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Nerve growth factor improves ligament healing.

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Abstract
Previous work has shown that innervation participates in normal ligament healing. The present study was performed to determine if exogenous nerve growth factor (NGF) would improve the healing of injured ligament by promoting reinnervation, blood flow, and angiogenesis. Two groups of 30 Sprague-Dawley rats underwent unilateral medial collateral ligament transection (MCL). One group was given 10 microg NGF and the other was given PBS via osmotic pump over 7 days after injury. After 7, 14, and 42 days, in vivo blood flow was measured using laser speckle perfusion imaging (LSPI). Morphologic assessments of nerve density, vascularity, and angiogenesis inhibitor production were done in three animals at each time point by immunohistochemical staining for the pan-neuronal marker PGP9.5, the endothelial marker vWF, and the angiogenesis inhibitor thrombospondin-2 (TSP-2). Ligament scar material and structural mechanical properties were assessed in seven rats at each time point. Increased nerve density was promoted by NGF at both 14 and 42 days. Exposure to NGF also led to increased ligament vascularity, as measured by histologic assessment of vWF immunohistochemistry, although LSPI-measured blood flow was not significantly different from controls. NGF treatment also led to decreased expression of TSP-2 at 14 days. Mechanical testing revealed that exposure to NGF increased failure load by 40%, ultimate tensile strength by 55%, and stiffness by 30% at 42 days. There were no detectable differences between groups in creep properties. The results suggest that local application of NGF can improve ligament healing by promoting both reinnervation and angiogenesis, and results in scars with enhanced mechanical properties.

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