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Synergistic motor nerve fiber transfer between different nerves through the use of end-to-side coaptation

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ABSTRACT

End-to-end nerve repair is a widely used and successful experimental microsurgical technique via which a denervated nerve stump is supplied with reinnervating motor or sensory axons. On the other hand, questions are still raised as concerns the reliability and usefulness of the end-to-side coaptation technique. This study had the aim of the reinnervation of the denervated forearm flexor muscles in baboons through the use of an end-to-side coaptation technique and the synergistic action of the radial nerve. The median and ulnar nerves were transected, and the motor branch of the radial nerve supplying the extensor carpi radialis muscles (MBECR) was used as an axon donor for the denervated superficial forearm flexors. A nerve graft was connected to the axon donor nerve through end-to-side coaptation, while at the other end of the graft an end-to-end connection was established so as to reinnervate the motor branch of the forearm flexors. Electrophysiological investigations and functional tests indicated successful reinnervation of the forearm flexors and recovery of the flexor function. The axon counts in the nerve segments proximal (1038 ± 172 S.E.M.) and distal (1050 ± 116 S.E.M.) to the end-to-side coaptation site and in the nerve graft revealed that motor axon collaterals were given to the graft without the loss or appreciable misdirection of the axons in the MBECR nerve distal to the coaptation site. The nerve graft was found to contain varying, but satisfactory numbers of axons (269 ± 59 S.E.M.) which induced morphological reinnervation of the end-plates in the flexor muscles. Accordingly, we have provided evidence that end-to-side coaptation can be a useful technique when no free donor nerve is available. This technique is able to induce limited, but still useful reinnervation for the flexor muscles, thereby producing a synergistic action of the flexor and extensor muscles which allows the hand to achieve a basic gripping function.

Introduction

Brachial plexus injuries often result in severe functional movement deficits of the upper extremity. An old and reliable procedure with which to reinnervate distal targets involves end-to-end repair of a distal denervated nerve stump with the use of a proximal innervated nerve as axon donor (Tuttle, 1993). However, this approach has the drawback that it sacrifices a donor nerve and its target to provide reinnervation for the recipient nerve and target muscles.

End-to-side nerve repair is a microsurgical technique in which nerve fibers are transferred from an intact donor nerve to a denervated recipient nerve, usually via a nerve graft. In this case, the nerve graft is coapted to the recipient nerve by end-to-end neurorrhaphy. Although the value of end-to-side coaptation is debated in the literature, good functional results can be achieved when this technique is applied with special care to the donor nerve (Millesi and Schmidhammer, 2007). This method is effective when a motor or sensory nerve is used as function-restoring axon source (Kovacic et al., 2007; Schmidhammer et al., 2005b), and it should be applied when no suitable proximal nerve stump is available as axon source, for example in certain brachial plexus injuries. The use of mixed nerves as axon donor can lead to a variable outcome (Kelly et al., 2007) as the sprouting of the donor axons cannot be controlled.

Earlier experiments have revealed that, in the event of permanent defects of a proximal median nerve injury, end-to-side coaptation between the terminal deep branch of the ulnar nerve and the thenar branch of the median nerve provides an opportunity for the restoration of lost thenar motor functions with preserved hypothenar,

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interosseous and thumb adduction functions (Schmidhammer et al., 2005b).

Another possible application of this technique is to restore some degree of gripping function by using a motor branch of the radial nerve to the wrist extensors as axon donor when the functions of the median and ulnar nerves are completely missing. Although it does not result in complete reinnervation of the denervated muscles, end-to-side coaptation appears to be superior to the functional tendon transfer techniques because the function of the intact muscle groups is maintained. This procedure is based upon utilization of the partial synergistic function of this branch of the radial nerve to reinnervate the superficial flexor forearm muscles.

The present study had two aims: a search for evidence that collateral sprouts from a motor nerve supplying the wrist extensors can be guided via a nerve graft to a muscle originally supplied by a motor nerve innervating the wrist and finger flexors; and an investigation of whether a lost forearm flexor function can be restored to some extent by nerve fiber transfer through the use of end-to-side coaptation.

Experimental procedures

Animals

The experiments were carried out on 8 adult (on average 5 years old, and weighing 18 kg) male baboons (*Papio ursinus*) housed at the Laboratory Animal Centre, North-West University, Potchefstroom, South Africa, and lasted for an average period of 18 weeks. The animals were sedated in their homing cage with a single intramuscular dose (8–10 mg/kg body weight) of ketamine hydrochloride (Ketalar, Parke Davis Co., Ann Arbor, MI, USA) and then placed on the operating table in the supine position. Following intubation, they were connected to an animal respirator (Servoventilator, Siemens-Elema, Sweden) and their body temperature was maintained at 37 °C through use of a heating pad. General anesthesia was introduced with intravenous sodium pentobarbital solution (2–5 mg/kg/h) followed by halothane gas. The baboons also received 0.5 mg/kg morphine at the beginning of the operation. All animals received a single intramuscular dose of antibiotic (2.2 g of Augmentin, GlaxoSmithKline Pharma GmbH, Vienna, Austria).

All animals were monitored postoperatively until they had recovered from the anesthesia and were later returned to their cages. The baboons received 0.2 mg/kg/day meloxicam intramuscularly for 3 days following surgery, as anti-inflammatory and analgesic therapy.

As regards the care and use of animals for experimental procedures, the experiments were carried out with the advance approval of the Committee for Animal Experiments, University of North-West University, Potchefstroom Campus, South Africa. However, no negative control group was allowed to be set up in order to use the possible lowest numbers of animals. All the procedures were carried out with full accord with the Helsinki Declaration on Animal Rights. Adequate care was taken to minimize pain and discomfort during and after the operation.

Surgery

A midside skin incision was made on the medial aspect of the right upper arm and forearm. After transection of the upper arm fascia at the medial antebrachial cutaneous nerve (CAM), the median, ulnar and radial nerves were exposed. The palmaris longus (PL) muscle was identified and exposed for electrophysiological studies (Fig. 1A). This muscle was chosen for analysis because it produces strong palmar flexion of the wrist in baboons. The PL muscle induces powerful flexion of the metacarpophalangeal joints, pulling the strong subcutaneous fat pads connected to the palmar aponeurosis in the proximal direction. Additionally, the PL muscle seems to induce some flexion of the proximal interphalangeal joints. Next, the radial nerve was exposed on the radial side of the upper arm, and the superficial branch, the deep branch and the motor branch to the extensor carpi radialis longus and brevis muscles (MBECR) were dissected (Fig. 1B).

A needle electrode was placed into the PL muscle innervated by the median nerve, and the nerve trunks at the upper arm level were stimulated to detect any variation in innervation. The PL muscle appeared to be innervated only by the median nerve. Stimulation of the radial nerve showed that the extensor carpi radialis muscle group was innervated by the radial nerve alone.

The median and ulnar nerves were transected twice to create a 10 cm nerve gap at the upper arm level. The denervation of the forearm flexor muscles was assessed electrophysiologically. The median nerve with its motor branches was dissected in the forearm. In all animals three main motor nerve bundles were found. The needle electrode was inserted into the PL muscle again and each nerve bundle was stimulated electrophysiologically (NeuroMax-XLTEK, Oakville, ON, Canada). The motor branch bundle producing the strongest response in the PL muscle after electrical stimulation was chosen for end-to-end coaptation.

The medial antebrachial cutaneous nerve was harvested for nerve grafting. A tunnel for two nerve grafts was created on the palmar aspect of the forearm in the radial region of the elbow joint. End-to-side nerve coaptation for the graft and the MBECR was secured by two epineurial sutures (Ethilon 8-0/BV-2, Ethicon-Johnson & Johnson, Brussels, Belgium; Fig. 1B) after the creation of an incision in the epineurium with the help of an operating microscope (Leica M651, Leica Microsystems, Vienna, Austria). The nerve graft was carefully inserted into this epineural slit without damaging the nerve fascicles or the perineurium. The integrity of the perineurium was checked under the operating microscope. The nerve graft was then pulled into the prepared tunnel without any tension, and end-to-end neurorrhaphy was established with the identified motor branch group to the superficial layer of the forearm flexors (the PL muscle is the ulnarmost muscle in this group). The nerve graft not used for the grafting procedure was processed for histological evaluation. The wound was closed in layers in all animals, with single interrupted nylon skin sutures.

Each animal was re-anesthetized 18 weeks after surgery to investigate the characteristics of the nerves and nerve grafts electrophysiologically, and the nerves and part of the PL muscle were then removed for morphological analysis. The left radial and median nerves served as controls.

Electrophysiological analysis

At the end of the survival period, the electrophysiological analysis was repeated to assess the extent of reinnervation of the PL muscle via the nerve graft after end-to-side coaptation to the MBECR (radial nerve). The needle electrode was inserted into the PL muscle, and the amplitude, compound action potential area and nerve conduction velocity were determined.

Functional analysis

Four different tests of the wrist and hand functions were performed preoperatively, on the first day postoperatively and thereafter weekly during an 18-week period (see Table 1).

Morphological analysis

The removed nerve complex was immersion-fixed with 2.5% phosphate-buffered glutaraldehyde for 2 days and then stored in PBS. Pieces (3 mm long) of the nerve graft, the MBECR nerve branch before