

Functional MRI study on brain plasticity induced by different peripheral nerve injury patterns: What makes the difference?

R. Li¹, S. Jones², C. Pawela¹, M. Parkins², D. Shefchik¹, M. Boshous², J-G. Yan², S. S. Jaradeh³, H. S. Matloub², and J. S. Hyde¹

¹Biophysics, Medical College of Wisconsin, Milwaukee, WI, United States, ²Plastic Surgery, Medical College of Wisconsin, Milwaukee, WI, United States, ³Neurology,

Medical College of Wisconsin, Milwaukee, WI, United States

Introduction

Nerve regeneration and repair following peripheral nerve injury has been studied extensively in the surgery literature. Nevertheless, because of the complex anatomical structure and the nature of the peripheral nervous system (PNS), recovery after nerve repair is often slow with poor outcome. The impact of peripheral nerve injury and repair on the central nervous system (CNS) has not been extensively studied. Koretsky et al.^[1] using fMRI methods, demonstrated that total denervation of a forepaw or a hindlimb leads to inter-hemispheric reorganization in the rodent primary somatosensory cortex. A literature review did not reveal any fMRI studies focusing on brain plasticity in a context of specific surgical procedures such as partial nerve transfer or C7 transfer. This study reveals, for the first time using (fMRI), brain plasticity patterns that are induced by various peripheral nerve injuries. The methodology provides a laboratory basis for selection of optimum surgical procedures.

Method

Animal preparation: Twenty-four Sprague-Dawley rats were divided equally into four groups. For all the animals, the brachial plexus was exposed on both sides, and stainless-steel electrodes were attached to nerves as described previously^[2]. (See Fig. 1 for group detail.) Rats in groups 1 and 3 were scanned immediately after surgery to acquire data of brain activation following acute nerve injury. In groups 2 and 4, rats were allowed to recover from anesthesia. Two weeks after the initial surgery, electrodes were attached again on both sides and nerves were stimulated directly during scan. **Anesthesia:** Isoflurane (1.4%) was administered during the surgical portion of the protocol. Once the rat was transferred to the scanner, the isoflurane was turned off. A continuous infusion of pancuronium bromide (2 mg/kg/hr) and Domitor (0.1 mg/kg/hr) was used during the fMRI acquisition. **MRI parameters:** Gradient echo scans (single shot EPI), TE = 18.4 ms, TR = 2 s, matrix 128 x 128, FOV = 3.5 cm, number of repetitions = 110. Ten contiguous 1 mm scans were acquired on a 9.4T/30 cm Bruker MRI scanner. **Data analysis:** The EPI scans were registered to an anatomic image. The images for each nerve and stimulation protocol were averaged. Activation was determined by an F test with a P-value threshold of 0.005 using AFNI.

Results

Figure 2.1 shows activation immediately following median nerve injury. There is some residue brain activation, especially in the thalamus and central gyrus. This is thought to be related to pain and stress. Figure 2.2 shows that brain activation disappears two weeks after injury. Figure 2.3 shows brain activation following left-side median nerve stimulation (control) immediately following injury. Results are highly comparable to results of our previous study^[2]. Distinct and localized sensorimotor area activation can be seen. Two weeks following surgery (shown as Fig 2.4), distinct and localized sensorimotor-area activation still can be found. Activation during the chronic period is similar to activation in the acute stage. The difference in number of voxels shown in Figs. 2.7 and 2.8 is not significant, indicating that the representation of the same nerve on the control side does not change during the chronic period. Statistically significant change in brain activation can be found when comparing ulnar nerve activation in the acute and chronic stages after initial right median nerve injury. This suggests the expansion of brain representation foci of the ulnar nerve on the experimental side dominates brain plasticity under this condition. In Fig. 3.1 and 3.2, obtained immediately after the nerve bundle was cut and the proximal end of the nerve residue was stimulated, residual brain activation still could be found. This kind of activation was not observed in the chronic injury study. Figures 3.3 and 3.4 demonstrate brain activation in the acute and chronic injury stages while the left median and ulnar nerve bundles (the control side) were stimulated. It is apparent that brain activation in the chronic stage is intense and diffuse in the somatosensory areas representing median and ulnar nerve bundle of the control side. Figures 3.5 and 3.6 demonstrate the results of right-side radial nerve stimulation in two stages. We can see that brain activation in the chronic stage is intensified and the activated area increases. However, the activated area remains localized compared to the area shown in Fig 3.4. Statistical analysis shows significant change occurs in the representation of the median-ulnar nerve bundle of the control side. Although there is an increase in the activation area for the representation of the right radial nerve in the chronic stage, there is no significant difference compared with the acute stage. From Figs. 3.7 and 3.8, we can see that the activated area of the left radial nerve (control side) remains nearly unchanged during acute and chronic stages. This suggests the expansion of brain representation foci of median and ulnar nerve bundle on the control side dominates brain plasticity under this condition.

Conclusion and Discussion

Two major conclusions can be drawn from our study: When a nerve of the rat forelimb is injured, the nearby nerve responsible for a similar function (shown in Fig 2) compensates for the injured nerve and becomes significantly over-activated. When all of the nerves responsible for a certain function are injured, the same nerves on the contra-lateral side of the body become over-activated to compensate for the functional loss (showed in Fig 3). These significantly over-activated nerves then become optimum donors for nerve repair that can be potentially used during surgery. Additional studies will be aimed at this kind of function-privilege phenomenon that occurs in nerve repair and brain plasticity. Additional longitudinal experiments will be carried out done using implanted electrodes.

References

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2. Cho YR, Pawela CP et al. Refining the sensory and motor ratunculus of the rat upper extremity using fMRI and direct nerve stimulation. Magn Reson Med 2007;58(5):901-909.

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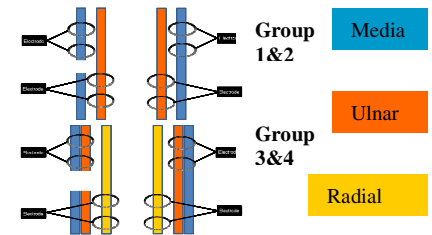


Fig. 1: Detailed group setting and electrode placement of all rats. Different nerves are marked with different colors. The white gap on the nerve trunk represents the nerve cutting site. Note in the left column (which is the right side of rats), electrodes are attached to the proximal end of the cut nerve (or nerve bundle).

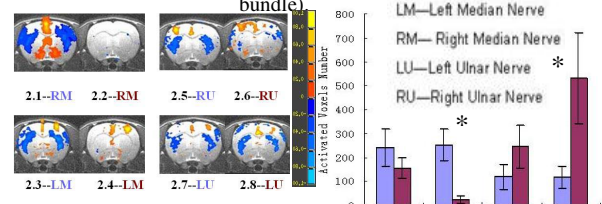


Fig. 2 Brain activation caused by median or ulnar nerve stimulation in acute and chronic stage of right median nerve damaged rats (group 1 and group2). Note the significant change of brain plasticity happens on right ulnar nerve (Fig 2.5 vs. 2.6, and RU group of voxel counting chart). (*) p<0.05

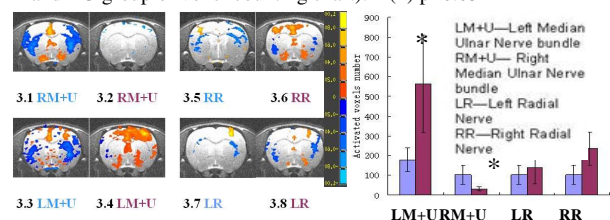


Fig. 3 Brain activation caused by median-ulnar nerve bundle or radial nerve stimulation in acute and chronic stage of right median-ulnar nerve bundle damaged rats (group 3 and group4). Note the significant change of brain plasticity happens on left median-ulnar nerve bundle (Fig 3.3 vs. 3.4, and RM+U group of voxel counting chart). (*) p<0.05