BOLD fMRI and fcMRI in the Pediatric Brachial Plexus Injury Population

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No Financial Disclosures

Introduction

- Brachial plexus birth palsy (BPBP) occurs in approximately 1/1000 live births[1,2]
- The most common of these palsies involve the C5-C6 roots of the brachial plexus[3]
- A number of surgical procedures for reconstruction have been introduced[4]
- Likewise, blood oxygen level dependent (BOLD) Functional MRI (fMRI) has provided a reliable method for indirectly studying task-induced cerebral neuronal activity[5-6]
- This imaging exploits changes in deoxygenated hemoglobin (dHb) concentrations, which, in turn, act as an endogenous paramagnetic contrast agent

Introduction

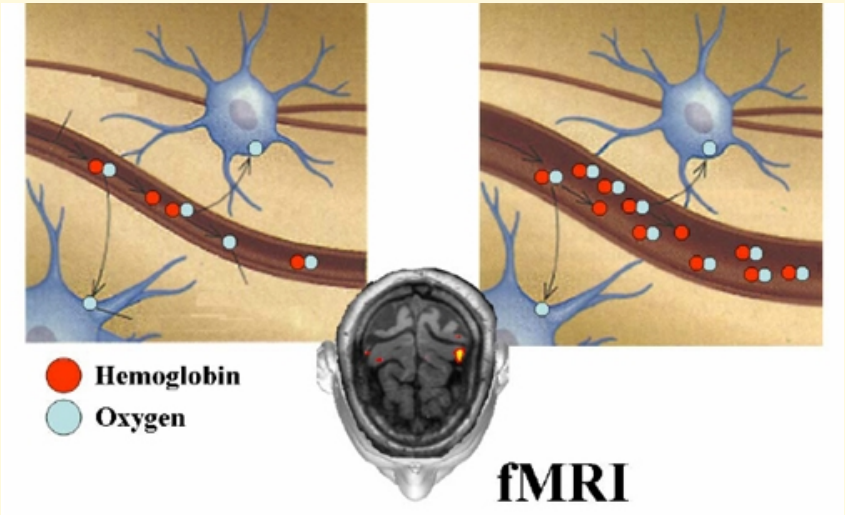

Figure 1. Signal in fMRI

Image: Astolfi et al. *IJBEM*. Vol. 6, No. 2. 2004

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Introduction

- Cortical metabolism is almost exclusively aerobic
- Thus, the local dHb to Hb ratio measured by fMRI can be interpreted as an indirect measurement of neuronal activity
- Likewise, Functional Connectivity MRI (fcMRI) uses spontaneous low frequency BOLD fluctuations to demonstrate cortical connectivity[7-9]
- Our laboratory has extensive experience utilizing fMRI to reveal cortical plasticity following peripheral nerve injury and repair[10-15]
- No human studies assessing cortical changes after BPBP exist

Introduction

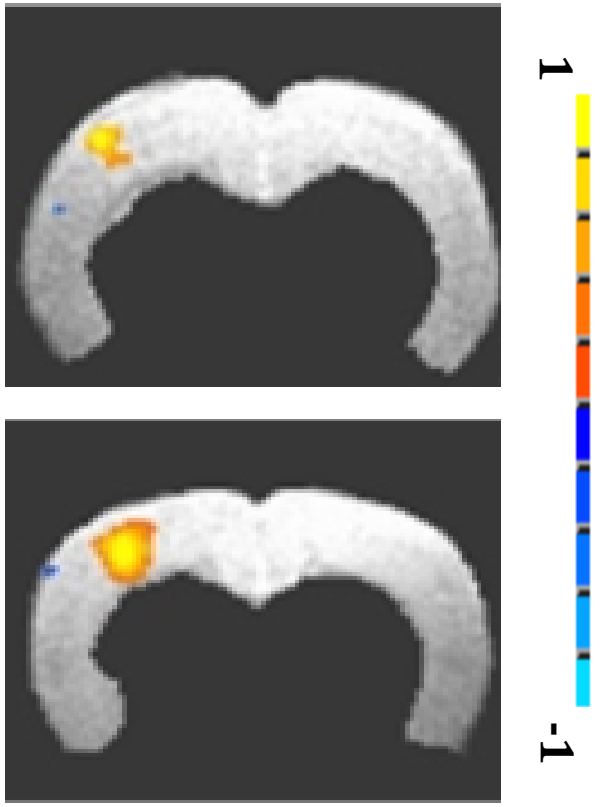

Figure 1. 9.4T fMRI during C7 (top) and median nerve stimulation (bottom)[10]
Li R, Machol IV JA, et al. *Muscle Nerve*. 2013

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Introduction

- We employ 3T BOLD fMRI and fcMRI in a pre-operative pediatric BPBP patient and a healthy adult
- Assess post-injury cortical changes using Air-Puffer somatosensory stimulation[16]
- Post central gyrus chosen as the region of principal evaluation (primary sensory cortex)[17]
- fMRI and fcMRI of the BPBP patient's injury side sensory cortex is contrasted to:
  - Non-injury side (internal control)
  - Healthy adult cortex
- **We hypothesize that there will be significant differences in BOLD signal noted for both comparisons**

Introduction

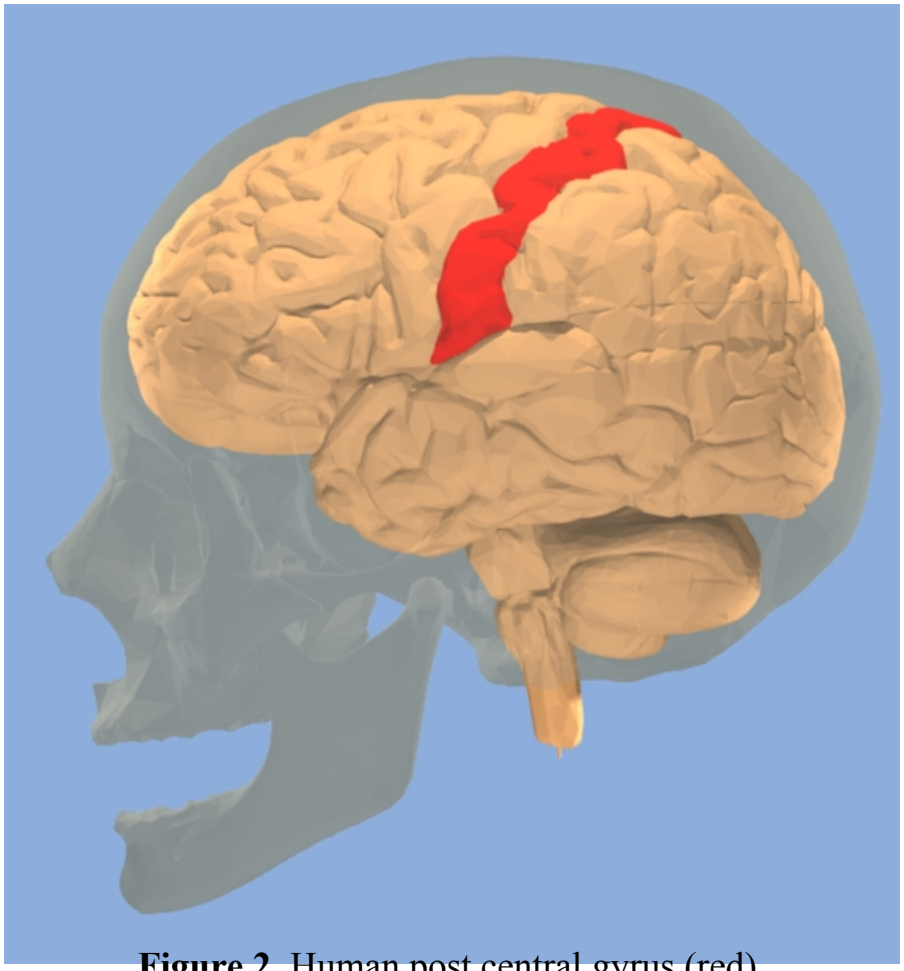

Figure 2. Human post central gyrus (red). Primary sensory cortex.

Image: http://commons.wikimedia.org/wiki/File:Postcentral_gyrus_3d.png

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Methods

- 10 mo Female
- Left C5-C6 BPBP
- 0/5 Ext. Rotators
- 0/5 Post. Deltoid
- No withdrawal with pinch of lateral deltoid
- Modified Mallet Classification
  - Global Abduction III
  - External Rotation III
  - Hand to Neck I
  - Hand to Spine II
  - Hand to Mouth I

Methods

Posterior Deltoid	Middle Deltoid	Anterior Deltoid	Supraspin.	External Rotators	Biceps & Brachialis	Brachiorad.
0	2	2	1	0	3	0
Supinator	Latissimus dorsi	Pectoralis major (clavicular)	Pectoralis major (sternal)	Pronator teres	Serratus anterior	ECRL
0	1	2	3	3	3	3
EDC	Triceps	APL	EPL	ECU	FCU	FCR
3	3	2	0	3	3	3
FPL	FDS	FDP	Interossei	APB	OPB	ADD
3	3	3	3	3	3	3

Table 1. Upper Extremity Functional Exam using the Medical Research Council (MRC) Scale for Muscle Strength.
0: no function – 5: contracts against full resistance. Testing was performed within the best ability given the patient's age.

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Methods

- Modified Mallet Classification
  - Global Abduction III
  - External Rotation III
  - Hand to Neck I
  - Hand to Spine II
  - Hand to Mouth I
- The C5-C6 pathology was verified with pre-operative EMG
- **Post-scan** surgical exploration and intra-operative EMG confirmed neuroma at C5-C6 (during nerve transfer)

Methods

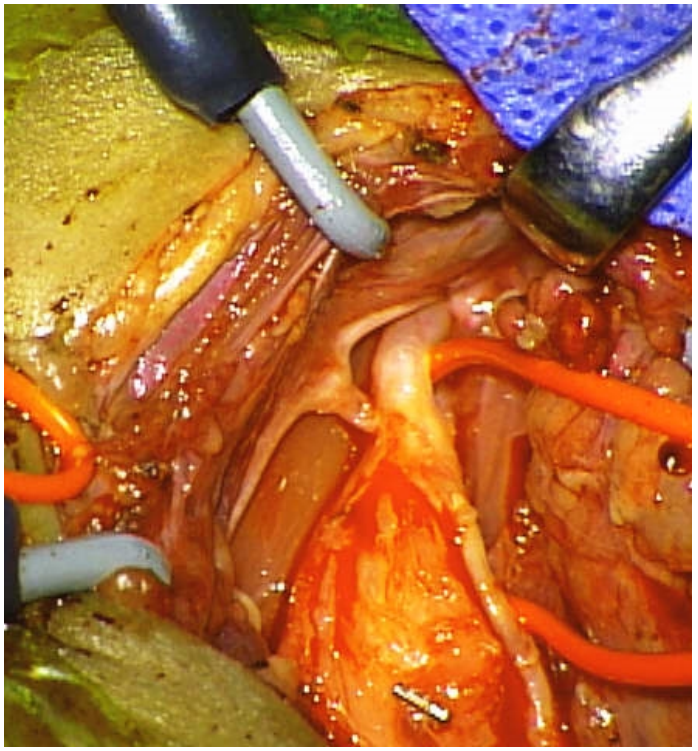

Figure 3. Intra-operative image of nerve transfer after identification of C5-C6 neuroma. Thoracodorsal n. to Axillary n. (side to side) with neurolysis was completed.

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Methods

- Children's Hospital of Wisconsin IRB and MCW MRI Safety approval obtained
- GE 3.0T short-bore utilized for MRI scans
- A timed air-puff stimulator using CO2 gas was connected to two tubes to intra-MRI arm cradles
- One tube was designated the RUE and the other was directed to the LUE
- The lateral deltoid was selected for stimulation
- C5-C6 dermatome

Methods

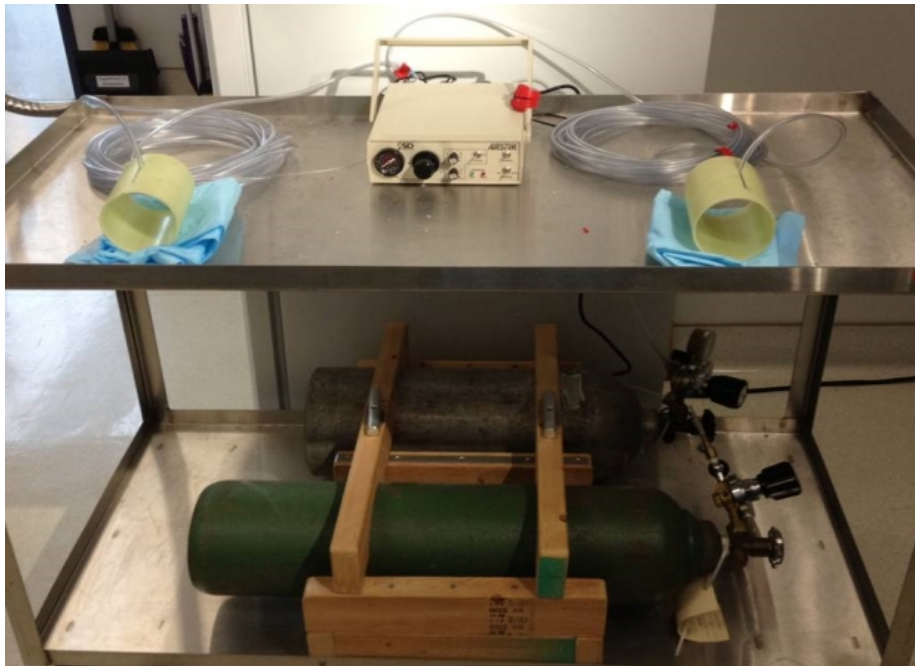

Figure 4. Air-Puffer Mechanism. AIRSTIM™ controlled L and R UE tubes to bilateral, intra-scanner, custom machined, G-10 fiberglass arm cradles. Each arm cradle was padded prior to use. This design prevented arm flexion and allow specific dermatome sensory targeting (C5 -C6). CO2 gas was regulated to 60psi.

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Methods

- **Pre-op** 3T BOLD fMRI imaging was performed (BPBP patient)
- Air-puff stimulus to the left (injury) and the right (non-injury) sides during the EPI phase - completed in duplicate during separate imaging runs
- fMRI of the pediatric **injury side cortex** was compared to the **non-injury side cortex**
- The injury patient's post-central gyrus cortical function was then compared to a **healthy 31 year old adult** using identical somatosensory stimulus BOLD fMRI protocols
- fcMRI was then performed to evaluate sensory connectivity differences between the healthy adult and the BPBP patient

Methods

- Echo Planar Image (EPI) data from each scan was averaged and masked using Analysis of Functional Neuro Images (AFNI) software[19]
- *P*-value threshold of ≤ 0.005 was set to determine significant Voxel activation (BOLD Signal) - Voxel – Represents 2.5 mm^3 (Similar to a 3D pixel)

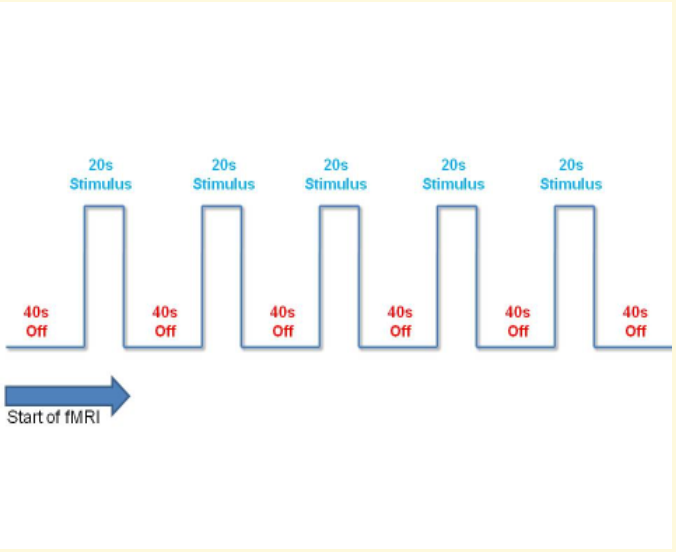

Figure 5. Air-Puffer Stimulus Timing during the EPI phase of the BOLD fMRI. The puffer remained off for 40 seconds, then on for 20 seconds. This was repeated five times followed by a rest period of 40 seconds. 60psi of CO2 was used as stimulus in the C5-C6 dermatome. (s = seconds)

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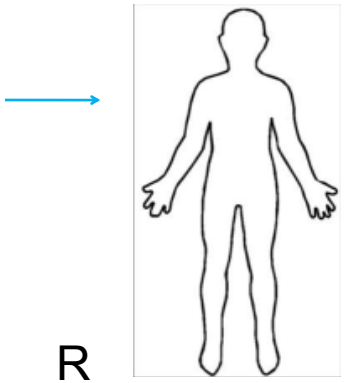
- Results
  - **Right deltoid (non-injury) somatosensory stimulus**
    - BOLD Signal noted in the patient's left post-central gyrus



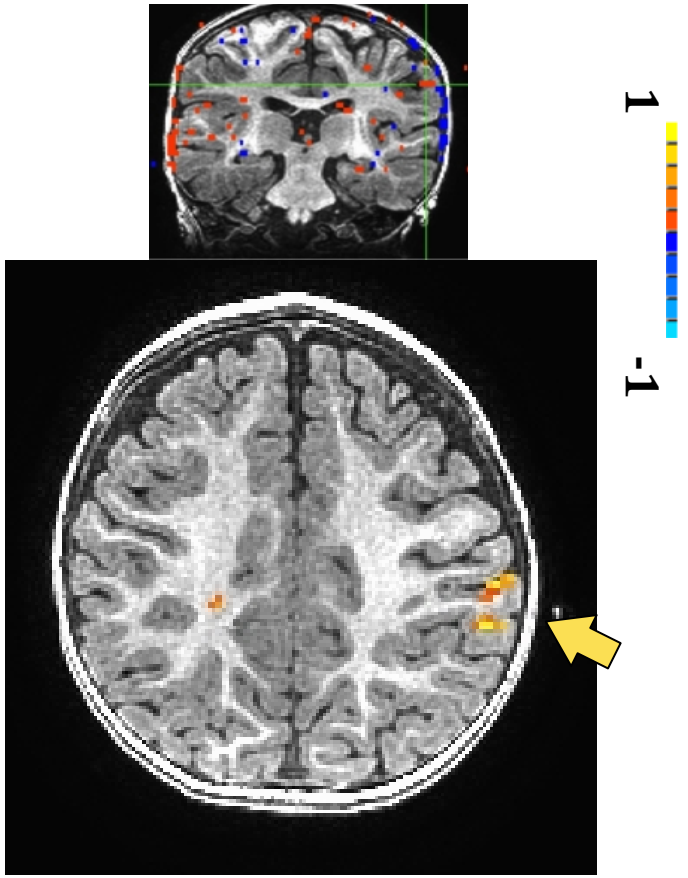


Figure 1. 10 Month Female BPBP.
Coronal (above) and Axial (below) fMRI during healthy right deltoid air-puff stimulation.
BOLD signal noted in left post central gyrus.
(crosshairs and arrow denote signal)

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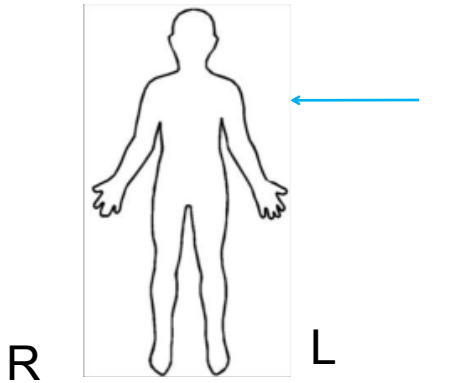
- Results
  - **Left deltoid (injury) somatosensory stimulus**
  - Lack of BOLD signal in the post central gyrus in the right cortex
  - Intra-cortical changes noted as compared to the non-injury cortex



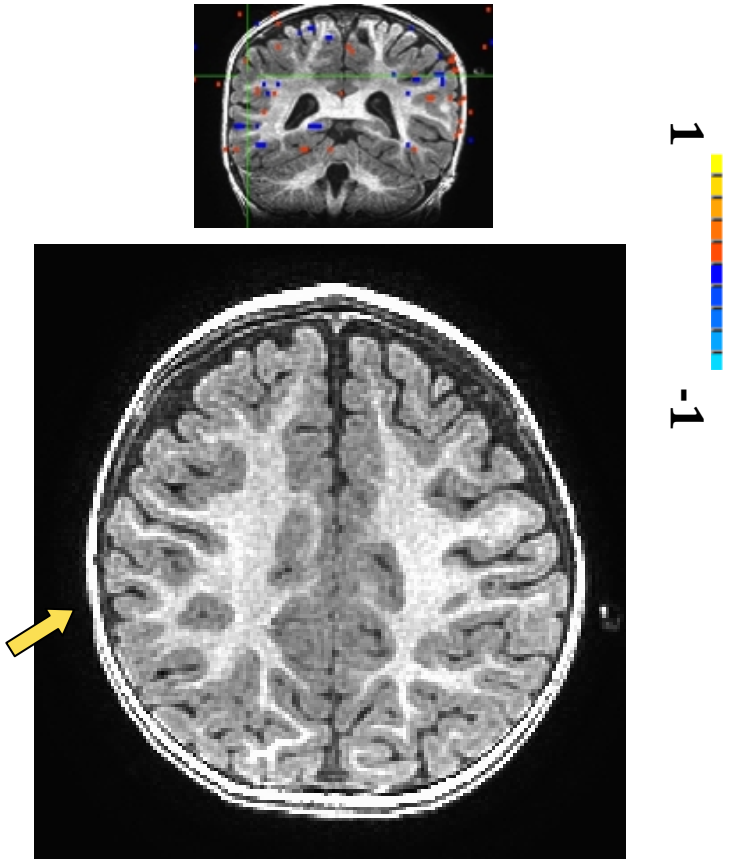


Figure 2. 10 Month Female BPBP. Coronal (above) and Axial (below) fMRI during injury left deltoid air-puff stimulation. No BOLD signal noted in right post central gyrus. *(crosshairs and arrow denote signal)*

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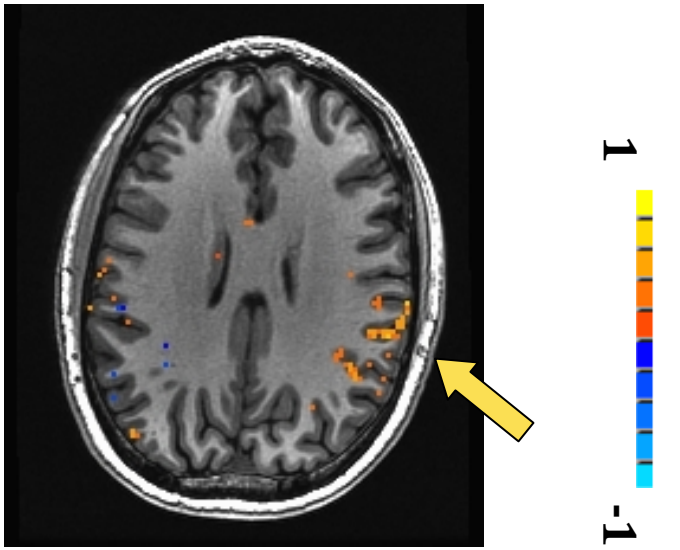
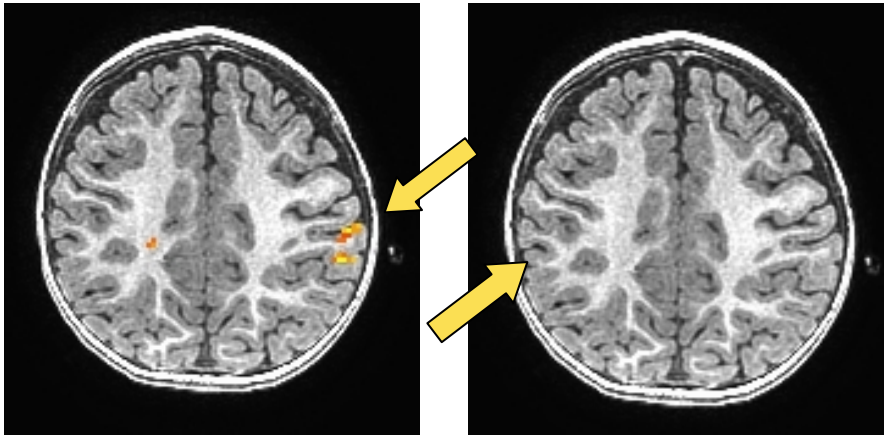
- **Intra-cortical variance was also illustrated when compared to a healthy adult subject**
- The BOLD signals during the healthy limb studies appeared to closely match (**top and bottom left**)
- Whereas, the somatosensory cortical representation of the pediatric injury side did not demonstrate BOLD signal at this significance, $P < 0.005$ (**top and bottom right**)
- **Figure 3.** BOLD fMRI of Axial Healthy Adult Left Deltoid stimulation vs. Healthy Pediatric side vs. Injury Pediatric Side



Healthy Adult R Side



Healthy Ped. R Side Injured Ped. L Side

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- fcMRI demonstrated connectivity difference between the healthy subject and the BPBP patient
- **Healthy Adult**: symmetrical, bilateral somatosensory networks are demonstrated using fcMRI techniques (**Top**)
- **BPBP Patient**: a similar sensory network is shown when the fcMRI seed was chosen from the healthy cortical side (**L cortex for R deltoid**)

However, the injury side cortical network has less organization (**Arrow, R cortex for L deltoid**)

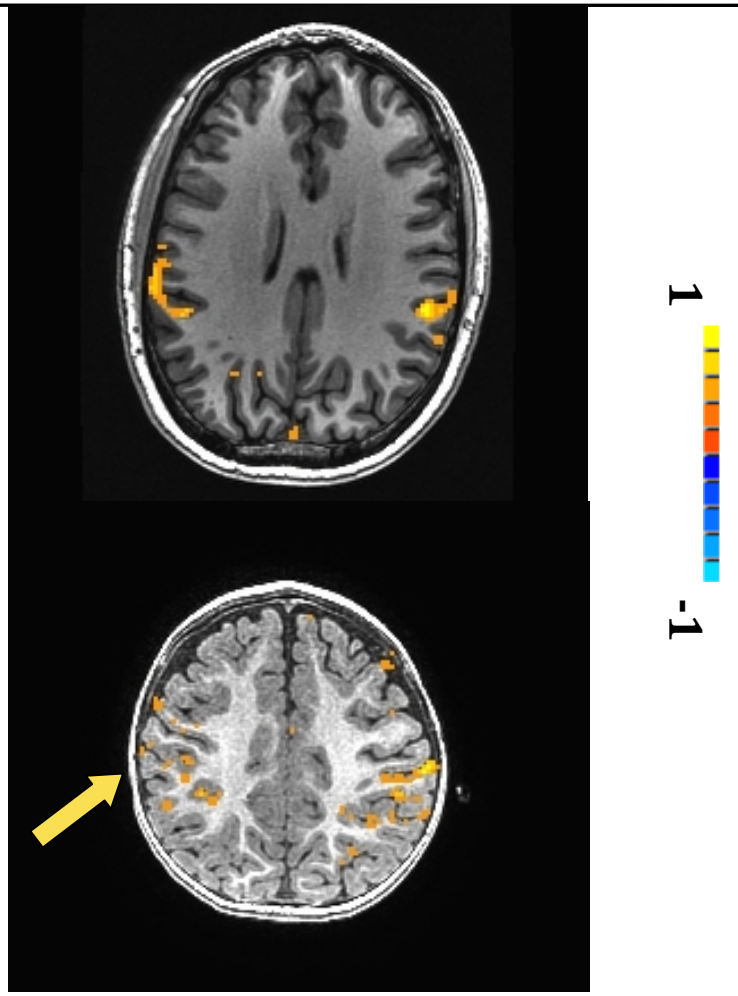

Figure 3. fcMRI of Axial Healthy Adult (above) with symmetric connectivity. Pediatric Left BPBP (below) with less network connectivity in the right cortex.

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Conclusions

- This novel application of 3T BOLD fMRI and fcMRI has demonstrated intra-cortical somatosensory functional and connectivity differences in a high BPBP patient
- The model proposed is applicable to demonstrate cortical sensory changes in the pre and post-operative patient with BP injuries

Conclusions

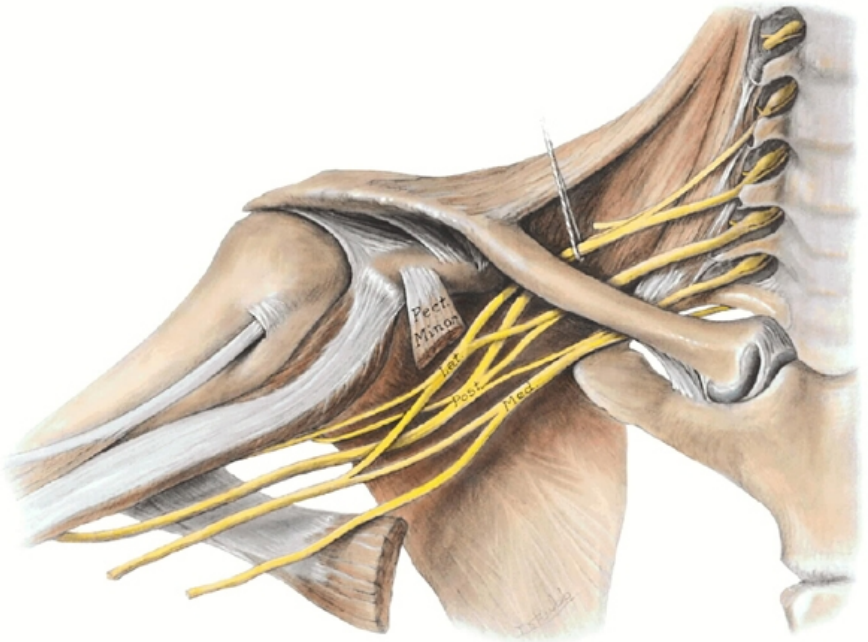

Image: Netter Atlas of Human Anatomy

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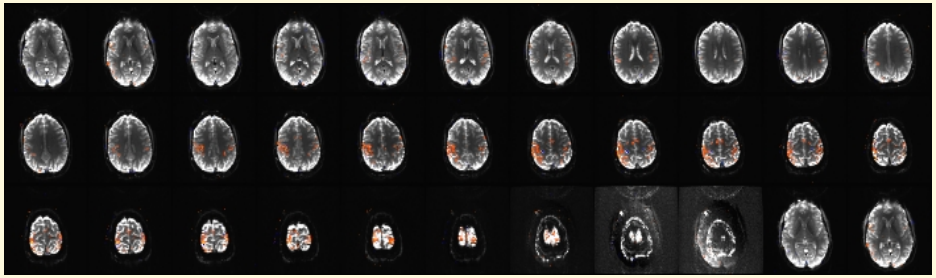
Conclusions

- Limitations: small patient sample size, comparison to adult, and no motor or post-operative imaging
- Represents the early phase of prospective pre and post-operative fMRI studies
- **<u>Goals</u>: Evaluate cortical plasticity after nerve transfer surgery for BP injury in the pediatric and adult populations**
- **Track treatment progress or assess candidacy for nerve transfer or other resconstructive procedures**



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