Remote Electromagnetic Control of Neural Activity for Treatment of Parkinsons Disease

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Country

USA

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Remote Electromagnetic Control of Neural Activity for Treatment of Parkinsons Disease

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NIH (NINDS)

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5

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Electromagnetics, neuroregulation, Ferritin, TRPV1 gene, Parkinson Disease

Research Abstract

Project Summary In this collaborative and interdisciplinary application, we propose to develop further a novel non-invasive method for cell regulation (NICR) that is suitable for preclinical

proof of concept studies. This technology potentially could be used to treat neurologic diseases and provide a less invasive alternative to deep brain stimulation (DBS) or optogenetics. We thus propose to refine the technology and develop a prototype device to test the use of NICR for the treatment of symptoms of Parkinson's Disease (PD) in mice. Cell activity is controlled by two components; the iron binding ferritin protein that spontaneously forms 5 nm iron nanoparticles and TRPV1, a temperature and mechano-sensitive channel. By tethering ferritin to TRPV1, one can gate the channel with radiofrequency (RF) (which heat or induce mechanical motion of ferritin) or a magnet (which induces motion). The method has been shown to be capable of controlling neural activity in vitro and in vivo, the latter by increasing neural firing. In addition, we have introduced a mutation into TRPV1 that converts it into a chloride channel, and the use of the mutant channel makes it possible to inhibit neural activity using electromagnetic waves (e.g., RF). Because the system is genetically encoded, one can regulate the activity of cells into which the two protein components of the system have been delivered by recombinant Adeno-Associated Virus (AAV) strains. AAV has been used in numerous human studies including patients with PD. Thus NICR could provide a less invasive alternative to implanted electrodes (DBS) or implanted light devices (optogenetics) for the modulation of neural activity (deep brain stimulation) and also be used to simultaneously control several different nodes in a neural circuit. In this application, we propose a set of preclinical proof-of-concept studies for the treatment of PD including: 1) refinement of the technology to improve its efficiency and to create suitable AAV strains to ameliorate the symptoms of PD. We also propose to increase the sensitivity of the system by using channels that can be gated with lower field strength and by identifying variants of ferritin with enhanced sensitivity to an electromagnetic field; 2) development of a prototype device that would create local electromagnetic fields of suitable strength with the aim of enabling the use of the method in routine laboratory settings and ultimately as a portable/wearable device; 3) testing the ability of the improved method and suitable instrumentation to alleviate the symptoms of PD in mice; and 4) creating knockin mice with cre dependent expression of the constructs to assess the safety of long term TRPV1 and ferritin expression. The validation of this technology could also lead to its use for the treatment of other diseases at sites within and outside the nervous system to either increase or decrease cell activity or regulate protein production. Finally, the further development of NICR could impact basic research by allowing the non-invasive activation or inhibition of cells by simply mating genetically modified mice and exposing them to RF or magnetic fields.

Lay Summary
Project Narrative We have developed a new method, Nanoparticle Induced Cell Regulation (NICR), that enables remote activation or inhibition of cells using radio waves or a magnet. We propose to further develop the technology and fabricate a suitable device to enable preclinical proof of concept studies of the efficacy of NICR for treating Parkinson's disease. We will also develop mouse strains that will allow us to assess the safety of the method and enable the application of the method in standard laboratory settings.

Further information available at:

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United States of America

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Parkinson's disease & PD-related disorders

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