Intraoperative microelectrode recording (MER) for targeting during deep brain stimulation (DBS) procedures

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Bejjani BP, Dormont D, and B. Pidoux (2000) reported bilateral subthalamic stimulation for Parkinson's disease by using three-dimensional stereotactic magnetic resonance imaging and electrophysiological guidance. Several methods are used for stereotactically guided implantation of electrodes into the subthalamic nucleus (STN) for continuous high-frequency stimulation in the treatment of Parkinson's disease (PD). The authors present a stereotactic magnetic resonance (MR) method relying on three-dimensional (3D) T1-weighted images for surgical planning and multiplanar T2-weighted images for direct visualization of the STN, coupled with electrophysiological recording and stimulation guidance.

Gross RE, Krack P, Rodriguez-Oroz MC, et al. (2005) performed a review of electrophysiological mapping for the implantation of deep brain stimulators for Parkinson's disease and tremor.
The vast majority of centers use electrophysiological mapping techniques to finalize target selection during the implantation of deep brain stimulation (DBS) leads for the treatment of Parkinson's disease and tremor. The review discusses the techniques used for physiological mapping and addresses the questions of how various mapping strategies modify target selection and outcome following subthalamic nucleus (STN), globus pallidus internus (GPi), and ventralis intermedius (Vim) deep brain stimulation. Mapping strategies vary greatly across centers, but can be broadly categorized into those that use microelectrode or semi microelectrode techniques to optimize position prior to implantation and macrostimulation through a macro electrode or the DBS lead, and those that rely solely on macrostimulation and its threshold for clinical effects (benefits and side effects). Microelectrode criteria for implantation into the STN or GPi include length of the nucleus recorded, presence of movement-responsive neurons, and/or distance from the borders with adjacent structures. However, the threshold for the production of clinical benefits relative to side effects is, in most centers, the final, and sometimes only, determinant of DBS electrode position. Macrostimulation techniques for mapping, the utility of microelectrode mapping is reflected in its modification of electrode position in 17% to 87% of patients undergoing STN DBS, with average target adjustments of 1 to 4 mm. Nevertheless, with the absence of class I data, and in consideration of the large number of variables that impact clinical outcome, it is not possible to conclude that one technique is superior to the other in so far as motor Unified Parkinson's Disease Rating Scale outcome is concerned. Moreover, mapping technique is only one out of many variables that determine the outcome. The increase in surgical risk of intracranial hemorrhage correlated to the number of microelectrode trajectories must be considered against the risk of suboptimal benefits related to omission of this technique.

A discrepancy between the final physiological target after micro recording and the target chosen by MRI can help to reach the surgical target leading to the best clinical outcome. Such discrepancy was assessed by Guridi J, Rodríguez-Oroz MC, and Ramos E. (2002).
Thirty patients with PD and motor complications were operated with stereotactic surgery by MRI and micro recording. In 19 patients, the target chosen was the subthalamic nucleus (STN) and in 11 others the target was globus pallidus internus (GPi). In this work it is considered that the electrode has a current field below usual parameters of 1.5 mm radius. Consequently, when the distance error between the final

physiological target and the MRI target, is between 1.5 and 3 mm was considered as partial discrepancy and distances of 3 mm or more were considered as total discrepancy.
Partial discrepancy for STN and GPi were in 25 and 33% of the cases respectively and total discrepancy was 57 and 42% for each nucleus. The average distance error between both targets, final and image, for X stereotactic coordinate (mediolateral distance) was 1.54 mm for STN and 0.8 mm for GPi. The average distance for Y coordinate (anteroposterior distance) was 2.3 mm for STN and 2.2 mm for GPi.
There is a significant discrepancy between the final physiological target after micro recording and the target chosen by MRI during surgery for alleviating PD that may induce variations or absence of clinical efficacy in parkinsonian patients submitted to the DBS surgery. Authors suggest the necessity of the microelectrode recording in order to reach the surgical target with the best clinical condition.

More recently, there is a growing need for accurate localization of the optimal targets in functional neurosurgery. Since deep brain stimulation (DBS) of the Vim thalamic nucleus has been proposed for the treatment of Parkinson's disease, the target has evolved toward the globus pallidus and subthalamic nucleus (STN) and the therapeutic indications have enlarged to include psychiatric disorders such as Tourette syndrome, obsessive compulsive disorders and depression. In these pathologies, the target has been restrained to smaller functional sub territories (G Alexander and M Crutcher, 1990) of the basal ganglia, requiring more refined techniques to localize smaller and smaller brain regions, often invisible in routine clinical MRI. Different strategies have been developed to identify such deep brain targets. Direct methods can identify structures in the MRI itself, but only the larger ones. Indirect methods are based on the use of anatomical atlases. Bardinet E, Bhattacharjee M, D. Dormont et al. (2009) described a tri dimensional histological atlas coupled to the MRI of the same brain specimen using deformation methodology to fit the atlas toward the brain of any given patient.
Magnetic resonance images of the brain specimen were obtained before extraction from the skull and histological processing. Adaptation of the atlas to individual patient anatomy was performed by reshaping the atlas MR images to the images obtained in the individual patient using a hierarchical registration applied to a region of interest centered on the basal ganglia, and then applying the reshaping matrix to the atlas surfaces.
Results were evaluated by direct visual inspection of the structures visible on MR images and atlas anatomy, by comparison with electrophysiological intraoperative data, and with previous atlas studies in patients with Parkinson disease. The method was both robust and accurate, never failing to provide an anatomically reliable atlas to patient registration. The registration obtained did not exceed a 1-mm mismatch with the electrophysiological signatures in the region of the subthalamic nucleus.

Li XY, Zhuang P, Li YJ. Zhonghua and Yi Xue Za Zhi (2008) explored the patterns of neuronal activity in the basal ganglia nucleus in parkinsonian patients with levodopa-induced dyskinesia (LID).
Sixteen idiopathic parkinsonian patients, 11 males and 5 female: 5; aged 56.1 +/- 11.9, with the mean disease duration of (10.1 +/- 6.6). years and Hoehn & Yahr score ranging 2 -4, all with the symptoms of tremor, rigidity, and bradykinesia, 8 with severe LID [with the mean unified Parkinson's disease rating scale (UPDRS) IV score of 6.8 +/- 1.5] underwent pallidotomy (n = 8) or subthalamic nucleus (STN) deep brain stimulation (DBS) implantation (6 bilaterally and 2 unilaterally). Microrecording was performed in the globus pallidus internus (GPi) and STN. Electromyogram (EMG) on the contralateral limbs to surgery was simultaneously recorded. Single unit analysis was performed. The interspike interval (ISI) and coefficient of variation (CV) of ISI were calculated. One-way ANOVA and rank test were employed to compare the ISI and CV among the patients.
Two hundred and thirty-eight neurons were identified from the GPi (n = 8) and STN (n = 14). 22.6% of them were tremor-related neurons, 33.8% were rapid tonic neuronal activity-related, and 29.0% were

irregular neuronal activity-related. It was discovered that 8. 0% of the neurons from GPi and STN were with grouped discharge following long period pause with the CV of 87 +/- 0.55, and 7.5% of the neurons were with low frequency firing with the mean frequency of (17.7 +/- 5.9) Hz. ANOVA revealed that in the STN the CV of the neurons with irregular with grouped discharge was significantly higher than those of the neurons with irregular neuronal activity and with low frequency firing (both $P < 0.05$), the ISI of the neurons with irregular grouped discharge was significantly higher than that of the neurons with low frequency firing and significantly higher than that of the neurons irregular neuronal activity (both $P < 0.05$); and in the GPi the CV of the neurons with irregular grouped discharge was significantly lower than those of the neurons with irregular neuronal activity and those with low frequency firing and the ISI of the neurons with irregular grouped discharge was significantly higher than those of the other groups (all $P < 0.05$). Chi square test showed that majority of the neurons with grouped discharge and neurons with low frequency firing mainly existed in the GPi and STN of the PD patients with LID (all $P < 0.05$).
The altered neuronal activity in the basal ganglia nucleus of GPi and STN plays an important role in the pathophysiology of PD and LID.

Welter ML, P. Burbaud et al. (2011) found that subthalamic neuronal activity correlates with symptoms severity and predicts high-frequency stimulation efficacy. Functional and connectivity changes in corticostriatal systems have been reported in the brains of patients with obsessive-compulsive disorder (OCD); however, the relationship between basal ganglia activity and OCD severity has never been adequately established. It was recently showed that deep brain stimulation of the subthalamic nucleus (STN), a central basal ganglia nucleus, improves OCD. Here, single-unit subthalamic neuronal activity was analyzed in 12 OCD patients, in relation to the severity of obsessions and compulsions and response to STN stimulation, and compared with that obtained in 12 patients with Parkinson's disease (PD). STN neurons in OCD patients had lower discharge frequency than those in PD patients, with a similar proportion of burst-type activity (69 vs 67%). Oscillatory activity was present in 46 and 68% of neurons in OCD and PD patients, respectively, predominantly in the low-frequency band (1-8 Hz). In OCD patients, the bursty and oscillatory subthalamic neuronal activity was mainly located in the associative-limbic part. Both OCD severity and clinical improvement following STN stimulation were related to the STN neuronal activity. In patients with the most severe OCD, STN neurons exhibited bursts with shorter duration and interburst interval, but higher intraburst frequency, and more oscillations in the low-frequency bands. In patients with best clinical outcome with STN stimulation, STN neurons displayed higher mean discharge, burst and intraburst frequencies, and lower interburst interval. These findings are consistent with the hypothesis of a dysfunction in the associative-limbic subdivision of the basal ganglia circuitry in OCD's pathophysiology.

Welter ML, Schüpbach M, Czernecki V, et al. (2014) compared locations of therapeutic contacts with 1-year motor, cognitive, and psychiatric outcomes, preoperative PD clinical features, MRI measures and surgical procedure in order to determine optimal target localization for subthalamic stimulation in patients with Parkinson disease. From a cohort of 309 patients with PD who underwent DBS-STN between 1996 and 2009 pre- and postoperative results were obtained in 262 patients with PD.
The best motor outcome was obtained when stimulating contacts were located within the STN as compared with the zona incerta (64% vs 49% improvement). Eighteen percent of the patients presented a postoperative cognitive decline, which was found to be principally related to the surgical procedure. Other factors predictive of poor cognitive outcome were perioperative confusion and psychosis. Nineteen patients showed a stimulation-induced hypomania, which was related to both the form of the disease (younger age, shorter disease duration, higher levodopa responsiveness) and the ventral contact

location. Postoperative depression was more frequent in patients already showing preoperative depressive and/or residual axial motor symptoms.
Conclusion: In this homogeneous cohort of patients with PD, this study showed that (1) the STN is the best target to improve motor symptoms, (2) postoperative cognitive deficit is mainly related to the surgery itself, and (3) stimulation-induced hypomania is related to a combination of both the disease characteristics and a more ventral STN location.

Bour LJ, Contarino MF, Foncke EM et al. (2010) investigated long-term experience with intraoperative micro recording during DBS neurosurgery in STN and GPi. Intraoperative microelectrode recording (MER) for targeting during deep brain stimulation (DBS) procedures has been evaluated over a period of 4 years, in 57 consecutive patients with Parkinson's disease, who received DBS in the subthalamic nucleus (STN-DBS), and 28 consecutive patients with either dystonia (23) or Parkinson's disease (five), in whom the internal segment of the globus pallidus (GPi-DBS) was targeted.
The procedure for DBS was a one-stage bilateral stereotactic approach using a combined electrode for both MER and macrostimulation. Up to five micro/macro-electrodes were used in an array with a central, lateral, medial, anterior, and posterior position. Final target location was based on intraoperative test stimulation.
For the STN, the central trajectory was chosen for implantation in 50% of the cases and for the globus pallidus internus (GPi) in 57% of the cases. Furthermore, in 64% of the cases, the channel selected for the permanent electrode corresponded with the trajectory having the longest segment of STN MER activity. For the GPi, this was the case in 61%. The mean and standard deviation of the deepest contact point with respect to the magnetic resonance imaging (MRI)-based target for the STN was 2.1 ± 1.5 mm and for the GPi was −0.5 ± 1.2 mm.
The author concluded that MER facilitates the selection of the final electrode location in STN-DBS and GPi-DBS, and based on the observed MER activity, a pre-selection could be made as to which channel would be the best candidate for macro-test stimulation and at which depth should be stimulated. The choice of the final location is based on intraoperative test stimulation, and it is demonstrated that regularly it is not the central channel that is chosen for implantation. On average, the target as defined by MER activity intensity was in accordance with the MRI-based targets both for the STN and GPi. However, the position of the best MER activity did not necessarily correlate with the locus that produced the most beneficial clinical response on macro electrode testing intra operatively.

Bibliography

-Bilateral subthalamic stimulation for Parkinson's disease by using three-dimensional stereotactic magnetic resonance imaging and electrophysiological guidance. Bejjani BP, Dormont D, Pidoux B, Yelnik J, Damier P, Arnulf I, Bonnet AM, Marsault C, Agid Y, Philippon J, Cornu P. J Neurosurg. 2000 Apr; 92(4):615-25.

-Retrospective cross-evaluation of an histological and deformable 3D atlas of the basal ganglia on series of Parkinsonian patients treated by deep brain stimulation. Bardinet E, Dormont D, Malandain G, Bhattacharjee M, Pidoux B, Saleh C, Cornu P, Ayache N, Agid Y, Yelnik J. Med Image Comput Assist Interv. 2005; 8(Pt 2):385-93.

-A three-dimensional, histological and deformable atlas of the human basal ganglia. I. Atlas construction based on immunohistochemical and MRI data. Yelnik J, Bardinet E, Dormont D, Malandain G, Ourselin S, Tandé D, Karachi C, Ayache N, Cornu P, Agid Y. Neuroimage. 2007 Jan 15; 34(2):618-38.

-A three-dimensional histological atlas of the human basal ganglia. II. Atlas deformation strategy and evaluation in deep brain stimulation for Parkinson disease. Bardinet E, Bhattacharjee M, Dormont D, Pidoux B, Malandain G, Schüpbach M, Ayache N, Cornu P, Agid Y, Yelnik J. J Neurosurg. 2009 Feb; 110(2):208-19.

-Functional architecture of basal ganglia circuits: neural substrates of parallel processing. G Alexander, M Crutcher. Trends Neurosci, 13 (1990), pp. 266–271

-Basal ganglia dysfunction in OCD: subthalamic neuronal activity correlates with symptoms severity and predicts high-frequency stimulation efficacy. Welter ML, Burbaud P, Fernandez-Vidal S, Bardinet E, Coste J, Piallat B, Borg M, Besnard S, Sauleau P, Devaux B, Pidoux B, Chaynes P, Tézenas du Montcel S, Bastian A, Langbour N, Teillant A, Haynes W, Yelnik J, Karachi C, Mallet L; French Stimulation dans Trouble Obsessionnel Compulsif (STOC) Study Group. Transl Psychiatry. 2011 May 3; 1:e5

-Optimal target localization for subthalamic stimulation in patients with Parkinson disease. Welter ML, Schüpbach M, Czernecki V, Karachi C, Fernandez-Vidal S, Golmard JL, Serra G, Navarro S, Welaratne A, Hartmann A, Mesnage V, Pineau F, Cornu P, Pidoux B, Worbe Y, Zikos P, Grabli D, Galanaud D, Bonnet AM, Belaid H, Dormont D, Vidailhet M, Mallet L, Houeto JL, Bardinet E, Yelnik J, Agid Y. Neurology. 2014 Apr 15; 82(15):1352-61.

-Electrophysiological mapping for the implantation of deep brain stimulators for Parkinson's disease and tremor. Gross RE, Krack P, Rodriguez-Oroz MC, Rezai AR, Benabid AL. Mov Disord. 2006 Jun; 21 Suppl 14:S259-83. Lancet. 2005 Oct 22-28; 366(9495):1420-2.

-Long-term experience with intraoperative microrecording during DBS neurosurgery in STN and GPi. Bour LJ1, Contarino MF, Foncke EM, de Bie RM, van den Munckhof P, Speelman JD, Schuurman PR. Acta Neurochir (Wien). 2010 Dec; 152(12):2069-77.

-[Patterns of neuronal activity in the basal ganglia nucleus in parkinsonian patients with levodopa-induced dyskinesia]. Li XY, Zhuang P, Li YJ. Zhonghua Yi Xue Za Zhi. 2008 Jun 17; 88(23):1607-12.

-[Discrepancy between imaging and neurophysiology in deep brain stimulation of medial pallidum and subthalamic nucleus in Parkinson's disease]. Guridi J, Rodríguez-Oroz MC, Ramos E, Linazasoro G, Obeso JA. Neurologia. 2002 Apr; 17(4):183-92.