Prefrontal Connectivity Analysis of the Evolving Stereotactic Capsulotomy Target for Refractory OCD

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2018 AANS Annual Scientific Meeting
Disclosures

None

Acknowledgements

National Institutes of Health (T35 AG044303)

Dr. James Noble, Dr. Stuart Fischer, and the Columbia University College of Physicians and Surgeons Summer 2017 Research Program

All the members of the Sheth Lab
Introduction

Most obsessive-compulsive disorder (OCD) patients are well controlled with pharmacological and cognitive behavioral therapy, but 10-20% remain severe and refractory.

For decades, stereotactictic capsulotomy has been a viable option for these patients, although the involved networks remain uncertain.

We used diffusion tensor imaging (DTI) to identify the networks affected by capsulotomy targets over time, with an emphasis on orbitofrontal cortex (OFC), a region implicated in cortico-striato-thalamo-cortical (CSTC) models of OCD.
Methods

1. Stereotactic coordinates for 5 anterior capsulotomy targets spanning 13 years were obtained by literature review.

2. We modeled representative spherical lesions with 3mm radii at each target and performed probabilistic tractography on DTI from 40 randomly-selected subjects from the Human Connectome Project (HCP).

Fig. 1: Location of modeled lesions in coronal cross-section. Orange and white are the same lesion, shown bilaterally for ease of visual comparison with adjacent targets.
Methods

3. For each modeled lesion, a lesion-connectome was created by averaging tractography from the 40 HCP subjects.

4. The percentage of tracts terminating in the grey matter of Brodmann Area 11 (BA11; OFC) out of tracts terminating in the grey matter of all frontal Brodmann Areas was calculated for each target.

Fig. 2: Lesion-connectome heatmap for yellow modeled lesion. Yellow target voxel coordinates: (77,135,66) (103,135,66)
Results

On average, 84.1% of tracts represented in frontal grey matter were localized to BA11. Values ranged from 47.5% in the earliest reported target to 96.8% in the second-most-recent target.

Kendall rank correlation between year of procedure and BA11 connectivity yielded a positive association trending towards significance (p<0.08, τ=0.80).

<table>
<thead>
<tr>
<th>Targets from least to most recent with bilateral voxel coordinates (x,y,z)</th>
<th>Frontal grey matter within BA11</th>
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</thead>
<tbody>
<tr>
<td>Cyan: (72,142,77) (108,142,77)</td>
<td>47.5%</td>
</tr>
<tr>
<td>Red: (70,140,68) (110,140,68)</td>
<td>89.9%</td>
</tr>
<tr>
<td>Purple: (72,136,68) (108,136,68)</td>
<td>92.2%</td>
</tr>
<tr>
<td>Yellow: (77,135,66) (103,135,66)</td>
<td>96.8%</td>
</tr>
<tr>
<td>Orange: (73,140,68) (107,140,68)</td>
<td>94.2%</td>
</tr>
<tr>
<td><strong>MEAN</strong></td>
<td><strong>84.1%</strong></td>
</tr>
</tbody>
</table>

*Table 1: Percent of gray matter tracts localized to Brodmann Area 11 for each modeled lesion.*
Results

Fig. 3: Representative sagittal, coronal, and axial cross-sectional views showing overlap of Brodmann Area 11 (cyan) and lesion-connectome seeded from yellow modeled lesion.
Discussion

In the CSTC model of OCD, there is an imbalance favoring increased tone of the direct (excitatory) pathway over the indirect (inhibitory) pathway.¹

The newer, more ventral capsulotomy targets exhibit more OFC involvement than the older, dorsal targets.

The nature of this modulation cannot be presumed – it is tempting to assume that ablation would categorically inhibit a given pathway, but it could also amplify it by reducing “signal noise”. However, it does appear that small differences in target location result in significantly altered regions of modulation.

Discussion

Technical limitations:

- Diffusion tensor imaging and tractography are not perfect representations of anatomy
- Transformation errors when mapping individual subject DTI scans onto standard coordinate space

Design limitations:

- Territory of orbitofrontal cortex difficult to define
- Dearth of capsulotomy target coordinates recorded in the literature
Conclusions

The frontal networks affected by capsulotomies appear primarily to involve the OFC, supporting the CSTC models of OCD.

Over time, the migration of capsulotomy targets has trended towards maximizing OFC modulation.

Future studies will aim to correlate these structural findings with clinical responses prospectively, which will further our understanding of the networks modulated by capsulotomy and improve its efficacy.