Muscular reflexes elicited by electrical stimulation of the anterior cruciate ligament in humans

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Dyhre-Poulsen, Poul, and Michael R. Krogsgaard. Muscular reflexes elicited by electrical stimulation of the anterior cruciate ligament in humans. J Appl Physiol 89: 2191–2195, 2000.—Anterior cruciate ligament (ACL)-deficient knees have impaired proprioception, and, although mechanoreceptors have been found in the ACL, the existence of a reflex elicited from these receptors has not been directly demonstrated in humans. In eight patients that underwent knee arthroscopy and had no sign of ACL disease, thin wire electrodes were inserted into the proximal and mid parts of the ACL. Postoperatively, the sensory nerve fibers inside the ACL were stimulated electrically while motor activity in the knee muscles was recorded using electromyography. In seven of the eight patients, a muscular contraction of the semitendinosus muscle could be elicited with stimulus trains consisting of at least two stimuli. The latency was 95 ± 35 ms. Stimulation during isometric contraction of either extensor or flexor muscles elicited a short, complete inhibition of the muscle activity in the contracting muscles. The latency of the inhibitory responses was 65 ± 20 ms in the semitendinosus muscle and 70 ± 15 ms in the rectus femoris muscle.

knee joint; physiology; proprioception

The functional role of the anterior cruciate ligament (ACL) is to restrain forward translation of the tibia in relation to the femur. However, the ACL can only sustain loads of ~1,735–2,000 N (19, 28), and it is, therefore, often torn, especially during dynamic loading. Given the limited protection possible through the mechanical properties of the ligament, it has been suggested that muscular contractions, possibly of reflex origin, are necessary to protect the ACL and to improve the dynamic stability of the knee (10, 23). Furthermore, proprioception is impaired in the knee of patients with ACL lesion (2), and histological studies have proved the existence of abundant nervous tissue and mechanoreceptors in the ACL (15, 29). Because most thick myelinated afferents arising from the ACL are activated by application of local pressure to discrete sites of the ligament (14), the ACL may serve both as a sensory receptor element that signals load and a movement-restraining mechanical device. It is therefore conceivable that articular mechanoreceptor reflexes are “significantly involved in the normal reflex coordination of muscle tone in posture and movement” (4).

In 1958, Palmer et al. (20) suggested that afferent signals from the medial collateral ligament (MCL) of the knee were able to modify the activity in the muscles around the knee. Pulling the MCL with a suture sewn into it or tapping the ligament elicited activity in the hamstrings muscles in decerebrated cats. Ekholm et al. (3) also reported such effects and suggested that the effects were mediated via the γ-muscle spindle system rather than directly onto the skeleton moto-neurons. The same suggestion was further stressed by Freeman and Wyke (4). The idea gained experimental support from Sjölander et al. (24), who showed that low and moderate changes in the tension of the MCL and the lateral collateral ligament (LCL) evoked fusimotor effects, without concomitant activation of skeleton moto-neurons. The fusimotor activations were potent enough to significantly alter the sensitivity of muscle spindle afferents from both the extensor and flexor muscles around the knee. Stener (26) described a method to selectively pull the MCL, but he was unable to elicit any muscular reflex from the MCL in neither cats (1) nor humans (22). However, stimulation of nerve fibers next to the MCL did, in fact, induce strong muscular activity in the extensor and flexor muscles around the knee.

Solomonow et al. (25) were the first to show that information from sensory receptors in the ACL influences electromyographic (EMG) activity in the hamstring muscles. By pulling the ligament with forces just below the rupture threshold, EMG activity in the hamstrings could be elicited in anesthetized cats. Miyatsu et al. (17) found that even low traction forces can induce changes in both knee flexor and extensor muscle activity in spinalized cats, and they suggested that the effects were primarily directed onto γ-motoneurons. In humans, a hamstring muscle response to traction of the ACL during open surgery has also been observed (8). Thus, from animal studies, there are enough experimental data to confirm the existence of “ligamento-muscular reflexes,” probably through low-threshold mechanoreceptors that influence muscle activity via the γ-muscle spindle system, whereas high-
METHODS

activated the sensory nerve fibers in the ACL with directly into the ACL under visual control. We selectively present study, we implanted stimulus electrodes di-

EMG activity of the muscles around the knee. In the humans and to record any subsequent changes in the selectively stimulate the sensory nerves in the ACL in healthy young people during muscular activity.

Threshold mechanoreceptors may exert effects directly onto the skeleton motoneurons. However, the existence of an “ACL reflex” in humans remains uncertain (9). A major problem in establishing its existence is that it is not possible to selectively stimulate the sensory receptors in the ACL by mechanical methods because sen-
sory receptors in other ligaments, the capsule, and the muscles will also be stimulated (23).

ACL injuries occur in young and active patients, and reconstruction of the torn ligament is often necessary to gain mechanical stability of the knee. Thus, if nerv-

ous activity elicited from the receptors in the ACL modulates motor activity in knee muscles under normal activities, reconstructions should be approached in a way that makes reinnervation of the ACL possible, and rehabilitation programs that reestablish dynamic knee function should be applied. It is, therefore, of interest to determine whether an ACL reflex exists in healthy young people during muscular activity.

The aim of this study was to establish a method to selectively stimulate the sensory nerves in the ACL in humans and to record any subsequent changes in the EMG activity of the muscles around the knee. In the present study, we implanted stimulus electrodes directly into the ACL under visual control. We selectively activated the sensory nerve fibers in the ACL with electrical stimuli and recorded subsequent changes in EMG activity during rest and during isometric muscle contractions in knee flexors and extensors.

METHODS

Eight patients, suspect of a meniscus lesion and admitted to the Department of Orthopedic Surgery for knee arthroscopy, participated in the study. All subjects had stable knees on clinical evaluation. None had acute injury. The age and gender distribution of the participants in the study are shown in Table 1. In all cases, the cruciate ligaments appeared normal when viewed and probed arthroscopically. Two 200-μm, multistranded, Teflon-insulated stainless steel wires with 3-mm exposed tips were inserted during arthroscopy in the proximal and mid parts of the ACL. Visual control ensured that the uninsulated tips of the electrodes were embedded completely inside the ACL. The measurements were performed 6–8 h after the operation, when the effects of anesthesia had subsided. Self-adhesive, surface EMG electrodes (Medicotest QA10) were mounted, with an interelec-
trode distance of 3 cm, over the medial head of the quadriceps femoris, the rectus femoris, the long head of the biceps femoris, the semitendinosus, and the medial head of the gastrocnemius muscles. The recording electrodes were placed over the midparts of the muscle bellies, and the ground electrode was placed over the bony part of the tibia. EMG was preamplified by small amplifiers taped to the skin and then lead to custom-built amplifiers (amplification 2,000, frequency 20 Hz to 1 kHz, input impedance >100 mΩ, and CCIR >120 dB). A constant voltage stimulator (DISA Min-
istim) was used to stimulate the ACL through the implanted wires. EMG was sampled at 4 kHz by using a standard personal computer. The sweep started 100 ms before the stimulus, lasted 600 ms, and was displayed after every stimu-

lus. Each stimulus consisted of a train of 1–8 monopolar stimuli, with an interstimulus interval of 5 ms. The sensory threshold, defined as the lowest amplitude at which the patient could feel the stimulus, was found for a stimulus train of 4 stimuli. The stimulus amplitude was held constant at two times the sensory threshold during the experiments. In all cases, the stimulus amplitude was <10 V. The stimuli produced a clearly perceived sensation inside the knee, and subjects reported the feeling as a tap that felt very different from pain. When the stimulus amplitude was increased to four times the sensory threshold, the subjects reported a sensation of pain inside the knee. The number of stimuli in each stimulus train was constant during the experiments. Finally, in one subject, we placed stimulus electrodes that floated freely in the joint fluid anterior to the femoral notch as a control for the specificity of the responses.

An experimental session consisted, in random order, of 10 sweeps while the knee was fully extended (patient supine with extended hip), 10 sweeps while the knee was flexed 30° (patient supine with the knee resting on a splint and with 30° flexion of hips and knees), and 10 sweeps while it was flexed 90° (patient sitting with hip flexed 90° and the leg hanging freely). The sessions were then repeated while the patient maximally activated the knee extensors and then while the patient maximally activated the knee flexors. The experi-

menter manually inhibited movements in the knee joint, so the contractions were isometric. The force was not measured. Most of the patients felt a slight postoperative pain in the knee, and, consequently, their maximal effort was limited. In every position of the knee, at least 5 sweeps were recorded so that the average of the responses could be calculated after the experiment. Latency was defined as the time interval from the second stimulus to the beginning of the muscular response.

The study was approved by the local ethics committee. The patients received written and oral information according to the Helsinki Declaration.

RESULTS

Trains of electrical stimuli given to the ACL pro-
duced a clearly visible contraction in the hamstrings in seven of the eight patients who were relaxed and rest-
sing supine with the knee flexed 30°. The EMG recordings showed a reflex response latency of 95 ± 35 ms (mean ± SD) in the semitendinosus muscle (Fig. 1). At least two stimuli were required to evoke either a visible muscle contraction or a response in the EMG recordings. The latency did not change when the number of stimuli was increased. One stimulus never elicited any response.

When the knee flexors were isometrically activated voluntarily, the response changed to a total inhibition

Table 1. Arthroscopic diagnoses and analgesia type for each patient

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Gender</th>
<th>Analgesia Type</th>
<th>Arthroscopic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>M</td>
<td>spinal</td>
<td>medial meniscus lesion</td>
</tr>
<tr>
<td>43</td>
<td>M</td>
<td>spinal</td>
<td>osteochondritis</td>
</tr>
<tr>
<td>22</td>
<td>F</td>
<td>general anesthesia</td>
<td>medial synovial plica</td>
</tr>
<tr>
<td>29</td>
<td>M</td>
<td>general anesthesia</td>
<td>medial meniscus lesion</td>
</tr>
<tr>
<td>37</td>
<td>M</td>
<td>spinal</td>
<td>medial meniscus lesion</td>
</tr>
<tr>
<td>29</td>
<td>M</td>
<td>spinal</td>
<td>lateral/medial meniscus lesions</td>
</tr>
<tr>
<td>28</td>
<td>F</td>
<td>spinal</td>
<td>subluxation of patella</td>
</tr>
<tr>
<td>35</td>
<td>M</td>
<td>general anesthesia</td>
<td>medial meniscus lesion</td>
</tr>
</tbody>
</table>

M, male; F, female.
of the active hamstring muscles in all eight patients (Fig. 2). The inhibition had a latency of 65 ± 6 ms and lasted ~35 ms. Latency was often followed by a short burst of activity lasting ~30 ms and then another ~35-ms silent period before the EMG returned to pre-stimulus activity. The silent period in the flexor EMG activity was equivalent to a marked drop in force that was felt by the investigator providing resistance against the flexion and was also clearly visible on the EMG. Similarly, when the subjects were voluntarily contracting the knee extensor muscles, stimulation of the ligament produced silent periods in the EMG of those muscles in all eight subjects (Fig. 3). The latency was 70 ± 15 ms, and the drop in activity lasted ~60 ms. In most cases, the silent period was followed by a short burst of activity and then another short silent period. There was a complete inhibition of the gastrocnemius muscle after stimulation under both active extension and flexion (Figs. 2 and 3). Changing the position in the knee joint to 0° or 90° influenced neither the amplitude nor the latency of the EMG responses.

In the subject that had the stimulus electrodes placed in the joint fluid, no motor responses were elicited with stimulus amplitudes five times higher than those normally used to elicit the ACL reflex.

DISCUSSION

It was observed that activation of afferent nerve fibers in the proximal part of the ACL influenced the motor activity in the muscles around the knee in humans. In this model, with electrical stimulation of sensory nerve fibers of the ligament, it was possible to demonstrate the existence of an ACL reflex in awake humans. The low-stimulus amplitudes and the location of the uninsulated part of the stimulus electrodes inside the ACL made it likely that the stimulation was of selective nerve fibers within the ACL. The proximal electrode in the ACL was placed at least 10 mm from the posterior capsule, and the distal electrode was placed in the center of the knee. When the stimulus electrodes were placed in the joint fluid of one subject, no motor responses were elicited by a stimulus with an amplitude five times higher than the stimulus that elicited a reflex from the ACL. It is therefore unlikely that sensory receptors of the capsule, muscles, or collateral ligaments were activated.

Because the experiments were performed shortly after surgery and the patients felt postoperative pain, afferent input from sensitized, group III pain receptors may have influenced the response (3). However, the patients did not report pain after the low-amplitude stimuli used in the present experiments, which indi-
cates that no Aδ or C pain fibers were activated. Therefore, the muscular responses were most likely elicited by stimulation of group II or III fibers, presumably mechanoreceptors.

Evidence for both facilitatory and inhibitory influences on the activity in the α-motoneurons was found, depending on the character of the ongoing activity. The latency of the responses varied between 65 and 95 ms, indicating that responses were of reflex rather than voluntary origin. The observation that at least two stimuli were needed to produce an excitation or inhibition and the rather long latency suggests that the reflexes were polysynaptic or long-loop reflexes, giving the central nervous system abundant possibilities to modulate muscle activity. At rest, impulses elicited in the ACL produced activation of the hamstring muscles, supporting the contention of an automatic ACL-hamstring synergy. However, with stimulus amplitudes two times the sensory threshold, as used in this experiment, this synergy was only present during rest and changed to an inhibition during motor activity.

Considering a reflex latency of 70 ms, at least 110 ms (reflex time + electromechanical delay) would pass before substantial forces could be produced by the muscles after application of load to the ACL. Therefore, the excitatory reflex demonstrated in this study cannot serve as an automatic protective mechanism for the ACL. In most situations, this reaction would be too slow to prevent rupture of the ligament. The long latency further suggests that direct regulation of force would be unlikely.

It has been suggested by many authors (3, 4, 12, 24) that mechanoreceptors in joint capsules and ligaments contribute to normal coordination of muscle activity in movements and posture. Johansson et al. (11) showed that electrical stimulation of joint afferent fibers running in the posterior articular nerve of the cat exert influence on the activity of the γ-motoneurons that project to both the flexors and extensors of the knee. Thus articular mechanoreceptor reflexes operating via the γ-loop may contribute to the regulation of muscle stiffness and joint stability.

Gómez-Barrena et al. (5) have shown that, in the cat, afferent impulses from the ACL are directed to lumbar segments 5–7. These segments correspond to the sciatic and femoral nerves. On the basis of this finding, Gómez-Barrena and co-workers suggested that afferent impulses from the ACL are important for an optimal balance between the hamstrings (innervated by the sciatic nerve) and the quadriceps (innervated by the femoral nerve). We have demonstrated, in this study, that stimulation of the afferent nerve fibers in the human ACL induced changes in the hamstrings and quadriceps muscles.

Experiments in cats present conflicting results regarding a link between afferent nerves from the MCL and ACL and the muscles around the knee. In some experiments, such a link could be demonstrated (3, 17, 25), and, in others, it could not be found (1, 6, 23). One reason for the contrasting findings may be that the experimental designs differ. In some experiments, the cats were decerebrated, and, in others, they were also spinalized (3, 17). In one experiment (23), the cats were anesthetized with high doses of chloralose, which is known to influence the excitability of α-motoneurons (18). Notwithstanding the conflicting results from animal studies, it is always hazardous to apply animal data to humans. However, it was recently shown that nonnoxious stimulation of the glenohumoral joint capsule in the shoulder of human subjects produces inhibition of ongoing motor activity (27).

The latency of the reflex demonstrated in our experiment was much longer than the latency found by Solomonow et al. in cats (25). In that study, a short latency reflex was elicited when the ACL was pulled with forces that were close to the rupture threshold of the ligament. These high forces may elicit the sensation of pain and may be equivalent to much higher stimulus amplitudes than we used in the present study.

Input from muscle and joint afferents converge with cutaneous input on the α-motoneurons, and reflex reversal that is dependent on motor activity is well known and described during walking (7). Lundberg et al. (16) showed that volleys in the posterior articular nerve in feline knees may facilitate transmission in both excitatory and inhibitory reflex pathways from Ib
afferents and that input from joint afferents may influence tension regulations from Golgi tendon organs. Instead of a direct protective function, it is more likely that sensory input plays an important role in the updating and formation of motor programs (12) that instruct humans to reactivate the muscles properly and to protect the knee during the next step. The maximal motor output in the knee extensors is substantially smaller during static and slow movements than is expected from the force velocity curve. Therefore, it is suggested that neural mechanisms restrict the maximal muscle tension (21). Protective reflexes originating from the knee ligaments may be responsible for this drop in maximal static force. Training rapidly increases the maximal motor output, and it is possible that training also modulates the inhibitory neural feedback (i.e., sensory inputs may help the neuromuscular system create the patterns of muscular activity that are the basis for normal movements). The ACL reflex may, therefore, be an essential part of normal knee function.

The hamstring muscles are normally regarded as key to dynamic knee stability. The observed inhibition of the gastrocnemius muscle after stimulation of the nerves of the ACL during both active extension and flexion suggests that this muscle also plays an important role in functional knee stability. Patients with good knee function (13). Training of both hamstrings and the gastrocnemius muscles functions should be considered in rehabilitation programs.

In this experiment, we have demonstrated that the activity in the muscles around the knee is influenced by sensory input from afferent nerves in the ACL. Further experiments are needed to characterize this ACL reflex and to establish its functional significance.

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REFERENCES