INTRODUCTION

Charcot arthropathy is a severe degenerative arthritis that occurs in patients with sensory neuropathy. Although Charcot believed the disease was caused by a loss of trophic substances derived from the nerves, leading to atrophy of the joint tissues, Volkmann and Virchow subsequently developed the consensus argument that the loss of limb sensation compromises muscular function in the limb leading to mechanical damage of the joint (Resnick 1988). Acceptance of this hypothesis has, in turn, has led to more recent speculations that a subtle, subclinical form of neuromuscular or sensory deficit may be a cause or contributing factor in the development of idiopathic osteoarthritis (OA).

Age is the highest risk factor for OA and 27%, 34% and 44% of persons exhibit radiographic osteoarthritis of the knee in the 7th, 8th and 9th decades of life respectively (Felson et al. 1987). Age-related loss of neurons from the central nervous system is a well-established phenomenon, but has not been widely documented in the peripheral nervous system.

Experiments in our laboratory revealed that in mice (and rats), innervation of the knee joint can be accurately and consistently quantified by retrograde tracing with the fluorescent dye Fluoro-Gold (FG). Using this technique in C57BL/6 mice of different ages, we found a 60% loss of joint afferents over the life span of the mouse (Salo and Tatton 1993).
Further denervating the limb by excising the L3 dorsal root ganglion (which contains 80% of the knee joint afferents in this species) significantly worsened the degenerative changes (Salo et al. 2002).

This led us to examine the effect of selective joint denervation in an animal model less prone to spontaneous OA (the rat). Selective joint denervation can be done by injection of the joint with an immunotoxin such as OX7-saporin, which selectively destroys rat sensory neurons. Up to 88% of knee joint afferents can be ablated with this technique (Salo et al. 1997).

We subsequently followed a group of rats that had been denervated in this way for up to 24 months. The rats were exercised on a treadmill for 30 minutes, 3 times a week. Interestingly, in control rats we found on average, a spontaneous loss of 42% of joint afferents. In the denervated group we documented a reduction by 69%. Careful histologic examination and grading of the knee joints of control and denervated rats revealed some degenerative change in almost all joints, but on average these changes were significantly worse in the denervated joints (Salo et al. 2002)(Fig. 3).

**SUMMARY**

Age-related loss of joint innervation occurs in both mice and rats. Surgical or chemical denervation of the knee joint promotes the development and progression of OA changes in these animals.

**REFERENCES**


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Fig. 3 Sagittal sections through the medial compartment of rat tibiofemoral joints. (a) control rat, showing mild central loss of cartilage matrix staining and superficial fibrillation. (b) denervated rat, showing major loss of cartilage matrix staining, disruption and loss of matrix down to tidemark, torn meniscus.