Published in final edited form as:

Muscle Nerve. 2014 January ; 49(1): 40–46. doi:10.1002/mus.23864.

C7 Nerve Root Sensory Distribution in Peripheral Nerves: A BOLD fMRI Investigation at 9.4T

Rupeng Li, MD, PhD¹, Jacques A Machol IV, MD², Xiping Liu, MD, PhD³, Patrick C Hettinger, MD², Nicholas A Flugstad, MD², Ji-Geng Yan, MD, PhD², Hani S Matloub, MD², and James S Hyde, PhD¹

¹Department of Biophysics, Medical College of Wisconsin 8700 Watertown Plank Road 53226 Milwaukee, WI, USA

²Department of Plastic Surgery, Medical College of Wisconsin 8700 Watertown Plank Road 53226 Milwaukee, WI, USA

³Department of Anesthesiology, Medical College of Wisconsin 8700 Watertown Plank Road 53226 Milwaukee, WI, USA

Abstract

Introduction—We aimed to elucidate the linear makeup of each major nerve of the upper limb by the C7 root through sensory stimulation and functional MRI in a rat model.

Methods—The C7 nerve root and major nerves of the right forelimb were stimulated electrically. Blood oxygen level dependent functional magnetic resonance imaging (BOLD fMRI) was performed concurrently. Voxel overlap within the primary sensory cortex was calculated.

Results—C7 comprises sensation in less than 1% in the musculocutaneous nerve, 6% in the ulnar nerve, 16% in the radial nerve, and 19% in the median nerve ($P < 0.005$ for each).

Conclusions—The overlap is always under 25% for each major nerve.

Clinical relevance—This study helps explain why C7 is a suitable donor for brachial plexus injury treatment and why there is only a transient sensory deficit after transfer.

Keywords

fMRI; C7 nerve root; peripheral nervous system; central nervous system; sensory

Introduction

The brachial plexus is an essential, complex group of nerves originating from the spinal roots of C5-T1 that provides the upper extremity with motor and sensory function. Auto or motorcycle accidents are the most common cause of traumatic injury, but brachial plexus damage may also occur after falls or in contact sports. Obstetric brachial plexus injuries also occur in about 1 in 1000 births.^{1–4} Total brachial plexus nerve root damage has the most devastating consequences, as it cannot be repaired primarily.

In the case of severe root avulsion injuries, the contralateral C7 (cC7) nerve root is identified as a possible donor for nerve transfer. It has been observed that isolated C7 nerve root injury is associated with transient weakness and sensory deficit, and the notion of invading a healthy nerve to use as a donor is controversial.^{5–9} It is of interest to peripheral nerve surgeons as to how the cC7 root can serve as a “spare nerve” in a highly structured and efficient nerve complex. It has been found that donor nerve fibers can gradually compensate

for the functional deficit when 30–50% of the nerve fiber is transected and used as a donor to repair other nerves.^{10–11}

Others have investigated the cortical changes that occur in response to the cC7 nerve root transfer procedure using invasive techniques.^{12–15} Due to the constraints of these approaches, it is difficult to obtain quality data that elucidates sensory and motor cortical plasticity with great precision. Blood oxygen level dependent functional magnetic resonance imaging (BOLD fMRI) has provided a reliable method for indirectly studying task-induced cerebral neuronal activity.^{16–17} This imaging exploits changes in deoxygenated hemoglobin (dHb) concentrations, which, in turn, act as an endogenous paramagnetic contrast agent. The local dHb to hemoglobin (Hb) concentration ratio measured by fMRI can be interpreted as an indirect measurement of neuronal activity. This imaging method has been utilized in a rat model to identify cortical topographical maps during peripheral stimulation.^{18–19} Importantly, this imaging has also been used to reveal cortical plasticity following nerve injury and repair.^{20–23}

It is well understood that the body surface is portrayed in cortical and subcortical fields in highly organized topographical maps.^{24–26} Given that the rat and the human share a homologous brachial plexus, the rat has provided an excellent model for study of human upper extremity nerves.^{27–28} Our institution used fMRI to identify specific cortical activities associated with direct stimulation of median, ulnar, radial, and musculocutaneous terminal nerve branches of the brachial plexus in a rat model.^{23, 29, 30} As each terminal branch receives contributions from multiple nerve roots, theoretically, a smaller, more specific area of cortical activation should be seen with more proximal brachial plexus stimulation.

Based on these antecedent studies, we aimed to elucidate the linear relationship in the makeup of each major upper limb nerve (ulnar, median, radial, and musculocutaneous) by the C7 nerve root cortical map by means of sensory stimulation. We hypothesize that if the linear C7 contribution is less than the 25% to each nerve (well below the acceptable deficit of 30–50% per nerve^{10, 11}), then this will help to explain why cC7 is a suitable donor for brachial plexus injury treatment.

Methods

Animal and Preparation

Institutional Review Board approval was obtained, and all studies were performed in compliance with the guidelines of our institution's animal care and use committee. 28 male Sprague-Dawley rats (150–200 g) were studied. Five groups were created: median, radial, musculocutaneous, n=5 each; ulnar, n=6; C7, n=7.

Anesthesia protocol—Isoflurane general anesthesia was administered through a vaporizer in an animal chamber (Halocarbon Laboratories, River Edge, NJ). The animal was then transferred supine to a heated operating table where 1% isoflurane vaporized into 30–70% O₂/N₂ was provided continuously through a nose cone during surgery. During the scan session, isoflurane was tapered off; each animal was then placed on a mechanical ventilator (MRI-1 Ventilator, CWE, Ardmore, PA). A continuous intravenous infusion of DEXDOMITOR® (Pfizer, USA) at 0.1 mg/kg/hr and pancuronium bromide (Hospira, Lake Forest, IL) at 2 mg/kg/hr was used for maintenance of anesthesia. The purpose for using muscle relaxant was to eliminate possible interference of the MRI signal caused by muscle movement and maximize the fMRI signal-to-noise ratio.

Surgical procedure

After anesthesia was administered, the right neck and axilla were clipped, prepped, and draped in a typical sterile fashion. A 2.0 cm incision was placed longitudinally in the right neck, extending obliquely into the right axilla. The subcutaneous tissues were divided to the level of the pectoralis major. The brachial plexus was identified at the level of the terminal branches, immediately lateral to the border of the pectoralis major muscle. The pectoralis major muscle was divided sharply parallel to its fibers, and the nerve roots were identified deep to this muscle. An operating microscope was utilized to isolate the brachial plexus and the C7 nerve root (Figure 1. A). A 125 μ m diameter stainless steel bipolar electrode (Plastics 1, Roanoke, VA) was placed circumferentially around the C7 nerve root (Figure 1. B). Following electrode placement, the overlying skin was closed using interrupted 3–0 nylon sutures. The pedestal of the implantable electrode was left exposed through the skin. A cable was attached to the pedestal to allow for direct C7 nerve stimulation. Of note, this same technique was used in our previous study to place the same electrodes on the ulnar, median, radial, and musculocutaneous nerves 1cm proximal to the elbow.³⁰ The distance between the major nerve stimulation site and the C7 nerve root stimulation site was 15–20 mm. This junction was also the most distal location for access to the C7 nerve root.

Prior to fMRI acquisition, the right femoral artery and vein of each rat were cannulated for blood pressure monitoring and continuous intravenous drug administration. Tracheostomy was performed to allow for mechanical ventilation during scanning. Immediately following the operation, the animal was transferred to a Bruker 9.4 Tesla small-animal MRI scanner (Biospec Avance 94/31; Bruker, Karlsruhe, Germany). fMRI was then performed during direct sensory nerve stimulation.

MRI Image Acquisition

A custom-designed cradle fabricated with G-10 fiberglass, a material that has a magnetic susceptibility similar to air, was used. The cradle was equipped with a warming pad controlled by a water-pump-driven temperature regulator (Medi-Therm III, Gaymar Industries, Orchard Park, NY).

Mild electrical stimulation at 10 Hz frequency, 0.5 mA current, and 1 ms duration was applied to each peripheral nerve in all groups using a square-pulse electrical stimulator (S88 Square Pulse Stimulator, Grass Telefactor, West Warwick, RI).^{21,23,30,31} This stimulation intensity is proven to be non-noxious by our previous fMRI studies and can generate distinct cortical responses under 9.4T high field strength fMRI scan. This task does not require the participation of sensory bodies in the skin and cutaneous tissue, which generate most of the painful sensation. Furthermore, we confirmed the maintenance of a non-noxious stimulation state via physiological monitoring. Throughout the stimulation session, there were no significant changes in arterial blood pressure, core temperature, or heart rate. Each nerve stimulation sequence began with an OFF period of 40 seconds followed by 3 repetitions of ON for 20 seconds and OFF for 40 seconds (Figure 2). The total scan time protocols were 3 minutes 40 seconds for the ulnar, median, radial, and musculocutaneous nerve testing. This time sequence defines a reference waveform. These were computer-controlled with LabVIEW software (National Instruments, Austin, TX) and initiated by a trigger pulse delivered by the scanner.

The 9.4 Tesla MRI system with a 31 cm horizontal bore was employed for scanning as mentioned. A Bruker linear transmit-coil (T10325) was positioned on top of the skull with the iso-center located 3mm anterior to the external ear canal. After a quick localization scan with flash sequence, a high-resolution scan with spin-echo rapid acquisitions with relaxation enhancement (RARE) pulse sequence was employed to acquire images in the sagittal plane.

This localized accurately the anterior commissure (AC) to ensure repeatability in slice positioning among different rat brains.

Next, the same RARE sequence and scanning parameters were employed to acquire 10 slices with the following acquisition parameters: Repetition time (TR) 2500 ms, echo time (TE) 50.8 ms, number of average 2, field of view (FOV) 38.4 × 38.4 mm², matrix size 256×256, slice thickness 1 mm in the coronal plane with the AC directly on the 7th slice. After the anatomical scan, EPI (echo-planar) scans were taken with the same setup and scanning parameters except TR 2000 ms, TE 18.76 ms, single average and matrix size 96 × 96 (it is zero filled into 128×128 to compare with previously published data) were employed. The number of repetitions = 110, and 10 contiguous 1 mm scans were acquired. Two sets of gradient echo (GE) data were collected for each stimulation scan in order to ensure the reproducibility of our results. Each set of GE data consists of a time course of images.

In fMRI, a pixel time course waveform can be formed from the intensity of a given pixel in each image of an image time course. Cross-correlation of the reference waveform with every pixel time course was performed on each individual animal before group analysis was done. Colorized correlation coefficients were overlaid on an anatomical image to produce an fMRI image.

Data Analysis

EPI scans were registered to an ideal anatomy using the Oxford Center for Functional Magnetic Resonance Imaging of the Brain (FMRIB) Linear Image Registration Tool (FLIRT) software.³² Data from individual animals were averaged and masked using Analysis of Functional NeuroImages (AFNI) software.³³ Activation was determined a *P*-value threshold of 0.005 after multiple comparison correction for the group study. Voxels were classified as active if the statistic was above threshold and counted as activated voxels (3dmaskave) through all slices. Voxel color-coding was determined by the amplitude of the fit coefficient. Regions of interest (ROIs) were drawn by consulting the activation map and cross-referencing it with the Paxinos and Watson Rat Atlas.³⁴ In this study, bilateral somatosensory areas of the forelimb (S1FL) were selected as primary ROIs. With this method, the degree of brain activation in different functional areas can be quantified by the area (or number) of activated voxels. Reprocessed fMRI data from prior ulnar, median, radial, and musculocutaneous nerve sensory groups served as the comparison for prospectively obtained cortical C7 sensory overlap data. Overlap is defined as the voxels within S1FL that activate in both C7 nerve root stimulation and corresponding prior peripheral nerve stimulation, as shown by following equation:

$$\text{Cortical fMRI Overlap} = \frac{\text{C7 Cortical BOLD fMRI} \cap \text{Nerve trunk BOLD fMRI} \left(\frac{\frac{M}{B}}{\frac{U}{MC}} \right)}{\text{Nerve trunk BOLD fMRI} \left(\frac{\frac{M}{B}}{\frac{U}{MC}} \right)} * 100\%$$

Results

BOLD fMRI activation results through 10 consecutive slices were averaged across all animals (Figure 3A–E). A focal area of activation in S1FL is identified in two slices (0.24m–0.76mm rostral of bregma, circled red). Voxel counts yielded a result of 52±9 voxels (*p*<0.005). Figures 3B, 3C, 3D and 3E are cortical BOLD fMRI results from stimulating each individual terminal nerve branch of forelimb. The stimulating protocol and scan parameters of these two studies were kept the same to guarantee the consistency of the

experiments.³⁰ It is clear that each terminal branch shows BOLD activation in multiple slices when being stimulated. Figure 3F is the atlas corresponding to each slice showing the anatomical structure of rat brain with the S1FL area being highlighted.³⁴

Table 1 shows the voxel number that reacted to the nerve stimulation when each of the 4 major nerves of the forelimb was stimulated. The fMRI overlap in the cortex was calculated with the equation provided in Methods. The final column in table 1 is the percentage of active voxels in each of the 4 separate nerve stimulations that were also significantly active during the C7 stimulation. All voxel analyses were completed with a $P < 0.005$.

The radial, ulnar, median, and musculocutaneous nerves receive contributions from multiple nerve roots. When they were stimulated peripherally, we found a large area of activation, extending from slice 2 to slice 8 in response to radial nerve stimulation (Figure 3B), from slice 1 to slice 3 from median nerve stimulation (Figure 3C) and from slice 1 to slice 4 from ulnar nerve stimulation (Figure 3D). At the same stimulation intensity, previous results of musculocutaneous nerve stimulation do not demonstrate obvious sensory activation in S1FL (Figure 3E).

Interestingly, we found overlap in slice 2 in median, ulnar, and radial nerve trunk stimulation results when comparing the territory of each terminal nerve trunk to the cortical territory of the C7 nerve root (Figure 3A). However, the C7 nerve root cortical representation area only occupies a very small amount of total activated area in all nerve maps. As hypothesized, the overlap is always under 25% for each major nerve (Table 1).

The C7 contribution to each of the 4 major nerves in the forelimb is demonstrated in Figure 4. Possible distribution pathways of the C7 nerve root to the 4 major nerves that subserve forelimb sensory functions were marked in yellow. Importantly, of four major nerves of the forelimb, the median and radial nerve have the most C7 cortical representation within S1FL of 19% and 16%, respectively. The ulnar nerve is 6%, and the musculocutaneous nerve is less than 1%.

Discussion

In histological studies, the posterior division of the C7 nerve root has been shown to supply approximately 50% of its axons to the radial nerve, thus making it the single greatest contributor to that nerve.⁹ A comparable innervation pattern is also found in median, ulnar, and musculocutaneous nerves, and each terminal nerve branch always receives contributions from multiple nerve roots. However, the cortical representation area of the C7 nerve root has not been studied in depth previously. It is known that a well-functioning extremity requires not only a healthy peripheral nervous system (PNS) with muscular and sensory end-organs, but also a healthy central nervous system (CNS). It has been accepted that as long as a peripheral nerve repair procedure is carried out with care and technical skill, CNS factors such as cortical plasticity and functional re-education contribute considerably to the overall clinical outcome.^{35–38}

This investigation used BOLD fMRI to demonstrate the linear quantitative contribution of the C7 nerve root in cortical sensory representations of all major peripheral nerves of the brachial plexus (Figure 3A–E). It is clear that for the sensory component of the C7 nerve root is made up of less than 25% of any given individual nerve: less than 1% from the musculocutaneous, 6% from the ulnar, 16% from the radial, and 19% from the median nerve. For every major forearm nerve, over 80% of its sensory function is conducted through other nerve roots, hence, the percentages are not 100% of C7. Preceding studies have demonstrated that donor nerve fibers can compensate for the functional deficit when

30–50% of a major nerve fiber is transected and used as donor to repair other nerves.^{10–11} When using the C7 nerve root as a donor, the central sensory deficit will be less than 25%. This is entirely within the ability of each major nerve to compensate, as we have hypothesized, and it is likely a reason why C7 is a suitable donor for repair of brachial plexus injury.

As expected, the radial and median nerves are most affected by the cC7 nerve transection procedure. Clinically, patients with isolated C7 injuries often complain of transient paresthesias in median and radial nerve distributions.³⁹ The overlap of cortical activation between C7 and other nerves provides an alternative, potentially improved, means to demonstrate objectively and study further this phenomenon. Anatomic variability in the brachial plexus may be found in pre-(C4–C8) and post-fixed (C6–T2) elements. These variations will likely change the C7 makeup of each nerve. For example, a pre-fixed plexus could have increased C7 contribution to intrinsic hand function, and a post-fixed plexus may have increased musculocutaneous influence.

A limitation of this study is that only sensory mapping was performed. Peripheral nerve stimulation, as completed in this study, will trigger motor function. However, it is rather difficult to conduct nerve stimulation of motor fibers antidromically into the motor cortex and cause neuronal activity. For this reason, fMRI studies of the motor cortex in animals are markedly difficult; they are much easier in human studies, as humans can follow commands. In order to obtain optimal fMRI sensory results, muscle relaxants were administered to block the neuromuscular junction and eliminate any confounding motor signals. Unlike previous histological studies, the fMRI data are based on the actual nerve function with both PNS and CNS distribution considered. Thus, there could be variations in the central C7 nerve distribution pattern acquired by fMRI when compared with peripheral histological studies.

Functional imaging methodology could also be applied to any nerve or nerve root to obtain specific cortical distribution information. Using this technique, it is possible to not only discover the underlying physiologic foundation of the C7 nerve transfer procedure, but also to evaluate the donor potential of other nerves. Future application of this modality in human studies would be especially beneficial for evaluation of pre-and post-operative patients with brachial plexus birth palsy and in demonstrating overall cortical plasticity.

Conclusion

This study demonstrated that the sensory component of the C7 nerve root contributes less than 25% of any given major upper extremity nerve: less than 1% in musculocutaneous, 6% in ulnar, 16% in radial, and 19% in median nerves. When using the C7 nerve root as a donor, the central sensory deficit will be less than 25%. This is entirely within the ability of each major nerve to compensate and is likely a reason why cC7 is a suitable donor for brachial plexus injury repair.

Acknowledgments

This work was supported by grant R01 EB000215 of National Institute of Health to James S. Hyde.

Abbreviations

AC	anterior commissure
AFNI	analysis of functional neuroImages

BOLD	Blood oxygen level dependent
C4-C8	No.4 th -No. 8 th cervical nerve
CNS	central nervous system
dHb	deoxygenated hemoglobin
EPI	echo planar imaging
FLIRT	linear image registration tool
fMRI	functional magnetic resonance imaging
FMRIB	functional Magnetic Resonance Imaging of the Brain
FOV	field of view
GE	gradient echo
Hb	hemoglobin
MC	musculocutaneous nerve
PNS	peripheral nervous system
RARE	rapid acquisitions with relaxation enhancement
ROIs	regions of interest
S1FL	primary sensory area of forelimb
T2	2 nd thoracic nerve
TE	echo time
TR	repetition time

References

1. Foad SL, Mehlman CT, Ying J. The epidemiology of neonatal brachial plexus palsy in the United States. *J Bone Joint Surg Am.* 2008 Jun; 90(6):1258–64. [PubMed: 18519319]
2. Hoeksma AF, ter Steeg AM, Nelissen RG, van Ouwerkerk WJ, Lankhorst GJ, de Jong BA. Neurological recovery in obstetric brachial plexus injuries: An historical cohort study. *Dev Med Child Neurol.* 2004 Feb; 46(2):76–83. [PubMed: 14974631]
3. Gilbert WM, Nesbitt TS, Danielsen B. Associated factors in 1611 cases of brachial plexus injury. *Obstet Gynecol.* 1999 Apr; 93(4):536–40. [PubMed: 10214829]
4. Wolf H, Hoeksma AF, Oei SL, Bleker OP. Obstetric brachial plexus injury: Risk factors related to recovery. *Eur J Obstet Gynecol Reprod Biol.* 2000 Feb; 88(2):133–8. [PubMed: 10690670]
5. Narakas AO, Hentz VR. Neurotization in brachial plexus injuries. indication and results. *Clin Orthop Relat Res.* 1988 Dec.(237):43–56. [PubMed: 3056647]
6. Gu YD, Zhang GM, Chen DS, Yan JG, Cheng XM, Chen L. Seventh cervical nerve root transfer from the contralateral healthy side for treatment of brachial plexus root avulsion. *J Hand Surg Br.* 1992 Oct; 17(5):518–21. [PubMed: 1479244]
7. Gu YD, Ma MK. Nerve transfer for treatment of root avulsion of the brachial plexus: Experimental studies in a rat model. *J Reconstr Microsurg.* 1991 Jan; 7(1):15–22. [PubMed: 2013862]
8. Bertelli JA, Ghizoni MF. Concepts of nerve regeneration and repair applied to brachial plexus reconstruction. *Microsurgery.* 2006; 26(4):230–44. [PubMed: 16586502]
9. Gu YD. Contralateral C7 root transfer over the last 20 years in china. *Chin Med J (Engl).* 2007 Jul 5; 120(13):1123–6. [PubMed: 17637236]

10. Lutz BS, Chuang DC, Chuang SS, Hsu JC, Ma SF, Wei FC. Nerve transfer to the median nerve using parts of the ulnar and radial nerves in the rabbit--effects on motor recovery of the median nerve and donor nerve morbidity. *J Hand Surg Br.* 2000 Aug; 25(4):329–35. [PubMed: 11057998]
11. Mackinnon SE, Novak CB, Myckatyn TM, Tung TH. Results of reinnervation of the biceps and brachialis muscles with a double fascicular transfer for elbow flexion. *J Hand Surg Am.* 2005 Sep; 30(5):978–85. [PubMed: 16182054]
12. Beaulieu JY, Blustajn J, Teboul F, Baud P, De Schonen S, Thiebaud JB, et al. Cerebral plasticity in crossed C7 grafts of the brachial plexus: An fMRI study. *Microsurgery.* 2006; 26(4):303–10. [PubMed: 16671052]
13. Jiang S, Li ZY, Hua XY, Xu WD, Xu JG, Gu YD. Reorganization in motor cortex after brachial plexus avulsion injury and repair with the contralateral C7 root transfer in rats. *Microsurgery.* 2010 May; 30(4):314–20. [PubMed: 20058301]
14. Zuo CT, Hua XY, Guan YH, Xu WD, Xu JG, Gu YD. Long-range plasticity between intact hemispheres after contralateral cervical nerve transfer in humans. *J Neurosurg.* 2010 Jul; 113(1): 133–40. [PubMed: 20136390]
15. Wang M, Li ZY, Xu WD, Hua XY, Xu JG, Gu YD. Sensory restoration in cortical level after a contralateral c7 nerve transfer to an injured arm in rats. *Neurosurgery.* 2010 Jul.67(1):136, 43. discussion 143. [PubMed: 20559101]
16. Ogawa S, Lee TM, Nayak AS, Glynn P. Oxygenation-sensitive contrast in magnetic resonance image of rodent brain at high magnetic fields. *Magn Reson Med.* 1990 Apr; 14(1):68–78. [PubMed: 2161986]
17. Ogawa S, Tank DW, Menon R, Ellermann JM, Kim SG, Merkle H, et al. Intrinsic signal changes accompanying sensory stimulation: Functional brain mapping with magnetic resonance imaging. *Proc Natl Acad Sci U S A.* 1992 Jul 1; 89(13):5951–5. [PubMed: 1631079]
18. Bandettini PA, Wong EC, Hinks RS, Tikofsky RS, Hyde JS. Time course EPI of human brain function during task activation. *Magn Reson Med.* 1992 Jun; 25(2):390–7. [PubMed: 1614324]
19. Kwong KK, Belliveau JW, Chesler DA, Goldberg IE, Weisskoff RM, Poncelet BP, et al. Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proc Natl Acad Sci U S A.* 1992 Jun 15; 89(12):5675–9. [PubMed: 1608978]
20. Jones SR, Li R, Pawela CP, Shefchik DL, Matloub HS, Yan J-G, Jaradeh SS, Hyde JS. Cortical plasticity of the brain after median nerve transection using fMRI at 9.4T by direct nerve stimulation. *Proc Intl Soc Mag Reson Med.* 2008; 16:2441.
21. Li R, Jones SR, Pawela CP, Shefchik DL, Yan J-G, Jaradeh SS, Matloub HS, Hyde JS. Functional MRI detection of acute and chronic brain plasticity following median and ulnar nerve transection using direct nerve stimulation at 9.4T. *Proc Intl Soc Mag Reson Med.* 2008
22. Parkins, MA.; Li, R.; Pawela, CP.; Matloub, HS.; Yan, JG.; Hyde, JS. A peripheral nerve repair model using fMRI in rats. 17th Annual International Society for Magnetic Resonance in Medicine Meeting; Honolulu, HI. USA. 2009.
23. Pawela CP, Biswal BB, Hudetz AG, Li R, Jones SR, Cho YR, et al. Interhemispheric neuroplasticity following limb deafferentation detected by resting-state functional connectivity magnetic resonance imaging (fcMRI) and functional magnetic resonance imaging (fMRI). *Neuroimage.* 2010 Feb 1; 49(3):2467–78. [PubMed: 19796693]
24. Kaas JH. Topographic maps are fundamental to sensory processing. *Brain Res Bull.* 1997; 44(2): 107–12. [PubMed: 9292198]
25. Kaas JH. Plasticity of sensory and motor maps in adult mammals. *Annu Rev Neurosci.* 1991; 14:137–67. [PubMed: 2031570]
26. Kaas JH. What, if anything, is SI? organization of first somatosensory area of cortex. *Physiol Rev.* 1983 Jan; 63(1):206–31. [PubMed: 6401864]
27. Bertelli JA, Mira JC, Gilbert A, Michot GA, Legagneux J. Anatomical basis of rat brachial plexus reconstruction. *Surg Radiol Anat.* 1992; 14(1):85–6. [PubMed: 1589853]
28. Bertelli JA, Taleb M, Saadi A, Mira JC, Pecot-Dechavassine M. The rat brachial plexus and its terminal branches: An experimental model for the study of peripheral nerve regeneration. *Microsurgery.* 1995; 16(2):77–85. [PubMed: 7783609]

29. Cho YR, Jones SR, Pawela CP, Li R, Kao DS, Schulte ML, et al. Cortical brain mapping of peripheral nerves using functional magnetic resonance imaging in a rodent model. *J Reconstr Microsurg*. 2008 Nov; 24(8):551–7. [PubMed: 18924070]
30. Cho YR, Pawela CP, Li R, Kao D, Schulte ML, Runquist ML, et al. Refining the sensory and motor ratunculus of the rat upper extremity using fMRI and direct nerve stimulation. *Magn Reson Med*. 2007 Nov; 58(5):901–9. [PubMed: 17969116]
31. Hettinger PC, Li R, Yan JG, Matloub HS, Cho YR, Pawela CP, Rowe DB, Hyde JS. Long-term vascular access ports as a means of sedative administration in a rodent fMRI survival model. *J Neurosci Methods*. 2011 Sep 15; 200(2):106–12. [PubMed: 21726581]
32. Jenkinson M, Bannister P, Brady M, Smith S. Improved optimization for the robust and accurate linear registration and motion correction of brain images. *Neuroimage*. 2002 Oct; 17(2):825–41. [PubMed: 12377157]
33. Cox RW, Hyde JS. Software tools for analysis and visualization of fMRI data. *NMR Biomed*. 1997 Jun-Aug;10(4–5):171–8. [PubMed: 9430344]
34. Paxinos, G.; Watson, C. The rat brain in stereotaxic coordinates. 5. Burlington, MA: Elsevier Academic Press; 2009.
35. Lundborg G, Richard P. Bunge memorial lecture. Nerve injury and repair--a challenge to the plastic brain. *J Peripher Nerv Syst*. 2003 Dec; 8(4):209–26. [PubMed: 14641646]
36. Rosen B, Lundborg G. Sensory re-education after nerve repair: aspects of timing. *Handchir Mikrochir Plast Chir*. 2004 Feb; 36(1):8–12. [PubMed: 15083384]
37. Rosen B, Lundborg G. Enhanced sensory recovery after median nerve repair using cortical audio-tactile interaction. A randomized multicenter study. *J Hand Surg Eur Vol*. 2007 Feb; 32(1):31–7. [PubMed: 17134797]
38. Alvarez FJ, Bullinger KL, Titus HE, Nardelli P, Cope TC. Permanent reorganization of Ia afferent synapses on motoneurons after peripheral nerve injuries. *Ann N Y Acad Sci*. 2010 Jun.1198:231–41. [PubMed: 20536938]
39. Gu YD. Distribution of the sensory endings of the C7 nerve root and its clinic significance. *J Hand Surg Br*. 1994 Feb; 19(1):67–8. [PubMed: 8169483]

Figure 1.

A. The healthy right rat brachial plexus, C5-T1. **B.** The C7 root and middle trunk are shown isolated in the plexus. An electrode is placed for sensory mapping.

Figure 2.

Electrical stimulation of 10Hz, 0.5mA, and 1ms was applied during a 20 second 'ON' period for 3 times. A 40 second 'OFF' time was applied between each 'ON' time and completed the block design. The duty cycle is kept at 27.3%, and each scan lasts for 220 seconds.

Figure 3.

fMRI detection of direct C7 nerve root and terminal nerve branch stimulation. Data were acquired through group averages for each nerve. Activation was found in only 2 slices (circled in red) within the S1FL area when C7 nerve root was stimulated (**A**). Compare this extremely localized C7 nerve root cortical representation with the BOLD fMRI results acquired when Radial (**B**), Median (**C**), Ulnar (**D**) and Musculocutaneous (**E**) nerves were stimulated individually under the same stimulation intensity. Overlapped cortical activation can be found between the C7 nerve root and radial/median/ulnar nerve cortical representations. Musculocutaneous nerve cortical representation was not obvious at this stimulation level. $P < 0.005$ for all group images. (**F**) Brain atlas corresponding to each slice showing cortical structures. ROI of this study (S1FL) was highlighted. Images used with publisher's permission.³⁵

Figure 4.

C7 sensory contribution to each of the 4 major nerves with pathways highlighted in yellow. The sensory contribution was calculated through voxel analysis of the C7 nerve root contribution in median, ulnar, radial and musculocutaneous nerve cortical representations in S1FL. There is no overlap between the musculocutaneous nerve and the C7 nerve root in the S1FL area. MC=musculocutaneous nerve.

Table 1

BOLD fMRI voxel analysis of each of the 4 major nerves of the forelimb and their overlap with C7 nerve root stimulation. The result shows the percentage of sensory fibers originating from the C7 nerve root in all sensory fibers of each nerve ($P<0.005$). Note that the result of each individual nerve cannot be directly summed to 100%.

Nerve from upper limb	Activated BOLD fMRI voxel number	Overlapped voxel number with C7	Cortical overlap [mean (range)]
Median	275±41	53±10	19% (18–20%)
Ulnar	275±52	45±13	16% (14–18%)
Radial	257±47	16±8	6% (4–8%)
MC	170±37	1±1	<1% (0–1%)