SCIENTIFIC ARTICLE

Transhemispheric Cortical Plasticity Following Contralateral C7 Nerve Transfer: A Rat Functional Magnetic Resonance Imaging Survival Study

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Purpose To perform contralateral C7 nerve transfer in a controlled, survival rat functional magnetic resonance imaging model, so as to understand the extent of cortical plasticity after brachial plexus injury and surgical manipulation with this procedure.

Methods A total of 24 rats divided into 3 groups underwent surgery followed by functional magnetic resonance imaging in this study. Group I rats served as sham controls. Group II injury rats underwent complete right brachial plexus root avulsion. Group III repair rats underwent complete right brachial plexus root avulsion and then contralateral C7 nerve transfer to the right median nerve. We assessed cortical response to median nerve stimulation at 0, 3, and 5 months after injury using functional magnetic resonance imaging at 9.4 T. We concurrently performed sensory and motor functional testing.

Results We noted a progression in cortical activation in the repair rats over 0, 3, and 5 months. Initially, right median nerve stimulation in the repair group showed complete loss of activation in the contralateral somatosensory cortex. Nerve stimulation at 3 months produced primarily ipsilateral cortical activation; at 5 months, 3 patterns of cortical activation emerged: ipsilateral, bilateral, and contralateral activation. After right median nerve stimulation, injury rats maintained a lack of cortical activation and control rats maintained exclusive contralateral activation throughout all time points. Functional testing revealed a degree of return of sensory and motor function over time in the repair group compared with the injured group.

Conclusions A high degree of transhemispheric cortical plasticity occurred after contralateral C7 nerve transfer. There appears to be a predilection for the rat brain to restore the preinjury somatotopic representation of the brain.

Clinical relevance Understanding the cortical changes after nerve injury and repair may lead to specific pharmacologic or behavioral interventions that can improve functional outcomes.

Key words Brachial plexus, cortical plasticity, C7 nerve transfer, functional magnetic resonance imaging.

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Received for publication May 20, 2012; accepted in revised form December 11, 2012.

Supported by grant EB000125 from the National Institutes of Health.

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

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0363-5023/13/38A03-0007$36.00/0
http://dx.doi.org/10.1016/j.jhsa.2012.12.018

Brachial plexus root avulsion injuries present a complex problem for the upper extremity surgeon. Over 25 years ago, contralateral C7 root transfer was developed as a treatment option in these difficult cases.[1] Since that time, multiple authors have confirmed the use of the C7 transfer procedure.[2–5] However, there remains considerable variability in results, depending on factors such as age, time to reconstruction, length of grafts, and the specific target muscle group.[5–7] In addition to these factors, it is unclear what role the central nervous system has in the variability of outcomes after peripheral nerve reconstruction, specifically with respect to cortical plasticity.

Previous studies have shown that changes occur in the cerebral cortex after peripheral nerve injury and repair.[8,9] Moreover, these changes can be noninvasively observed using blood oxygen level–dependent functional magnetic resonance imaging (fMRI).[9,10] Whereas some authors have investigated cortical changes that take place in response to the contralateral C7 nerve transfer procedure, these studies have relied on invasive testing, few time points, or no controls.[11–14]

Our aim in this study was to perform the C7 transfer procedure in a controlled, survival rat fMRI model to elucidate how both brachial plexus injury and this specific nerve transfer procedure affect the brain. We hypothesized that a survival rat model can be successfully employed and that a high degree of transhemispheric cortical plasticity occurs and continues to adapt over time after contralateral C7 nerve transfer. Moreover, these cortical changes parallel functional recovery.

MATERIALS AND METHODS

All experiments were approved by the institution's Animal Care and Use Committee and performed in compliance with federal regulations.

Animal preparation

Anesthesia: We performed all surgeries under 2% isoflurane general anesthesia on 200-250-g Sprague-Dawley rats. On completion of the surgery, we transferred each rat to the MRI suite for scanning, during which the isoflurane was discontinued and anesthesia was maintained using subcutaneously administered dexmedetomidine at 100 to 200 μg/kg/h after a 20- to 40-μg bolus.[15] Once scanning was complete, we reversed dexmedetomidine with atipamezole. We achieved pain control with 1 injection of 0.05 mg/kg buprenorphine subcutaneously before reversal and dissolved 25 mg tramadol in gelatin, administered daily for 7 days. During all procedures, we continuously monitored pulse oximetry and maintained heart rate and temperature using a thermostatic heating pad. During MRI scanning sessions, additional pulmonary monitoring included respiratory rate and end tidal gases.

Operation: We chose a complete avulsion model because this mirrors clinical indications for C7 nerve transfer (Fig. 1). In addition, this provides certainty that any cortical activation during stimulation is the result of the nerve repair and not intraplexus regeneration or interference from other healthy nerve roots.

All animals received 1 dose of 50 mg/kg cefazolin subcutaneously for perioperative antimicrobial prophylaxis. We then clipped the surgical site with an electric razor and prepared it with povidone-iodine. We made a longitudinal incision over the right chest and axilla. Within the axilla, we carried the incision down to the lateral border of the pectoralis major, where we identified the terminal branches of the brachial plexus. Using the operating microscope, we isolated the median nerve branch and atraumatically dissected it free of the surrounding tissue.

At this point, control rats underwent placement of implantable electrodes (MS303-8-A-SPC; Plastics One, Inc, Roanoke, VA) on bilateral median nerves 1 cm proximal to the elbow. Injury rats also underwent placement of implantable electrodes on bilateral median nerves. In addition, in injury rats, we split the right pectoralis major parallel to the muscle fibers and retracted the pectoralis minor superiorly to expose the brachial plexus. We then avulsed nerve roots C5-T1 from the spinal column using forceps; we excised a 1-cm portion of the avulsed roots to prevent intraplexus nerve regeneration. Repair rats also underwent placement of implantable electrodes on bilateral median nerves and right brachial plexus avulsion. After this, we incised the left chest and axilla, split the left pectoralis major, and retracted the pectoralis minor superiorly to expose the left brachial plexus. Next, we harvested the right ulnar nerve and used it as a nonvascularized reversed interposition graft between a division of the left C7 nerve root and the right median nerve. We performed end-to-end repairs using 3 interrupted 11-0 nylon sutures. In all groups, we closed the skin with interrupted 5-0 nylon suture.

The pedestal of the implantable electrodes was left exposed through the skin to allow for connection to the electrical nerve stimulator during MRI scanning. On completion of the scanning period, we closed the skin over the electrode pedestals using 5-0 nylon suture. For later time points, we made an incision over the electrode pedestal and achieved access for stimulation without violating tissues near the original sites of nerve surgery.