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Magnetothermal nanoparticle technology alleviates parkinsonian-like symptoms in mice

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Abstract

Deep brain stimulation (DBS) has long been used to alleviate symptoms in patients suffering from psychiatric and neurological disorders through stereotactically implanted electrodes that deliver current to subcortical structures via wired pacemakers. The application of DBS to modulate neural circuits is, however, hampered by its mechanical invasiveness and the use of chronically implanted leads, which poses a risk for hardware failure, hemorrhage, and infection. Here, we demonstrate that a wireless magnetothermal approach to DBS (mDBS) can provide similar therapeutic benefits in two mouse models of Parkinson's disease, the bilateral 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and in the unilateral 6-hydroxydopamine (6-OHDA) model. We show magnetothermal neuromodulation in untethered moving mice through the activation of the heat-sensitive capsaicin receptor (transient receptor potential cation channel subfamily V member 1, TRPV1) by synthetic magnetic nanoparticles. When exposed to an alternating magnetic field, the nanoparticles dissipate heat, which triggers reversible firing of TRPV1-expressing neurons. We found that mDBS in the subthalamic nucleus (STN) enables remote modulation of motor behavior in healthy mice. Moreover, mDBS of the STN reversed the motor deficits in a mild and severe parkinsonian model. Consequently, this approach is able to activate deep-brain circuits without the need for permanently implanted hardware and connectors.

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Figures

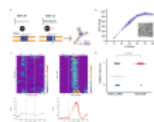


Fig. 1. In vitro magnetothermal control. A ...

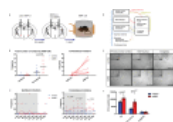


Fig. 2. Remote magnetothermal neuromodulation of

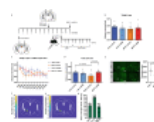


Fig. 3. Magnetothermal STN DBS alleviates mild...

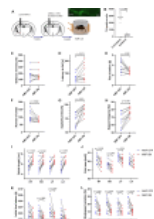


Fig. 4. Magnetothermal STN DBS alleviates severe...

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