Deep brain stimulation in mice using magnetic resonance imaging-compatible carbon electrodes

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Introduction

- Deep Brain Stimulation (DBS) delivers high-frequency electrical stimulation via implanted electrodes to brain circuits that are compromised by neuropsychiatric disorders
- Used effectively in the treatment of Parkinson's disease
- Under investigation for treatment of other disorders such as major depression and Alzheimer's disease
- Metal DBS electrodes render the use of Magnetic Resonance Imaging (MRI) unsafe and/or problematic (figure 1) due to their magnetic susceptibility
- Pre-clinical longitudinal studies evaluating the effects of DBS on brain structure could benefit from MRI-compatible electrodes

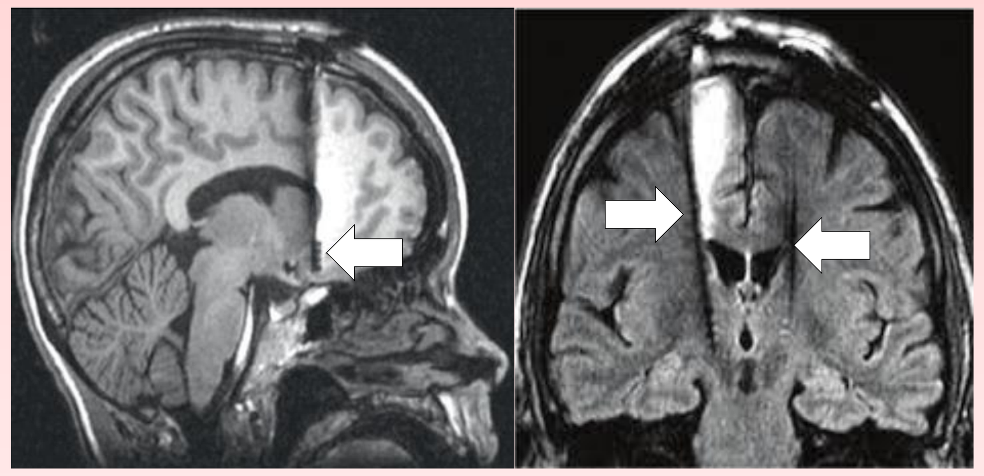

Figure 1. Sagittal (right) and coronal (left) MRI images of patients with DBS electrodes implanted. Differences in magnetic susceptibility between metallic electrodes and surrounding tissue create inhomogeneities in the magnetic field of the instrument, which manifest as distorted signal intensity and warping. Modified from Lipsman et al. 2013 (left) and Sarkar et al. 2014 (right).

Objective

- Construct functional electrodes that are compatible with MRI in terms of both safety and image quality

Electrode Construction

- Carbon fiber rods of 0.25 and 2 mm diameters (figure 2)
- Thicker rod serves as an attachment anchor for stimulation wires via alligator clips
- Thinner rod serves as the transcranial portion, allowing targeting of different brain structures
- Annealed together with conductive carbon epoxy
- Insulated with dip-dried polyvinyl alcohol
- Monopolar
- Contains no metal for better MRI imaging performance and safety

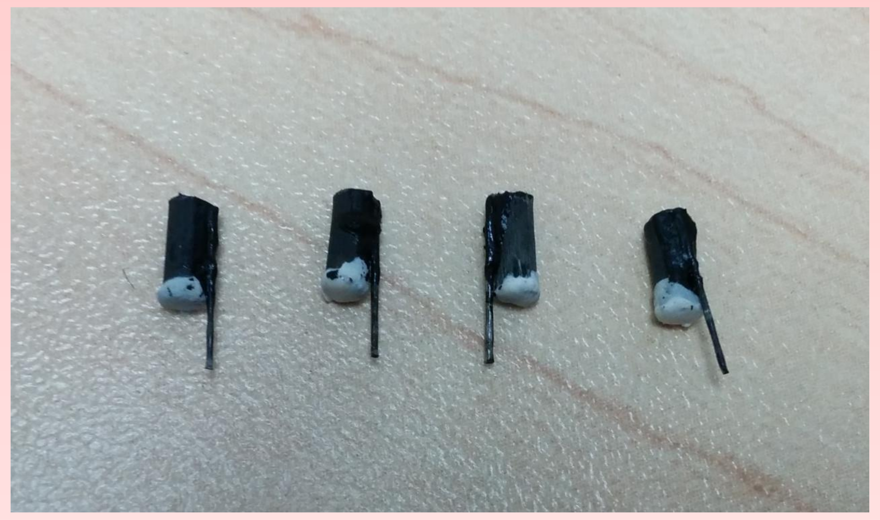

Figure 2. Finished carbon electrodes.

Surgery

- C57BL/6 mice, male and 8 weeks
- Stereotaxic surgery lasting ~40 min per mouse
- 2 electrodes implanted bilaterally +/- 1 mm at bregma, to a depth of 3.75 mm, perpendicular to the skull plane
- Targeting the body of the fornix
- Electrodes cemented directly to the skull (figure 3) with high grade dental cement (no screws or platform)

Figure 3. Male C57BL/6 mice post-surgery, with electrodes implanted and secured to the skull with high-grade dental cement.

Stimulation

- Awake, unrestrained mice for 1 hour (figure 4)
- Monophasic, 100 Hz, 100 µA, ~1 V with pulse width of 100 µs
- Custom pulse generator with live voltage feedback

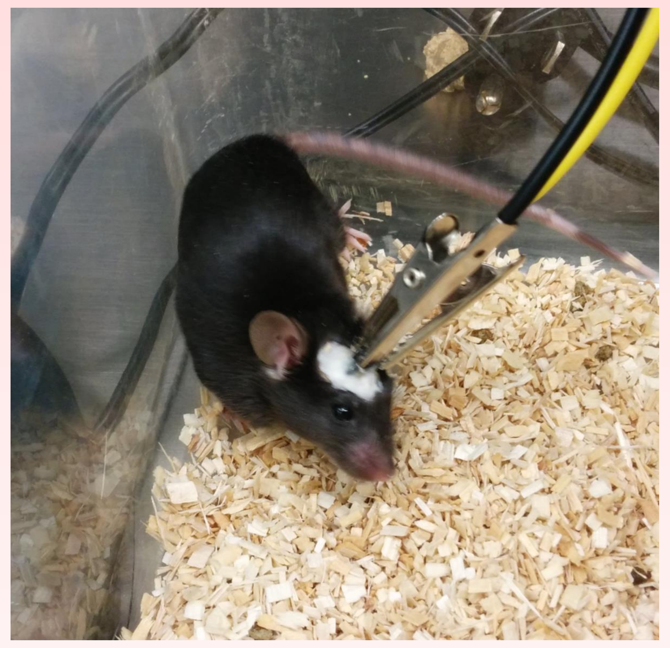

Figure 4. C57BL/6 mouse with implanted electrodes attached to pulse generator via alligator clips.

MRI Imaging

- 7T Bruker USR magnet with 30 cm bore with high performance imaging gradient kit
- Live animals under 1.5% isoflurane anesthesia
- 3D-FLASH (Fast Low Angle Shot) scan, 100 µm isotropic voxels (figure 5), 180x160x90
- TR = 20 ms, TE = 4.5 ms, FA = 20°
- $MnCl_2$ enhanced, fat suppressed
- Scan time < 15 min

Results

- Mean electrode resistance was 1379 Ω with standard deviation of 248 Ω
- Neither electrode implantation nor stimulation caused noticeable adverse side-effects in mice
- 100 µA stimulation required 1 V, less than comparable metal electrodes
- Total circuit resistance of ~5 kΩ
- High resolution (100 µm isotropic) MR images contained no major artifacts generated by the electrodes

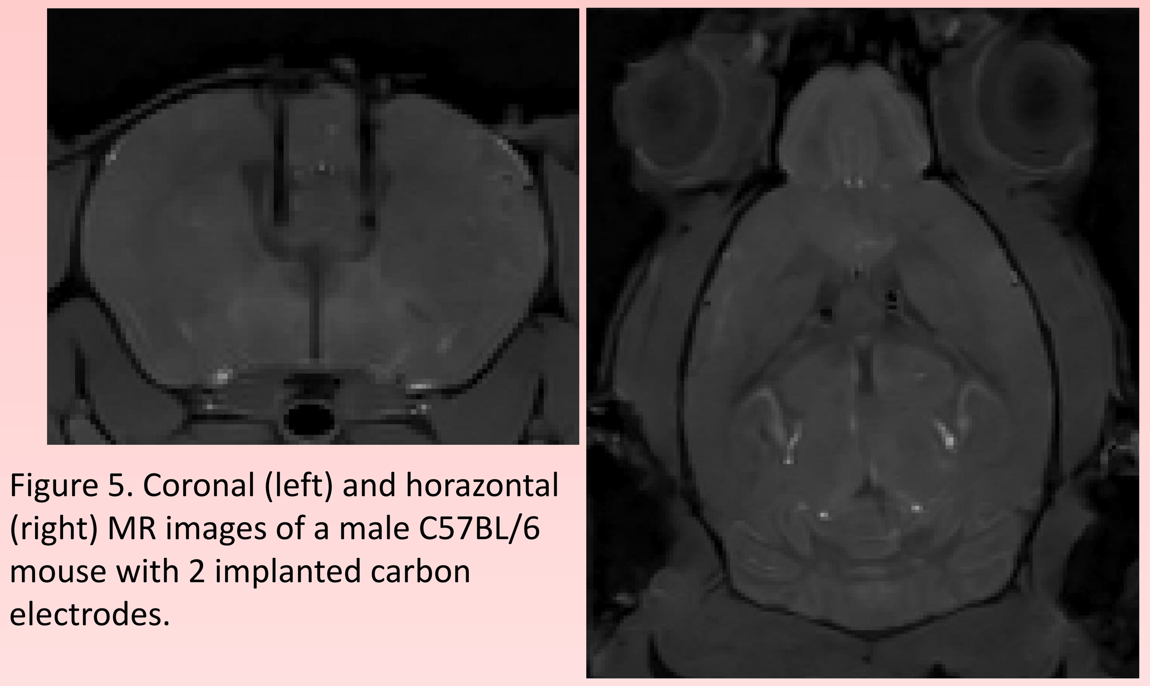

Figure 5. Coronal (left) and horazontal (right) MR images of a male C57BL/6 mouse with 2 implanted carbon electrodes.

Conclusion

- Our findings suggest carbon fibre to be an appropriate replacement material for metal in DBS electrodes due to its high conductivity, biocompatibility and the relative absence of MRI acquisition artifacts

References

- N. Lipsman et al. "Subcallosal cingulate deep brain stimulation for treatment-refractory anorexia nervosa: a phase 1 pilot trial," *Lancet*, Vol. 381, No. 9875, pp. 1361–1370, 2013.
- S. N. Sarkar, P. R. Sarkar, E. Papavassiliou, and R. R. Rojas. "Utilizing fast spin echo MRI to reduce image artifacts and improve implant/tissue interface detection in refractory parkinson's patients with deep brain stimulators," *Parkinson's Disease*, Vol. 2014, pp. 1–6, 2014.

Acknowledgements and Contact Info

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