Deep brain stimulation fMRI with a home-made two-channel tungsten microwire electrode

Hsin-Yi Lai[1], John Robert Yount[1], Yu-Chieh Jill Kao[1], and Yen-Yu Ian Shih[1]

[1]*Experimental Neuroimaging Laboraory, Department of Neurology and Biomedical Research Imaging Center, University of North Carolina, Chapel Hill, NC, United States*

INTRODUCTION Deep brain stimulation (DBS) is a procedure which is useful in the treatment of several neurological disorders, though the mechanism of effect continues to be unclear [1]. fMRI with simultaneous DBS in animal models may potentially reveal patterns of altered neural activity at regional and global levels, but this technique faces several technical challenges, including cost effectiveness, susceptibility artifact, and generalizability of findings under anesthesia and/or sedation [2-4]. In this study, we aimed to design a tungsten microwire electrode that can be used for preclinical DBS fMRI experiments and is bendable after implantation. A cost effective fabrication process was proposed and the BOLD frequency-tuning curves to thalamic DBS were performed under either isoflurane anesthesia or α-chloralose sedation to demonstrate the validity of DBS fMRI with this electrode under two physiological conditions. The tungsten microwire electrode creates less susceptibility artifact than a commercial MR-compatible product and is highly flexible, permitting use with a variety of RF probes.

ELECTRODE FABRICATION Tungsten microwires with polyimide insulation and a diameter of 50 μm (California Fine Wire Co., Grover Beach, CA) were straightened by hanging between two rubberized clamps, cut into two 3 cm pieces and soldered into two 1 cm long, 500 μm inner diameter silver tubing (OttoFrei, Grover Beach, CA) with a 2-pin IC socket used as electrode connectors. A small piece of thin plastic was placed between two pieces of silver tubing for insulation. The soldering spot was protected by hot-melt adhesive and the microwires were aligned in parallel, fixed with saturated sucrose solution and kept in 4°C refrigeration.

METHODS On the date of the experiment, the two-channel tungsten microwire electrode was removed from refrigeration and stereotactically implanted into the thalamus (3.0 mm posterior to bregma, 3.4 mm lateral to the midline, and 5.5 mm below the cortical surface) [5] and fixed with dental cement in six Sprague Dawley rats (350-450 g) under deep isoflurane anesthesia (2-2.5%). After implantation, electrode was bent caudally in parallel to the skull surface. *In the first study*, an additional MR-compatible platinum electrode MS303/9C-B (the smallest available MR-compatible product from the manufacturer: PlasticsOne, Roanoke, VA) was implanted into the contralateral thalamus for comparison. fMRI experiments were performed under 1-1.25% isoflurane anesthesia. *In the second study*, a BOLD frequency tuning curve to thalamic DBS was first obtained under 1-1.25% isoflurane and then repeated under □-chloralose sedation in the same subject (n=5). □-chloralose was administered (60mg/kg bolus and 30mg/kg/hr i.v.) after the isoflurane was discontinued and the fMRI experiment was started 40 min after the initiation of infusion. All subjects were intubated, paralyzed, and ventilated with medical air during imaging. $EtCO_2$, SpO_2 and body temperature were maintained within normal physiological ranges. MRI experiment was performed on a Bruker 9.4T/30 cm scanner. *In the first study*, data were acquired with a home-made surface coil (ID = 1.6 cm) using a double-sampled 4-shot gradient-echo EPI sequence (bandwidth=160 kHz, TR/TE=750/13 ms, matrix=128x128, FOV=2.56x2.56 cm^2, slice thickness=1 mm). *In the second study*, the imaging geometry is the same but a single-shot gradient-echo EPI sequence (BW=250 kHz, TR/TE=1000/14 ms, matrix=96x96 and zero-padded to 128x128) and a Bruker 4-channel phased array coil was used. DBS frequencies of 1, 5, 10, 15, 20, 25, 30 and 40 Hz were studied with a bipolar square-wave current of 2 mA and a pulse width of 1/f ms where f = frequency in Hz. The frequencies were performed in a pseudo-random manner. 2 to 5 repeated trials were performed for each stimulus parameter to improve measurement accuracy and SNR. The stimulation paradigm was 20 s initial rest, 10 s stimulation, 40 s rest, 10 s stimulation, followed by 40 sec rest and an additional 90 sec minimum resting interval between scans. Correlation coefficient (CC) maps were performed by correlating BOLD time courses to the stimulus paradigm after inter-subject coregistration, with a significance level at $p<0.05$ (Bonferroni corrected) and a temporal delay of 2 s. Threshold for CC colorbar was set at 0.3 to 0.8. Statistical analysis employed ANOVA followed by Fisher's LSD test. Error bars used were SEM.

RESULTS AND DISCUSSION This study successfully demonstrated fMRI response to thalamic DBS using tungsten microwire electrode. **Fig.A** shows a schematic plot of the DBS setup which does not require a high electrode implantation on the head. Our findings were **i)** reduced susceptibility artifact was found as compared to commercial platinum electrodes (**Fig.B**), and **ii)** peak BOLD response under α-chloralose was higher than under isoflurane (4% to 2%, respectively), but the peak frequency was identical (**Fig. C-E**). BOLD responses in this study were durable throughout the scan period and highly reproducible. The susceptibility artifact by tungsten microwire electrode was smaller, making visualization of nearby activation feasible. This electrode was flexible enough to use with commercial surface/array coils that do not have an opening for conventional electrode implantation on the head. The BOLD fMRI tuning curve observed with the microwire electrode were similar to those observed with the commercially available electrode [6]. α-chloralose is known to preserve better neurovascular coupling [7]. The baseline signal intensity exhibited 12.7% higher in isoflurane than α-chloralose caused by the CBF ceiling effect that may also result in higher BOLD responses obtained under α-chloralose [3]. The similar frequency-dependence and location of BOLD response indicates that anesthesia may have less impact on DBS fMRI because DBS bypassed the anesthetic confounds on the peripheral nervous system and ascending neurons in the spinal cord.

CONCLUSION: This study demonstrates the utility of the tungsten microwire electrode for DBS fMRI, with reduced susceptibility artifact, sufficient flexibility to be used with commercial RF coils and comparable BOLD response under isoflurane and α-chloralose. Our data support the validity of DBS fMRI with this electrode.

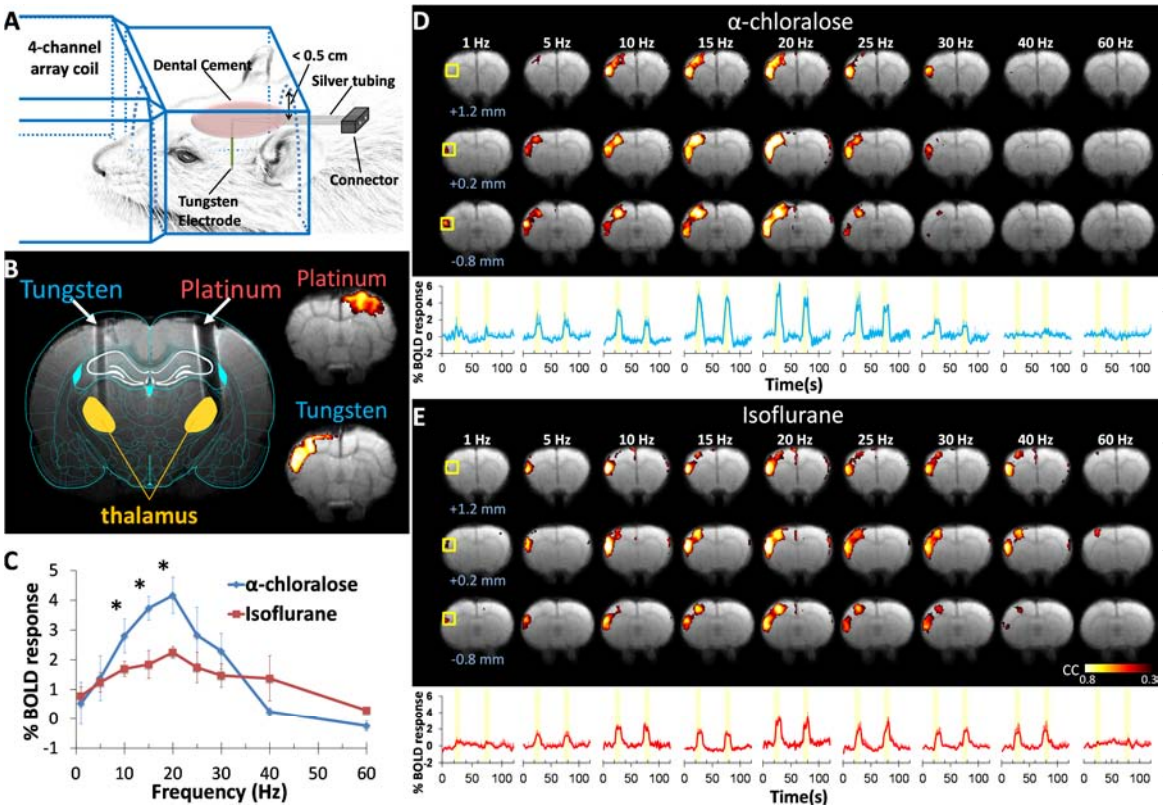

Figure (**A**) DBS fMRI setup using microwire electrode with a commercial array coil. (**B**) A T_2-weighted image with rat brain atlas showing MR artifact induced by a commercial platinum electrode (right) and a tungsten microwire electrode (left). Corresponding fMRI correlation maps are shown on right. (**C**) Group-averaged BOLD response under isoflurane was weaker but exhibited similar frequency dependency as under α-chloralose (n=5). (**D&E**) Group-averaged BOLD fMRI activation maps and time courses under α-chloralose and isoflurane, respectively (n=5). Yellow boxes indicate approximate ROIs (8x8 voxels).

REFERENCES: [1] DeLong et al., Ann, N.Y. Acad Sci. 2012, 1265-1. [2] Shyu et al., MRM 2004, 52:47. [3] Masamoto et al., Cereb Cortex 2007, 17:942. [4] Dunn et al., MRM 2009, 61:222-8. [5] Paxinos and Watson, The Rat Brain in Stereotaxic Coordinates, 2005. [6] Shih et al., ISMRM 2012, #0658. [7] Ueki et al., Acta Anaesthesiol Scand. 1992, 36:318-22.