Functional Brain Mapping During Acute Stimulation Through Chronic Electrode Implants in Rat

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INTRODUCTION

Chronic brain stimulation is used to treat people with various neurological disorders including movement etiologies, epilepsy and a variety of other behavioural anomalies. The use of chronic stimulation in animal models provides us with valuable insights into brain mechanisms, function and connectivity patterns that underlie such disorders (eg. [1]). To investigate the patterns of connectivity and the capacity of the brain to adapt to chronic stimulation, we developed an electrode that can be chronically implanted, deliver current, and record brain activity at 9.4T with minimal susceptibility artifact. We visualized connectivity using fMRI in response to stimulation delivered through a chronically implanted electrode.

METHODS

Carbon fiber electrodes were constructed in our laboratory. A monopolar electrode, approximately 400um in diameter and insulated with Kynar was inserted into the brain of male Long-Evans rats under ketamine/xylazine anesthesia. Implant locations included the sensorimotor neocortex and the corpus callosum. The electrode connection was fixed to the skull and the rats were allowed to recover for at least 1 week before MRI. During this time, the capacity to record EEG and to elicit an afterdischarge (seizure) through electrical stimulation was confirmed. For MRI, animals were anesthetized with isoflurane, spontaneously ventilated and monitored for respiration. MRI was done with a 9.4T Bruker Avance system, a 3 cm diameter surface coil, and a fast spin echo sequence (TR/TE = 4 sec/58.9 ms, FOV=3 cm^2, matrix size= 128x128). Stimulation was delivered using a Grass stimulator with a stimulus isolation unit which applied a 1 mA constant current with a stimulus train of 2ms square wave, 60Hz for 2s. Varying numbers of stimulation trains were repeated from single train to a set of 6 stimulation trains. Ten images were acquired prior to stimulation, 1 during stimulation and 10 images between stimulations. Images were analyzed for activation clusters using EvIdent software. This detects clusters of voxels with self-same intensity changes (correlation to average time course with $p<0.00005$) of positive or negative BOLD signal changes (2).

RESULTS

The electrode had minimal susceptibility artifact as seen in Fig 1. Patterns of activation as evidenced by cluster analysis varied with electrode location and with the pattern of stimuli train. With a single 2s train, all clusters with average intensity changes related to the stimulation conditions, exhibited positive BOLD changes. Positive BOLD effects occurred near the electrode site (Fig 2a) as well as at distant sites (Fig 3c). As the number of stimulation periods increased, regions showing marked negative BOLD effects appeared (Fig 2b,c). These negative effects were largely unilateral, and included cortex and striatum.

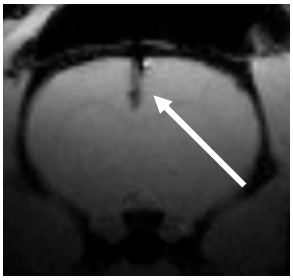


Figure 1: FLASH image of a brain slice containing the implanted electrode near corpus callosum showing minimal susceptibility artifact (TR/TE/α = 100 ms/ 4.5 ms/ 20°).

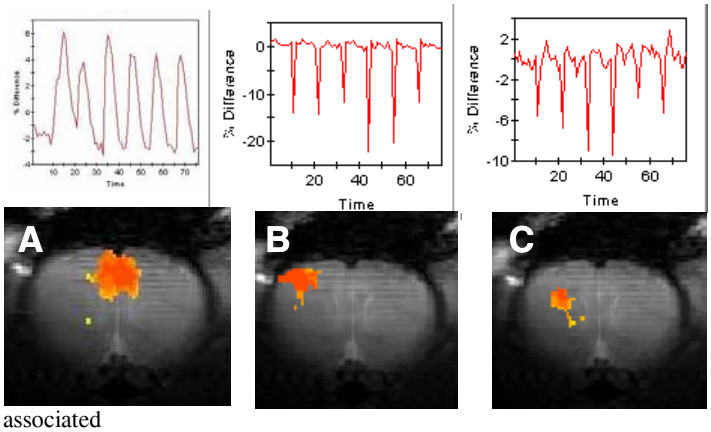
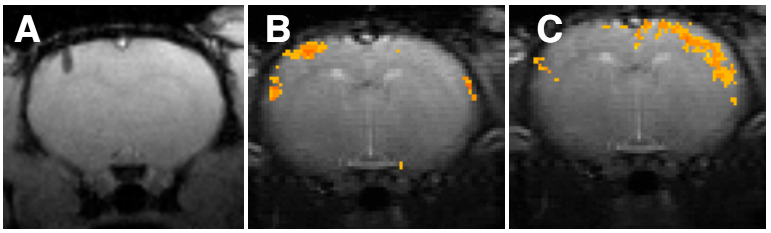


Figure 2: Example of activation responses observed from the subject in Fig 1, showing cluster based activation patterns. Top shows mean % BOLD signal change for the cluster with the x axis being scan number. Bottom shows the voxels of activation for each cluster: A) at electrode B) negative activation in lateral cortex C) negative unilateral response in the striatum.

associated

Figure 3: Example from an animal with the electrode implanted laterally in the somatosensory cortex. These clusters were observed with 6 repeated trains of stimuli: A) MRI showing electrode site B) positive activation 1 mm posterior, near electrode as well as bilaterally in parietal cortex C) strong positive contralateral cortical activation.



DISCUSSION

These examples are a subset of data showing complex response patterns elicited by stimulation from a chronically implanted electrode. Clusters of either activation or inhibition are seen in varying regions throughout the brain. These are often distant from the electrode, often unilateral and vary with the number of repeated trains of stimuli. Negative activation regions are seen both in cortex and thalamus such as Fig 1b,c, where it is possible that unilateral motor inhibition is moving through thalamic projections. Such chronic implants will allow us to assess activation patterns in brains that have recovered from the trauma of surgery, and will allow us to monitor changes in activation patterns through weeks of stimulation.

REFERENCES

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