



RETUNE CRC/TRR Initiative Berlin-Würzburg



#### International Graduate Program Medical Neurosciences

# Symptom specific tractography correlates with, and can be used to suggest optimal parameters for DBS programming and surgery

## Nanditha Rajamani<sup>1</sup>, Barbara Hollunder<sup>1,2,3</sup>, Vincent J.J. Odekerken<sup>4</sup>, Martin Reich<sup>5</sup>, Rob M.A. de Bie<sup>4</sup>, Jens Volkmann<sup>5</sup>, Clemens Neudorfer<sup>1</sup>, Petra Ritter<sup>6,7</sup>, Wolf-Julian Neumann<sup>8</sup>, Andrea A. Kühn<sup>1,2,3</sup>, Andreas Horn<sup>1,2</sup>

 Department of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany. 2. Einstein Center for Neurosciences Berlin, Charité Universitätsmedizin Berlin, Berlin, Germany. 3. Berlin School of Mind and Brain, Humboldt-Universität zu Berlin, Berlin, Germany. 4. Department of Neurology, Amsterdam University Medical Center, Amsterdam, The Netherlands. 5. Department of Neurology, University Clinic of Würzburg, Josef-Schneider-Str. 11, 97080, Würzburg, Germany. 6. Brain Simulation Section, Department of Neurology, Charité Universitätsmedizin and Berlin Institute of Health, D-10117, Berlin, Germany. 7. Bernstein Center for Computational Neuroscience, D-10117, Berlin, Germany. 8. Movement Disorders and Neuromodulation Unit, Department for Neurology, Charité University Medicine Berlin, Germany.

## INTRODUCTION

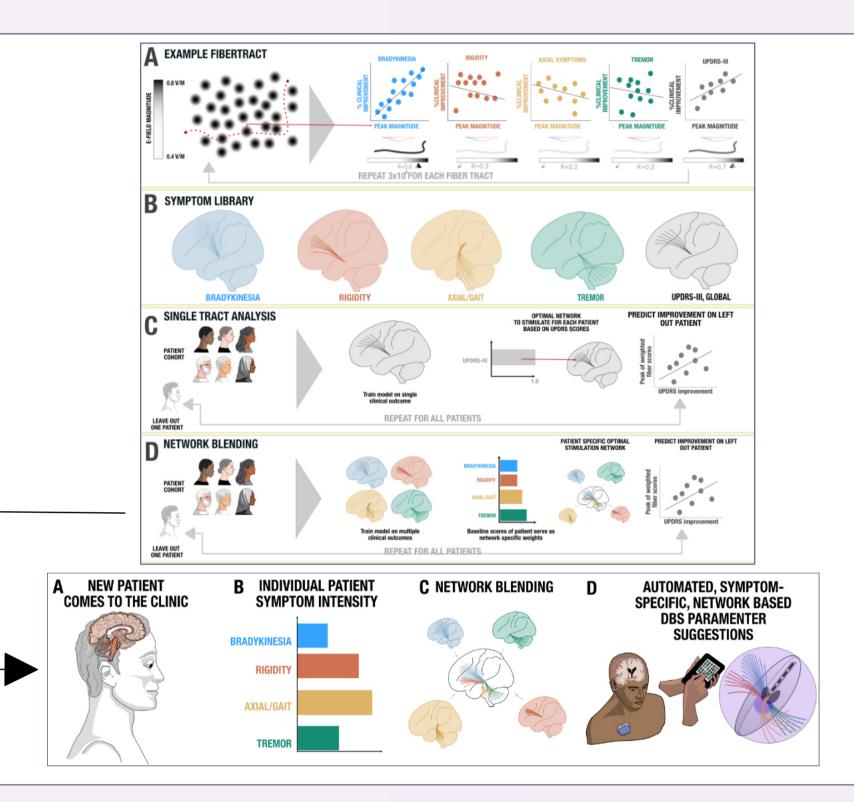
• Different symptoms map to different brain networks in Parkinson's Disease.

• Evidence is accumulating that DBS can differentially modulate these networks.

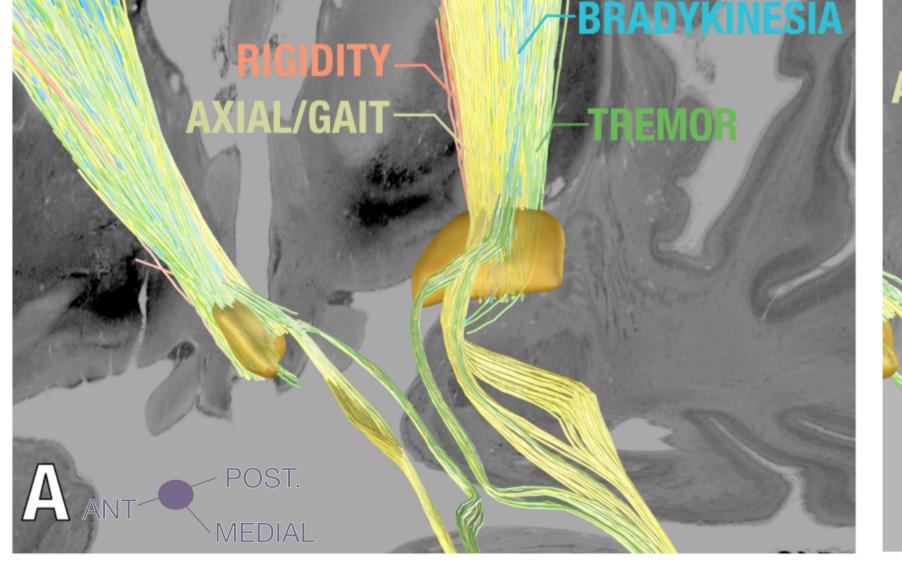
•Here, we introduce a novel method termed multi-symptom fiber filtering to test which symptoms map to which structural connections in the human brain.

### METHODS

- •3 Cohorts (N = 129) with STN-DBS.
- •Calculate electrical fields and stimulation volumes using a finite element model approach.
- Calculate percentage improvements in clinical sub-scores along four axes of motor symptoms in PD (Bradykinesia, Rigidity, Axial symptoms and Tremor) using pre- and post - operative UPDRS scores.
- Apply DBS fiber filtering (Baldermann et al., 2019) to identify specific tract connections in the subthalamic region using the connectome created above.
- Develop brute force bottom-up algorithm to suggest optimal DBS stimulation parameters that would maximally
  engage the symptom specific tracts relevant for individual patients.

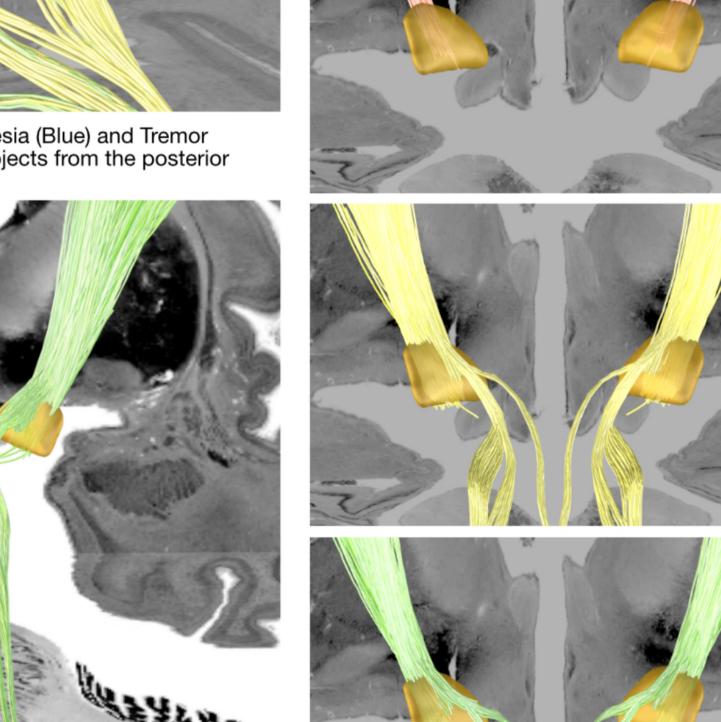


#### RESULTS

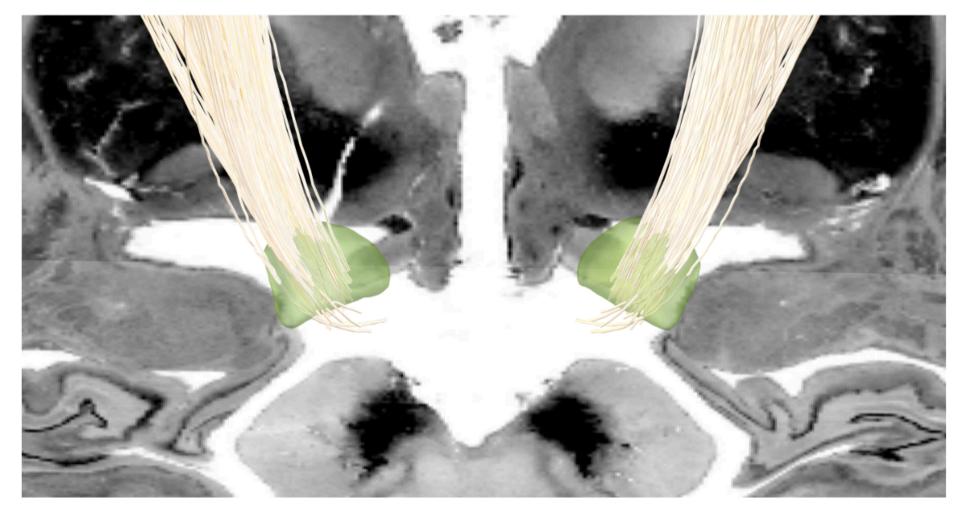


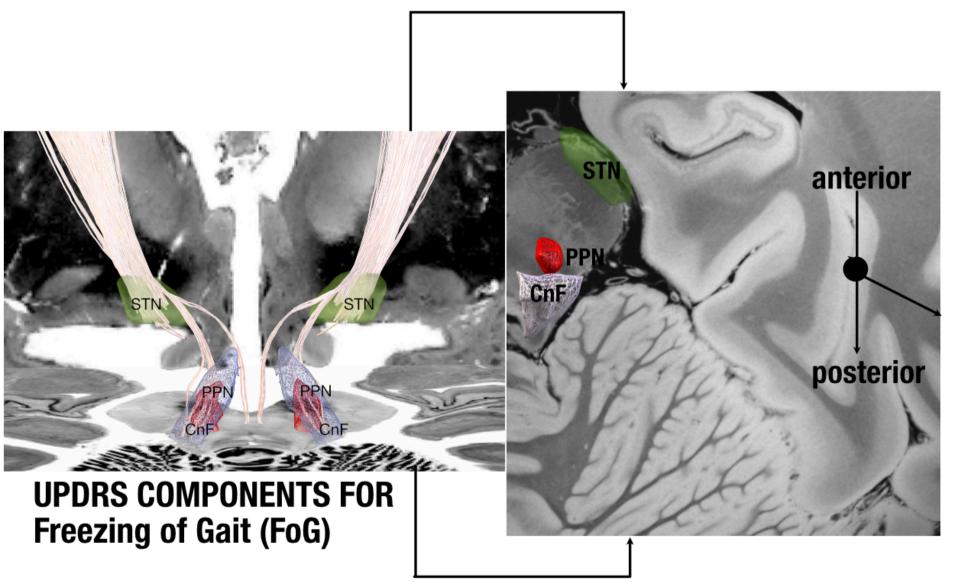


**PANEL A:** Left fig shows the blended fiber visualization: tracts corresponding to Rigidity (Red), Axial symptoms (Yellow), Bradykinesia (Blue) and Tremor (Green). Right fig shows a closed up view of the STN. Rigidity projects from the anterior region of the motor-STN and Tremor projects from the posterior region of the motor-STN.

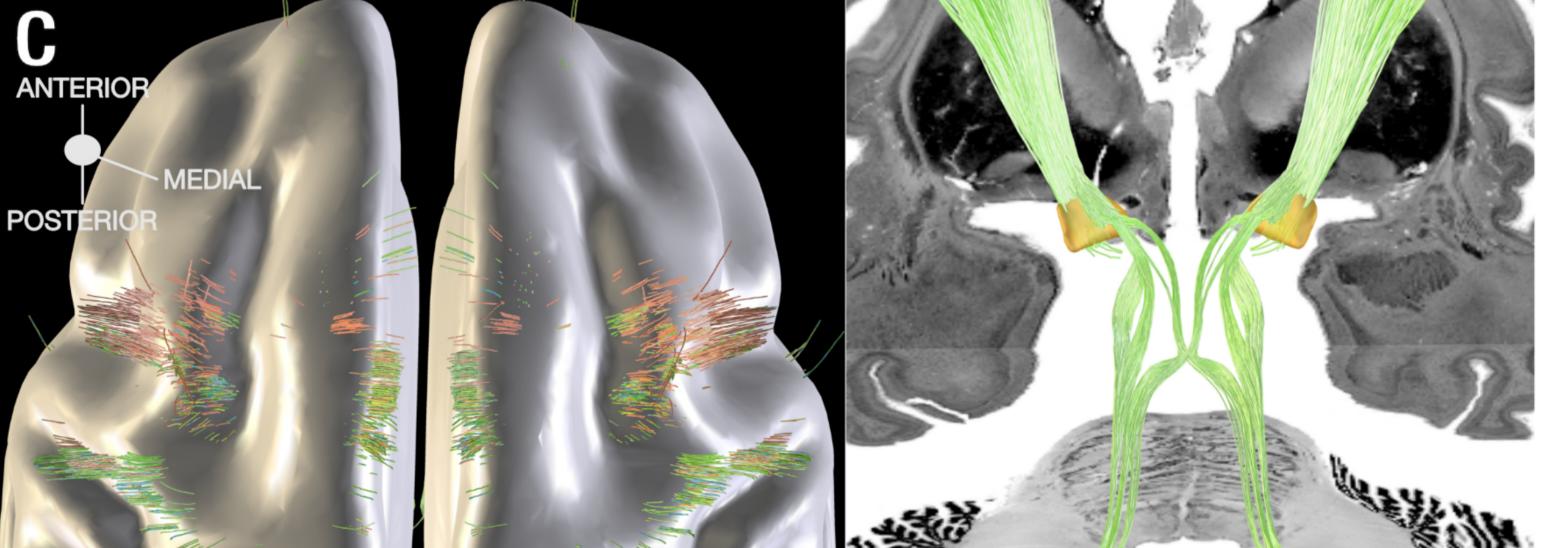


#### UPDRS COMPONENTS FOR POSTURE AND POSTURAL STABILITY





Tract representative of Freezing of Gait (FoG) passes through the pedunculopontine nucleus (PPN) and the cuneiform nucleus (CnF).





PANEL C: Left figure shows the cortical projections of the fiber tracts. Right figure shows unthresholded tracts corresponding to the improvement in tremor symptoms. These tracts form the DRT at the STN level and project to the M1 region at the cortical level.

**PANEL B(a-d):** Each sub-figure represents the projection of tracts corresponding to each of the sub-symptoms of the UPDRS, visualized separately but generated via the network blending method.

#### CONCLUSIONS

- Specific networks associate with symptom specific improvement.
  - 1. Tremor maps to M1 and Cerebellum via the cerebellothalamic pathway
  - 2. Bradykinesia and Rigidity map to premotor regions
  - 3. Axial symptoms map to midbrain regions.

Scan the barcode for software demo & to learn more about the Netstim laboratory!





• We can now pave the way for personalizing DBS with symptom adjusted treatment in individual patients.