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Probabilistic Mapping of the Effect of Deep Brain Stimulation in the Ventral Thalamus for Essential Tremor from Intraoperative Stimulation Data: a Proof of Concept.

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Background

Deep brain stimulation (DBS) is commonly used as a complement to medication in the management of symptoms of movement disorders such as Parkinson's disease (PD) and essential tremor (ET). Electrical stimulation is delivered in the brain via multi-contacts electrodes to structures of the basal ganglia. Stimulation tests during awake surgery allow to observe the symptomatic response. This approach has been the standard procedure for several decades, and generates large amount of data, with many contact positions and amplitudes tested. Most studies in the literature focus on analyzing data after surgery, which is less detailed in the spatial and stimulation amplitude dimensions.

We present a pipeline for creating probabilistic stimulation maps and exemplified it on the data from 6 essential tremor patients.

Material and Methods

The data from 19 patients (PD:13, ET:6) operated at the university hospital Clermont-Ferrand (France) who were implanted awake [1] with accelerometer-based [2] tremor recording was used in this work.

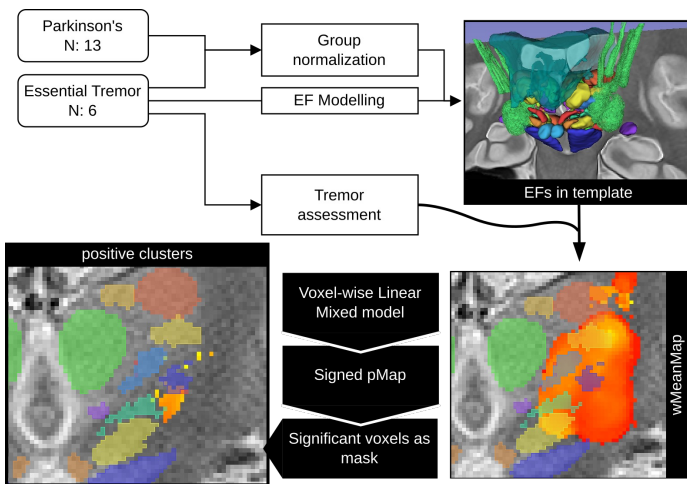


Figure 1: Probabilistic stimulation map workflow. The MRI data from all patients (PD and ET) was used for the creation of an anatomical template. The data from the 6 ET patients was used for EF simulations, and generation of the wMeanMap. In each voxel, a linear mixed model was then used to estimate the significance of the relation between EF norm and tremor improvement.

Group-Specific anatomical template:

- From all 19 patients (PD:13, ET:6)
- Iterative, non-linear registration [3]

Electric field simulations:

- patient-specific tissue conductivity derived from T1 MRI
- Finite element method, current conservation
- Activation variable: electric field norm (EF)
- EF resampled to rectilinear grid (0.5x0.5x0.5mm)

Tremor assessment:

- 3D acceleration sensor on contra-lateral wrist
- Metric: relative tremor suppression (%)

Normative analysis:

- EFs transformed to atlas space → many EF values for each voxel
- Average effect weighted by EF norm in each voxel → wMeanMap
- In each voxel: linear mixed model (LMM); tremor vs EF norm
- Significant voxels extracted, voxels with positive/negative slopes templates used. This was with only 6 patients but very dense data. With more patients, maps will more through validated dans used target prediction.

Verification:

- Comparison of tremor suppression predicted against actual
- Tremor suppression prediction: average of voxels from positive

significant cluster included in each EF (0.2V/mm threshold)

Linear regression between predicted and observed effect.

Comparison in left hemisphere with single cluster obtained by Nowacki [4] with dice overlap and distances between centers of mass of clusters.

Results

Positive clusters: taken at the largest section of the Vim, target for all 6 ET patients the map presents two clusters:

posterior subthalamic area (PSA)

at the junction between Vim, VO and VCM/VCL.

Mean tremor suppression scores are higher in the PSA cluster.

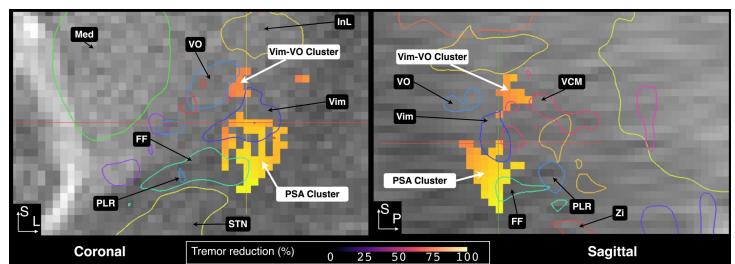
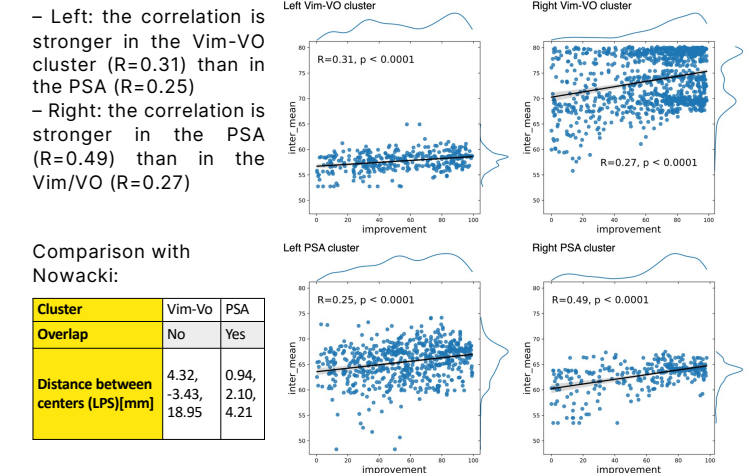


Figure 2: A. sagittal slice of the clusters significant for positive response to stimulation. B. 3D view of the positive (violet, black vertices) and negative (green, black vertices) clusters around Vim.

Verification:

Verification for the significant clusters are presented in Figure 3. On both sides, the linear regression for Vim-VO and PSA clusters result in significant correlation.



Comparison with Nowacki:

Cluster	Vim-Vo	PSA
Overlap	No	Yes
Distance between centers (LPS)[mm]	4.32,	0.94,
	-3.43,	2.10,
	18.95	4.21

Discussion

A group-specific workflow was implemented and allowed to identify the PSA and Vim/VO regions as positive clusters; these clusters allow to predict tremor suppression in the original data. Both clusters were compared to the cluster obtained in another study with post-operative simulation data and the PSA clusters are situated less than 5mm from each other. This difference is minimal and may be caused by the different anatomical templates used. This was with only 6 patients but very dense data. With more patients, maps will more through validated dans used target prediction.

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