Disruption of interhemispheric functional connectivity by peripheral nerve block

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Introduction
Determining functional connectivity with magnetic resonance imaging (fcMRI) has become a common topic in neuroimaging research [1]. Increasingly, measures of connectivity have been used to study disease states or damage within the brain in order to better determine the extent and effects of such disorders. Recently, a study in rats has shown that damage to the peripheral nervous system (PNS) can induce changes in the resting state connectivity of the brain [2]. In the study described here, we show a similar effect in the human brain after a temporary nerve block is applied to the subject. Functional connectivity between brain hemispheres in the motor cortex is disrupted while the block is in place.

Methods
A total of 8 healthy, right-handed subjects participated in this study after supplying informed consent. Each subject underwent three imaging sessions on a GE MR750 3T system using an 8-channel head coil. In each session, a set of standard anatomical images were acquired, as well as a series of functional scans which included a resting state scan (other functional tasks included actual and imagined finger tapping and are being analyzed as part of a larger study on the effects of the nerve block and PNS damage). The resting state functional scan consisted of a SENSE spiral sequence with TE=30ms, TR=2s, and FOV=240mm with 150 time points. Subjects were instructed to remain still with eyes open and maintain fixation on a crosshair presented on a screen. After the first session, subjects were removed from the scanner and the nerve block applied to their right arm. Subjects were placed supine, with the head of the bed slightly elevated, and the subject’s head turned to the contralateral side. After routine monitors were applied including electrocardiogram, noninvasive blood pressure, and pulse oximetry, an ultrasound-guided, in-plane supraclavicular nerve block was performed. Chloroprocaine 3% 30 ml with 3:400K epinephrine and sodium bicarbonate 2 ml in combined solution was administered incrementally after negative aspiration. Full motor and sensory blockade was confirmed prior to returning the subject to the scanner, and the second imaging session was performed with the block in place. The third session began at least two hours after the second session ended in order to allow the nerve block to clear. Data was pre-processed in SPM, including slice-timing correction, motion correction, and normalization. The analysis of functional connectivity was performed in two ways. First, an ROI was defined within the motor cortex of each hemisphere separately. From this ROI, a time course was generated that was then compared to the entire brain, producing a whole brain correlation map for each subject, which was then converted to z-scores and submitted to a second-level analysis in SPM. For the second analysis, a map of Brodmann areas was used to define multiple ROIs, and the correlations between each ROI were determined and a correlation matrix was produced.

Results and Discussion
Figure 1 displays the results from the connectivity analysis. The top image shows significant correlations from a seed in the left primary motor cortex for the pre-block group. Below that is the result from the block group, and on the bottom the result from the post-block group. The difference in connectivity is easily seen- before the block is applied, the hemispheres show strong connectivity between them. After the block, this cross-hemisphere connectivity is significantly reduced. Similar results were found for an ROI in the right hemisphere and this result can be seen in individual subjects as well as the group result shown here. Figure 2 is a matrix showing connectivity strength between a number of ROIs for both the pre-block (left image) and block group. These images were set to the same threshold, and represent areas in both the right and left hemisphere. Again, it can be seen that during the block, functional connectivity is greatly reduced.

Conclusions
We have shown that a peripheral nerve block produces changes in the resting state connectivity within the human brain. This is similar to previous results in deafferented rats, although our results show an immediate and reversible change. These results have implications for studies of PNS injury and human brain plasticity, as well as for the role of fcMRI in future studies.