

Plasticity of the rat sensory cortex at 9.4T demonstrated in a survival model of brachial plexus injury and repair with contralateral C7 nerve transfer

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Introduction

Brachial plexus nerve root avulsion results in severe functional deficit of the upper extremity. Nerve root avulsion cannot be primarily repaired and thus nerve transfers are the mainstay of treatment. Contralateral C7 nerve root transfer is shown to improve outcomes for total brachial plexus avulsion and has become a first line therapy (1). It is known that after nerve repair, recovery is often slow and variable. Furthermore, the response of the brain to peripheral nerve injury and repair is an area of wide inquiry. Previously, our group has reported observations of cortical plasticity after injury and repair of individual peripheral nerves in the rat forepaw (2,3). In this study, a rat survival model for brachial plexus avulsion injury with and without contralateral C7 nerve transfer surgery was designed and implemented. BOLD fMRI was used to record remodeling of the primary sensory cortex of the forepaw (S1FL) over 7 months' time.

Methods

24 Sprague-Dawley rats were divided into three groups for this survival study: control, injury, and injury & repair. The control group underwent sham surgery with electrode placement on both median nerves. The injury group underwent complete brachial plexus root avulsion on the right forelimb and electrode placement on both median nerves. The injury & repair group underwent complete brachial plexus root avulsion on the right forelimb followed by left C7 nerve root transfer to the right median nerve via an ulnar nerve interposition graft across the chest followed by electrode placement on both median nerves. The electrodes were implanted beneath the skin on the lateral chest so that they could be accessed at each time point. Using a 9.4 Tesla MRI scanner, the rats then underwent BOLD fMRI imaging with electrode stimulation at 0, 3, 5, and 7 months.

Scanning Protocol: Functional scans were performed with stimulation of individual median nerves via implanted electrodes at 10 Hz, 0.5 mA, and 1 msec duration. This was done in three repetitions of 20 seconds on, 40 seconds off with a four minute resting time between stimulations. Gradient echo scans (single shot EPI, TE = 18.4 ms, TR = 2 s, matrix 96 x 96, FOV = 3.5 cm, number of repetitions = 110, 10 contiguous 1 mm scans) were acquired on a 9.4T/30 cm Bruker MRI scanner. Two sets of gradient echo images were acquired for each stimulation protocol. The EPI scans were registered to ideal anatomy. Multiple comparisons using AlphaSim were done to display activation at $p < 0.005$.

Results

6 of 8 injury and repair rats survived to 7 months. Speed of recovery and cortical activation pattern varied between the individual rats. Figure 1 shows BOLD fMRI images of 2 representative rats from the injury & repair group during right median nerve stimulation. Time points 0, 3, 5, and 7 months are included. At 0 months, there is no sign of cortical activation with median nerve stimulation. At 3 months, both rats show small ipsilateral cortical activation in S1FL. At 5 months post op, Rat 1 shows bilateral activation and rat 2 shows contralateral activation. At 7 months, both rats display only native, contralateral activation.

Discussion

BOLD fMRI was used to detect cortical changes after brachial plexus avulsion and repair with cross C7 nerve graft. The S1FL region, which represents the primary sensory cortex of the forepaw, displayed a progression of cortical plasticity as recovery took place in each rat. At 3 months' recovery cortical activation was ipsilateral, representing the surgically created pathway of the nerve graft. At 5 months' and at 7 months' recovery the group progressed toward bilateral and ultimately to native contralateral activation. Initially, the neural pathway follows the transferred nerve and stimulation activates the ipsilateral cortex, but over time, it appears that the cortex remodels to more closely restore the native somatotopy. The brain responds to the functional mismatch of non-anatomic sensory input and, through undefined pathways, undergoes higher level reorganization to more closely restore the native sensory cortex. This restoration of contralateral activation took place in all rats in this group, but the speed of remodeling varied among individual rats.

In humans, recovery after peripheral nerve injury and repair is a slow and variable process due to patient, injury, and surgical factors. Variable recovery of individual rats over time, and in strength of BOLD signal is reflected in our results. We believe the rodent model of cortical plasticity closely translates to human brain recovery mechanisms after nerve injury and repair. Future work may include modulation of post-injury cortical remodeling through various therapies to encourage more robust functional recovery.

References

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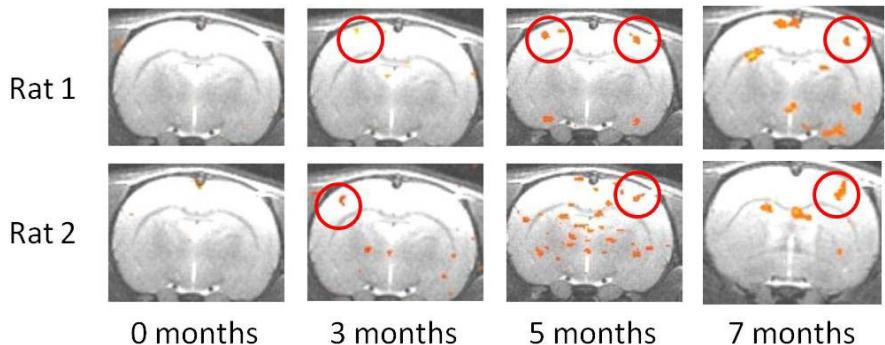


Figure 1: BOLD fMRI displaying cortical remodeling in rats with brachial plexus injury and cross C7 nerve transfer over 7 months.