## SYMPTOM NETWORK MODULATION BY DEEP BRAIN STIMULATION IN OBSESIVE-COMPULSIVE DISORDER

Barbara Hollunder<sup>1,2,3</sup>, Garance Meyer <sup>4</sup>, Ningfei Li <sup>1</sup>, Nanditha Rajamani<sup>1</sup>, Clemens Neudorfer<sup>4,5</sup>, Cristina Nombela<sup>6</sup>, Philip Mosley<sup>7,8,9,10</sup>, Harith Akram<sup>11,12</sup>, Nicola Acevedo<sup>13,14</sup>, Benjamin Borron<sup>15</sup>, Tina Chou<sup>15</sup>, Jürgen Germann<sup>16</sup>, Juan Pablo Castaño Montoya 16, Bryan Strange 17, Juan A. Barcia 17, Himanshu Tyagi<sup>11,12</sup>, David Castle<sup>19,20,21</sup>, Susan Rossell<sup>14,22</sup>, Peter Bosanac 14,23, Carsten Finke 1,2,3, G. Rees Cosgrove 4,24, Andrea A. Kühn<sup>1,2,3,24</sup>, Jens Kuhn<sup>26,27</sup>, Veerle Visser-Vandewalle<sup>28</sup>, Stephan Chabardes <sup>29,30</sup>, Martijn Figee<sup>31</sup>, Darin D. Dougherty <sup>15</sup>, Shan H. Siddiqi<sup>4</sup>, Andres M. Lozano<sup>16,32</sup>, Ludvic Zrinzo<sup>11,12</sup>, Eileen Joyce 11,12, Mircea Polosan 29,30,33, Juan Carlos Baldermann 26,34, Michael D. Fox <sup>4</sup>, Andreas Horn <sup>26,27</sup>

### INTRODUCTION



Heterogeneity of symptom presentation in patients with obsessive-compulsive disorder (OCD) is a key source of outcome variability following deep brain stimulation (DBS) [1].



While targeting a dedicated fiber bundle in the internal capsule is successful in "average" patients [2,3,4], personalized treatment may require modulating a blend of multiple symptom tracts [5].

To segregate the global OCD response tract into a set of subcircuits related to improvements of obsessions, compulsions, depression, anxiety, and global functioning

### METHODS

**PATIENT COHORT:** 



N = 70 OCD patients with bilateral DBS to five different stereotactic targets – anterior limb of the internal capsule (ALIC), bed nucleus of the stria terminalis (BNST), inferior thalamic peduncle (ITP), subthalamic nucleus (STN), & ALIC / STN combined

#### SYMPTOM IMPROVEMENTS:



Obsessions vs. compulsions (Yale-Brown Obsessive Compulsive Scale), depression (Beck Depression Inventory / Montgomery Åsperg Depression Rating Scale / Hamilton Depression Inventory), anxiety (Hamilton and Beck Anxiety Inventories / state section of the State-Trait Anxiety Inventory), and general level of functionality (Global Assessment of Functioning)

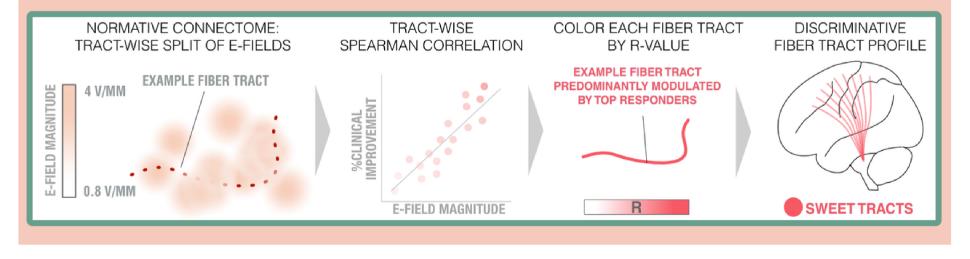


LEAD-DBS BASED PREPROCESSING

PIPELINE [6]: Electrode reconstructions & estimation of local DBS impact (electric field modeling)

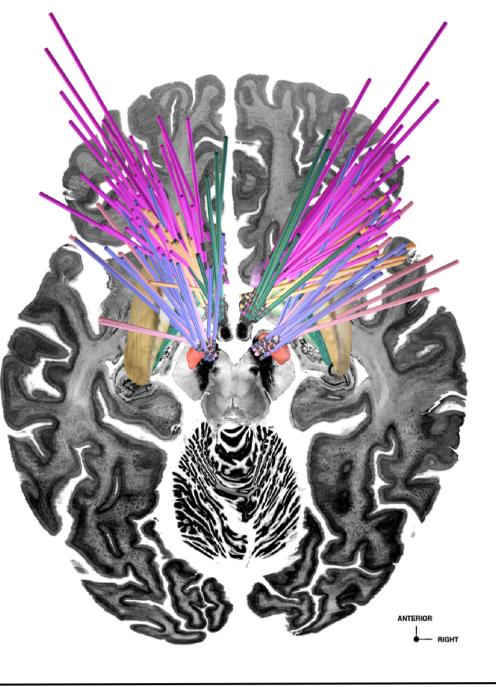


**DBS FIBER FILTERING** [7]: Identification of streamlines from a normative group connectome discriminative for beneficial stimulation effects per symptom domain and confirmation of these tract models using in-sample correlations as well as five-fold cross-validations (CV)



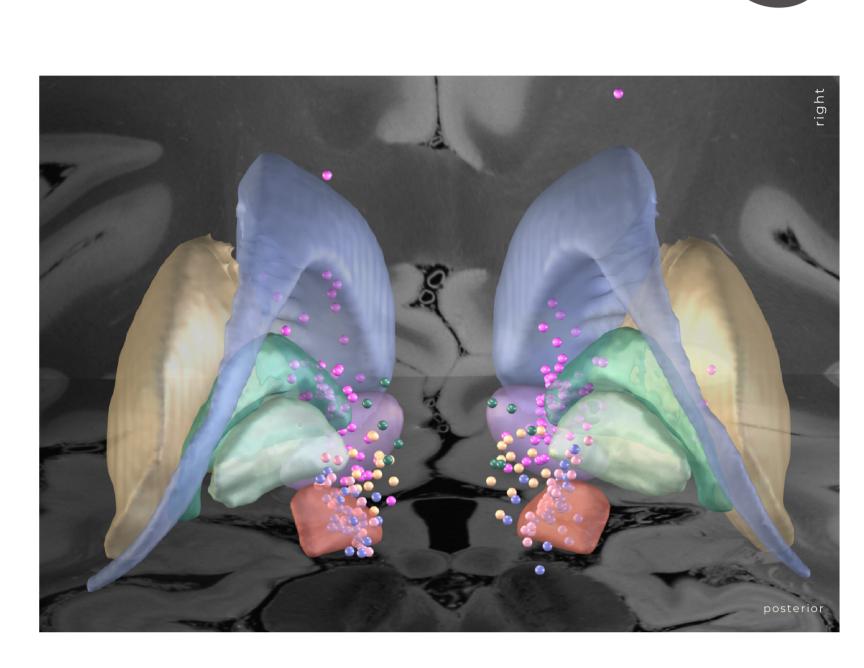
#### ELECTRODE PLACEMENT IN MULTICENTRIC OCD-DBS PATIENT COHORT

**OCD COHORTS BY DBS TARGET ZONE** 



**ATLAS STRUCTURES** STN ALIC GPe

Putamen



RESULTS 3

THERAPEUTIC SYMPTOM NETWORK SPECTRUM IN DBS FOR OCD

Across variable DBS electrode placement as a function of centers and surgeons (see panel A), therapeutic stimulation effects on global obsessive-compulsive symptomatology converged on a shared prefronto-cortical streamline bundle passing through the ALIC (see panel B.a).

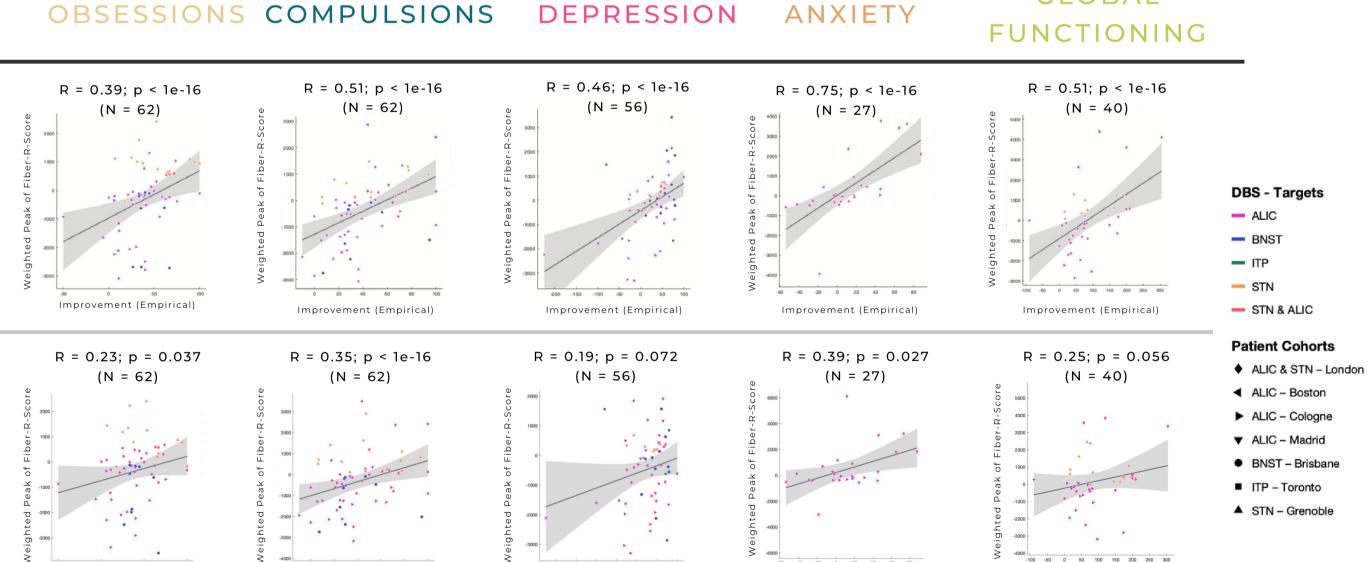
This model showed positive insample associations (R = 0.46, p < 1e-16) and was robust to fivefold CV (R = 0.28, p = 0.024).

This global OCD response tract could be segregated into symptomwise bundles (see panel B.b).

SEGREGATION BY OCD SUB-SYMPTOMS

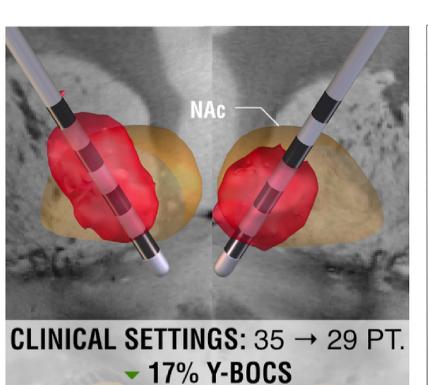
**TRACT** 

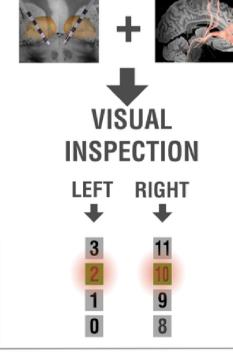
**OCD RESPONSE** COMPULSIONS VALIDATION OF SYMPTOM-NETWORK MAPPINGS GLOBAL



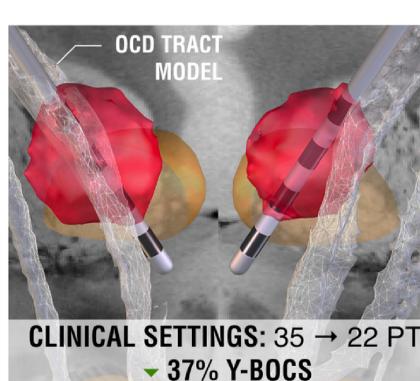
#### PROSPECTIVE VALIDATION OF GLOBAL OCD RESPONSE TRACT MODEL (N = 1)

Improvement (Empirical)

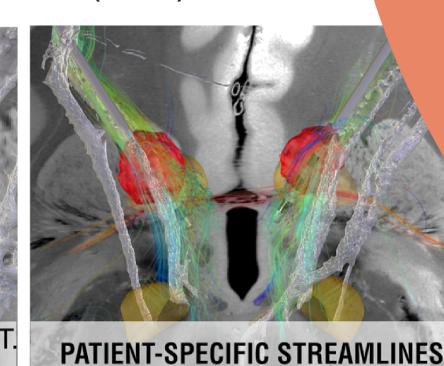




Improvement (Empirical)



Improvement (Empirical)



PRISM BREAKS UP THE LIGHT, DBS CAN BE **USED AS A TOOL** TO SEGREGATE **BRAIN CONNEC-**TOMES INTO SYMPTOM

JUST LIKE A

TRACTS.

# DISCUSSION

- Presented networks may improve our understanding of the underlying pathophysiology and mechanism of action of DBS attributed to various OCD symptoms.
- Further, they may prove valuable in the context of transdiagnostic symptoms or in personalized tailoring of treatment to symptom constellations of individual patients [1,5].

### GET IN TOUCH:



@nestim\_org & @b\_hollunder



http://www.netstim.org



barbara.hollunder@charite.de

