Posterolateral Trajectories Favor a Longer Motor Domain in Subthalamic Nucleus Deep Brain Stimulation for Parkinson Disease

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■ OBJECTIVE: **The clinical outcome of patients with Parkinson disease (PD) who undergo subthalamic nucleus (STN) deep brain stimulation (DBS) is, in part, determined by the length of the electrode trajectory through the motor STN domain, the dorsolateral oscillatory region (DLOR). Trajectory length has been found to correlate with the stimulation-related improvement in patients' motor function (estimated by part III of the United Parkinson's Disease Rating Scale [UPDRS]). Therefore, it seems that ideally trajectories should have maximal DLOR length.**

■ METHODS: **We retrospectively studied the influence of various anatomic aspects of the brains of patients with PD and the geometry of trajectories planned on the length of the DLOR and STN recorded during DBS surgery. We examined 212 trajectories and 424 microelectrode recording tracks in 115 patients operated on in our center between 2010 and 2015.**

■ RESULTS: **We found a strong correlation between the length of the recorded DLOR and STN. Trajectories that were more lateral and/or posterior in orientation had a longer STN and DLOR pass, although the DLOR/STN fraction length remained constant. The STN target was more lateral when the third ventricle was wider, and the latter correlated with older age and male gender.**

■ CONCLUSIONS: **Trajectory angles correlate with the recorded STN and DLOR lengths, and should be altered toward a more posterolateral angle in older patients and atrophied brains to compensate for the changes in STN location and geometry. These fine adjustments should yield a longer motor domain pass, thereby improving the patient's predicted outcome.**

INTRODUCTION

It is generally accepted that precise lead location in subthalamic nucleus (STN) deep brain stimulation (DBS) determines motor outcome in patients with Parkinson disease (PD)[1] as validated by improvement in the United Parkinson's Disease Rating Scale (UPDRS) part III (motor) score.[2] The optimal STN target is a subject of unresolved controversy.[3] Although most centers target the dorsal motor part of the STN, some aim to different targets, including extra-STN areas, such as the zona incerta.[4-6] Therefore, it should come as little surprise that several studies have failed to find an association between changes in UPDRS scores and target coordinates.[7] Other studies have shown a strong association between UPDRS scores and beta band oscillatory activity in the STN dorsolateral oscillatory region (DLOR).[8,9] Therefore, the DLOR area, representing the

Key words
- Beta oscillations
- DBS
- Local field potential
- Parkinson disease
- STN
- Trajectory

Abbreviations and Acronyms
%DLOR: the fraction of the DLOR length out of STN length
3D: Three-dimensional
AC: Anterior commissure
DBS: Deep brain stimulation
DLOR: Dorsolateral oscillatory region
MCP: Midcommissural point
MER: Microelectrode recording
MRI: Magnetic resonance imaging
PC: Posterior commissure
PD: Parkinson disease
STN: Subthalamic nucleus
UPDRS: United Parkinson's Disease Rating Scale

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motor subdivision of the STN, is believed to be the preferred target for DBS implantation.[10,11]

By this reasoning, directing implantation of the lead contacts to the longest recordable DLOR should be a central operative objective. Anatomic magnetic resonance imaging (MRI) used for preoperative target and trajectory planning as well as diffusion tensor imaging protocols are not yet routinely capable of differentiating between subterritories of the STN.[12,13] Therefore, microelectrode recording (MER) is still the only method to accurately detect and validate the DLOR target, thus avoiding suboptimal clinical results.

Factors affecting STN targeting are believed to include variable target selection between different neurosurgeons,[3] effects of anesthesia on STN MER,[14-16] the type of imaging used for preoperative planning of target and trajectory,[17-20] and awake MER-guided versus asleep intraoperative MRI-guided DBS implantation.[21-23] Some studies have discussed trajectory planning in the context of adverse effects,[24-26] as a result of proximity to blood vessels, eloquent brain areas and the ventricles, and others have discussed trajectory planning for DBS targets other than the STN, such as globus pallidum internus[27] and ventralis intermedius nucleus.[28] However, none of these studies has investigated the effects of patient-specific characteristics on STN geometry as shown by intraoperative STN physiologic recordings.

The STN, first characterized by Jules in 1865, is a lens-shaped diencephalic structure. It contains around 430,000 neurons, comprising a volume of 100–130 mm^3.[12] The STN lies between the zona incerta posterodorsally, the internal capsule laterally, and the substantia nigra anteroventrally. Its long axis extends from anterolateral (in its dorsal portion) to posteromedial (in its ventral portion). Despite its preserved anatomy across species, some variation in its postural angle is evident within and between patients.

Age has a particularly important effect on the anatomy of the STN in both healthy individuals as well as in patients with PD. The volume of the STN as well as its neuronal count decreases with age, with small variations between healthy human individuals.[12] The distance of the STN from the midsagittal plane increases with age, becoming more lateralized. The latter finding is observed in patients with PD as well as in healthy controls.[29]

In addition to age-related STN changes, other subcortical structures also tend to change morphometrically with age. These changes include decreased thalamic height and increased third ventricle width. In contrast, the anterior commissure (ACC)–posterior commissure (PC) length seems to be stable within various age groups.[30] All these anatomic alterations inevitably affect the way we target the STN and plan out trajectories. Intuitively, they should also have an effect on the recorded STN length and may have an effect on DLOR length as well. Brain atlases (Schaltenbrand-Wahren and Schaltenbrand-Bailey) that were based on a limited, nondiverse patient population, and are still being used for indirect targeting by some centers, should be viewed as inherently inaccurate.

Driven by the finding that STN beta activity is directly correlated with the clinical outcome of patients with PD undergoing STN DBS,[8] and by a recent case report that indicated a dramatic effect of trajectory angles on the side effect profile of STN DBS,[24] we investigated the possible contribution of patient-specific demographic and anatomic factors on intraoperative STN physiology. We studied the contribution of 3 groups of factors: 1) demographic (patients' age, gender, and PD duration); 2) anatomic (third ventricle length [AC-PC length], third ventricle width [both maximal width and width at midcommissural point (MCP)], and laterality [right versus left hemisphere, and first versus second operated side]); and 3) trajectory-related (anteroposterior [ring] and mediolateral [arc] trajectory angles used to target the STN, and microelectrode location [relative to the Microdrive BenGun central track]).

METHODS

Data Collection

This study was authorized and supervised by the institutional review board of Hadassah Medical Center (reference code 0168-10-HMO). The charts and operative reports of all patients with PD who had undergone STN DBS at the Hadassah Hebrew University Medical Center in 2010–2015 were retrospectively reviewed. All patients signed informed consent and release forms for participating in studies that included analysis of data related to their clinical records and MERs.

Overall, 115 patient data sets were included in this study. Most patients were implanted bilaterally, usually both sides in the same session or in some cases as a staged procedure. Trajectory was defined as a single pass to the target, having a specific set of trajectory angles (arc and ring). Routinely, we use 2 microelectrodes in the microdrive BenGun (AlphaOmega Engineering; Nazareth, Israel), thus all trajectories had 2 MER data sets: one located centrally in the BenGun, and the other being either anterior (ventral) or posterior (dorsal) to the central microelectrode. Most patients had 1 pass to each brain target (right or left). However, a few patients required a second pass, because of unsatisfactory MERs or clinical response to macrostimulation in the first. In these cases, a new set of trajectory angles might be used. Overall, 212 trajectories and 424 MER tracks were included in our data analysis.

DBS Surgery and MER

Surgery and MER techniques used are similar to those previously reported.[31] Stereotactic localization was performed based on fusion of preoperative MRI (either 1.5-T or 3-T axial and coronal slices using 2 × 0.4 × 0.4 mm isotropic T1-weighted and T2-weighted magnetic resonance sequences) and stereotactic computed tomography (performed on the morning of surgery, after fixation of a Cosman Robert Wells stereotactic frame [Radionics, Burlington, Massachusetts, USA]), using Framelink 5 software (Medtronic, Minneapolis, Minnesota, USA).

STN target coordinates were chosen based on direct visualization on the T2 MRI (targeting for the posterior dorsolateral STN). Trajectories were planned to avoid penetrating sulci, ventricles, blood vessels (as seen in T1 MRI with contrast media) and also eloquent brain areas. In some cases, trajectory angles were slightly modified during surgery, because of cortical blood vessels. Both the preoperative targeting coordinates and MER-defined STN borders used in the analysis were those originally used for planning and treatment and thus were blind to the goals of this study.