# Refining the Sensory and Motor Ratunculus of the Rodent Upper Extremity: Evaluation of the C7 Nerve Root using fMRI and Direct Nerve Stimulation

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**Introduction** The purpose of this study is to further define the ratunculus by observing cortical activity using BOLD fMRI during direct stimulation of the C7 nerve root. In 2007, Cho et al. showed large areas of motor and sensory activation when direct nerve stimulation was applied to the terminal branches of the brachial plexus, including the ulnar, radial, median, and musculocutaneous nerves (1). While each of these nerves exists as its own structure, anatomically each nerve receives contributions from multiple nerve roots, as shown in the following table (see also Fig. 1A).

| Branch | Nerve Root Contributions | |
|---|---|---|
| Musculocutaneous: | C5, C6, C7 | |
| Radial: | C5, C6, C7, C8, (T1) | Parentheses indicate inconsistent contribution. |
| Median: | (C5), C6, C7, C8, T1 | |
| Ulnar: | (C7), C8, T1 | |

Theoretically, when stimulating more proximally at the level of the nerve root, a more specific area of activation should be seen since each terminal branch receives contributing axons from multiple nerve roots. The redundancy of these nerve roots has led to the adoption of the C7 nerve root as a donor nerve in brachial plexus injuries (2).

**Methods** *Animal Preparation:* Following an acclimation period of 1 week, 7 male Sprague-Dawley rats weighing 200-250g underwent exposure and dissection of the brachial plexus at the level of the nerve roots. Following skin incision, the nerve root was exposed through blunt dissection through the pectoralis major muscle. After adequate dissection of the nerve root, each rat underwent placement of an implantable electrode (AISI 304, Plastics1, Roanoke, VA) on the C7 nerve root (see Fig. 1B). All animals then underwent fMRI with direct nerve stimulation protocol as described below.

*Anesthesia:* Isoflurane (1.4%) (Halocarbon Laboratories, River Edge, NJ) was administered during the surgical portion of the procedure. Following transfer of the rat to the MRI scanner, isoflurane was discontinued. At this point, a continuous IV infusion of dexmedetomidine (Orion Corp., Espoo, Finland) (100mcg/kg/hr) along with pancuronium bromide (Hospira, Inc., Lake Forest, IL) (2mg/kg/hr) was initiated to maintain anesthesia during image acquisition.

*MRI Parameters:* The BOLD response to electrical stimulation in the primary sensory and motor regions was studied. Each nerve stimulation sequence began with an OFF period of 40s followed by three repetitions of ON for 20s and OFF for 40s for a total of 3min40s for each sequence. During each ON period, two separate electrical stimulation protocols were used for each rat. The first protocol included a current of 1 mA, frequency of 5Hz, and duration of 1 ms, while the second protocol changed only frequency to 10Hz. A rapid acquisition with relaxation enhancement (RARE) anatomical image was acquired with a 256x256 matrix, TE=12.5ms, TR=2.5s, and the same slice geometry as the echo planar imaging (EPI) sequence. Gradient recalled EPI scans were acquired using a Bruker AVANCE 9.4TMRI scanner with a 30cm bore. Images were acquired using a Bruker receiving surface coil (T9208) and a linear transmit coil (T10325). The EPI scans were registered to an ideal anatomy. The images for each nerve stimulation protocol were averaged. A total of 10 images were obtained with 1mm thick slices. The averaged data for each nerve and stimulation level were then masked using AFNI. Activation was then determined by an F-test (3dDeconvolve) with a p-value threshold of 0.005 (using AFNI). Statistical significance for the number of activated voxels was determined using an unpaired t-test with a p-value of $<0.05$.

**Results** Figures 1C and 1D demonstrate BOLD response to nerve stimulation in coronal slices 2 (Bregma -0.36) and 3 (Bregma +0.64), respectively. In slice 2, a small area of activation is seen within the contralateral S2 region. Slice 3 shows an area of activation within the cortex located at the contralateral S1FL region. M1/M2 region activation is seen in multiple slices including 2 and 3.

**Discussion** The C7 nerve root contributes to the sensory and motor function of the upper extremity. The sensory representation of the C7 nerve root is seen in only a small area in the S1FL region compared to those of the terminal branches of the brachial plexus. The area of activation in the S1FL region is consistent with that seen during stimulation of the 2nd and 3rd digits, as shown by Li (3). Interestingly, humans who undergo division of the C7 nerve root complain of transient index and middle finger numbness, suggesting a similar sensory distribution of the human C7 nerve root (2). With regard to motor contribution, we see a large area of activation throughout the M1/M2 regions of the cortex. There is considerable overlap with the M1/M2 areas activated during stimulation of the musculocutaneous, median, radial, and ulnar nerves, showing contribution of C7 to each of these nerves (1). As seen in human studies, C7's motor contribution assists in multiple actions, including shoulder extension/abduction, elbow flexion/extension, wrist pronation/flexion, and intrinsic hand function. The complex branching pattern of the brachial plexus ensures sufficient redundancy in motor and sensory function such that utilization of the C7 nerve root as a donor nerve results in deficits that can be overcome by the remaining uninjured nerves. Despite its use as a donor nerve, however, clinical outcomes have been inconsistent in terms of restoring function to the injured extremity. One reason for inconsistent outcomes could be the significant cortical reorganization that would be necessary for a donor nerve to restore function to a contralateral injured upper extremity. For this reason, mapping of the C7 cortical representation in the rat brain not only adds to the on-going development of the motor and sensory ratunculus, it also provides an important foundation to study subsequent C7 donor nerve models.

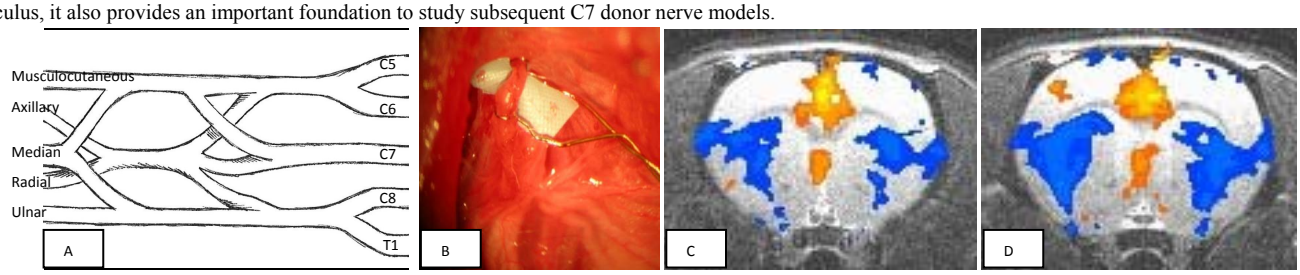


**Figure 1 A**. Brachial Plexus Schematic **B**. Closeup of implanted electrode on C7 nerve root. **C**. Slice 2 (Bregma -0.36mm) showing contralateral S2 activation. **D**. Slice 3 (Bregma +0.64mm) showing contralateral S1FL activation.

**References**

1) Cho, YR et al. Magnetic Resonance in Medicine. 2007. 58: 901-909.
2) Gu, YD et al. Journal of Hand Surgery – British Volume. 1992. 17(5): 518-21.
3) Li, R. Medical College of Wisconsin. Private Communication.