Connectivity Analysis of Cingulotomy Lesion Using Tractography: Do More Effective Targets Exist?

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Introduction

- Cingulotomy procedures for the treatment of depression, pain, and OCD consists of 1-3 bilateral lesions in the dorsal anterior cingulate cortex and an underlying WM tract called the cingulum bundle (CB)
- While cingulotomy is effective, the exact region responsible for symptom relief is unclear
- The CB has long been implicated in the pathophysiology of psychiatric disorders and certain CB regions, such as the rostral dorsal CB, have greater connectivity than others, to cortical and subcortical structures associated with mood and thought
- This study uses tractography to assess connectivity of standard cingulotomy lesions, compared to subdivisions of the rostral dorsal CB, to help shed light on pathways responsible for the therapeutic effects of cingulotomy and to determine if other regions of the CB might be more effective targets

Figure 1. Regions of Interest for Tractography Analysis
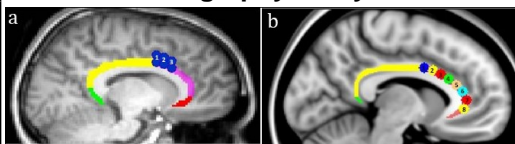
Region of interest masks replicating three standard cingulotomy lesions (a), and 8 equally-sized subdivisions of the rostral dorsal CB (b)

Methods

- Ten healthy volunteers underwent T1 and diffusion-weighted MRI
- Regions of interest (ROIs) were created to replicate three cingulotomy lesions and eight equally-sized subdivisions of the rostral dorsal CB (Figure1)
- Subdivisions (1-3) coincided respectively with the bottom halves of the three lesions
- Deterministic tractography was performed to assess connectivity of each ROI to 11 cortical and subcortical brain structures

Results

- Deterministic tractography was performed seeding from three bilateral cingulotomy lesions and eight bilateral rostral dorsal CB subregions
- All three cingulotomy lesions showed greatest connectivity to three cortical areas: posterior cingulate cortex (PCC) for lesion 1, followed by dorsal anterior cingulate cortex (dACC), and then dorsomedial frontal cortex (dmFC); dACC for lesions 2&3, followed by dmFC and PCC (Table1)
- The CB subregion with the greatest connectivity to the PCC was subregion 1, but it showed equivalent connectivity to dACC as well. Subregions 2-5 showed greatest connectivity to dACC (Table 2)

Table 1. Cingulotomy Lesion Connectivity

	Amygdala	Thalamus	dlFC	dmFC	dACC	sACC	PCC	FP	m/cOFC	lOFC	vlPFC
Cingulotomy_1	0.0%	1.6%	1.6%	60.7%	70.5%	3.3%	82.0%	1.6%	1.6%	0.0%	1.6%
Cingulotomy_2	0.0%	1.7%	1.7%	57.6%	96.6%	3.4%	49.2%	3.4%	1.7%	0.0%	1.7%
Cingulotomy_3	0.0%	1.8%	0.0%	59.7%	94.7%	7.0%	28.1%	3.5%	1.8%	1.8%	1.8%

0   10   20   30   40   50   60   70   80   90   100
Fraction of total streamlines leaving seed ROI

Fraction of total streamlines from cingulotomy lesions 1-3, that are connected to each cortical or subcortical location; dlFC, dorsolateral frontal cortex; dmFC, dorsomedial frontal cortex; dACC, dorsal anterior cingulate cortex; sACC, subgenual anterior cingulate cortex; PCC, posterior cingulate cortex; FP, frontal pole; m/cOFC, medial/central orbitofrontal cortex; lOFC, lateral orbitofrontal cortex; vlPFC, ventrolateral prefrontal cortex.

Table 2. Rostral Dorsal Cingulum Bundle Subregion Connectivity

	Amygdala	Thalamus	dlFC	dmFC	dACC	sACC	PCC	FP	m/cOFC	lOFC	vlPFC
Subregion_1	0.0%	2.9%	2.9%	45.7%	74.3%	5.7%	74.3%	2.9%	2.9%	0.0%	2.9%
Subregion_2	0.0%	3.0%	3.0%	48.5%	97.0%	6.1%	54.6%	6.1%	3.0%	0.0%	3.0%
Subregion_3	0.0%	3.2%	0.0%	48.4%	96.8%	9.7%	38.7%	6.5%	3.2%	0.0%	0.0%
Subregion_4	0.0%	3.0%	0.0%	48.5%	97.0%	18.2%	15.2%	9.1%	3.0%	3.0%	3.0%
Subregion_5	0.0%	2.9%	0.0%	54.1%	47.1%	11.8%	20.6%	2.9%	2.9%	0.0%	0.0%
Subregion_6	0.0%	2.8%	0.0%	36.1%	66.7%	36.1%	8.3%	36.1%	2.8%	5.6%	0.0%
Subregion_7	0.0%	0.0%	0.0%	20.0%	34.3%	94.3%	5.7%	57.1%	8.6%	5.7%	0.0%
Subregion_8	0.0%	0.0%	0.0%	7.5%	20.0%	82.5%	5.0%	67.5%	17.5%	15.0%	0.0%

0   10   20   30   40   50   60   70   80   90   100
Fraction of total streamlines leaving seed ROI

Fraction of total streamlines from rostral dorsal CB subregions 1-8

Discussion

Based on their connectivity, the therapeutic effects of cingulotomy lesions may be due to disruption of connections to dACC, dmFC, & PCC. Thus, since subregions 2-5 all show highest connectivity to dACC, and subregion 1 shares highest connectivity to dACC and PCC, it is possible that cingulotomy lesions positioned more anteriorly to currently placed lesions, may produce more effective results by further disrupting pathways traveling to dACC.

Conclusion

Tractography based connectivity analysis of cingulotomy lesions compared to subregions of the rostral dorsal CB, showed highest connectivity predominantly to dACC.

This suggests that therapeutic effects of cingulotomy lesions results from disruption of the connections to the dACC, and that perhaps lesions made more anteriorly to current cingulotomy targets, might further optimize the therapeutic efficacy of the results.

References

Heilbronner SR, Haber SN. Frontal cortical and subcortical projections provide a basis for segmenting the cingulum bundle: implications for neuroimaging and psychiatric disorders. J. Neurosci. 2014;34(30):10041-10054.

Yang JC, Ginat DT, Dougherty DD, et al. Lesion analysis for cingulotomy and limbic leucotomy: comparison and correlation with clinical outcomes. J Neurosurg. 120: 152-164, 2014.

Mayberg HS, Liotti M, et al. Reciprocal limbic-cortical function and negative mood: converging PET findings in depression and normal sadness. Am J Psychiatry. 1999 May;156(5):675-82

Zhang Y, Schuff N, et al. Diffusion tensor imaging of cingulum fibres in mild cognitive impairment and Alzheimer's disease. Neurology. 2007;68:13–18.

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