Combined TMS/MRI for image-guided brain circuit neuromodulation

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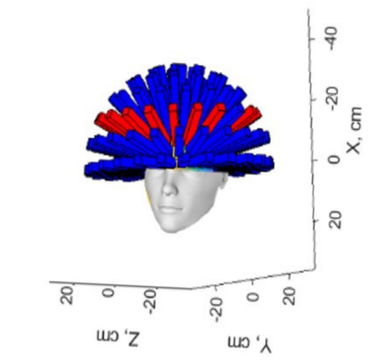
Purpose

Magnetic resonance researchers have identified brain tract patterns associated with various mental health and neurological disorders. Early clinical data suggest that transcranial magnetic stimulation (TMS) can increase the integrity of damaged tracts and alleviate symptoms. Existing neuromodulation methods are ill-suited to direct neuromodulation therapy at entire tracts with high anatomic accuracy. We are therefore working on building novel image-guided therapy systems that combine tract-based neuromodulation with built-in MRI guidance.

Methods



Electropermanent module (EPMM) systems were constructed with magnetizable cores and high current coils. The EPMMs allow magnetic fields to stay on without the need for continuous current supplies.

A quasi-static magnetic field B_0 (of about 50 mT) as well as magnetic gradients for MRI can be created with the EPMMs. The EPMMs can create TMS pulse trains with current amplitude up to 2 kA. Using AI-based software analyzing obtained MRI images and defining which EPMMs should be activated, targeted stimulation to entire tracts is possible. Experimental data as to the electric field maps generated by the EPMMs were used to simulate delivery to tracts, in which timing of the pulses could be used to generate bi-phasic electric pulses at some locations and mono-phasic pulses at other locations. Neurons are more sensitive to mono-phasic pulses than to bi-phasic pulses, enabling differential activation.

Results

A system containing five EPMMs (a full human system will require about 100 EPMMs) was used to generate TMS magnetic fields sufficient to open the blood-brain barrier (BBB) in mice (to Gadobutrol) and to open an *in vitro* BBB model to gene therapy.

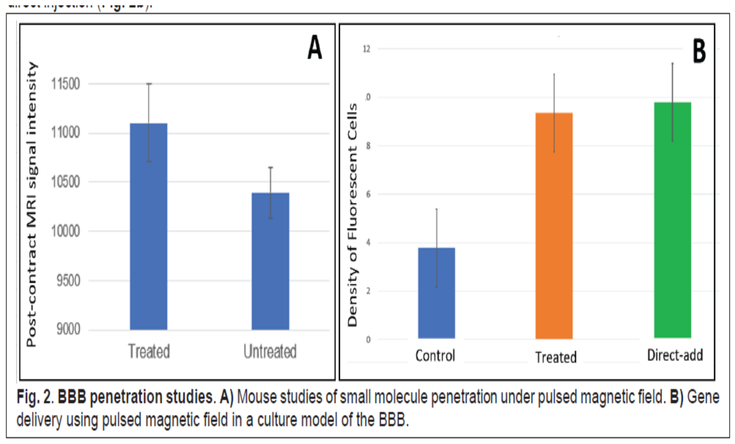
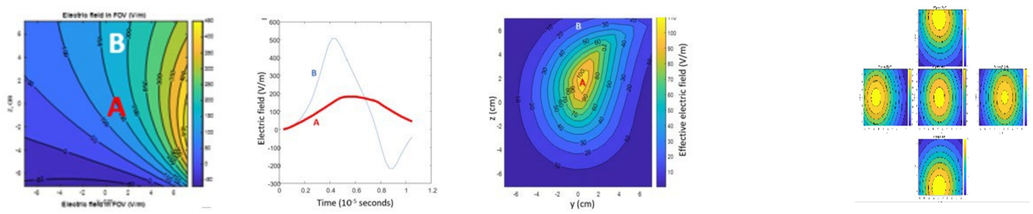


Fig. 2. BBB penetration studies. A) Mouse studies of small molecule penetration under pulsed magnetic field. **B)** Gene delivery using pulsed magnetic field in a culture model of the BBB.

The EPMMs provided magnetic resonance images of a phantom with 2-mm spatial resolution The ability of phased EPMM activation to implement bi-phasic electric pulses at some locations and mono-phasic pulses at other locations was simulated to explore the capability of differentially exciting neurons according to the MRI-derived anatomic brain maps. The simulations of tract-based TMS delivery suggest that neuromodulation of entire tracts can be done anywhere in the human head.



Discussion

A compact mobile or office-based MRI-TMS system would be capable of delivering neuromodulation to specific brain tracts, with personalized treatment enabled by built-in magnetic resonance tractography.