OPTIMAL FUNCTIONAL CONNECTIVITY PROFILES IN SUBTHALAMIC DBS

Min Jae Kim[1], Clemens Neudorfer[2,3], Barbara Hollunder[3], Nanditha Rajamani[3], Konstantin Butenko[1], Garance Meyer[1], Ningfei Li[3], and Andreas Horn[1-3]

1. Department of Neurology, Brigham and Women's Hospital, Harvard Medical School, Boston, USA
2. Department of Neurosurgery, Massachusetts General Hospital, Harvard Medical School, Boston, USA
3. Movement Disorder and Neuromodulation Unit, Department of Neurology, Charité – Universitätsmedizin Berlin, Berlin, Germany

BACKGROUND

DBS network mapping is a technique that correlates whole-brain normative functional connectivity profiles seeding from DBS sites with clinical improvements. The result has often been reported in form of a map of optimal connectivity, expressed by voxel-wise correlation coefficients ("R-maps"),[1] and these maps have been reported across disorders such as Parkinson's Disease (PD),[2] Essential Tremor[3] and Obsessive Compulsive Disorder (OCD).[4] **However, given intrinsic correlational structures within the functional connectome of the human brain, it remains unclear how different the profiles of R-maps could theoretically be.** To probe how specific the results of DBS network mapping could potentially be for subthalamic DBS, we apply DBS network mapping to *synthetic data* that can systematically probe profiles for hypotherical optimal stimulation sites within the entire nucleus.

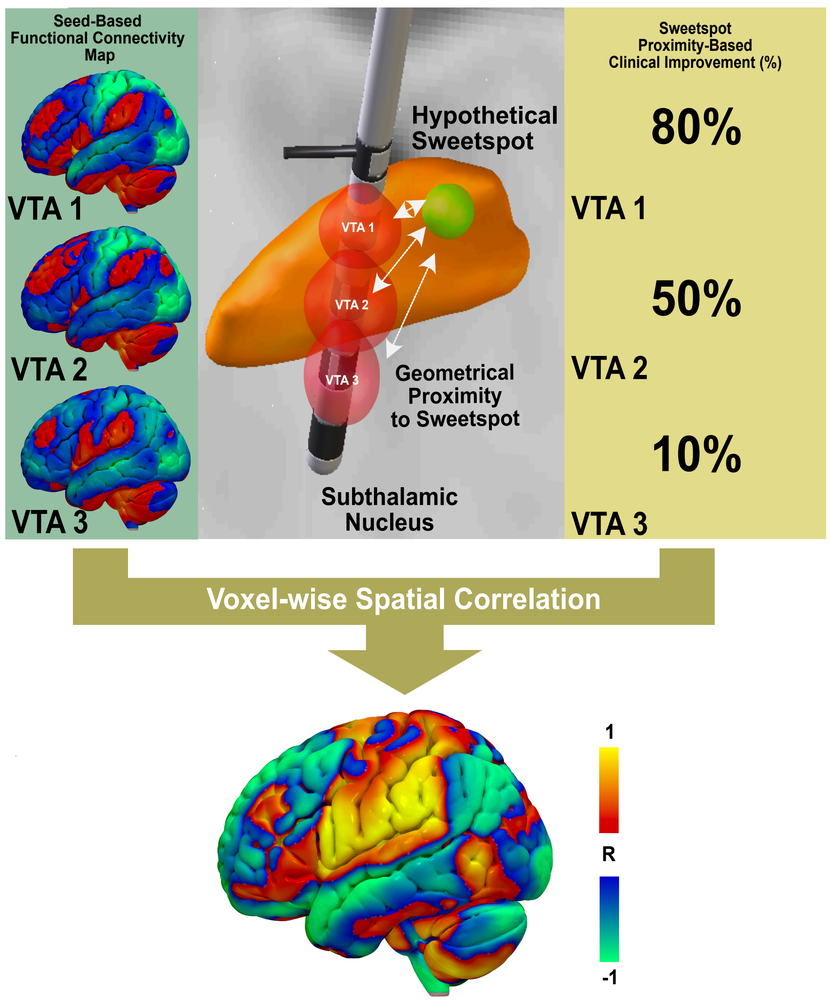

Figure 1. R-map Generation. **(1)** For a given hypothetical sweetspot, volumes of tissue activated (VTA) are generated based on activated DBS contact and stimulation parameters. **(2)** VTAs can further be used as a seed to produce functional connectivity (FC) "fingerprints". **(3)** Based on geometrical proximity of VTAs a clinical sweetspot, clinical improvement post-DBS can be assumed. **(4)** After performing voxel-wise spatial correlation with each FCs and improvement, R-map can be generated.

METHODS

250 synthetic volumes of tissue activated (VTA) and 1000 ground-truth spherical sweetspots were randomly and symmetrically generated across the bilateral STN. Iterating across sweetspots, based on the spatial overlap between each VTAs and the respective sweet spot, (synthetic) improvement scores were assigned to each synthetic VTA. Functional connectivity (FC) analysis was performed by seeding individual VTAs in the GSP1000 normative connectome, and R-maps were generated by correlating connectivity profiles with (synthetic) improvements.[2] This led to 1000 R-maps, each associated with one (synthetic) sweet-spot.

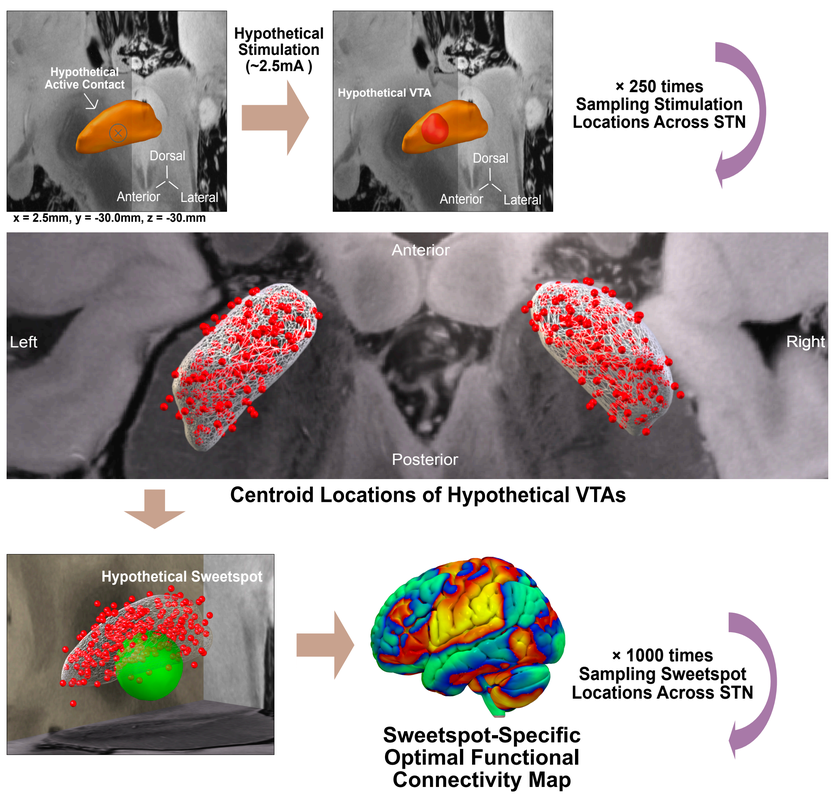

Figure 2. Methodology for Sweetspot-Specific R-map Generation. (A) 250 random coordinates in bilateral STN were sampled and seeded to produce 250 hypothetical VTAs (stimulation parameter: ~2.5 mA, 60μsec, 130 HZ) **(B)** 1000 random coordinates in bilateral STN were sampled and seeded to produce 1000 spherical hypothetical sweetspots (radius ~ 4.15mm, 2mm gaussian filter). For each sweetspot locations, R-maps were produced.

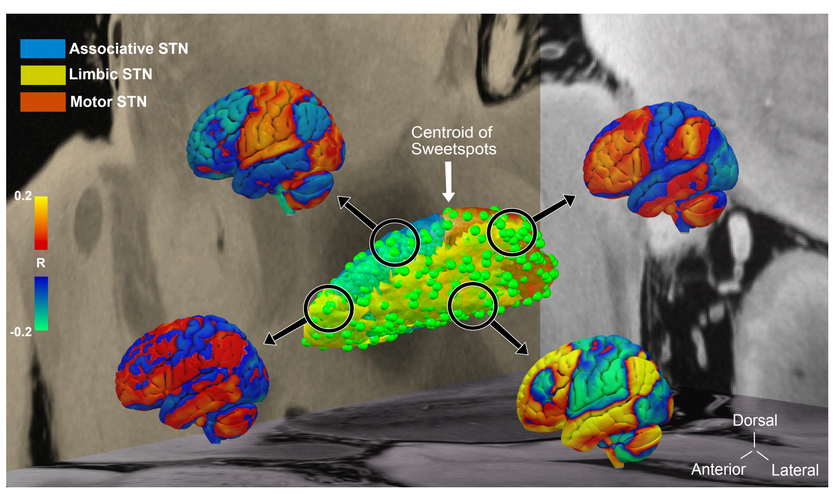

Figure 3. Sweetspot Centroid Locations and R-Maps. Centroids of 1000 randomly generated sweetspots (green) are visualized relative to STN subregions (associative, limbic, motor). R-maps produced from sweetspots sampled across different axis of STNs are shown.

RESULTS

1000 R-maps associated with each of 1000 sweetspots were subjected to a principal component analysis. Resulting principle components represent the potential 'connectivity landscape' that could result from any type of STN-DBS network mapping analysis (no matter which target, disease or clinical outcomes).

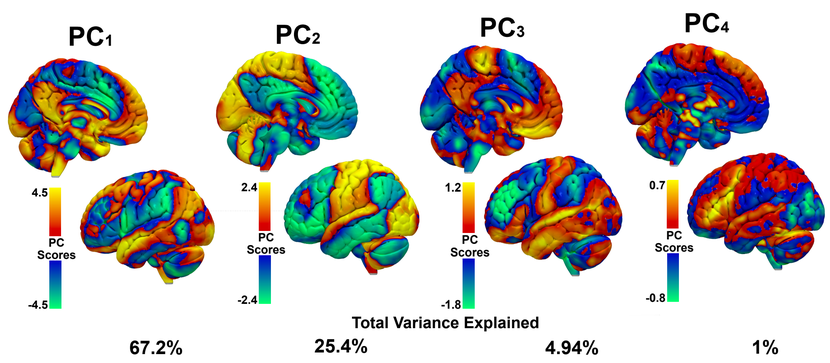

Figure 4. R-map Landscape of Subthalamic DBS Network Mapping. PCA analysis revealed four distinct patterns that could theoretically emerge from subthalamic DBS network mapping (no matter which target, disease or clinical outcomes).

With four PCs, 98.5% of the total variance across the 1000 R-maps could be explained (PC_1: 67.2%, PC_2: 25.4%, PC_3: 4.94%, PC_4: 1%).

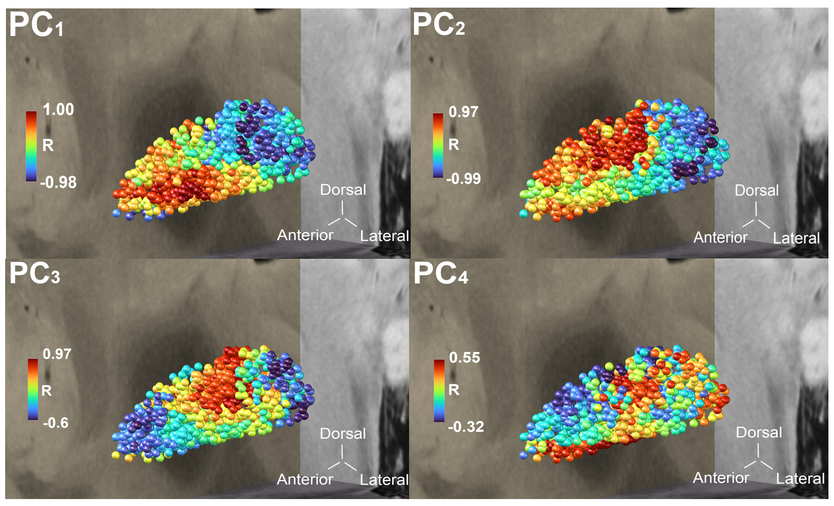

Figure 5. **Spatial Similarity of R-maps.** Each of 4 PC maps were spatially correlated with individual R-maps produced from 1000 sweetspots across the STN. Results highlight discrete regions in STN sharing similar characteristics with PC maps, and these regions altering from PC1 to PC4 maps.

Spatial correlation between PCs and 1000 R-maps revealed a spatio-topographic representation of PCs across the antero–posterior axis of the STN. PC_3 maximally pointed to the established stimulation site for PD, while PC_1 would best match the stimulation target for neuropsychiatric disorders such as OCD.

CONCLUSIONS

Based on synthetical modeling, DBS network mapping seems able to reveal only four different spatial maps, which were distributed across (synthetic) optimal stimulation sites along the anterior-posterior axis of the nucleus. Our results help identify potential patterns associated with responses from DBS to the subthalamic nucleus.

REFERENCES

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