Structural connectivity of the basal ganglia from patient-individual tractography for predicting therapeutic effects of deep brain stimulation in Parkinson's Disease

Ricardo Loução[1], Martin Kocher[1], Josef Mana[2], Pablo Andrade[1], Ondrej Bezdicek[2], Robert Jech[2], Veerle Visser-Vandewalle[1], David Linden[3]
1 – Department of Stereotactic and Functional Neurosurgery, University Hospital Cologne, Cologne, Germany
2 – Department of Neurology, Charles University, Prague, Czech Republic
3 – Department of Psychiatry, University Hospital Maastricht, Maastricht, The Netherlands

Aims, research questions, and working hypothesis

Motor control is achieved through the interplay of multiple nodes of the cortico-basal ganglia-thalamocortical loop. Therapeutic approaches for PD patients include deep brain stimulation (DBS) of the subthalamic nucleus (STN). However, the mechanisms underlying the therapeutic effects of STN-DBS are not completely understood. In this work, we investigate the patient-specific structural connectivity associated with DBS and its links to therapeutic effects. We hypothesise that DBS modulates activity in specific STN-related fibre tracts, consequently leading to a clinical improvement.
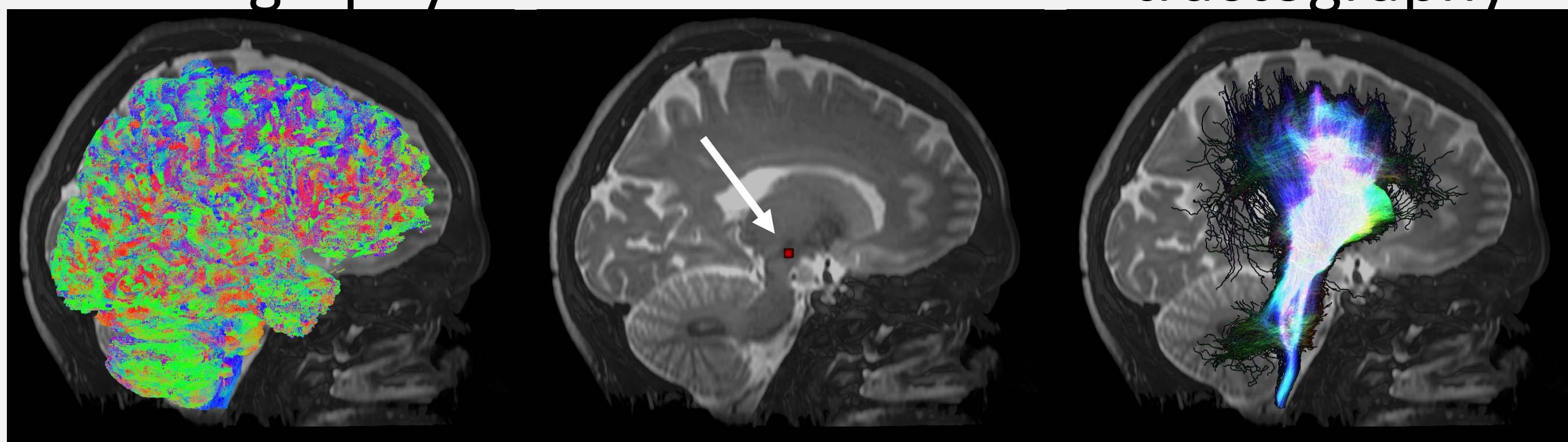
Methods implemented by the consortium

STN-DBS patients from Cologne (N = 69) and Prague (N = 53)
- Pre-op MRI (DWI)
- Post-op CT
- Pre- and post-op clinical assessments:
  - UPDRS — Whole score
  - BDI — Sub-scores
  - PDQ8 etc. — Single item

VTA connectivity

Whole brain tractography | Volume of tissue activated | Filtered tractography

Treatment-induced disconnectivity: Proportion of VTA-targeted fibres to/from STN

Pathways
- ■ Direct
- ■ Indirect
- ■ Hyperdirect

$$Dis(\%) = \frac{N_{Total} - N_{VTA}}{N_{Total}} * 100\%$$
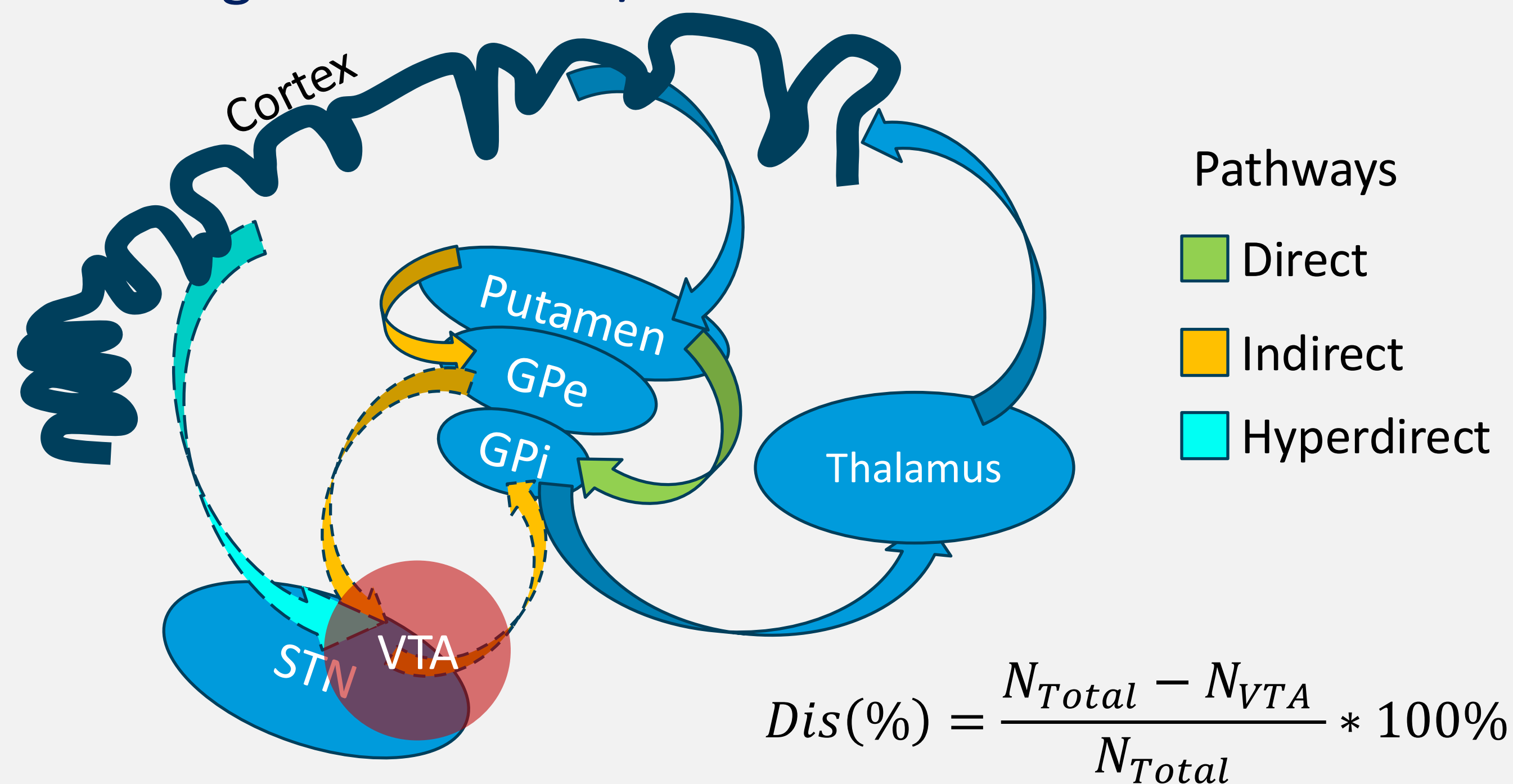
Statistical analysis
- Correlation between (dis-)connectivity values and clinical outcome
- Group analysis:
  - Better vs worse responders
 - Best, average, and worst responders
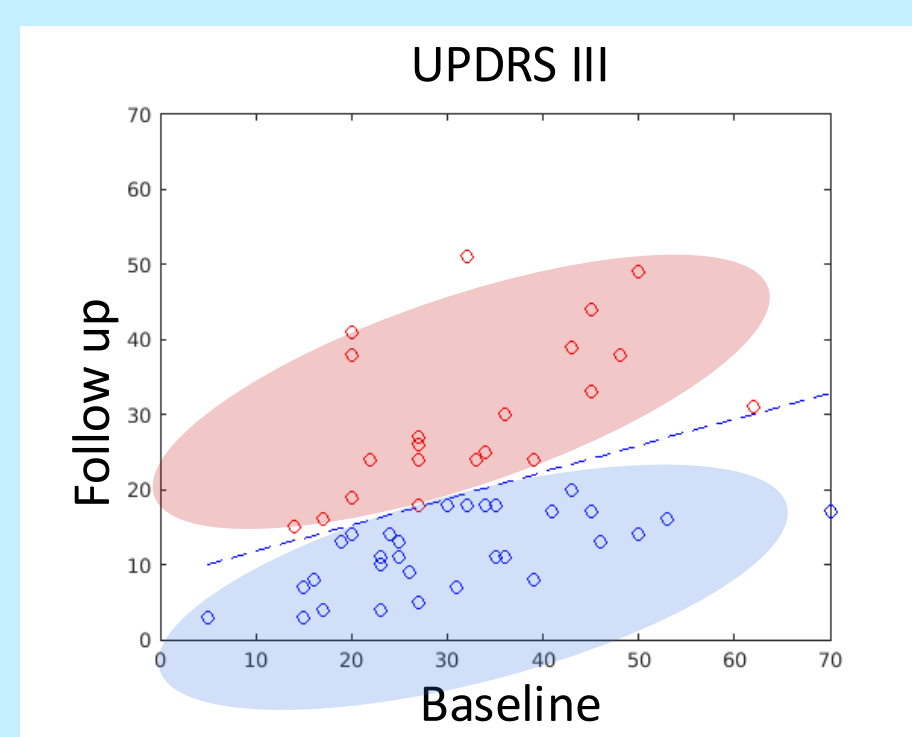
Significance and impact of work on the field

Largest study of STN-DBS PD patient-specific tractography to date. Collaborative nature of the project ensures that the results obtained by one group can be validated by another, increasing applicability to other centres. VTA (dis-)connectivity profiles and the clinical outcome predictive model have the potential to advance the understanding of DBS on PD, potentially guiding therapy.

Current outcomes of the project

Interim results of Cologne's dataset

Cortical projections … | … vs UPDRS - III

… vs bradykinesia | … vs tremor | …vs gait | .. vs posture | … vs rigidity
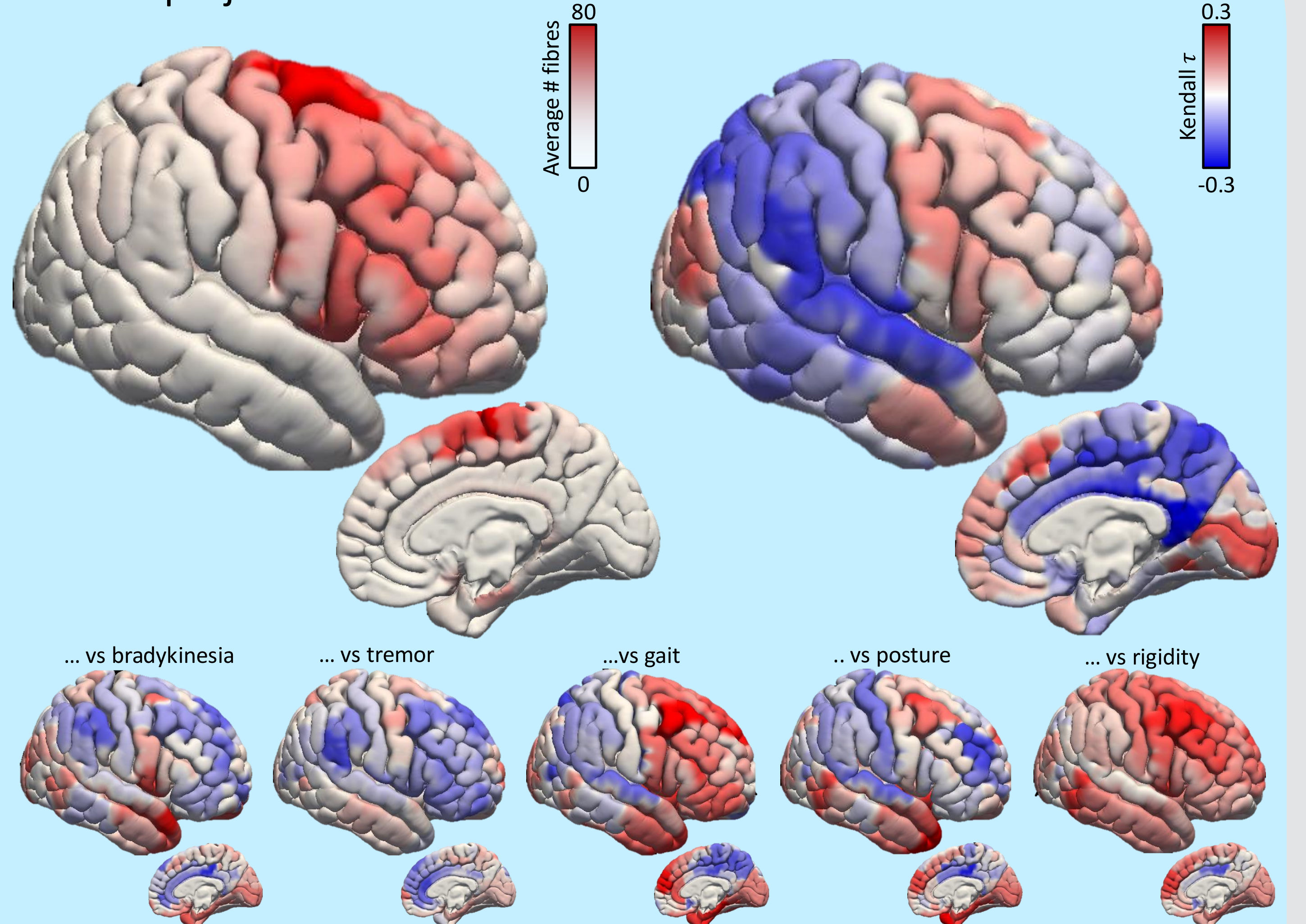
Fibres hit by the VTA have cortical projections mostly in the SMA and pre-motor regions. Correlations between cortical terminations and clinical outcomes reveal different patterns for different outcomes.

Positive correlations between symptom improvement and degree of disconnectivity from STN to SMA, preSMA, and pre-motor cortex.
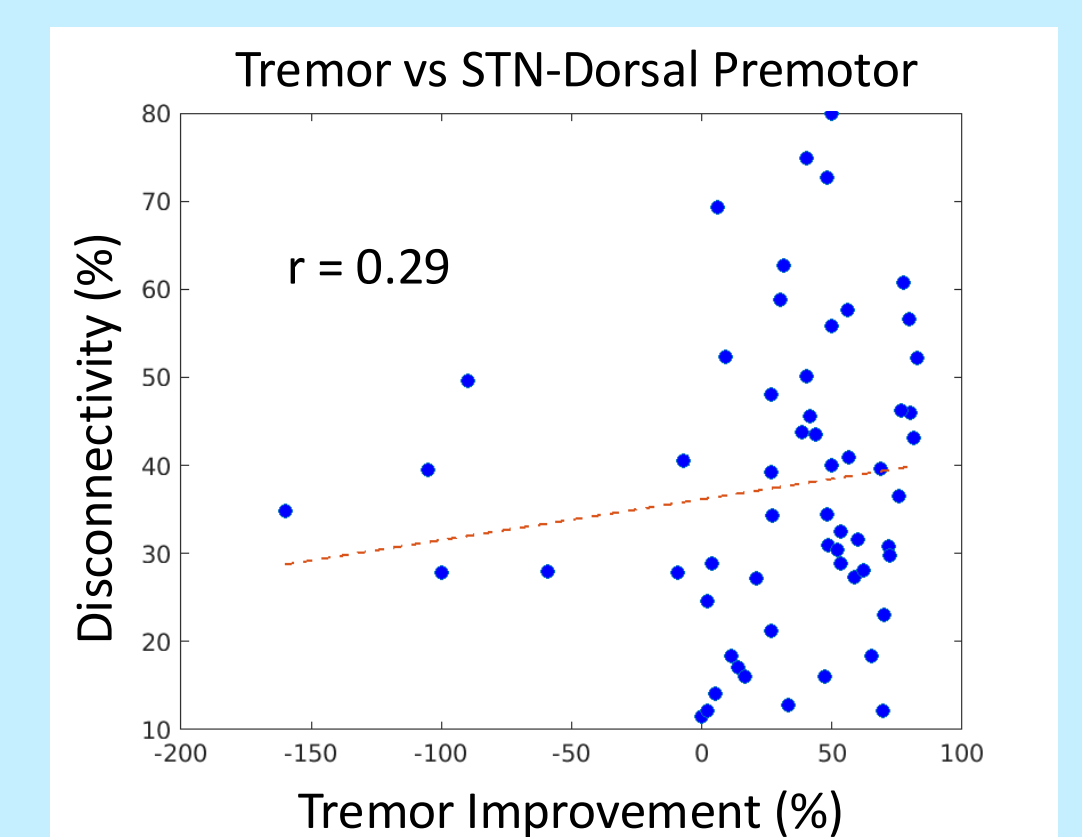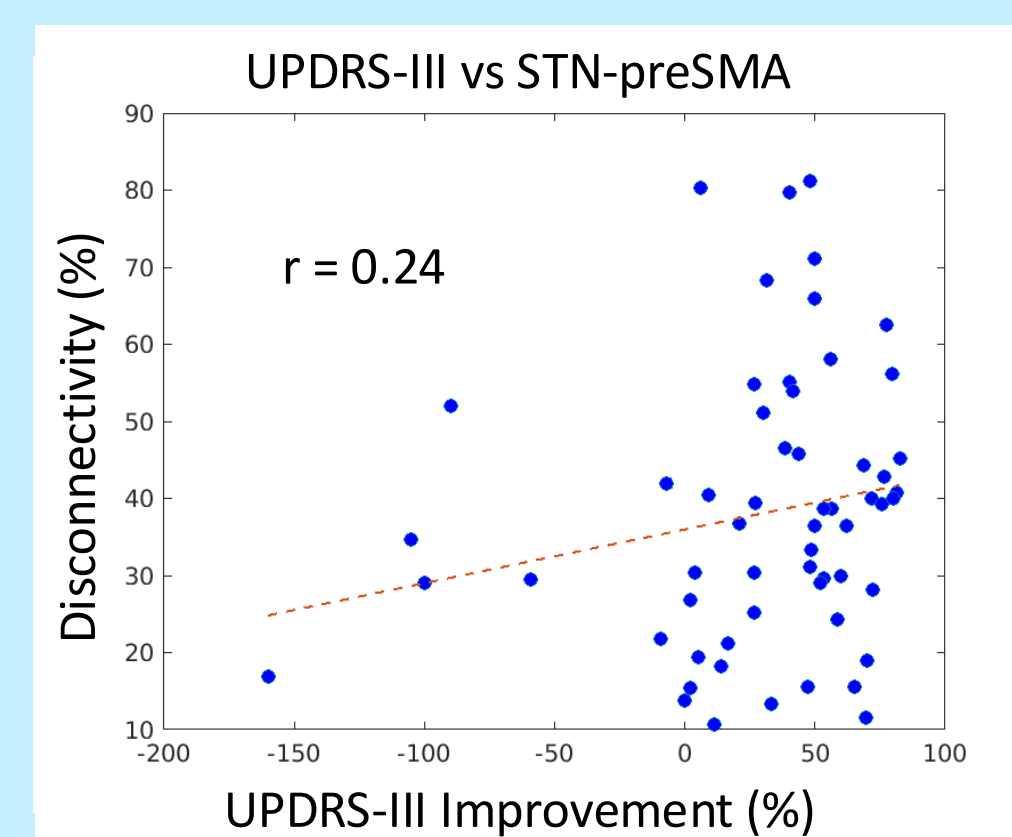
Good responders showed significantly increased disconnectivity between STN and SMA, preSMA, pre-motor cortex, and even GPi and GPe
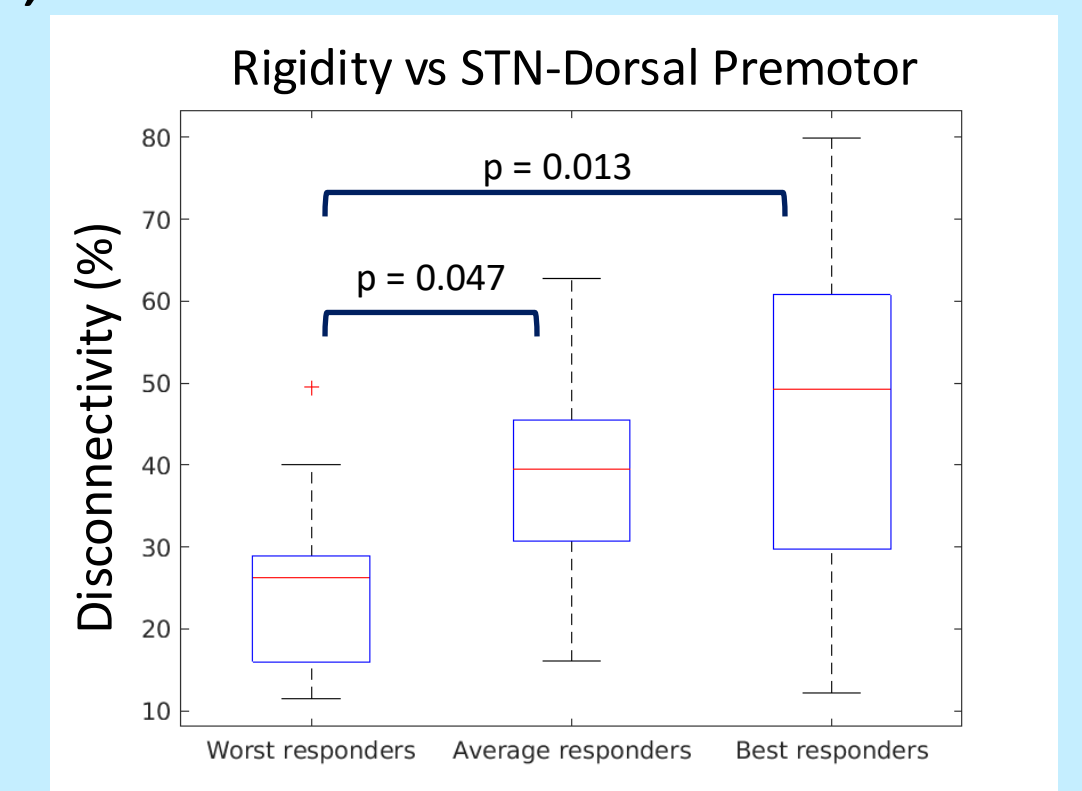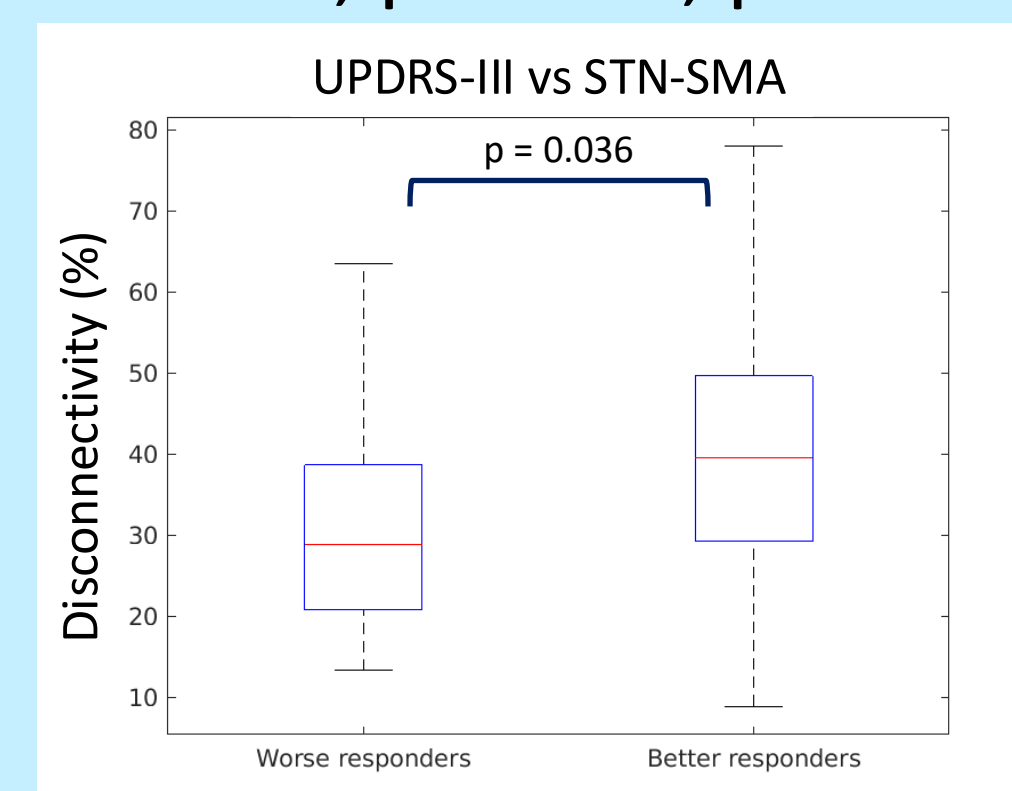
Next steps and future challenges

The next steps will focus on incorporating non-motor symptoms into the analysis, along with the development of symptom-specific predictive models.