Abstract of a PhD Dissertation

Deep Brain Stimulation: Neurosurgical Advancement and Study of Mechanism Using 7.0 Tesla MRI in Humans and Molecular Neuroimaging in Animal Models.

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Deep brain stimulation (DBS) is an emerging neurosurgical technique for several neuropathologies, particularly Parkinson's disease (PD). In spite of its well-established clinical efficacy, however, the mechanism underlying DBS remains poorly understood. Furthermore, from a practical perspective relating to DBS implantations, it is difficult to precisely target electrodes due to an insufficient resolution necessary to accurately delineate the desired deep brain target nuclei. This often leads to indirect approximations of stereotactic targets. This increases the difficulty of studying and understanding how DBS works.

With the recent development of ultra high field (UHF) MRI, such as 7.0 Tesla (T) MRI, it is now possible to acquire ultra-high resolution *in vivo* images of the human anatomy. This facilitates a direct visualization of detailed structures, and thereby allows us to enhance diagnostic and surgical accuracy. Additionally, most recently, high-resolution functional neuroimaging techniques, such as microPET and voltammetry, have become available for visualizing the brain activities, including global energy metabolism change and neurotransmitter release, in small animals.

The present study was designed to improve neurosurgical methods using UHF 7.0 T MRI by substantially enhancing resolution and sensitivity as well contrast, thereby enabling identification of target nuclei, such as the subthalamic nucleus (STN), and the application of direct targeting.

We also performed *in vivo* neuroimaging studies in order to understand the DBS mechanism. Using this knowledge as a framework, we then explored a specific hypothesis regarding DBS of the STN for the treatment of PD. This hypothesis states that therapeutic benefit is achieved, at least in part, by activation of surviving nigrostriatal dopaminergic neurons, subsequent striatal dopamine release, and resumption of striatal target cell control by dopamine.

We envisage that direct visualization, or the possibility of direct targeting of electrodes onto the target nuclei, will not only be beneficial during operations

but will also improve the treatment outcome and post-treatment management of DBS PD patients. We additionally propose that by understanding the mechanism of DBS, we will be able to improve existing technologies and develop new technologies to further advance this treatment approach.