SCIENTIFIC ARTICLE

Reverse End-to-Side Nerve Transfer: From Animal Model to Clinical Use

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Purpose Functional recovery after peripheral nerve injury is predominantly influenced by time to reinnervation and number of regenerated motor axons. For nerve injuries in which incomplete regeneration is anticipated, a reverse end-to-side (RETS) nerve transfer might be useful to augment the regenerating nerve with additional axons and to more quickly reinnervate target muscle. This study evaluates the ability of peripheral nerve axons to regenerate across an RETS nerve transfer. We present a case report demonstrating its potential clinical applicability.

Methods Thirty-six Lewis rats were randomized into 3 groups. In group 1 (negative control), the tibial nerve was transected and prevented from regenerating. In group 2 (positive control), the tibial and peroneal nerves were transected, and an end-to-end (ETE) nerve transfer was performed. In group 3 (experimental model), the tibial nerve and peroneal nerves were transected, and an RETS nerve transfer was performed between the proximal end of the peroneal nerve and the side of the denervated distal tibial stump. Nerve histomorphometry and perfused muscle mass were evaluated. Six Thy1-GFP transgenic Sprague Dawley rats, expressing green fluorescent protein in their neural tissues, also had the RETS procedure for evaluation with confocal microscopy.

Results Nerve histomorphometry showed little to no regeneration in chronic denervation animals but statistically similar regeneration in ETE and RETS animals at 5 and 10 weeks. Muscle mass preservation was similar between ETE and RETS groups by 10 weeks and significantly better than negative controls at both time points. Nerve regeneration was robust across the RETS coaptation of Thy1-GFP rats by 5 weeks.

Conclusions Axonal regeneration occurs across an RETS coaptation. An RETS nerve transfer might augment motor recovery when less-than-optimal recovery is otherwise anticipated. *(J Hand Surg 2011;36A:1631–1639. Copyright © 2011 by the American Society for Surgery of the Hand. All rights reserved.)*

Type of study/level of evidence Therapeutic I.

Key words Nerve regeneration, nerve transfer, neurorrhaphy, peripheral nerve, reverse end-to-side.

Additional material is available online.

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We would like to provide a special thanks to the Citizen Potawatomi Nation and tribal chairman John A. Barrett for their financial support of Andrew Yee.

Received for publication December 14, 2010; accepted in revised form June 24, 2011.

No benefits in any form have been received or will be received related directly or indirectly to the subject of this article.

Part of this work was presented by S.S.K. at the annual meeting of the American Society for Surgery of the Hand and was awarded the Joseph H. Boyes Award for best overall paper.

A. Y. received salary support through a grant from the Citizen Potawatomi Nationce:grant-sponsor> and tribal chairman John A. Barrett.

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0363-5023/11/36A10-0010$36.00/0
doi:10.1016/j.jhsa.2011.06.029

Distal end-to-end (ETE) nerve transfers (Fig. 1A) have been recommended for proximal nerve injuries in which the likelihood of functional recovery is poor.[1–4] There are, however, greater numbers of nerve injuries in which some, but not normal, functional recovery is predicted. In these situations, a technique to augment motor recovery would be advantageous.

This study evaluates the feasibility of augmenting[5] motor nerve regeneration using a reverse end-to-side (RETS) technique (Fig. 1B). The aim of this study was to assess the feasibility of RETS nerve transfer by analyzing nerve regeneration through the RETS coaptation site. Especially in situations of severe or recurrent cubital tunnel syndrome, the ability to augment additional motor axon regeneration to the intrinsic muscles of the hand would be useful. We designed this study with that specific scenario in mind, and we present a clinical case in which an RETS nerve transfer was performed to aid functional recovery following recurrent cubital tunnel surgery. In addition, we present our surgical technique for RETS nerve transfer of the anterior interosseous nerve (AIN) to the motor component of the ulnar nerve.

MATERIALS AND METHODS

Animals

Animal care complied with the guidelines set forth by the National Institutes of Health and our institution's animal studies committee.

Surgical model

Thirty-six male Lewis rats (Charles River Laboratories, Inc., Wilmington, MA) were randomized into 1 of 3 treatment groups (Fig. 2). The right leg served as the surgical side and the left leg as a nonsurgical control for each animal.

The animals were anesthetized by subcutaneous delivery of ketamine and dexmedetomidine. Standard sterile technique was used for all procedures. We exposed the sciatic nerve through a longitudinal incision, posterior and parallel to the femur. The incision was carried through the muscle fascia, and the biceps femoris muscle was retracted in an posterior direction to expose the sciatic nerve. We dissected the sciatic nerve distal to its trifurcation to mobilize the tibial, peroneal, and sural nerves. We then transected the tibial nerve proximal to a consistent distal side branch, which served as a landmark in all groups. In all animals, the proximal stump of the tibial nerve was doubly ligated, cauterized, and sewn into a blind-ending silicone cap to prevent regenerating fibers from reaching the distal stump. The capped proximal stump was then buried deep within the surrounding muscle.

The animals then had one of the following procedures. Animals in group 1 (n = 12) served as a negative control. Only tibial nerve transection with capping was performed, with no repair. The muscles innervated by the tibial nerve were left permanently denervated. Animals in group 2 (n = 12) served as a positive control. The peroneal nerve was transected distally and coapted to the distal stump of the tibial nerve in an end-to-end fashion, using 11-0 nylon epineurial sutures. The level of this coaptation was 2.5 mm proximal to the landmark tibial nerve side branch. Animals in group 3 (n = 12) served as the experimental group. The peroneal nerve was transected distally and coapted to a perineurial window in the side of the distal tibial nerve at a level 2.5 mm proximal to the tibial nerve side branch. At the conclusion of surgery, the surgical wound was irrigated thoroughly and closed in layers. Anesthesia was reversed, and the animal was allowed to recover on a warming pad. Six Thy1-GFP transgenic Sprague Dawley rats, whose neural tissues expressed green fluorescent protein, also had RETS nerve transfer and were used for all experiments requiring confocal imaging.

Histomorphometry

Labeled nerve specimens (Fig. 2) from the distal tibial nerve near its branching point were preserved in glutaraldehyde, postfixed in osmium tetroxide, embedded in epoxy, and sectioned with an ultramicrotome, as described previously.[6,7] For each harvested nerve segment, 3 sections were selected for quantitative analysis with semi-automated histomorphometric algorithms. This system used a series of semi-automated algorithms to distinguish axons, myelin, nerve sheath, and debris. Processed cross-sections were digitized and assessed for total fascicular area and total fiber number. Samples were harvested from half of the animals (n = 6 per group) at 5 weeks and the remaining half at 10 weeks.

Muscle mass

Immediately following nerve harvest, the animals had transcardiac perfusion with 400 mL 0.1M phosphate buffer followed by 400 mL 4% paraformaldehyde. Muscles innervated by the tibial nerve (gastrocnemius, soleus, and deep flexor of digits) were harvested from both the surgical and nonsurgical limbs. All muscles were weighed using an analytic balance. Muscle mass from the surgical side was normalized to the nonsurgical side for each animal.