn transmit excitatory impulses to the homonymous α -motoneuron pool via Ia afferent fibers (Fig. 2). Normal function of the γ -loop is necessary to achieve full muscle activation during voluntary contractions. Thus, impaired transmission along this pathway may contribute to AMI (3,44,105).

To investigate the importance of the γ -loop to muscle activation, a number of authors have used prolonged vibration to experimentally attenuate the excitability of Ia afferent fibers. A vibratory stimulus, applied to the muscle or its tendon, temporarily blocks transmission in Ia affer-

ent fibers by increasing presynaptic inhibition, raising the activation threshold of Ia fibers, and/or causing neurotransmitter depletion at the Ia afferent terminal ending (125). In healthy subjects, prolonged vibration (20-30 minutes) causes a reduction in EMG activity (3,126,127), motor unit firing rates (126), and muscle force output (3,126-128) during subsequent maximum voluntary contractions. However, in patients who have ruptured their ACL, prolonged vibration has no effect on quadriceps force output or EMG activity. This suggests a deficit in the transmission of Ia input to the motoneuron pool and has been termed γ -loop dysfunction (3). Similar findings have been confirmed in patients after ACL reconstruction up to 20 months postsurgery (129-131). Interestingly, it has been demonstrated that γ -loop dysfunction occurs bilaterally in ACL-injured and ACL-reconstructed patients (129,130) but that transmission in the contralateral γ -loop may be (at least partially) restored 18 months after surgery (129). It is currently unknown whether γ -loop dysfunction contributes to AMI in other knee joint pathologies.

A number of potential neural mechanisms can be considered to explain γ -loop dysfunction. Researchers have suggested that structural damage to the ACL results in a loss of excitatory feedback from ligamentous mechanoreceptors to quadriceps γ -motoneurons and/or supraspinal centers that diminishes α - γ coactivation during strong muscle contractions (3,4,44,105). In support of this conjecture, Konishi and colleagues (3,108) have shown that injecting undamaged knee joints with 5 mL of local anesthetic reduced maximum isometric quadriceps torque and integrated EMG. However, the same infusion of local anesthetic into knee joints with an isolated ACL rupture had no effect on quadriceps torque or EMG. Furthermore, prolonged vibration of the infrapatellar tendon in subjects with uninjured but anesthetized knee joints did

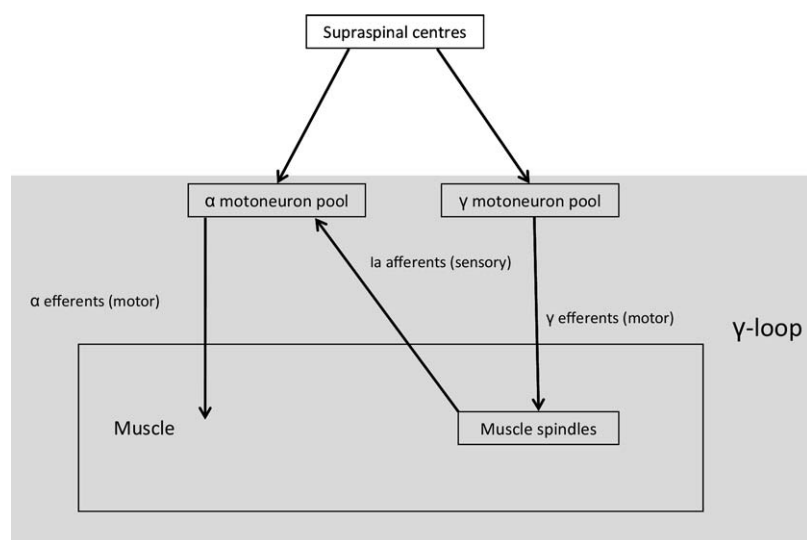


Figure 2 Schematic diagram of the γ -loop (shaded area). During voluntary muscle contraction, supraspinal centers coactivate the α -motoneuron and γ -motoneuron pools. The γ -motoneuron pool in turn innervates muscle spindles via γ efferents, enhancing their firing. Muscle spindles provide a tonic excitatory input to the homonymous α -motoneuron pool via Ia afferent fibers.

not diminish maximum quadriceps force output or EMG amplitude. These observations led Konishi and coworkers (3) to conclude that excitatory output from sensory receptors within the ACL may be critical to the maintenance of normal γ -loop function. Given the relatively sparse innervation of the ACL compared with other structures in the knee joint (50,51), this seems unusual. It remains to be determined if other sensory receptors in the knee joint could also be involved.

Alternatively, or perhaps concurrently, an increase in the discharge of nociceptive joint afferents may contribute to γ -loop dysfunction. Scott and coworkers (132) have shown that low-intensity stimulation of the posterior articular nerve in the cat, sufficient to activate group II and III knee joint afferents, has a net excitatory effect on extensor γ -motoneurons of the calf. However, if a second, high-intensity stimulus (activating group IV joint afferents) was applied beforehand, the excitatory effect of group II and III afferents was abolished or reduced. Thus, the discharge of group IV afferents may suppress the excitatory effects of low-threshold joint receptors on extensor γ -motoneurons (132). Whether this occurs in humans is not known.

Finally, transmission in the afferent limb of the quadriceps γ -loop may be impaired by an increase in Ia afferent presynaptic inhibition. Presynaptic inhibition involves spinal inhibitory interneurons that project to the synaptic terminals of Ia afferent fibers, adjusting the quantity of neurotransmitter released in response to an afferent volley, thus modulating synaptic efficacy (for review see (133)). As activity from a wide range of peripheral receptors, including joint receptors (134), can modify the excitability of presynaptic inhibitory interneurons, a change in articular afferent discharge could theoretically impair quadriceps γ -loop function via this mechanism (135). However, the evidence supporting this theory is limited and findings to date are conflicting. Poststimulus time histograms from single quadriceps motor units have shown that electrical stimulation of knee joint afferents before femoral nerve stimulation does not change the amplitude of the initial, purely monosynaptic component of the resulting H-reflex response (136). This suggests that joint afferent discharge does not alter presynaptic inhibition of quadriceps Ia afferents. In contrast, using a modified H-reflex protocol, Palmieri and coworkers (135) found that quadriceps paired reflex depression increased after experimental knee joint infusion. This finding led Palmieri and coworkers to conclude that an increase in presynaptic inhibition may contribute to AMI. However, this interpretation can be challenged on methodological grounds and should be considered with caution.

In summary, γ -loop dysfunction contributes to AMI in patients with an ACL rupture and after ACL reconstruction. There is evidence to suggest that ACL injury disrupts the flow of excitatory joint afferent output to the quadriceps γ -motoneuron pool and/or supraspinal centers, attenuating γ -motoneuron discharge and, ultimately, Ia

afferent facilitation of the quadriceps α -motoneuron pool. A change in joint afferent discharge could theoretically enhance quadriceps Ia presynaptic inhibition, contributing to γ -loop dysfunction. However, this has yet to be clearly determined. Future research should investigate the presence of γ -loop dysfunction in other knee joint pathologies and aim to achieve a stronger understanding of its underlying neurophysiological causes.

Supraspinal Influences on AMI

Joint afferents are known to have extensive supraspinal as well as spinal projections (137-141). Research to date has largely focused on the spinal mechanisms behind AMI. However, supraspinal centers are highly likely to be affected by changes in joint afferent discharge. Importantly, descending pathways have widespread projections to interneurons and motoneurons at the spinal level (for reviews see (97,110,111)) and thus have the potential to strongly influence AMI.

Changes in Corticospinal Excitability

Transcranial magnetic stimulation (TMS) of the motor cortex has recently been used to quantify changes in corticospinal excitability associated with chronic knee joint pathology (142,143). Fascinatingly, it was found that quadriceps corticospinal excitability was higher in patients with chronic anterior knee pain (average duration, 3.5 years) than in healthy control subjects (143). This was despite lower quadriceps EMG amplitude during maximal contractions and diminished patellar tendon reflexes in subjects with joint pathology. Similarly, Heroux and Tremblay (142) investigated quadriceps corticospinal excitability in chronic ACL-injured subjects (median time since injury, 22 months) and found that resting motor threshold was significantly lower in the injured compared with the uninjured limb. No significant differences were found between limbs in healthy control subjects. While these findings show that corticospinal excitability is increased, the location of the observed changes (ie, motor cortex versus motoneuron pool) is not easily determined using single-pulse TMS. However, as the quadriceps α -motoneuron pool is likely to be inhibited, it is reasonable to suggest that chronic knee joint pathology paradoxically increases excitability in the area of the primary motor cortex projecting to the quadriceps motoneuron pool. While speculative, it is possible that enhanced cortical excitability allows the central nervous system to increase corticospinal drive to the quadriceps to counteract α -motoneuron inhibition by spinal reflex pathways.

Brainstem Modulation of the Flexion Reflex

Descending brainstem pathways typically exert a tonic inhibitory control over spinal neurons involved in pain processing and the flexion reflex, including wide dynamic range neurons (97,134,144). Injury or inflammation

greatly enhances descending input from brainstem pathways that has both inhibitory and facilitatory components (97,144-148). Thus, it is possible that joint damage leads to a reduction in the effectiveness of descending inhibition (4) and/or enhanced descending facilitation to wide dynamic range neurons, increasing excitability in the flexion reflex pathway and amplifying AMI.

Investigations in animals have shown that acute arthritis (3-48 hours) results in a net increase in descending inhibition to wide dynamic range neurons (144,146-148) that may help to limit central sensitization of wide dynamic range neurons and suppress flexion reflex excitability. However, with time, descending inhibition returns to baseline levels (146,149), subsiding as early as 1 week after inflammation commences despite continued hyperalgesia (149). Likewise, time-dependent changes in the efficacy of diffuse noxious inhibitory controls (DNICs) have been observed following the induction of experimental arthritis in the rat (145). DNICs are considered an endogenous form of pain control and refer to the widespread, brainstem-mediated inhibition of spinal and trigeminal wide dynamic range neurons that is triggered by the stimulation of peripheral nociceptors. Danziger and colleagues (145) showed that in the acute stages of arthritis (24-48 hours) DNIC-mediated inhibition of convergent trigeminal neurons was enhanced compared with control conditions. However, in animals with chronic arthritis (3-4 weeks), DNIC-mediated inhibition decreased to normal levels despite continued hyperalgesia. Similarly, a reduction in the efficacy of DNIC-mediated inhibition has been noted in humans with chronic OA of the hip (150). These authors used a pressure algometer to induce graded mechanical stimulation of the soft tissue overlying the hip. The threshold for pressure-mediated pain was found to be significantly lower in arthritic patients compared with a healthy control group. Ischemic arm pain was then induced in both groups, a procedure commonly used in laboratory studies to evoke DNIC-mediated inhibition of wide dynamic range neurons. As expected, the threshold for pressure-mediated pain rose significantly in healthy control subjects. However, in patients with chronic arthritis, ischemia had no effect on pressure-mediated pain, suggesting dysfunction in the descending inhibition of wide dynamic range neurons.

However, in a similar study, Leffler and coworkers (151) found no evidence for DNIC dysfunction among subjects with RA. As expected, RA patients had significantly lower pressure pain thresholds over their thigh compared with healthy, age- and gender-matched controls. In this study, DNIC-mediated inhibition was evoked by immersing the contralateral hand in a bath of ice cold water (the cold-pressor test), after which pressure pain thresholds were reassessed in both groups. After cold water immersion, pressure pain thresholds increased significantly in both RA and healthy control subjects, suggesting preserved function of DNIC-mediated inhibition in patients with RA. These findings are at odds with the

previous observations in OA patients (150) and experimental arthritis (145) described above. As suggested by Leffler and coworkers (151), this discrepancy may relate to the populations tested (OA versus RA versus animal models of experimental arthritis), the duration and location of joint disease, or differences between methods of inducing pressure pain and DNIC-mediated inhibition.

Nevertheless, the balance of evidence suggests that chronic joint pathology be associated with dysfunction in the brainstem modulation of wide dynamic range neurons involved in pain perception and the flexion reflex pathway. The net effect of brainstem regulation appears to be influenced by the stage of joint injury, suggesting a possible role for brainstem pathways in the maintenance of flexion reflex hyperexcitability after articular damage (Fig. 1). In turn, this may contribute to the long-lasting AMI that is often observed after knee injury, after surgery, and in patients with arthritis.

Reduced Voluntary Effort

Studies investigating changes in quadriceps activation rely on the motivation of their participants. It has been suggested that reductions in quadriceps strength and activation may be partly due to a subconscious adjustment in voluntary effort, perhaps for fear of damaging or eliciting pain from the injured joint (4,24,116). Intuitively, this seems reasonable and a decrease in voluntary effort may well contribute to reduced quadriceps activation. However, it should be remembered that a strong reflex component to AMI has been established by a number of studies (7,8,61,71). Moreover, Wood and coworkers (64) found no evidence that a reduction in voluntary effort contributes to AMI when utilizing an experimental model of joint effusion. In this study, the knee joint was distended with different volumes of saline and dextran or local anesthetic. Subjects were blindfolded throughout the testing procedure and were kept unaware of the volume of fluid injected. Both the subjects and the tester were unaware of the nature of fluid injected. The presence of saline and dextran within the knee joint caused marked reductions in maximal isokinetic torque at all velocities tested. However, subsequent injection of anesthetic almost completely restored force to pre-effusion values. In addition, when anesthetic was infused before saline solution, quadriceps torque remained stable over time. As subjects were unaware of the nature of fluid injected, the authors concluded that the observed reductions in quadriceps activation were due to reflex actions of articular afferents, not to changes in volition.

Therapeutic Interventions That May Counter AMI

Therapeutic interventions that may counter AMI can be divided into 2 groups, those that modulate joint afferent discharge and those that stimulate the quadriceps muscle directly.

Afferent Modulation

Aspiration

In the first 3 to 5 days after meniscectomy, aspiration of fluid from the knee (range, 36–85 mL) has been found to consistently reduce (although rarely abolish) quadriceps AMI (24). Similarly, a recent case study showed that aspirating 150 mL of fluid from the knee a week after sustaining an acute injury produced large increases in quadriceps strength and activation (77). However, in patients with chronic inflammatory arthropathies, aspiration may have no significant effect on AMI (84) or produce moderate (14–18%) increases in quadriceps strength (73,90). This may relate to the volume of fluid aspirated in these studies, which was typically lower than in studies involving acute injury. Alternatively, it may be that chronic joint pathology leads to changes in capsular compliance (56,84) and/or damage to articular receptors that reduces the afferent response to swelling. Thus, while aspiration appears to be an effective way to reduce AMI in patients with an acutely swollen knee joint, its clinical benefit is questionable in patients with chronic arthritic joint disease, particularly where effusion is expected to reoccur within a short time frame.

Intra-Articular Corticosteroid Injection

In patients with RA, intra-articular corticosteroid injection has been shown to increase quadriceps peak torque and EMG by ~30% after 14 days, an effect attributed to a reduction in AMI (89). However, in OA patients, corticosteroid injection was found to produce only marginal improvements in quadriceps strength that did not reach statistical significance (152). This may be related to the lack of notable joint inflammation for many patients with OA. Corticosteroid injection may be more effective in patients with advanced OA, when inflammation is more prevalent (153).

Nonsteroidal Anti-Inflammatory Drugs

There is conflicting evidence regarding the use of NSAIDs to reduce AMI. Suter and coworkers (30) found that 7 days of NSAIDs (naproxen sodium, 550 mg) taken twice daily reduced pain but failed to diminish AMI in a group of patients with anterior knee pain. In contrast, there is indirect evidence that NSAIDs may help to reduce AMI after knee surgery. Ogilvie-Harris and coworkers (154) investigated the effects of twice daily doses of a NSAID (naproxen sodium, 550 mg) for 6 weeks compared with placebo after arthroscopic meniscectomy. Patients in the NSAID group had significantly less pain ($P < 0.001$), swelling ($P < 0.001$), and quadriceps atrophy ($P = 0.01$) compared with the placebo group and returned to work or sport quicker ($P \leq 0.002$). Similarly, in a double-blind, placebo-controlled study, Arvidsson and Eriksson (155) showed that daily doses of an NSAID (piroxicam, 20 mg) led to significantly increased isokinetic quadriceps torque

values compared with placebo across a range of joint angular velocities at 3, 7, 11, and 21 days after open meniscectomy. Finally, while strength was only measured semi-quantitatively, 10 days of twice daily NSAIDs (naproxen sodium, 550 mg) was found to significantly improve quadriceps strength after arthroscopy compared with placebo ($P < 0.05$) (156). Intuitively, it seems reasonable that NSAIDs may help to reduce AMI, particularly in the acute stages after joint damage or when there is a strong inflammatory component to articular pathology. However, the use of NSAIDs may also have negative consequences. NSAIDs have been shown to reduce pain but increase knee joint loading during gait in patients with OA (157). Furthermore, a recent observational study (158) reported that OA patients taking diclofenac for >180 days had a 3.2-fold greater risk of knee joint OA progression when factors such as age, gender, body mass index, baseline OA, follow-up time, and dosage were taken into account.

Local Anesthetic

Following experimental joint infusion (8,64), meniscectomy (36) and in patients with OA (90), the intra-articular injection of local anesthetic has been used to partially silence afferent impulses from the joint, effectively reducing AMI. However, a more recent study found that while local anesthetic reduced AMI in patients with OA, the improvements were not statistically different from placebo (99). Furthermore, the invasive and short-lasting nature of this treatment (a few hours) makes it clinically impractical. A number of injections would have to be administered to achieve an appropriate therapeutic effect, increasing the risk of sequelae such as joint infection.

Cryotherapy

Like local anesthetic, cryotherapy may temporarily reduce AMI but has the added benefit of being noninvasive. Thirty minutes of cryotherapy has been shown to reverse the decline in quadriceps H-reflex amplitude that is seen after swelling, an effect that lasts for at least 30 minutes after the ice is removed from the joint (72). Hopkins (66) showed that 30 minutes of cryotherapy negated the reductions in peak torque, power, and quadriceps that EMG caused by swelling during a semirecumbent stepping task performed at 36% of maximum intensity. More recent work (69,159) has established that cryotherapy reduces AMI during maximum effort voluntary contractions. Icing experimentally infused knee joints for 20 minutes led to a significant increase in quadriceps peak torque and muscle fiber conduction velocity compared with control subjects ($P < 0.05$) (69). These findings were notable in that quadriceps torque returned to within ~6% of baseline measures. Similarly, in patients with OA, 20 minutes of icing was found to significantly reduce AMI compared with a control condition (159). Thus, if cryotherapy is applied to the knee joint immediately be-

fore quadriceps strengthening, it may provide a therapeutic window during which more complete activation of the quadriceps musculature is permitted. Yuktaran and Kocagil (100) have shown that repeated applications of ice may lead to improved quadriceps activation in subjects with chronic OA. In this study, subjects received ice massage to 4 standard acupoints for a total of 20 minutes per session, 5 sessions per week for 2 weeks. After the 2-week treatment period, maximum effort quadriceps strength was found to improve by 22% compared with the placebo/sham treatment group's improvements of ~7% ($P < 0.001$).

Transcutaneous Electrical Nerve Stimulation (TENS)

Following open meniscectomy (24) and ACL reconstruction (98), high-frequency TENS has been shown to increase quadriceps activation during subsequent maximal voluntary contractions. Furthermore, Hopkins and coworkers (160) have found that high-frequency TENS (120 Hz, pulse width, 0.1 seconds) prevents the decline in quadriceps H-reflex amplitude seen after the infusion of fluid into the knee joint. Recently, the application of high-frequency (150 Hz, pulse width, 0.15 seconds) TENS to OA knee joints has been shown to significantly improve quadriceps activation when applied during maximal voluntary contractions ($P < 0.05$) (159). The improvement in quadriceps activation with TENS (~11%) was greater compared with a matched control group of OA patients (~1%) who did not receive an intervention ($P < 0.05$).

Low-frequency (4 Hz, pulse width, 1 second), acupuncture-like TENS has been reported to increase quadriceps force output by 71% in OA patients after 2 weeks of treatment (20 minutes per day, 5 days per week) (100). Such large changes in quadriceps strength in just 2 weeks suggest a substantial improvement in voluntary activation. It remains unknown whether low-frequency TENS may be effective in reducing AMI in patients with other knee joint pathologies.

Altering Fluid Distribution/Capsular Compliance

McNair and coworkers (62) showed that infusing 60 mL of saline and dextrose into undamaged knee joints reduced quadriceps isokinetic peak torque by approximately 30%. However, peak torque returned to preinjection levels after a 3- to 4-minute period of submaximal flexion and extension movements of the knee. Magnetic resonance imaging scans of the knee joint at each measurement interval showed that the volume of fluid within the joint capsule was largely unchanged, suggesting that submaximal exercise may modulate mechanoreceptor discharge by increasing the compliance of the joint capsule and/or by redistributing fluid throughout the knee joint, reducing local capsular strain (56,62). Thus, in patients with an effused knee, a series of non-weight-bearing, sub-

maximal movements of the joint may serve to reduce AMI before quadriceps strengthening.

Muscle Stimulation

Neuromuscular Electrical Stimulation (NMES)

The therapeutic advantage of NMES is that it activates the muscle directly, circumventing the inhibited motoneuron pool (4). Thus, while it is unlikely to affect AMI itself, NMES may help to minimize quadriceps atrophy after joint damage, thereby reducing quadriceps weakness. It should be noted that in many cases, voluntary exercise is as effective, if not more effective, than NMES in improving quadriceps strength (for review see (161)). However, there is some evidence (41,162-165) that after knee injury and surgery the combination of NMES and volitional training may achieve greater gains in quadriceps strength when compared with volitional training alone. If isometric protocols are used, NMES may obtain superior results when performed with the knee partially flexed (163) compared with full extension (162). Additionally, the benefits of NMES appear to be dose-dependent, with high-intensity, maximally tolerated stimulations proving more effective than those performed at lower intensities (41,163). A relatively unexplored alternative to NMES is peripheral magnetic stimulation of the quadriceps. Preliminary evidence (166) suggests that magnetic stimulation may be significantly more comfortable and achieve greater quadriceps activation than NMES. Further research is indicated.

Transcranial Magnetic Stimulation

Urbach and coworkers (167) have shown that TMS improves quadriceps activation following TKA when it is applied during maximum voluntary quadriceps contractions. Statistically significant improvements in quadriceps peak torque and a trend toward increased voluntary activation were found to persist up to 60 minutes after 3 single pulses of TMS were applied to the motor cortex. While improvements were modest (<10% increase in quadriceps torque), the dose of TMS used in this study (single treatment session, 3 pulses, 60% of maximum stimulator output) was low. These findings indicate a need for further research, investigating the effect of different stimulation parameters on AMI in subjects with knee joint pathology and at different stages after joint damage. The major disadvantage of transcranial magnetic stimulators is their cost, which may prohibit the widespread use of this technique in clinical settings.

DISCUSSION

AMI remains a significant barrier to effective rehabilitation in patients with arthritis and following knee injury and surgery. AMI contributes to quadriceps atrophy and prevents full activation of the muscle, playing a major role in the marked quadriceps weakness that is commonly ob-

served in these patients. Moreover, AMI may delay or prevent effective quadriceps strengthening. This is particularly apparent in the first few months after trauma or in the case of extensive joint damage when AMI may be severe and quadriceps strengthening protocols are often ineffective. While the magnitude of AMI appears to diminish with time, it is clear that quadriceps inhibition often persists for months or even years after acute knee injury and surgery. This may lead to long-lasting quadriceps weakness that impairs physical function and increases the risk of further joint damage.

AMI is caused by a change in the discharge of sensory receptors in or around the damaged knee joint. Factors that may alter afferent discharge include swelling, inflammation, joint laxity, and damage to articular sensory receptors. Abnormal output from knee joint afferents may alter the excitability of spinal reflex pathways that in turn decrease quadriceps α -motoneuron excitability and prevent full activation of the muscle. To date, 3 major reflex pathways have been implicated in AMI. These are the group I nonreciprocal (Ib) pathway, the flexion reflex, and the γ -loop. While it seems likely that each of these plays a role in AMI, the relative importance of these (and possibly other) reflex pathways remains to be discovered and may well vary across different knee joint pathologies. The potential influence of supraspinal centers on AMI is vast but has only just begun to be explored. Preliminary findings suggest that chronic joint pathology paradoxically increases quadriceps motor cortex excitability and may be associated with changes in the modulation of spinal interneurons by descending brainstem pathways.

Some of the most promising interventions to mitigate the effects of AMI include cryotherapy, TENS, and NMES. Intra-articular corticosteroids and NSAIDs may also be effective when a strong inflammatory component is present with joint pathology. To allow the development of improved therapeutic strategies, it is important to attain a greater understanding of AMI's underlying neural mechanisms. This will augment current rehabilitation practice by allowing clinicians to target AMI directly, thus minimizing muscle atrophy and enhancing quadriceps strength gains after knee injury, after surgery and in patients with arthritis.

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