Functional MRI demonstrates a consistent pattern of activation in deep brain motor structures during DBS electrode stimulation of the subthalmic nucleus in patients with Parkinson's disease.

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Background: Placement of deep brain stimulators (DBS) in the subthalamic nucleus (STN) for the treatment of Parkinson's disease (PD) has become part of the standard of care. Despite the frequency of this procedure, relatively little is known about the mechanism(s) of action of DBS. Due to safety concerns for potential heating at the DBS electrode tip and possible brain injury, few imaging studies have been done patients with DBS implants. Our group has extensive experience with safety testing in DBS, and we have thoroughly tested the lead systems used in the present study in a previously described gel phantom.[(1,2)] At present, there is only one report of functional MRI at 1.5T in patients with unilaterally placed DBS for PD. [(3)] In vivo evaluation of DBS using fMRI may allow for a better understanding of the mechanism of DBS and potentially lead to optimization DBS for improved symptom relief.

Purpose: To study the pattern of activation produced by DBS electrode stimulation in the STN using fMRI.

Methods: Four patients with percutaneously-extended bilateral DBS electrodes in the STN for the treatment of PD were studied using a 3T Siemens Allegra MRI (Erlangen, Germany) on the first or second postoperative day. The externalized lead system was extended through the waveguide to an external pulse generator in the MRI control room. Stimulation parameters were determined by extensive testing prior to MRI to determine optimal stimulation for alleviation of symptoms. Scanning consisted of: 1) three-dimensional anatomic data set with leads disconnected from the pulse generator the follow parameters: 3D turboflash, 120 1.2mm thick axial slices, matrix=128x256, fov=24cmx24cm, TE/TR/TI/flip=1.74ms/1900ms/900ms/8°, receive bw=125KHz; and 2) BOLD fMRI with a single lead connected to the pulse generator and follow parameters: 2D grad echo epi, 180 volumes of 32 3.8 mm-thick axial slices,TE/TR/flip=29ms/2000ms/90°matrix=64x64, FOV=24cmx24cm, receive bw=125KHz. BOLD images were acquired using prospective motion correction. fMRI examinations were performed with a block style paradigm consisting of 5 stimulator off and 4 stimulator on 32 second epochs with 10 seconds placed between the stimulator off and stimulator on conditions in order to gradually ramp the stimulator to the optimal stimulation level. Gradual ramping was employed for patient comfort and to decrease patient motion. Images acquired during the ramping process were discarded prior to image analysis. All data were spatially filtered with a Hamming filter that increased BOLD contrast to noise. The MRI time series at each pixel was fit using least squares to a boxcar reference function plus a slope and intercept.

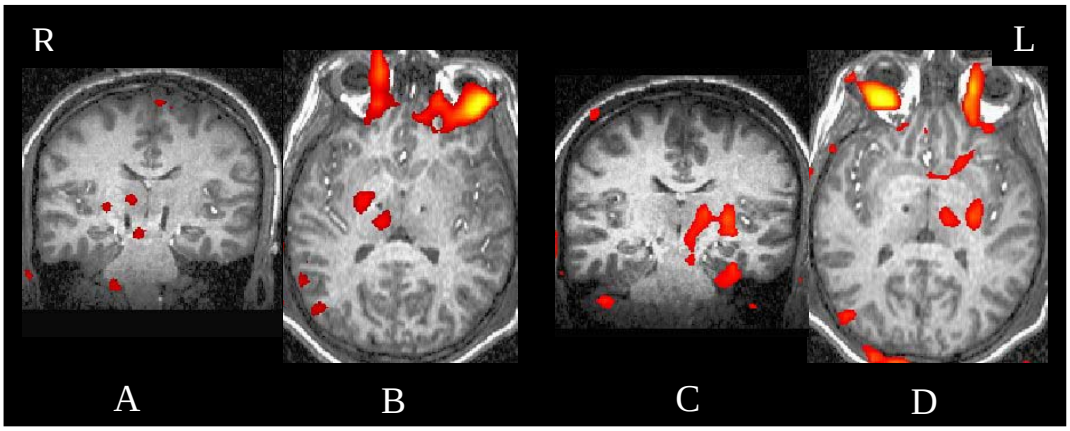

Figure 1.Images from a typical subject. Images A) and B) are coronal imaging and axial images showing activation within the right posterior globus pallidus, posterior putamen and thalamus during stimulation of the right-sided STN electrode. Images C) and D) are coronal imaging and axial imaging showing activation within the left posterior globus pallidus, posterior putamen and thalamus during stimulation of the left -sided STN electrode.

Results: All four of the patients were able to complete the study. Good activation was demonstrated from 6 of the 7 electrodes stimulated. In all cases activation was demonstrated in the anterior thalamus and posterior portions of the globus pallidus and putamen . Four of the electrode stimulations demonstrated additional activation in the subthalmic nucleus/substantia nigra (SN) region adjacent to the electrode tip. For two electrode stimulations activation was seen in the contralateral superior cerebellum. Typical activation results are displayed in Figure 1.

Discussion: Activation was consistently identified in the ipsilateral posterior globus pallidus, posterior putamen and thalamus. Jech et al. demonstrated this pattern in two out of four of their subjects.[(3)] Additionally, activation was seen in the ipsilateral STN/SN region and contraleral cerebellum. Areas of activation noted by Jech et al. in the dorsal lateral prefrontal cortex, superior colliculus, and contralateral caudate nucleus were not seen.[(3)] Importantly, the present study demonstrates activation only ipsilateral to stimulating electrode suggesting that artifact secondary susceptibility effects is unlikely to explain the activation results.

Conclusion: Stimulation of therapeutically effective contacts of a DBS electrode in the STN produces a consistent pattern of ipsilateral activation deep brain motor structures.

Reference: 1. Finelli et al AJNR Am J Neuroradiol 2002;23:1795-1802. 2. Rezai et al. J Magn Reson Imaging 2002;15:241-250.3.Jech et al. Mov Disord 2001;16(4):1126-11.