

Neural response of mechanoreceptors to acute inflammation in the rotator cuff of the shoulder joint in rabbits

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We examined with electrophysiological techniques the effects of experimentally induced inflammation on the mechanosensitive afferent units in the rotator cuff of the shoulder joint of 21 rabbits.

We identified 21 mechanosensitive units belonging to group III. 12 units had mechanical thresholds of > 7.0 g and 9 units had thresholds of < 7.0 g. After injection of inflammatory agents, kaolin and carrag-

enan, into the joint space, ongoing afferent discharge rates increased in all units. The average discharge rate increased significantly from 7 imp/s to 15 imp/s after injection. 5 units had a decreased mechanical threshold after the injection.

Acute inflammation seems to have an excitatory and sensitizing effect on the high- and low-threshold units in the rotator cuff.

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Acute shoulder pain is usually thought to be related to nonspecific or mechanical events, while persistent or chronic shoulder symptoms may be caused by inflammation in the tissues in and around the shoulder joint, such as subacromial bursitis and tendinitis of the rotator cuff and biceps tendon.

Experimentally induced inflammation has been studied electrophysiologically in somatosensory units of the knee joint (Coggeshall et al. 1983, Schaible and Schmidt 1985, Grigg et al. 1986, Rang et al. 1991) and lumbar facet joint (Ozaktay et al. 1994, Cavanaugh et al. 1997) as well as in the muscle (Berberich et al. 1988). However, the shoulder joint has not been studied.

Previously, we identified and characterized the mechanosensitive afferent units in the shoulder joint and adjacent tissues of the rabbit using electrophysiological techniques (Yamashita et al. 1995, Minaki et al. 1996). That study showed that the rotator cuff, the supraspinatus and infraspinatus muscles contained high-threshold slowly conducting units which may serve a nociceptive function and low-threshold afferent units which may serve a proprioceptive function.

We have now examined the effects of acute experimental inflammation on the mechanosensitive afferent units in the rotator cuff of the rabbit shoulder joint using electrophysiological techniques.

Animals and methods

The study was carried out on 21 adult male Japanese White rabbits weighing 3.0–3.5 kg. They were sedated with an intramuscular injection of ketamine hydrochloride (28 mg/kg body weight) and xylazine (3.5 mg/kg body weight). After venous cannulation, they were anesthetized with intravenously administered sodium pentobarbital (5.5 mg/kg body weight). Additional doses of sodium pentobarbital were given as needed to maintain a deep level of anesthesia throughout the experiment. Ringer's solution was continuously infused through the cannula. Atropine (0.45 mg/kg body weight) was subcutaneously injected to suppress upper respiratory secretion, and the animals were tracheally intubated to minimize respiratory compromise. Body temperature was maintained at 37 °C with a heated blanket. The experiment was approved by the Committee for Animal Experimentation of Sapporo Medical University.

The operation

A longitudinal incision was made over the shoulder joint. The trapezius and deltoid muscles were cut and the rotator cuff, adjacent supraspinatus muscle and infraspinatus muscle were exposed. The rabbit was clamped at the scapula and L7 spinous processes by means of a spine-holding device. The suprascapular nerve was released from surrounding tissues and cut

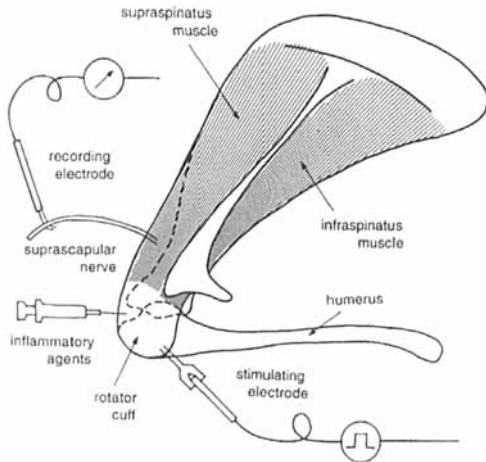


Figure 1. A schematic diagram of the systems for recording and stimulation. The afferent activities were recorded from the suprascapular nerve with a bipolar recording electrode. The shoulder joint was electrically and mechanically stimulated to identify the units. Inflammatory agents, kaolin and carrageenan, were injected into the shoulder joint space.

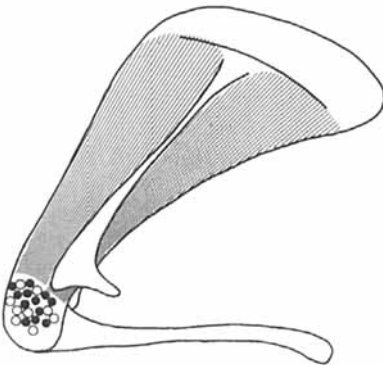


Figure 2. Diagram showing the locations of the receptive fields identified at the rotator cuff of the shoulder joint. Filled circles units with mechanical thresholds of > 7.0 g; open circles units with mechanical thresholds of < 7.0 g.

at the proximal end. A pool was formed from the skin flap, and the nerve was covered by warm (37°C) paraffin oil.

Recording and identification of the units

The suprascapular nerve was split and draped over a bipolar recording electrode. Afferent impulses from nerve fibers were amplified, monitored on an oscilloscope and an audiometer, and recorded on an FM tape-recorder. Afferent discharge frequency was analyzed by a window discriminator. The receptive fields of the mechanosensitive units in the shoulder joint were sought and located with glass probes of 1 mm diameter. The center of the area responsive to probing was plotted on the diagram of the shoulder (Fig. 1-2).

When the receptive fields were identified, they were stimulated electrically with a bipolar electrode

to obtain conduction velocities. In the search for units, a 5-10 V-stimulus of 0.1 ms duration was used. To calculate the conduction velocities, the distance (mm) between stimulating and recording electrodes was measured; this was divided by the latency (ms) of the evoked response. Sensory nerve fibers that had a conduction velocity of < 2.5 m/s were classified as group IV units, those with a velocity of 2.5-20 m/s as group III units, those with a velocity of 20-70 m/s as group II units, and those with a velocity of > 70 m/s as group I units (Schaible and Schmidt 1983, Martin 1985, Sessle and Hu 1991).

The receptive fields were stimulated with a set of 17 nylon filaments to determine the threshold to mechanical stimulation. The nylon filaments were 38 mm long and 0.4-1.2 mm in diameter, with a force ranging from 0.008 to 279 g when applied to receptive fields (Semmes-Weinstein Monofilaments, North Coast Medical, Inc., San Jose, CA, USA). The filaments were applied vertically to the receptive fields until they buckled slightly and were held in that position for at least 1.5 s. They were applied at least three times in each receptive field.

Induction of the inflammation

After characterizing a unit electrophysiologically, 0.2 mL of 4% kaolin and 0.2 mL of 2% carrageenan were injected into the shoulder joint space of the rabbit using a 25-gauge needle.

At 2 hours after the injection, frequencies of afferent discharge and mechanical thresholds of the units were examined and compared with those before the injection.

Results

Receptive fields and physiological properties of the units

21 mechanosensitive afferent units were identified and characterized in the shoulder joint. The receptive fields of all these units were localized in the rotator cuff area (Figure 2).

The average conduction velocities of these units was 8 (4.1-22) ms, SD 4.0. All units belonged to group III.

The average mechanical thresholds of these units was 7 (2.4-13) g, SD 2.9. Of 21 units, 12 units had thresholds of > 7.0 g and 9 units had thresholds of < 7.0 g.

Changes in the ongoing discharge rate

All 21 units had ongoing discharges before the injection of kaolin and carrageenan, average 6.9 (SD 1.3)

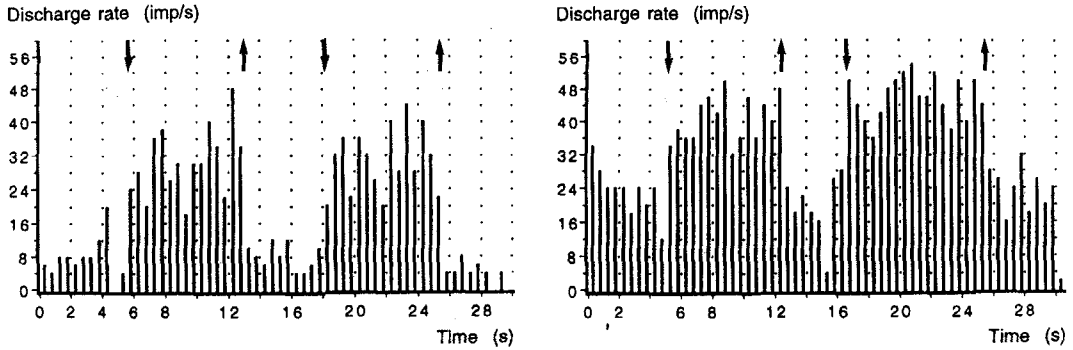


Figure 3. Discharge rate versus time histogram illustrating the responses of afferent units to mechanical stimulation of the receptive fields with a glass probe. Before the injection of kaolin and carrageenan (left) and 2 hours after the injection of kaolin and carrageenan (right). Arrow pointing down onset of stimulus, arrow pointing up stimulus stopped. Bin width 0.5 s.

imp/s. After the injection, ongoing discharge rates were increased in all units (Figure 3). The average discharge rate was 15 (SD 2.5) imp/s, higher than that before injection ($p < 0.001$, Student's *t*-test).

Changes in the mechanical threshold

Of the 21 units, 5 units had a decreased mechanical threshold after the injection of kaolin and carrageenan. Of these 5 units, 4 had a threshold of > 7.0 g and 1 unit had a threshold of < 7.0 g before the injection. For these units, the average magnitude of decrease in the threshold by inflammation was 2.8 g (Figure 4).

Discussion

In a previous electrophysiological study using rabbits, we identified and characterized mechanosensitive af-

ferent units in the tissues in and around the shoulder joint, such as the rotator cuff, the supraspinatus and infraspinatus muscles (Yamashita et al. 1995, Minaki et al. 1996). Group III units with mechanical thresholds higher than 7.0 g may serve as nociceptors, and units with lower thresholds may serve as proprioceptors (Burgess and Perl 1967, Perl 1968, Schaible and Schmidt 1983). We found nociceptive units in all the tissues of the shoulder joint that we examined. Noxious mechanical stimuli to the shoulder joint, such as excessive motion and mechanical contusion, may activate nociceptive units and generate acute shoulder pain. On the other hand, prolonged or chronic shoulder pain may be caused by inflammation that continuously stimulates the nociceptive units.

In the laboratory, an inflammatory response can be produced by injecting the tissue or joint with carrageenan, a sulfated polysaccharide, and kaolin, a mineral product containing silica. This model results in edema, leukocytic infiltration, and the release of histamine, bradykinin and prostaglandins into extracellular tissue (Cavanaugh et al. 1997). Keele and Armstrong (1964) showed that histamine, serotonin and bradykinin, injected subcutaneously, elicit pain in man. Serotonin can be released from blood platelets and mast cells during tissue damage and can either sensitize or directly activate nociceptors (Rang et al. 1991). Bradykinin is one of the most potent pain-producing substances present in inflammatory exudates and damaged tissue (Steranka et al. 1988). Bradykinin, serotonin, and histamine directly stimulate chemosensitive primary afferent nociceptive fibers via specific B_1 (or B_2), 5-HT₂ (or 5-HT₃), and histamine receptors, respectively (Kontinen et al. 1994). To our knowledge, the response of sensory nerves to inflammation has never been studied in the shoulder joint.

In our study, all mechanosensitive units in the rotator cuff of the shoulder joint were activated by acute

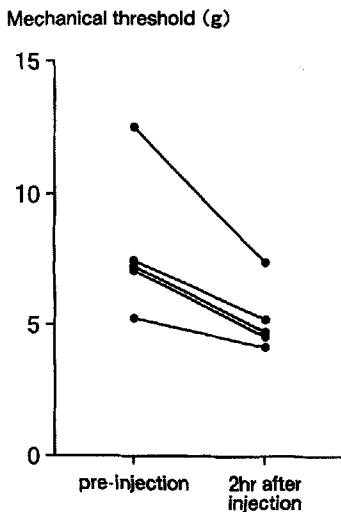


Figure 4. Changes in the mechanical threshold of 5 units due to injection of kaolin and carrageenan.

inflammation. This indicates that these units are "polymodal receptors" which respond to both mechanical and chemical stimuli (Kelly 1985). Coggeshall et al. (1983) and Grigg et al. (1986) showed that afferent discharge rates were much higher in the group III and group IV mechanosensitive units in an inflamed knee joint than those in the normal control joint. Cavanaugh et al. (1997) reported that average ongoing discharge rates of mechanosensitive units were 18 imp/s in the inflamed lumbar facet joints and 9.3 imp/s in the controls. Ozaktay et al. (1994) also examined the effects of acute inflammation on the units in the lumbar facet joint and showed that ongoing discharge rates had increases that consisted of 2 phases: a first phase from 0 to 30 min and a second phase from 45 to 150 min. In our study, both the nociceptive units and proprioceptive units were excited by acute inflammation of the shoulder joint. Inflammation may cause constant pain of the shoulder joint by exciting nociceptive units in the shoulder joint. On the other hand, it is presumed that activation of proprioceptive units may cause a dull or heavy sensation in arthritis of the shoulder.

One-fourth of the units showed lowered mechanical thresholds after injection of the inflammatory agents in our study. This indicates that inflammation sensitized the units to mechanical pressure. Ozaktay et al. (1994) showed that the thresholds of the units in the lumbar facet joint decreased with time after application of carrageenan. Yamashita et al. (1993) reported that one-third of the units in the lumbar facet joint showed decreased thresholds after application of substance P that induced neurogenic inflammation in the joint. According to Kontinen et al. (1994), inflammatory compounds, such as prostaglandin E_2 (PGE_2) and PGI_2 , can sensitize group III and IV afferent fibers to subsequent mechanical, chemical or thermal stimulation. Thus, nociceptors in the joints that would normally only fire when mechanical stress is clearly noxious will fire at much lower stresses in the presence of inflammation and maintain an ongoing discharge even without mechanical stress. This peripheral sensitization may be a mechanism for the persistence of pain.

Coggeshall et al. (1983) showed that the thresholds for activation by joint movements were considerably lowered by acute inflammation in the units of the cat knee joint. Cavanaugh et al. (1997) reported that a more vigorous multi-unit response to joint movement occurred in inflamed lumbar facet joints than in the controls. We examined the effects of inflammation on mechanosensitive units in the shoulder only at rest.

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