Restoration of elbow flexion by performing contralateral lateral thoracic and thoracodorsal nerve transfers after experimental musculocutaneous nerve transection

Ecole Nationale Vétérinaire d’Alfort; and Ecole Nationale Vétérinaire de Lyon, France

Object. The immediate transfer of the right lateral thoracic nerve (LTN) and the thoracodorsal nerve (TDN) to the transected left musculocutaneous nerve (MCN), leading to nerve cross-neurotization, was performed in cats to evaluate reinnervation of the biceps brachii muscle (BBM).

Methods. Surgery to produce cross-neurotization of the MCN was performed in 12 cats (treatment group). Transection of the MCN was performed without attempts at neurotization in three cats (control group). Reinnervation of the BBM was assessed by performing electromyography (EMG) 6 months (14 cats) and 26 months (one cat) postsurgery. True Blue retrograde axonal tracing studies, tensile force measurements (muscle extensometry), and histopathological analyses were performed.

All cats in the treatment group recovered voluntary contraction of the BBM and regained elbow flexion. Electromyography revealed no abnormal spontaneous activity in the BBM. Muscle evoked potentials were recorded in that muscle after right C-8 ventral branch stimulation. The muscle contraction strength in the left BBM varied from 108 to 557 g. The BBMs regained their normal appearances. The region of the MCN distal to the anastomosis displayed a normal histological appearance. Fluorescence was detected in the ventral horn of the spinal cord in the right C-8 and T-1 segments. In contrast, in all cats in the control group there was atrophy of the BBM, no EMG signal, and no clinical sign of recovery. There was no contraction of the BBM, no labeled neuron in the spinal cord, and the MCN displayed major degenerative changes.

Conclusions. These findings demonstrate that the LTN and TDN can be used to neurotize injured contralateral brachial plexus nerves and obtain successful reinnervation in cats.

Key Words • nerve cross-transfer • lateral thoracic nerve • thoracodorsal nerve • musculocutaneous nerve • brachial plexus injury • cat

TRAUMATIC brachial plexus injuries in both humans and animals are well documented in the neurosurgical literature. Traction injuries put severe tension on nerves of the brachial plexus, possibly tearing the nerve roots from the spinal cord. The rootlets are more susceptible to damage after being stretched than the peripheral nerve, and the ventral root is more susceptible than the dorsal root. Various nerves of the brachial plexus can be affected to different degrees, and the combination of these multiple deficits causes a number of abnormal limb postures. The so-called BPA is the most dramatic situation; it corresponds to an avulsion of the rootlets from their site of insertion in the spinal cord, leaving a gap separating the spinal cord from the avulsed root. Brachial plexus avulsion results in the permanent paralysis of muscles innervated by the avulsed roots and in sensory loss in the corresponding dermatomes.

Various surgical techniques have been designed to treat BPA. These include avulsed spinal nerve root reimplantation into the spinal cord, or specific C-7 nerve cross-transfer. The choice between the latter two techniques remains controversial and depends on the exact location and extent of the avulsion.

Most of these surgical methods first must be developed in experimental animal models before they can be performed in human patients. The anatomy of the brachial plexus displays great variations in the root contribution to individual peripheral nerves in animals; however, functionally, the brachial plexus can be divided into two parts. The cranial portion of the plexus originates from ventral branches of the spinal nerves C-5, C-6, and C-7. In particular it controls shoulder mobility and elbow flexion. The caudal portion of the plexus commands elbow extension and carpus and digit mobility. The caudal portion is more important to locomotion because elbow extension is essential in bearing the weight of the individual. Cranial or caudal BPA can be treated successfully by a C-7 nerve cross-transfer in hu-
Restoration of elbow flexion in cats

and by a C-8 nerve cross-transfer in the cat; however, treatment of cranial BPA by nerve cross-transfer has not been studied in an animal model.

In a recent study we showed that the feline brachial plexus anatomy is relatively constant. This experimental model can therefore be used to explore a novel surgical technique in which the LTN and the TDN are used as sources for re-generating axons in cases of cranial BPA. The MCN innervates the BBM, which is the major muscle necessary for elbow flexion and the most important nerve in the cranial portion of the brachial plexus. The LTN arises from the caudal portion of the brachial plexus and innervates the cutaneous trunci muscle. The TDN arises from the caudal portion of the plexus and innervates the latissimus dorsi muscle. These two nerves are not essential to locomotion.

The goal of this study was to assess the efficiency of a novel technique of brachial plexus reconstruction after cranial BPA, based on the principles of nerve cross-transfer. We attempted to evaluate whether the procedure is technically possible in cats, whether it induces problems in the donor side of the patient, whether it can lead to reinnervation of the BBM in the affected limb, and whether it enables satisfactory functional recovery.

Materials and Methods

All surgical, behavioral, and electrophysiological procedures performed in the animals were approved by the Scientific Committee of the National Veterinary School of Alfort, France.

Experimental Animals

The study was conducted using 15 European cats (seven males and eight females), each weighing between 2.5 and 3.5 kg, which had been provided by a licensed experimental cat breeder. The cats were maintained in accordance with European Union legislation (CEE Council 24/11/86, article 5). They were divided into two groups: a treatment group (12 animals) and a control group (three animals).

Surgical Procedure

Anesthesia. General anesthesia was induced by an intramuscular injection of 15 mg/kg ketamine (Imalgène 1000, Merial SAS, Lyon, France) and 0.05 mg/kg midazolam (Hynnovel; Roche, Neuilly-sur-Seine, France), and was maintained by inhalation of halothane (Rodhia Organique Fine Ltd., Avonmouth, United Kingdom), which was administered in 100% oxygen through a tracheal tube via a semipneum Bain-type circuit. Lactated Ringer solution was administered intravenously at a rate of 0.5 ml/kg/min throughout the procedure. For all procedures that could induce pain, pre- and postoperative analgesia was provided using intramuscular injections of morphine chloridate (1 mg/kg) and ketoprofen (0.2 mg/kg body weight im). For all procedures, anaesthesia was maintained in a Bain-type circuit (Bain-Espine, Aesculap, Tuttlingen, Germany), during which the BBM was the only muscle that contracted. The nerve was then sectioned 0.8 cm from its termination in the BBM.

Constitution of the Animal Groups and Cross-Neurotization. At this point in the procedure, the cats were randomly allocated to either the treatment group or the control group.

In the treatment group (Fig. 1), the right TDN and LTN were moved to the opposite side of the animal by pulling these nerves between the trachea and the longus colli muscle. The peripheral stumps of both nerves were then anastomosed to the central stump of the left MCN by using one microsurgical epiperineural, simple interrupted suture made of No. 9-0 monofilament nylon to position the nerves in continuity inside a recolonization tube (Tube de recolonisation; Imedex Biométrieux, Chaponost, France). In the control group, the distal stump of the left MCN was sutured to the BBM. The proximal stumps of the left MCN and the right LTN and TDN were sutured to the right sternohyoid muscle.

The surgical incisions were closed in layers by using No. 2-0 polyglactin 910 (Vicryl) for the muscles and subcutaneous tissues and No. 3-0 nylon for the skin.

Clinical Methods of Evaluation

Clinical Assessment. This assessment was performed daily for the first 2 weeks, followed by weekly over a period of 6 months, and then monthly until the end of the study in one cat. Each forelimb was examined in turn by a visual assessment of locomotion, use of the limb, and the cat’s ability to flex its elbow. The withdrawal reflex of...
After application of the tracer, the exposed area was washed out several times with saline and the incision was closed in multiple layers. Five days later, the cats were killed by administering an overdose of pentobarbitone 20% (60 mg/kg injected intravenously). The heart was approached from the left side by performing a thoracotomy and the left ventricle was cannulated. Each cat was perfused with a heparinized 0.9% saline solution, followed by 4% paraformaldehyde in 0.1 M phosphate buffer. The spinal cord was removed and kept in the same fixative; later it was placed in a 30% sucrose solution for 24 hours. Each spinal cord segment between C-5 and T-2 was cut into cross-sections 40 μm wide. In each section, labeled neurons with visible nuclei were counted using fluorescence microscopy.

**Statistical Analysis**

No statistical tests were performed on the clinical data. Muscle mass and tension were statistically analyzed. They are believed to be associated with functional recovery. To rule out individual variations in muscle weight and compensatory muscular hypertrophy, which probably depends on multiple factors including the activity and weight of the cat, we calculated the left/right muscle weight ratio in the treated group and the control group. An analysis of variance was performed using SAS software (SAS Institute, Cary, NC). When an overall test was significant at the 5% level, we tested differences between the groups. The comparison error rate was fixed at 0.05/3 (= 0.017).

**Results**

The duration of the study was 6 months for all but one cat, No. 13 in the treatment group, which was killed 26 months after surgery.

**Clinical Assessment**

A clinical deficit was identified in the operated limb in all cats. The animals lost elbow flexion in that limb and were particularly affected when climbing an obstacle or ambulating upstairs.

A compensatory movement of the shoulder was visible with a slight rotation of this articulation. In all cats, the panniculus reflex disappeared after surgery and was not recovered. Sensitivity of the left first digit was absent throughout the study in all cats.

One month after surgery, lameness gradually diminished in all cats in the treatment group; by the end of the experiment five cats were capable of normal elbow flexion and six were capable of partial elbow flexion (Fig. 2). The withdrawal reflex, which is associated with active flexion of the elbow, was reestablished 6 months postoperatively in cats in the treatment group. In the control group none of the cats demonstrated any decrease in lameness or in active elbow flexion.

**Electrophysiological Evaluation**

All preoperative parameters were within normal ranges. Normal muscle evoked potentials were recorded in the left and right BBMUs after left and right C-7 ventral branch transcutaneous stimulations, respectively.

After surgery, spontaneous activity (fibrillation potentials) was recorded within the BBMUs of all cats. These muscles displayed abnormal activity, ranging from weak to strong. No activity was detected in the other forelimb muscles and, furthermore, no muscle evoked potentials were detected in the BBMUs after stimulation of the right C-8 ventral branch.

A final EMG evaluation revealed no abnormal sponta-

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P. Moissonnier, et al.
neous muscle activity in any animal. Muscle evoked potentials were recorded in the BBM of cats in the treatment group after stimulation of the right C-8 ventral branch (Fig. 3 upper right). There were no recordings of muscle evoked potentials in the BBM after an identical stimulation in the control cats (Fig. 3 lower left). Postoperative recordings of muscle evoked potentials were compared with preoperative recordings (Fig. 3 upper left).

Muscular Contractions and Atrophy

The muscle contraction strength in the left BBM among animals in the treatment group varied from 108 g (Cat 2) to 557 g (Cat 1) at 6 months postsurgery (mean 201.63 g), whereas it was 0 g in the control group (Fig. 4).

At the end of the study, muscle atrophy was observed in the left limbs of control cats, whereas in the treated cats the BBMs had regained their bulky appearance.

The histological appearance of the BBM was normal in treated cats (Fig. 5 lower). Muscle atrophy, fibrosis, and chronic inflammation were observed in the BBM of control cats (Fig. 5 upper).

Histological Evaluation of Neural Tissues

Musculocutaneous nerves collected distal to sutures in cats in the treatment group were histologically normal (Fig. 6 center) when compared with MCNs located on the right side of the same cats (Fig. 6 left). In the control group, the same portions of left-sided nerves were studied. They were very small in diameter, exhibited complete histological disorganization, and demonstrated connective tissue proliferation (Fig. 6 right).

In the spinal cord, fluorescence was detected in the ventral horn of the right C-8 segment. The number of positively stained neurons in the right horn was compatible with the number of myelinated axons counted in the LTNs and TDNs (980 and 1200 myelinated axons, respectively). No
True Blue fluorescence was detected in the left horn or in the other medullary segments, C-6 to T-2 of the spinal cord.

**Discussion**

In the present study, the clinical examination showed that sectioning the MCN caused loss of elbow flexion during the first 2 months postoperatively. Electrophysiological studies undertaken during the postoperative period revealed denervation lesions in the left BBM. This model therefore reproduces the deficits encountered in cranial brachial plexus trauma. Improvements obtained by the cross-transfer of LTNs and TDNs were evaluated objectively. The EMG results returned to normal (no spontaneous activity detected) and nerve conduction studies revealed a progressive improvement in the conduction of the MCN, with normal muscle evoked potentials in the BBM at the end of the study. Measurements of the strength and mass of the BBM also demonstrated that muscular activity returned to a level similar to that in the right limb in most of the treated cats. It is clear that motor function was restored by reinnervation by axons originating from motor neurons located in the right C-8 and T-1 spinal cord segments. Results from the retrograde staining study showed that axons arising from the right C-8 and T-1 segments could grow into the right LTN and TDN and link up with the left MCN.

We can, therefore, conclude from this work that using the LTN and TDN to cross-neurotize an avulsed MCN in cats leads to the restoration of function through the provision of

**Fig. 3.** Recordings of muscle evoked potentials obtained in a normal cat left BBM after left C-8 nerve stimulation (upper left). Six months postoperatively in a cat treated with cross-neurotization, the muscle evoked potential is normal (upper right). Six months postoperatively in a control cat, there is no muscle evoked potential (lower left). A1 = monofilament electrodes; A2 = concentric bifilament electrodes.
axons arising from cell bodies in the contralateral side of the spinal cord.

Experimental Design

The experimental model chosen here is a preclinical model. The avulsion of the cranial portion of the brachial plexus (C6–7) was mimicked by sectioning the MCN. Many nerves originate from the cranial part of the brachial plexus: axillary, pectoral, subscapular, suprascapular, and musculocutaneous among others. It is therefore possible that the observed improvement in neurological signs may be less important in the case of a complete cranial BPA. Nevertheless, clinical experience has shown that the MCN is functionally the most important nerve of the cranial portion of the brachial plexus. Recovery of elbow flexion cannot originate from another nerve.

In our study, the nerves were sutured immediately after transection. This situation differs from that sometimes encountered in the clinical situation. On the one hand, the advantages of an immediate (or primary) repair of a sharply transected plexus injury are numerous. In a clinical study better results were achieved in patients in whom a sharp injury was immediately sutured end to end compared with patients in whom surgical treatment was delayed. The latter treatment resulted in the need for a nerve graft, a factor that worsened the prognosis.

On the other hand, an immediate suture tends to remove major stimuli for nerve regrowth. Moreover, neurotmesis causes a release of inflammatory mediators and debris from sites of Wallerian degeneration, two factors that probably negatively influenced the results of reinnervation in the present experiment. We therefore cannot form an opinion about the real impact of immediate suture on the results of our study, but we believe that it is of little influence compared with the fact that brachial plexus lesions are not caused by sectioning, but rather by traction injuries, which cause substantially worse nerve lesions than a sharp transection.

Nevertheless, the present model offers a description of a
It does not necessitate an approach. In that study, none of the patients contralaterally to the lesion, and the ventral roots, caudal to the lesion—both also, in some cases, sensory function—contra-lateral C-7,8 in humans or C-8 in cats—nerve transfer is currently the technique of choice in the surgical treatment of a BPA; however, C-7 nerve cross-transfer is a two-staged surgery that always necessitates a secondary nerve graft to bridge the gap separating the ventral root from the neurotized nerve. In comparison, TDN and LTN cross-neurotization provides selective neurotization of the MCN by pure motor nerves (LTN and TDN). The axons provide a significant gain in reinnervation time and also in the selectivity of reconnection, so that the recovery of muscle after denervation should be improved. On the other hand, like a C-7 nerve cross-transfer, these axons arise from neurons on the opposite side of the patient. This necessitates a period of adaptation to allow the patient to compensate and reorganize the supraspinal nervous system. This is probably possible in the cat.

It is difficult to compare the various experimental or clinical techniques used to repair a BPA. Cross-neurotization, however, offers a number of advantages. From a technical standpoint, LTN and TDN cross-transfer appears simpler to perform than lateral intramedullary root reimplantation. It does not necessitate an approach to the vertebral canal, thus eliminating the risks of a spinal cord lesion, unlike that which can occur with reimplantation techniques. The LTN and TDN are sufficiently long to allow a distal connection, and therefore, an early reconnection for regrowing axons to muscle. Thus, denervated muscles can rapidly recover their function before they undergo severe atrophy. In our study, reinnervation of the left BBM in animals in the treatment group started within 1 month postoperatively. This delay does not appear excessive when considering the risks of irreversible fiber atrophy and the inability to recover initial muscle mass despite reinnervation. For this reason, LTN and TDN cross-neurotization offers major advantages when compared with other techniques. After root reimplantation, the number of neurons sending axons into the reimplanted nerve root is lower and the regrowth time is longer because the axons have to follow the ventral root and branch to the brachial plexus before reaching the peripheral nerves. In contrast, when the LTN and TDN are used for cross-neurotization the procedure is performed very distally; it reduces the distance between donor axons and the effector muscle so that regrowth is achieved more rapidly, increasing the chances of success.

Using reimplantation technique, regrowing axons may follow the wrong path and enter the dorsal branch or the communicating branch (ramus communicans). Nevertheless, the reimplantation techniques have been used in humans suffering from traumatic plexus injuries. Some of these patients recovered not only motor function—via a peripheral nerve autograft implanted between the spinal ventral horn, rostral to the lesion, and the ventral roots, caudal to the lesion—but also, in some cases, sensory function. Contra-lateral C-7,8 (in humans) or C-8 (in cats) nerve transfer is currently the technique of choice in the surgical treatment of a BPA; however, C-7 nerve cross-transfer is a two-staged surgery that always necessitates a secondary nerve graft to bridge the gap separating the ventral root from the neurotized nerve. In comparison, TDN and LTN cross-neurotization provides selective neurotization of the MCN by pure motor nerves (LTN and TDN). The axons provide a significant gain in reinnervation time and also in the selectivity of reconnection, so that the recovery of muscle after denervation should be improved. On the other hand, like a C-7 nerve cross-transfer, these axons arise from neurons on the opposite side of the patient. This necessitates a period of adaptation to allow the patient to compensate and reorganize the supraspinal nervous system. This is probably possible in the cat.

It is important to know if our procedure can be used in human patients. Anatomically there are differences between humans and cats. The lateral thoracic nerve innervates the cutaneous trunci muscle. This muscle is relatively undifferentiated in humans. For this reason, the LTN can probably not be used in humans. The TDN innervates the latissimus dorsi muscle and its use in the procedure leads to thoracodorsal muscle palsy. In our study, we did not observe a functional deficit on the side on which the TDN was transected. The same observation was made in human patients in whom an MCN section was treated by an end-to-end suture to the ipsilateral TDN. In that study, none of the patients complained of functional weakness with shoulder adduction and/or internal rotation.

We can assume that it would be the same in human patients treated by TDN and LTN cross-neurotization; however, it must be shown to be acceptable for the human patient.

The only contraindication for TDN cross-neurotization would be if the latissimus dorsi muscle was needed for another secondary procedure such as a shoulder external rotation transfer.

The major benefit of performing this technique is the fact that a nerve graft does not appear to be required. A nearby viable nerve source provides faster nerve regeneration to the target muscle, thus ensuring more timely muscle reinnervation. The thoracic outlet differs anatomically between the cat and human. Additional anatomical studies in humans are needed to assess the feasibility of direct nerve anastomosis or whether a nerve graft should be used. In the case
of the latter, a more realistic model should include a graft and the results would be less encouraging.

Currently, we consider that the result of TDN and LTN neurotization would probably be similar to that observed in ipsilateral TDN transfer, which was first described by Lurje\textsuperscript{31} for the treatment of traumatic brachial plexus injuries. Using this procedure, Novak, et al.,\textsuperscript{37} showed that biceps reinnervation was successful in all six patients studied. In one case the Medical Research Council muscle grade was 5, in four cases it was Grade 4, and in one case it was Grade 2. The Medical Research Council muscle grade is difficult to assess in animals, but our results demonstrate that muscle contractile force was restored after the TDN and LTN cross-neurotization. A comparison with other techniques used to repair the MCN in humans was made.\textsuperscript{39} Transfers to the MCN and axillary nerve have been attempted using the collateral branches of the brachial plexus, the upper intercostal nerve, or the accessory nerve. The rate of recovery for the MCN was 50\% when the intercostal nerve was used, 65\% when the accessory nerve was used, and 90.4\% when collateral branches of the brachial plexus were used. A significant difference was only found in comparison with other techniques used to repair the MCN in humans. Based on our findings we suggest that nerve transfer of collateral branches, when possible, may be the method of choice, yielding better results in cases of an MCN lesion. The goal of our study was to assess the technical difficulties and therapeutic possibilities associated with the cross-transfer of the LTN and the TDN to MCN of the contralateral limb. Our results show that the procedure is technically feasible in cats. In all cats that underwent the technique, satisfactory functional recovery was obtained. It will be useful to conduct further work on clinical cases.

Conclusions

The goal of our study was to assess the technical difficulties and therapeutic possibilities associated with the cross-transfer of the LTN and the TDN to MCN of the contralateral limb. Our results show that the procedure is technically feasible in cats. In all cats that underwent the technique, satisfactory functional recovery was obtained. It will be useful to conduct further work on clinical cases.

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