Changes in dorsal horn neuronal responses in an experimental wrist contracture model

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Abstract Joint contracture, a major complication after casting, usually makes the therapeutic outcome worse by causing a limited range of motion and related pain. We developed rat models of wrist contracture with fracture of the radius (group A) and wrist contracture without fracture (group B), and investigated whether contracture and fracture changed the characteristics of cervical dorsal horn neuronal responses and the behavior of the animals. After 4 weeks of immobilization, both groups showed wrist contracture and disuse tendencies in the treated forelimb. In an electrophysiological study, the responses of 403 cervical dorsal horn neurons to mechanical stimuli were examined. In normal (control) animals, the neurons had the following distribution: 63% were low-threshold (LT); 15% were high-threshold (HT); and 22% were wide-dynamic-range (WDR). In group A, the distribution of the neurons changed to 51% LT, 16% HT, and 33% WDR. Similar changes were observed for group B. Responses during wrist movement were also examined. Forty-one percent of cells in the control group were responsive to the movements, whereas the number of neurons responding to motion stimulus in both groups A and B was increased, to 77%. The changed population of WDR and LT neurons responding to wrist movement suggests that the characteristics of dorsal horn neurons may undergo plastic changes after contracture.

Key words Dorsal horn neuron · Joint pain · Disuse atrophy · Complex regional pain syndrome · Immobilization

Introduction

Despite advances in orthopedic therapy, casting (immobilization) is still commonly utilized because of its ease and wide application. However, it is well known that casting may also have harmful complications.1,2,4 One major complication is joint contracture. Because of morphological changes in joints and muscles, a limited range of joint motion is often observed after long-term immobilization.2 Symptoms include not only the limited range of motion (ROM) but also associated motion pain, especially after removal of the cast. Therefore, contracture may limit the therapeutic outcome and produce a low level of activity in daily life.

The pain in contractured joints is considered to be the result of the shortened muscle and the adhesion of joint and periarticular structures. Indeed, surgical release of the periarticular tissues resulted in successful pain relief in patients with painful post-traumatic contracture.6 Animal models of contracture have been developed for histological, biochemical, and biomechanical studies. Using these, several investigators have studied local changes in the contractured joint itself. Histologically, pressure necrosis of the articular cartilage and synovial adhesions were observed in contractured joint tissue.1,2,16

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It is well known that spinal sensitization develops after peripheral inflammation and increased peripheral input to the spinal cord.8,12 On the other hand, conditions of immobilization may decrease the peripheral input into the central nervous system. Recently, several researchers have been paying attention to immobilization-induced neurological changes. Butler et al.4 observed signs of complex regional pain syndrome (CRPS) and neglect-like states in healthy volunteers after 4 weeks of forearm immobilization.4 Also, Galer et al.9 observed neglect-like states in CRPS type 1 patients with disused extremities and proposed that changes within central nervous system structures may occur after abnormal activation of the peripheral and autonomic nervous systems. We suggest that the histological and biochemical changes that occur in the periphery and the reduced peripheral input to the spinal cord may alter the responses of dorsal horn cells during and after immobilization. However, to the best of our knowledge,
the neurophysiological changes that occur after contracture develops have not yet been investigated.

The aims of this study were: (1) to develop a model of radius fracture in rats and (2) to investigate the mechanism of contracture-induced sensory property changes, including nociception, by carrying out behavioral and electrophysiological studies. A preliminary report of these results has been made in abstract form.23

Materials and methods

The following investigation was carried out under a protocol approved by the Animal Care and Use Committee, University of Texas Medical Branch at Galveston.

Experimental animals and preparation

Twenty-four adult male Sprague-Dawley rats, weighing 300–400 g, were used in this study. The animals were housed in pairs in plastic cages with soft bedding and allowed free access to food and water. The rats were kept for at least 5 days under these conditions before the surgery and casting.

The rats were divided into three groups, as follows: Group A (n = 9), Three to four weeks of immobilization of the wrist joint at full flexion wrist position with a plastic cast after fracturing of the radius. Group B (n = 8), Three to four weeks of immobilization of the wrist joint at full flexion position with a plastic cast. Group Norm (n = 7), normal control untreated animals.

Immobilization

Rats were anesthetized with pentobarbital sodium (50mg/kg, i.p.) The left forearm was wrapped with soft cotton and gauze to prevent skin irritation. To keep the wrist joint immobilized at 90° of flexion, a plastic cast (Castlight 7; Alcare, Tokyo, Japan) was wrapped around the limb from the forearm to the left forepaw. To prevent the rat from chewing the cast and to avoid detachment of the cast, the rat’s trunk was included with the arm in the cast. After the casting, rats were returned to their cages for 3 to 4 weeks.

Fracture procedure

Before immobilization, a left radial fracture was made in group A. Sterile surgical procedures were used; rats were anesthetized with pentobarbital sodium (50mg/kg, i.p.) and placed in the prone position, and a lateral incision, 5-mm-long, was made in the distal left forearm. Care was taken to avoid tendon and other soft tissue damage while the proximal part of the radial styloid process was explored. Then, the distal radius was gently explored and the distal part of the radius was cut with small scissors, from 3–5 mm proximal to the wrist joint, to make a fracture with minimum damage to the soft tissue. After these procedures, the wound was closed with a 4-0 silk suture. The plastic cast was attached to minimize pain from the fracture. The healing of the fracture site was checked by X-ray after behavioral and electrophysiological studies were done.

Observation of general behavior

During the immobilization period, the animals’ behavior and fit of the cast were observed daily. After a period of immobilization, the posture of the immobilized paw and motion during walking and feeding were monitored while animals were in the cage. After removal of the plastic cast, walking posture and grooming behavior were observed for 10 min. Attention was paid to whether or not the rats could bear weight on the treated forepaw.

Measurement of wrist ROM

To measure passive range of motion (ROM) in the wrist, animals were anesthetized with pentobarbital sodium (i.p.) and then a wooden stick (diameter, 1.7mm; length, 100mm) was tightly fixed to the palm with bonding (cyanoacrylate glue). This stick was used as a lever, and, with the stick, full extension and flexion stress forces were applied to the wrist joint (approximate force of 10 g); a protractor was then used at the dorsal side of the wrist joint to measure the ROM in degrees.

Electrophysiological experiments

All rats in groups A, B, and Norm were used for the electrophysiological study after the behavioral study. In groups A and B, recordings were made from both the treated side and the untreated side of the cervical enlargement. Cells were divided into four groups according to the recording site, as follows:

Cells recorded from the treated side in group A animals: A-TR cells
Cells recorded from the treated side of group B animals: B-TR cells
Cells recorded from the untreated side of group A animals: A-UN cells
Cells recorded from the untreated side of group B animals: B-UN cells.