Advanced Neuroimaging Techniques for Central Neuromodulation

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KEYWORDS

• Brain mapping • Deep brain stimulation (DBS) • fMRI • DTI • 7 T MRI • Functional imaging

KEY POINTS

- The world of modern neuroimaging has seen rapid advances in capability and efficiency, made possible by the ongoing accumulation of discoveries in computational and basic science research.
- Because of the successes of this field, structural and functional image techniques have become the preferred means of evaluating and framing information collected about the function, in vivo, of the human brain.
- Applying these methods to the clinical field of neurosurgery can confer a measure of certainty to surgical undertakings on our patients' brains.
- We must move away from earlier eras when clinical observations were linked with data derived from basic neuroanatomy or animal models, which have resulted in conflicts, competing hypotheses, and incomplete knowledge about the mechanism of deep brain stimulation and the diseases it is used to treat.
- Familiarity with the new perspectives provided by advanced imaging techniques can help achieve a deeper understanding of neurologic and psychiatric disorders and refine both medical and neuromodulatory therapies.

INTRODUCTION

Deep brain stimulation (DBS) has become standard in the treatment paradigm of medically refractory movement disorders. Its efficacy has been proved not only for Parkinson disease (PD) but also for essential tremor and dystonia.[1–5] The remarkable effects produced by DBS on quality of life and motor function as well as its reversibility, and personalization of stimulation, have encouraged exploration of DBS as a treatment of other neurologic conditions such as psychiatric disorders, Alzheimer disease, chronic pain, refractory epilepsy, obesity, and addiction.[6–12]

Contemporary central neuromodulation has continually evolved from the foundation created by stereotactic neurosurgery for lesioning in the mid-twentieth century.[13] Techniques developed during that time, such as ventriculographic guidance and Talairach proportions, were considered the gold standard until the mid-1990s, when the advent of multimodality imaging such as computed tomography (CT) and magnetic resonance imaging (MRI) afforded millimetric precision, and obviated painful and variable contrast ventriculography.[14] This was the birth of direct targeting, which is one of 3 means of target identification and verification used in current practice. The

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second means of target verification is indirect targeting, in which each subcortical target has standardized atlas-based coordinates relative to the anterior commissure (AC) and posterior commissure (PC). The most commonly used systems are the Talairach coordinate system published in 1988 from the analysis of 1 brain and the stereotactic atlas developed in 1977 by Schaltenbrand and Wahren, which consists of photographs of microscopic sections of 2 cadaveric brains sliced with reference to the AC-PC planes.[15,16] After optimizing direct and indirect modalities, verification of the target occurs with microelectrode recording (MER), a technique described in 1961 by Albe-Fessard and colleagues,[17] and intraoperative stimulation testing.

Many studies over the past several decades have focused on validating the data used in the creation of such print atlases, and suggesting methods to improve, modify, and integrate both structural and functional data to facilitate multimodal mapping, as was the intention of Schaltenbrand and colleagues.[15,18,19] Although such population-based atlases have their place in the anatomic identification of targets and surrounding structures, they are useful only for a subset of patients, and inadequately address the well-documented problem of interindividual structure and functional variability of subcortical targets.[20–25] Advances in MRI technology and availability have helped to expose these differences. A study published in 2009 looking at the variability of subthalamic nucleus (STN) in patients with PD found that the MRI-derived position, size, and shape for the STN was statistically different compared with the Schaltenbrand and Wahren atlas coordinates.[25] These individual differences have been highlighted in many studies over the past decade.[26–29] Richter and colleagues[27] compared the position of STN borders on MRI with the atlases of Talairach and Tournoux and Schaltenbrand and Wahren and found that the lateral border on MRI was 3.1 mm more medial than predicted, and the position of the anterior border was 7.8 cm more posterior on MRI than was shown in the atlases. These positional differences are clinically significant because they are of a similar order of magnitude to the nucleus itself. The clinical impact of these differences is highlighted in the 2008 study by Patel and colleagues,[26] who reported that targeting STN based on atlas-based coordinates results in failure to identify the nucleus in 55% of initial MER passes.

The challenge of targeting is even more significant when trying to target certain subregions of the STN. An anteromedially placed electrode within the STN has been attributed to the emotional and cognitive side effects often seen with this target.[30,31] The optimal position for efficacy in PD is reported to be in the lateral anterodorsal portion of the STN.[32] Other reports describing efficacy have provided conflicting information as to the optimal location of stimulating electrodes within a scalable atlas of the STN.[33] Adding to the difficulty in optimal electrode placement within the STN is the limitation of standard 1.5-T MRI to reliably identify the nucleus, because its borders can often blend into the substantia nigra (SN).[27]

Such variability is even more profound in context of inconsistencies caused by aging, disease, sex, and handedness. In addition to these factors, there are potential influences of variances introduced by neurologic and psychiatric diseases such as depression, psychosis, and dementia, which are particularly relevant to the population of patients with DBS.[34–38] The presence of ventricular enlargement is commonly observed in such neurodegenerative and psychiatric conditions. The individual structural and functional variations in cortical and subcortical structures underscore the limitations of the existing anatomic atlases used in DBS targeting. Advances in neuroimaging modalities can provide a patient-specific solution for the lack of comprehensive targeting strategies.[20–22,24]

NEUROIMAGING TECHNIQUES

The gold standard for present-day DBS surgery remains a combination of indirect and direct targeting and MER. In keeping the techniques of the past, the long-standing controversy remains that has surrounded the imprecision of stereotactic surgery since its inception.[19,39] Although these techniques are certainly valid and account for the success of this therapy to date, they are limited in their ability to provide patient-specific details of subcortical targets, thus representing a potential limitation of current therapeutic strategies and thereby compromising, in part, the goal of DBS surgery: to provide excellent clinical outcomes with the lowest stimulation power required. Advances in neuroimaging techniques have already revolutionized the practice of medicine and are vital to the modernization of central neuromodulation by providing personalized target identification, segmentation of target subregions for network modulation, and understanding the mechanism of DBS and the diseases it treats. These advances include improvements in structural imaging capabilities with ultrahigh field (7-T) MRI for improved resolution and contrast for direct targeting, diffusion tensor imaging (DTI) to characterize and reconstruct white matter tracts surrounding