A Peripheral Nerve Repair Model using fMRI in Rats

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Introduction
The purpose of this study was to create a model for peripheral nerve injury and repair. This was done using a rat model and functional magnetic resonance imaging (fMRI). Many of the advances in peripheral nerve surgery have been based on rat models (1) due to the morphological and physiological homology with human nerves, as can be seen in Fig. 1. Blood oxygen level dependent (BOLD) fMRI was used to track cortical recovery of the repaired nerve (2).

Materials and Methods
Nineteen Sprague-Dawley rats underwent either median nerve repair or sham control surgery. The rats were separated into four groups: group A consisted of 4 rats that underwent sham control surgery and were imaged on the same day of surgery (0 weeks); group B consisted of 6 rats that underwent median nerve repair and were imaged on the same day of surgery (0 weeks); group C consisted of 5 rats that underwent sham control surgery and were imaged 2 weeks after surgery; and group D consisted of 4 rats that underwent median nerve repair and were imaged 2 weeks after surgery. For the rats in the repair group, the median nerve was dissected free from the surrounding tissues and transected at the level of the pectoralis major muscle. A repair of the median nerve was then performed using a surgical microscope and 11-0 nylon suture. For the sham control rats, the median nerve was dissected free from the surrounding tissues, but no transection or repair was performed. At designated time intervals, the rats were scanned in the 9.4T animal scanner. On the day of imaging, an electrode was surgically implanted on the median nerve distal to the site of repair or sham surgery. The BOLD response to task in the primary sensory forepaw region was studied (S1FL). Two separate electrical stimulation protocols were used. Each of the nerve stimulation sequences began with an OFF period of 40 s followed by three repetitions of ON for 20 s and OFF for 40 s (total scan time = 3 min 40 s). A rapid acquisition with relaxation enhancement (RARE) anatomical image was acquired with a 256 x 256 matrix, TE = 12.5 ms, TR = 2.5 s, and the same slice geometry as the echo planar imaging (EPI) sequence. Gradient echo scans (single shot EPI, TE = 18.76 ms, TR = 2 s, matrix size 128 x 128, FOV = 3.5 cm, number of repetitions = 110, 10 contiguous interleaved 1 mm slices, acquisition time = 3 min 40 s) were acquired using a Bruker AVANCE MRI scanner with a 30 cm bore. Two sets of gradient echo images were acquired for each stimulation protocol. Images were acquired using a Bruker receiving surface coil (T9208) and a linear transmit coil (T10325).

Results
Figure 2 demonstrates the change in activation in the S1FL region at 0 and 2 weeks for median nerve repair and sham control surgery. Figure 3 is a bar graph plot of the number of activated voxels in the S1FL region in response to median nerve stimulation. It can be seen that the number of activated voxels increases over time in the forepaw region with median nerve repair. The difference between sham control surgery and median nerve repair is statistically significant at each of the time points.

Discussion and Conclusions
The median nerve repair data show an increase in activation in the primary sensory forepaw region (S1FL) after just two weeks. This increase in activation is expected to continue as healing of the repaired nerve progresses. Previous studies have demonstrated return of cortical activation around 15 days in a rat nerve crush model (2). Our model involves complete transection of the nerve with repair; therefore, return of activation may take longer. We are collecting data on 4, 8, and 12 week time points and expect to see the activation of S1FL continue to increase with time. This model is exciting to the peripheral nerve surgical community because it can be used as a vehicle for evaluating different interventions that could improve nerve healing, such as application of neurotrophic growth factors or mechanical stress.

References