SUBTHALAMIC DEEP BRAIN STIMULATION: MAPPING NON-MOTOR OUTCOMES TO STRUCTURAL CONNECTIONS

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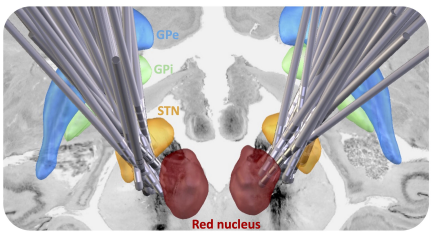
INTRODUCTION

- In Parkinson's disease, deep brain stimulation of the subthalamic nucleus reliably improves motor symptoms, but non-motor outcome is variable.
- Non-motor outcome could be improved by stimulating or avoiding specific brain circuits.
- However, this approach is limited since numerous non-motor symptoms would need to be accounted for.

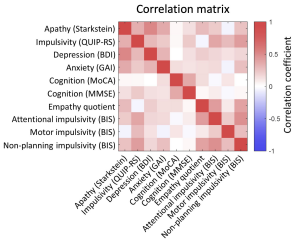
AIMS

- We aimed **to identify key dimensions** of neuropsychological and neuropsychiatric outcome.
- **We identified the structural connections** whose stimulation was associated with these dimensions.
- Finally, we tested whether stimulation of these structural connections **could predict individual symptom outcomes**.

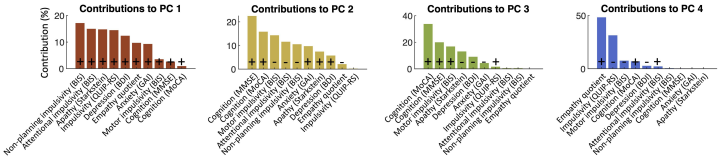
DBS electrode positions



Principal Component Analysis of outcomes



4 PCs retained (Eigen value >1, total explained variance 66.8% – +/- indicates the sign of the loadings)

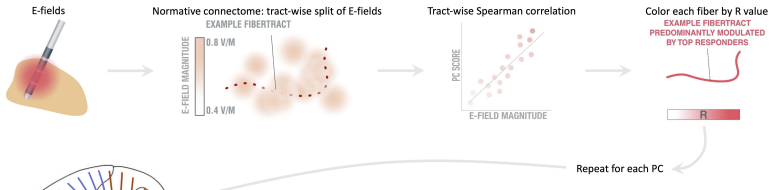


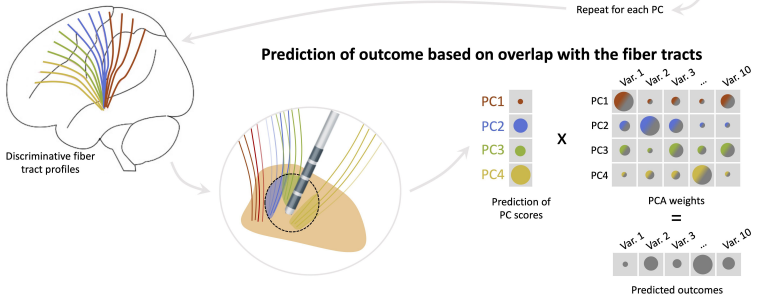
PC1: General non-motor improvement
PC2: Improvement of cognition and worsening of trait impulsivity, improvement of mood
PC3: Improvement of cognition
PC4: Improvement of empathy, worsening of ICBs

METHODS

- **Patients:** 59 Parkinson's Disease patients, assessed before and 6 months after deep brain stimulation surgery to the bilateral subthalamic nucleus (Brisbane, Australia).
- **Identification of the main dimensions of non-motor outcome:** Principal Component Analysis (PCA) applied on ten clinical scores assessing changes in cognition, appetitive behaviors, anxiety and mood, impulsivity, and empathy.
- **Localization of the DBS electrodes** and electric field (E-field) modeling using the Lead-DBS toolbox.
- **Structural connectivity analysis:** Identification of the fiber tracts whose stimulation was associated with the principal component (PC) scores based on a normative structural connectome ("Fiber-filtering"). Change in LEDD used as a covariate.
- **Prediction of individual symptom outcomes** based on overlap with the tracts and PCA decomposition.
- **Validation** in an independent cohort.

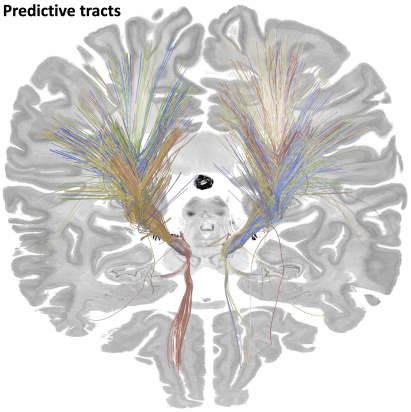
Fiber tracts associated with principal components

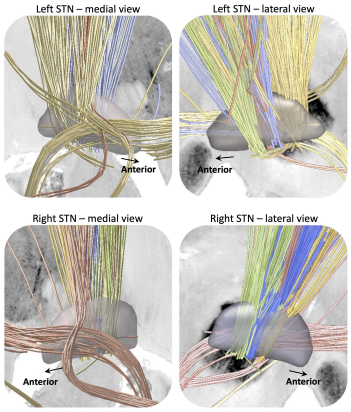




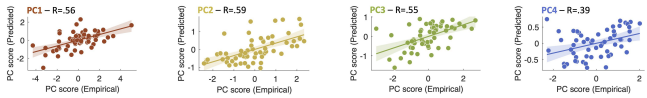
RESULTS

Predictive tracts



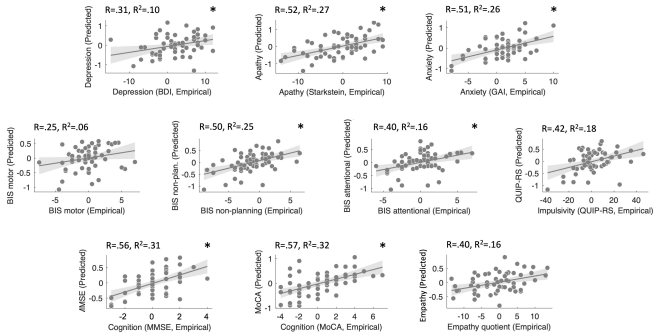


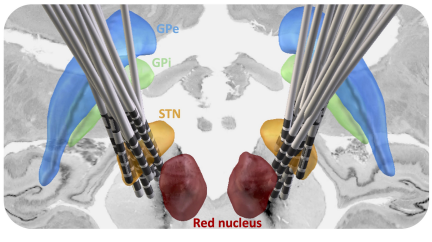
In-sample correlation between overlap with fiber tracts and PC scores



In-sample correlation with clinical outcomes

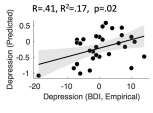
- Overlap with the identified tract bundles could explain variance in individual symptom outcomes.
- Permutation statistics showed that this model explained individual symptom outcomes better that can be expected by chance (as indicated by *).





Out-of-sample validation

- Independent cohort of 32 Parkinson's Disease patients with bilateral subthalamic stimulation assessed for depression (Berlin, Germany).
- Overlap with the identified tract bundles could predict changes in depression.



CONCLUSIONS

- Changes along an extensive neuropsychiatric score battery were mapped to the modulation of four tract bundles in the human brain.
- The degree of modulation of these tracts was able to explain variance in individual symptom outcomes both in-sample and out-of-sample.
- The proposed approach could pave the way towards personalized deep brain stimulation tailored at the patient's symptoms.

We propose a new approach to map changes along extensive clinical score batteries to the modulation of a small set of fiber tract bundles in the human brain - These tracts might be used to predict and improve the outcome of deep brain stimulation.

SCAN ME FOR MORE INFO!

Code available at github.com/netstim/leaddbs

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