END-TO-SIDE NERVE SUTURE — A TECHNIQUE TO REPAIR PERIPHERAL NERVE INJURY

Ulrich Mennen

End-to-side nerve suture (ETSNS) has until recently been extensively researched in the laboratory animal (rat and baboon). Lateral sprouting from an intact nerve into an attached nerve does occur, and functional recovery (sensory and motor) has been demonstrated.

We have demonstrated conclusively that ETSNS in the human is a viable option in treating peripheral nerve injuries, including injuries to the brachial plexus. Among the many advantages of this new technique are: (*i*) simple and short operation; (*ii*) shorter recovery time — suture is done closer to the target organs; (*iii*) nerve grafts to bridge injured gaps are eliminated, reducing the morbidity of nerve surgery to a minimum; (*iv*) innervation of paralysed muscles, for which there was previously thought to be no hope of recovery, opens up many new treatment options; and (*v*) certain aspects of nerve function and regeneration, unknown until recently, open new horizons and understanding.

ETSNS has given us new dimensions in the management of peripheral nerve injuries.

S Afr Med J 1999; **89**: 1188-1194.

Until recently it seemed that the technique and results of peripheral nerve suture had reached a dead end as far as further significant improvements were concerned. Among the factors contributing to this situation were practical limits to refinement in suture material, micro-instruments and magnification, and underestimation of the inherent abilities and potential of the peripheral nervous system to heal, regenerate and adapt to challenges.

End-to-side nerve suture (ETSNS) addresses both the above factors. The simplicity of the procedure means that further refinement of technique and equipment is not required and new avenues for nerve studies have been opened by the surprising finding, especially in the primate and the human,[1,2] that intact nerves have an inherent 'urge' to sprout laterally in order to

Department of Hand and Microsurgery, Medical University of Southern Africa, and Ga-Rankuwa Hospital, Pretoria

Ulrich Mennen, MBChB, FRCS (Glasg), FRCS (Edin), FCS (SA) Orth, MMed (Orth), MD (Orth)

populate distal neural tubes, the finding that axons can carry many more impulses, i.e. are not area-specific, the finding that the brain has the capacity to interpret impulses that arrive by detour routes, and the finding that selective orientation of axons regarding sensation and motor function is an integral function of the nerve and need not be imposed by surgical and chemical means. Many of these findings could only be made after ETSNS was performed in humans, with whom it was possible to communicate intelligibly. In animal studies, even in the primate, the interpretation of the various modalities of sensation and the voluntary contraction of muscles is not possible.

Many neurotrophic and neurotropic factors have been discovered.[3-5] These are essential for the maintenance of nerve structure and function, for promoting recovery of injured nerve, and for stimulating regeneration should it be needed.[6]

Neurotrophic factors mainly maintain the integrity of nerves. The end of a sectioned distal nerve produces neurotropic factors which 'recruit' axons to fill the neural tubes. This 'summoning force' is so overwhelming that the donor axons sprout out superfluous axons. Because of the abundance of these newly sprouted axons, only the minority will find an empty neural tube. The rest will atrophy.

The histological experimental results indicate that the majority of neural tubes are re-populated by the new sprouting axons, unlike the situation with end-to-end nerve sutures. The effect of the neurotropic factors is so strong that these lateral sprouts even cross through the epineurium.[7,8] However, it has been shown that the result of lateral sprouting and populating of the recipient nerve is more organised and abundant when an epineural 'window' is made before the neuroraphy is done[9-12] (and F Viterbo *et al.* — unpublished data).

Historically ETSNS has been practised on a very limited scale with only sporadic reports.[13-16] However, the exact technique and eventual results are not known for certain. Axonal damage probably occurred because of the large 'windows' created and the crude instruments available. Follow-up reports on results have not been forthcoming.

METHOD

The proximal end of the distal part of the injured nerve is 'freshened' by serial cuts with a sharp knife until a healthy-looking cut surface is seen.

An intact nearby matching nerve is selected to act as host nerve. An epineural window is created on the side of the host nerve on the same plane as the approaching receiving nerve. Care is taken not to damage any axons in the host nerve (Fig. 1).

The recipient nerve is sutured to the epineural window using four 8/0 Prolene sutures, in much the same way as an end-to-side arterial suture.[1,2] The suture line should be free of tension, and kinking of the nerve should be avoided (Fig. 2). The proximal end of the injured nerve is buried in soft tissue.

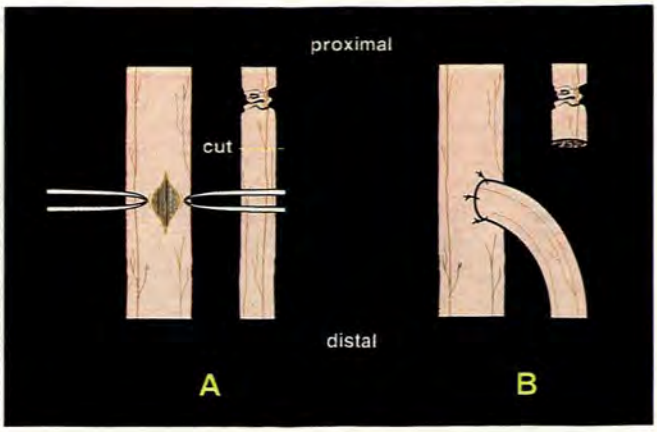


Fig. 1. The technique of end-to-side (ETS) suture. An epineural window is made to receive the proximal end of the distal part of the injured nerve. Four of five 8/0 Prolene sutures keep the ETS suture in place. Note: (i) *the axons of the host nerve should not be damaged;* (ii) *the ETS suture should not be under tension;* (iii) *the ETS suture should be done to the host nerve in the same plane as the approach of the injured nerve to prevent any kinking.*

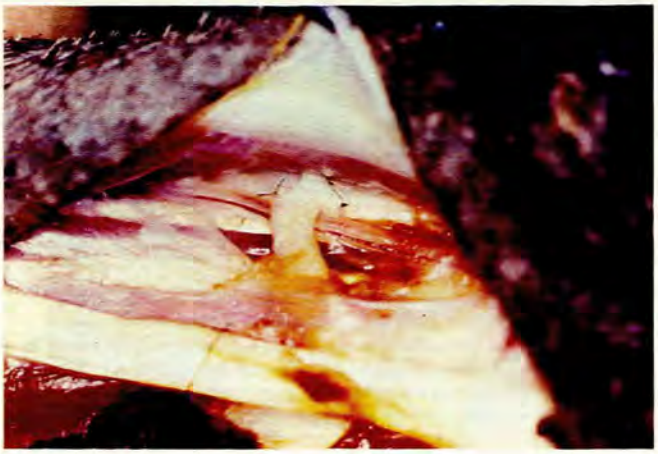


Fig. 2. Example of ETSNS in the baboon.

Postoperative care includes splinting for 14 days if the suture line is near a joint. After brachial plexus ETSNS surgery, a supportive sling is worn for 2 - 3 weeks.

MATERIAL

Experimental animal

As experimental model the chacma baboon (*Papio ursinus*) was used. The ETSNS technique was used in 12 baboons, i.e. to suture 24 nerves. Twelve ulnar nerves were sutured end-to-side (ETS) to the median nerve and 12 median nerves were sutured to the ulnar nerve at the wrist level.

These nerve sutures were used for a variety of experiments of various post-suture time intervals, including clinical observations for re-innervation, electroconduction and histology.

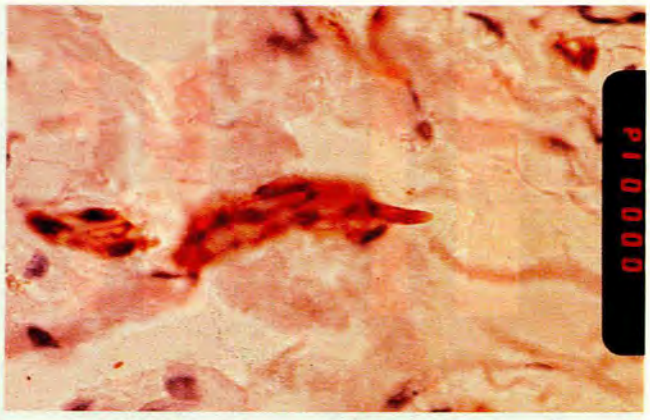


Fig. 3. S100 colouring clearly shows new sprouting of axon.

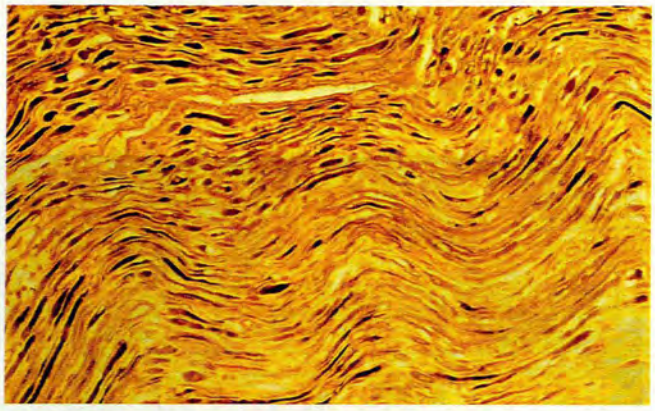


Fig. 4. Palmgren coloring indicating near normally populated recipient nerve. Black indicates new axons. Note normal wavy pattern of nerve. The same histology was seen after digital nerve to digital nerve ETSNS on patient 14. The patient requested amputation of the finger due to subsequent pathology, yielding the first human specimen for histological examination.

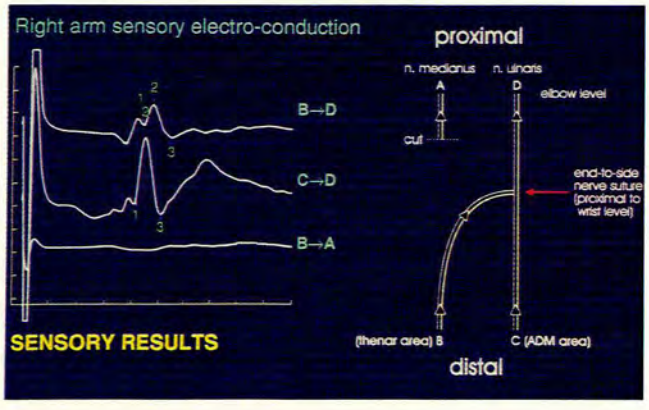


Fig. 5. Sensory electroconduction: the nerve impulse crossing the ETSNS (B to D).

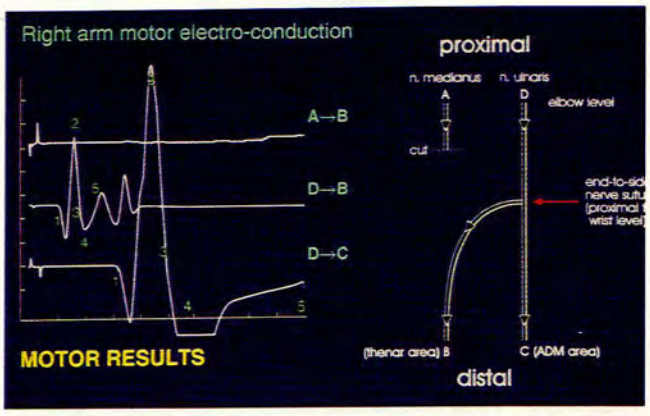


Fig. 6. Motor electroconduction: the nerve impulse crossing the ETSNS (D to B).

Among the findings were the following:

1. Early, prolific lateral sprouting of axons from the host nerve is seen (Fig. 3).

2. The recipient nerve is near normally populated by the new axons, which show the typical wavy pattern (Fig. 4).

3. The baboons did not show any signs of distress, did not mutilate themselves, had no trophic changes or ulcers, and used and moved their hands in the same way as they had before the operation. No evidence of loss of donor nerve function was noted.

4. Sensory electroconduction studies showed early recovery with a clear recordable pattern and conduction across the ETS suture line (Fig. 5).

5. Motor electroconduction studies showed a high contraction peak and typical scatter pattern due to demyelinisation. This is a normal phenomenon after nerve suture (Fig. 6).

6. Specimens taken 2 years after surgery do not show any evidence of loss or atrophy of donor axons beyond the suture line.

In the experimental animal it is obviously not possible to evaluate quality of sensation, modalities of sensation (e.g. two-point discrimination, vibration, proprioception, light touch), voluntary movements of extrinsic and intrinsic muscles, and any cross-over sensations or movements.

Human patients

To date 50 patients with a variety of peripheral nerve lesions have been operated on, but Table I reflects the first 33 cases (up to March 1999). The results in the first 22 cases[2] indicated remarkable recovery. This prompted us to use this technique as the method of choice in patients who might otherwise have needed a nerve graft or neurotisation.

Although this is not a homogeneous group, with the location and type of injuries all differing from each other and the timing of surgery dictated by a host of factors, the re-innervation of the

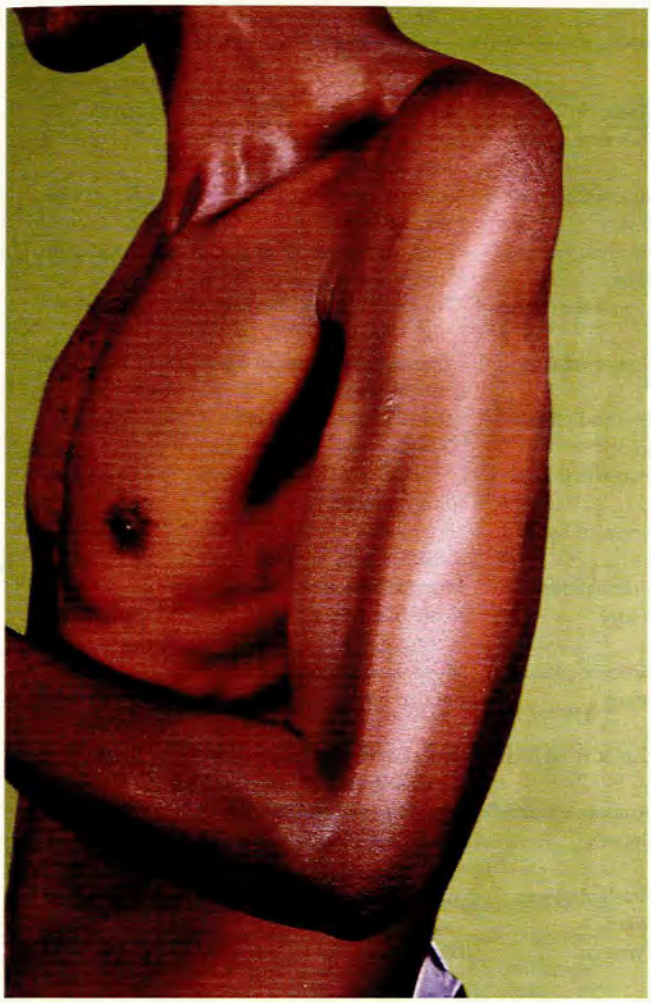
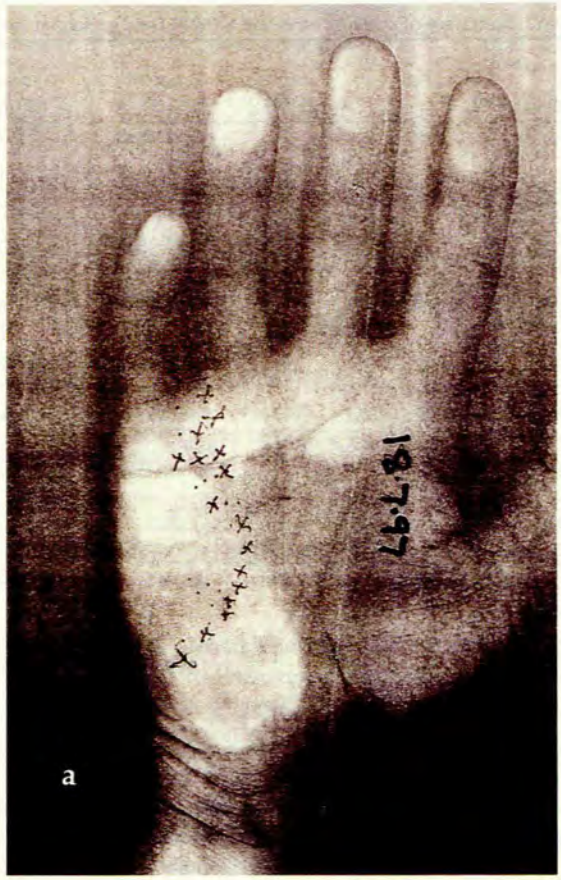


Fig. 7. Recovery of biceps muscle 2 years after ETSNS of the musculocutaneous nerve to the posterior cord of the brachial plexus.

target organs (skin and muscles) is most encouraging. The following results are observed:

1. Since ETSNS is done much closer to the target organs re-innervation occurs much sooner.
2. Axonal advancement is 1.5 - 2 mm per day on average, again contributing to earlier recovery.
3. Light touch recovers first when mixed nerves are sutured.
4. Sweat appears with or soon after sensory recovery.
5. Unpleasant feelings often seen with end-to-end nerve sutures, such as hypersensitivity, a burning sensation and paraesthesiae, have not been observed.
6. The sensory pattern has a normal anatomical distribution.
7. Crossover sensation is seen in some cases, i.e. a sensory stimulus in a re-innervated area may produce a similar feeling in an area supplied by the donor nerve. This is not an unpleasant experience and does not seem to bother the patient.
8. No sensory loss has been seen in the donor area.
9. The fingerprints recover with the sensory recovery. They look and feel normal.



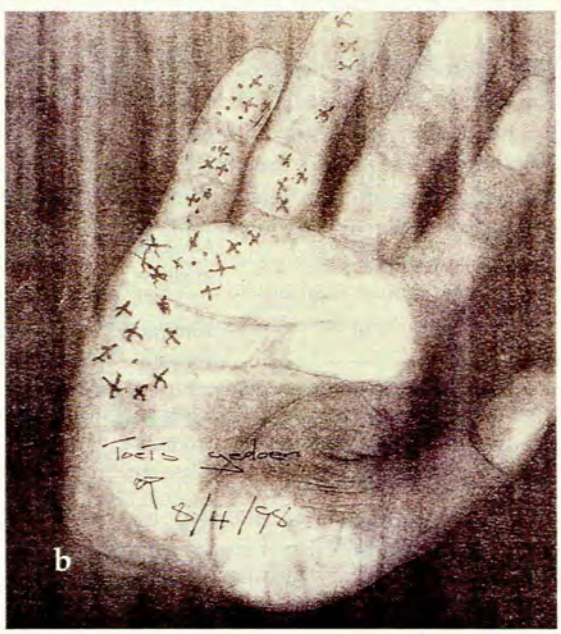


Fig. 8. ETSNS of ulnar nerve to median nerve at wrist level. This is a photocopy image of the patient's hand. The crosses represent sensation. On 18 July 1997 (a) clawing (ulnar negative hand) is clearly visible. On 8 April 1998 (b), 9 months after ETSNS, the clawing has disappeared, indicating re-innervation of the instrinsic muscles. (Reproduced from Hand Surgery *1998; 3(1), with permission.)*

Table I. Summary of patients who had ETSNS for a variety of conditions

Patient	No.	Age (yrs)	Gender	Side	Cause of injury	Date of injury	Area	Nerves sutured	Date of surgery
Me 1	1	26	F	1	Gun shot	5 Feb 1996	Forearm injury	Median nerve to ulnar nerve (prox. to wrist)	12 Feb 1996
Me 2	2	19	M	1	MVA	13 Oct 1989	Brachial plexus injury	Median nerve to ulnar nerve (prox. to wrist)	27 Jun 1996
Me 3	3	25	M		Knife stab	16 Jan 1996	Brachial plexus injury	Ulnar nerve to median nerve (prox. to wrist)	24 Oct 1996
He 1	4	55	M	1	Gun shot	15 Sep 1996	Upper arm injury	Ulnar nerve to median nerve (prox. to wrist)	23 Jan 1997
Le 1	5	50	M	1	Fan blade cut	4 Apr 1997	Forearm injury	Ulnar nerve to median nerve (prox. to wrist)	15 May 1997
Me 4	6	22	M	1	Infraclavicular stab	28 Sep 1996	Brachial plexus injury	Musculocutaneous nerve to posterior cord	3 Jun 1997
Me 5	7	33	M	1	Knife stab	15 Mar 97	Forearm injury	Ulnar nerve to median nerve (prox. to wrist)	14 Jul 1997
Me 6	8	23	M	r	MVA	1 Jul 1995	Forearm injury	Ulnar nerve to median nerve forearm (prox. to wrist)	18 Sep 1997
Le 2	9	32	F	1	MVA	29 Nov 1996	Brachial plexus injury	Musculocutaneous nerve to median nerve	16 Oct 1997
Be 1	10	24	M	r	MVA	6 Jan 1996	Brachial plexus injury	Musculocutaneous nerve to median nerve	28 Oct 1997
Me 7	11	30	M	1	Stab wound	24 May 1997	Cut at wrist level	Ulnar nerve to median nerve (at wrist level)	17 Nov 1997
Ce 1	12	37	M	1	Crush injury, middle finger	5 Feb 1995	Amputated middle finger	Ring finger digital nerve to index finger digital nerve	20 Nov 1997
Le 3	13	25	M	r	MVA	15 Jan 1996	Brachial plexus injury	Musculocutaneous nerve to long nerve of Bell	5 Dec 1997
Se 1	14	35	M	1	Angle grinder cut, palm of hand	26 Jan 1997	Palm cut	Digital nerve to digital nerve	11 Dec 1997
Me 8	15	26	M	1	MVA	20 May 1996	Brachial plexus injury	Upper trunk to middle trunk	11 Dec 1997
Me 9	16	44	F	r	Severance of ulnar nerve	3 Feb 1998	Forearm cut	Ulnar nerve to median nerve (prox. to wrist)	8 Feb 1998
Ne 1	17	4	M	1	MVA, degloving at elbow	15 Feb 1997	Ulnar nerve cut at elbow level	Ulnar nerve to median nerve (prox. to wrist)	11 Feb 1998
Me 10	18	32	M	1	Knife stab wound	1 Jan 1997	Ulnar nerve cut at elbow level	Ulnar nerve to median nerve (prox. to wrist)	12 Feb 1998
Ke 1	19	36	M	r	Knife stab wound	28 Aug 1997	Forearm open wound	Ulnar nerve to median nerve (prox. to wrist)	12 Feb 1998
Me 11	20	26	M	r	Glass cut, median nerve	15 Oct 1996	Forearm open wound	Median nerve to ulnar nerve (prox. to wrist)	5 Mar 1998
Ne 2	21	39	M	1	Glass cut, median nerve	21 Oct 1997	Forearm open wound	Median nerve to ulnar nerve (prox. to wrist)	16 Mar 1998
Ve 1	22	38	F		Cut ulnar nerve after neurolysis	20 Oct 1997	Elbow	Ulnar nerve to median nerve	17 Feb 1998
Ne 3	23	40	M	r	Cut ulnar nerve by grinder	25 Aug 1997	Forearm open wound	Ulnar nerve to median nerve (prox. to wrist)	26 Mar 1998
Me 12	24	30	M	1	Cut, ulnar nerve	14 Feb 1998	Forearm open wound	Ulnar nerve to median nerve	16 Jul 1998
He 2	25	42	M	1	Cut, digital nerve of index finger	15 Jan 1998	Wound on volar aspect of hand	Digital nerve to digital nerve	11 Jun 1998

Table I Continued

Me 13	26	26	M	l	Glass cut ulnar nerve	29 Mar 1998	Forearm open wound	Ulnar nerve to median nerve	15 Jun 1998
Ve 2	27	45	M	l	Glass cut ulnar nerve	23 Sep 1998	Forearm open wound	Ulnar nerve to median nerve	10 Dec 1998
We 1	28	38	F	r	MVA	31 Jul 1998	Cut elbow	Ulnar nerve to median nerve (prox. to wrist)	5 Nov 1998
Me 14	29	35	M	l	Stab wound	28 Jul 1998	Brachial plexus injury	Upper trunk to lower trunk of brachial plexus	19 Nov 1998
Me 15	30	40	F	r	Glass cut ulnar nerve	15 Oct 1998	Forearm open wound	Ulnar nerve to median nerve	6 Dec 1998
Ne 4	31	3	M	r	MVA passenger, car rolled	29 Dec 1998	Degloving forearm injury	Ulnar nerve to median nerve (prox. to wrist)	31 Dec 1998
Ne 5	32	21	M	r	Knife stab	25 Sep 1998	Brachial plexus injury	Musculocutaneous nerve to medial cord	15 Feb 1998
Re 1	33	13	M	r	Fractured humerus cut radial nerve	13 Mar 1998	Mid shaft humerus	Radial nerve to median nerve	14 Mar 1999

No. = sequence of surgery undertaken; M = male; F = female; l = left; r = right; MVA = motor vehicle accident; prox. = proximal.

10. Static two-point discrimination slowly improved over 2 years, even reaching 3 mm.

11. Motor function of large (i.e. biceps) (Fig. 7) and small (i.e. intrinsic hand) muscles recovered (Fig. 8, a and b). This recovery was observed even beyond 2 years, and was closely influenced by specific rehabilitative therapy, which concentrated on specific muscle rehabilitation rather than gross function, e.g. elbow flexion involving a group of muscles.

12. Co-contraction or functional confusion of muscles was not seen, again indicating that nerves may act as generalised conduits for impulses, rather than once-off area-dedicated conductors.

13. Although histologically the nerves at the suture area showed a neuroma-like pattern, no painful or sensitive neuromas or even hypersensitivity with percussion over the anastomosis site developed.

14. The results of re-innervation are less successful in patients treated more than 6 months after injury.

Discussion

ETSNS is a practical option to innervate motor and sensory end organs. Our results are very encouraging, and at least match those of end-to-end nerve suture and do better than nerve grafting. Patients had fewer side-effects such as neuroma formation at the suture site and unpleasant sensory feelings.

ETSNS is a simple alternative to re-innervate lost sensory and/or motor function. The possibility of 'borrowing' axons from virtually any neighboring intact nerve opens up a wide spectrum of options.

The ability and desire of an intact nerve to sprout laterally, to do this selectively for sensory and motor axons, to populate the injured distal recipient nerve fully, and to carry many more impulses than once thought, all without any unpleasant side-effects (e.g. neuromas), has been drastically under-estimated. Of course, much research and clinical observation still needs to be done to understand and quantify this remarkable phenomenon.

The importance of specific rehabilitation must be emphasised. Paralysed muscles and anaesthetic skin need to be re-educated. Paralysed muscles are often 'amputated in the brain' and need to be re-kindled, re-educated or awakened when innervation takes place. This form of therapy has been well documented.[17] Sensory rehabilitation is important. For both sensory and motor rehabilitation the professional skills of occupational therapists are strongly recommended.

No evidence of motor or sensory deficit was observed in the donor area. In the experimental animal (most recently the rat[18]) histology and actual counting of axons before and after ETSNS did not reveal any damage to the axons. How the nerve manages to carry impulses to and from various target organs remains a mystery, and here further neurophysiological investigations are required.

Nerves treated more than 6 months after injury do not respond as well as those treated more promptly. This is because increased fibrous tissue in the distal recipient nerve prevents axons from growing down neural tubes. Owing to the atrophy (Wallerian degeneration) of the recipient nerve, the amount of neurotropic factors which stimulate axonal sprouting is probably also reduced.

In this report I do not attempt to explain how all this happens. I merely report on experimental findings in the non-human primate and clinical findings over 3 years in a diverse group of patients. However, I do claim that this new technique to re-establish sensory and/or motor function does work in the human, that it simplifies many of our present techniques (e.g.

obviate nerve grafts), and that it presents us with new treatment options (e.g. motorising biceps and deltoid muscles, and restoring brachial plexus integrity in some avulsion injuries).

Conclusion

ETSNS is a well-established surgical technique to restore lost motor and sensory function. Technically it is a simple, easy procedure. Because any suitable neighboring intact nerve can be used as host for a distal injured nerve, many new management options become available, including the restoration of avulsed brachial plexus injuries and doing away with nerve grafts, thereby reducing morbidity and operation time. The functional results of ETSNS can only be fully evaluated in the human patient who is able to co-operate, especially in the rehabilitation phase, with whom it is possible to discuss the nuances of sensation.

A special word of thanks is due to Professor E J Raubenheimer, Head of the Department of Oral Pathology and Oral Biology, Faculty of Dentistry, MEDUNSA, for the meticulous histology investigations.

References

1. Mennen U. End-to-side nerve suture in the non-human primate. *Hand Surgery* 1998; **3**(1): 1-6
2. Mennen U. End-to-side nerve suture in the human patient. *Hand Surgery* 1998; **3**(1): 7-15.
3. Lundborg G. *Nerve Injury and Repair.* Edinburgh: Churchill Livingstone, 1988.
4. Lundborg G, Zhao Q, Kanje M, Danielsen N, Kerns JM. Can sensory and motor collateral sprouting be induced from intact peripheral nerve by end-to-side anastomosis? *J Hand Surg* 1994; **19B:** 277.
5. Dagum AB. Peripheral Nerve Regeneration, Repair, and Grafting. *J Hand Ther* 1998; **11:** 111-117.
6. Yin Q, Kemp GJ, Frostick SP. Neurotrophins, neurones and peripheral nerve regeneration. *J Hand Surg* 1998; **23B:** 433-437.
7. Noah EM, Williams A, Jorgenson C, Skoulis TG, Terzis JK. End-to-side neurorrhaphy: A histologic and morphometric study of axonal sprouting into an end-to-side nerve graft. *J Reconstr Microsurg* 1997; **13**(9): 99-106.
8. Zhao JZ, Chen ZW, Chen TY. Nerve regeneration after terminolateral neurorraphy: Experimental study in rats. *J Reconstr Microsurg* 1997; **13**(1): 31-37.
9. Viterbo F. End-to-side neurorraphy with removal of the epineural sheath. Experimental study in rats. PhD thesis, Botucatu, Faculdade de Medicina, Universidade Estadual Paulista, 1992.
10. Viterbo F, Trindade JCS, Hoshino K, Mazzoni Neto A. Latero-terminal neurorraphy without removal of the epineural sheath: Experimental study in rats. *Journal Sao Paulo Med* 1992; **110:** 267.
11. Viterbo F, Trindade JCS, Hoshino K, Mazzoni Neto A. End-to-side neurorraphy with removal of the epineural sheath: An experimental study in rats. *J Plast Reconstr Surg* 1994; **94:** 1038.
12. Viterbo F, Trindade JCS, Hoshino K, Mazzoni A. Two end-to-side neurorraphies and nerve graft with removal of the epineural sheath: Experimental study in rats. *J Brit Plast Surg* 1994; **47:** 75.
13. Kennedy R. On the restoration of co-ordinated movement after nerve-crossing, with interchange of function of the cerebral cortical centers. *Philos Trans R Soc London (Biol)* 1901; **194B:** 127.
14. Balance CA, Balance HA, Steward P. Remarks on the operative treatment of chronic facial palsy of peripheral origin. *J Brit Med* 1903; **1:** 1009.
15. Harris W, Low VW. On the importance of accurate muscular analysis in lesions of the brachial plexus, and treatment of Erb's palsy and infantile paralysis of the upper extremity by cross union of the nerve roots. *J Brit Med* 1903; **24:** 1035.
16. Gatta R. Laterotermínal anastomosis of nerve trunks. *Arch Ital Chir* 1938; **48:** 155.
17. Eggers IM, Mennen U. The motivational therapeutic apparatus system. *South African Bone and Joint Surgery* 1995; **5**(3): 53-55.
18. Tham SKY, Morrison WA. Motor collateral sprouting through an end-to-side nerve repair. *J Hand Surg* 1998; **23A:** 844-851.

Accepted 21 Sep 1999