

Have you got enough nerve?

– Implications of white matter integrity in Transcranial Magnetic Stimulation

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Objective

This project was a pilot study to determine whether a decline in white matter integrity may predict Transcranial Magnetic Stimulation outcome in patients with depression.

Introduction

- **Transcranial Magnetic Stimulation (TMS)** is a novel and non-invasive type of treatment for patients with depression
- It uses a wire coil to transmit electromagnetic pulses through the skin and the skull, stimulating the specific area within the cerebral cortex that the coil is held to
- Despite weekly sessions, a proportion of patients shows no response to TMS
- One explanation may be that the overall number of neurons present in a specific electrical pathway play a role in evoking dissimilar magnitudes of stimulation between patients despite using the same TMS pulse strength
- We therefore conducted a study to examine the integrity of white matter fibre tracts that connect distinct regions in the brains of TMS responders and non-responders

Methods

For my study I examined MRI scans from 7 responders to TMS and 7 non-responders to TMS.

Subject	BH	DM	DP	GG	GO	JA	KN	LH	LO	PM	RB	SM	SW	TS
Age	22	31	35	41	40	32	51	43	55	39	19	27	52	68
Sex	F	M	F	M	F	F	M	M	M	M	M	M	M	M

- In order to measure white matter integrity, I carried out **Diffusion Tensor Imaging (DTI)** on these MRI scans
- DTI tracks the diffusion of water molecules along neuronal tracts in the brain. Thus information about the extent of free water movement along white matter tracts can be used to draw implications on fibre structure and connectivity

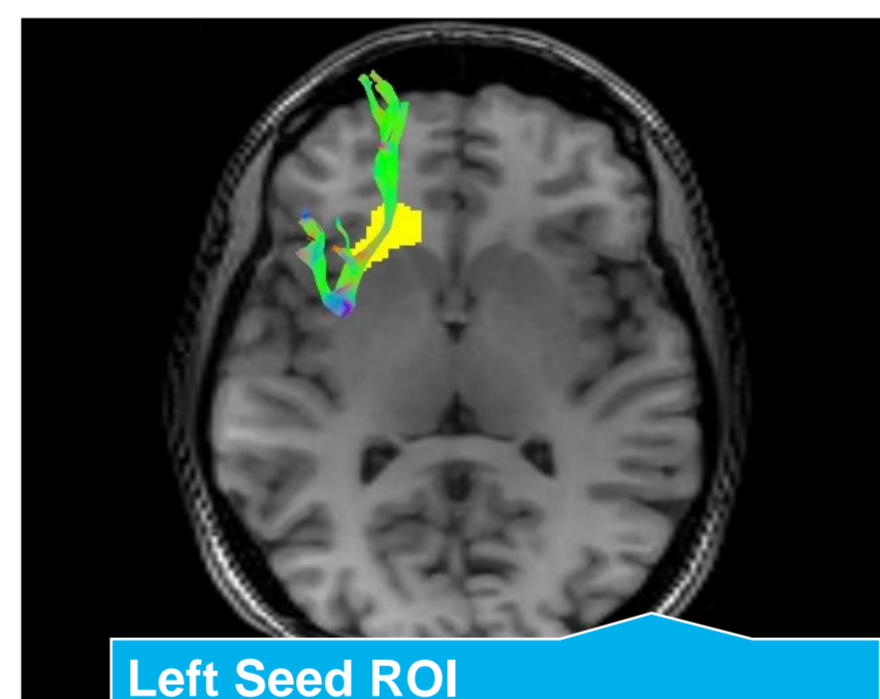
Obtaining the Data

My project targeted a tract called the **Uncinate Fasciculus (UF)**, which connects the orbitofrontal cortex with the temporal lobe of the brain as best depicted in *ROI 2*. The UF has been repeatedly linked to depression in the literature.

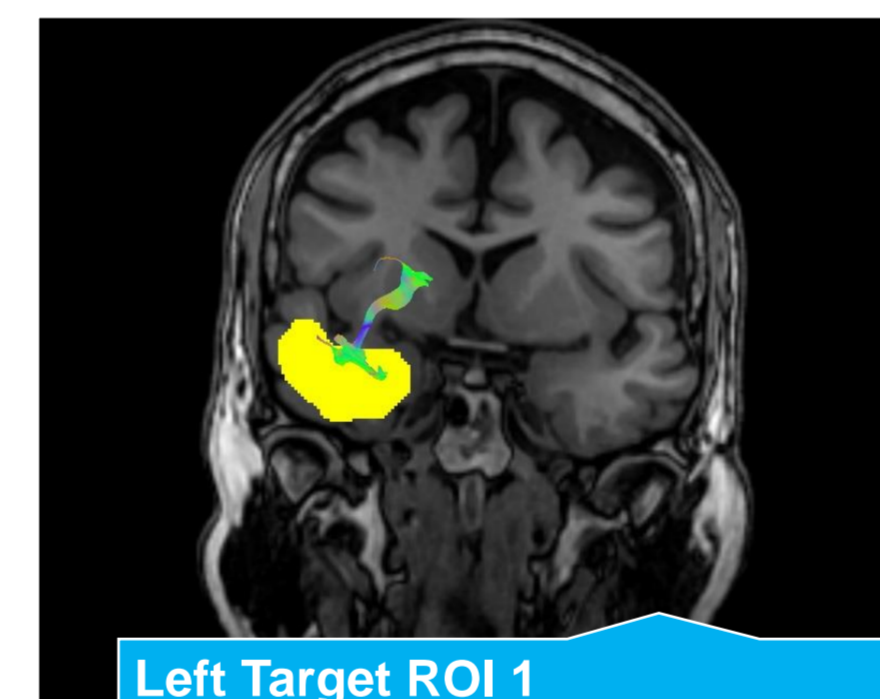
To specify the UF tract rather than examining whole brain water diffusion, I defined three **Regions Of Interest (ROIs)**. With a brain-imaging software I manually drew the ROIs onto both hemispheres on the scans (in yellow). The programme could then extract fibres that only run through the given ROIs.

I also defined a control tract to validate any possible differences between the two cohorts. The control tract was isolated using the same method as for the UF, however the ROIs were dissimilar.

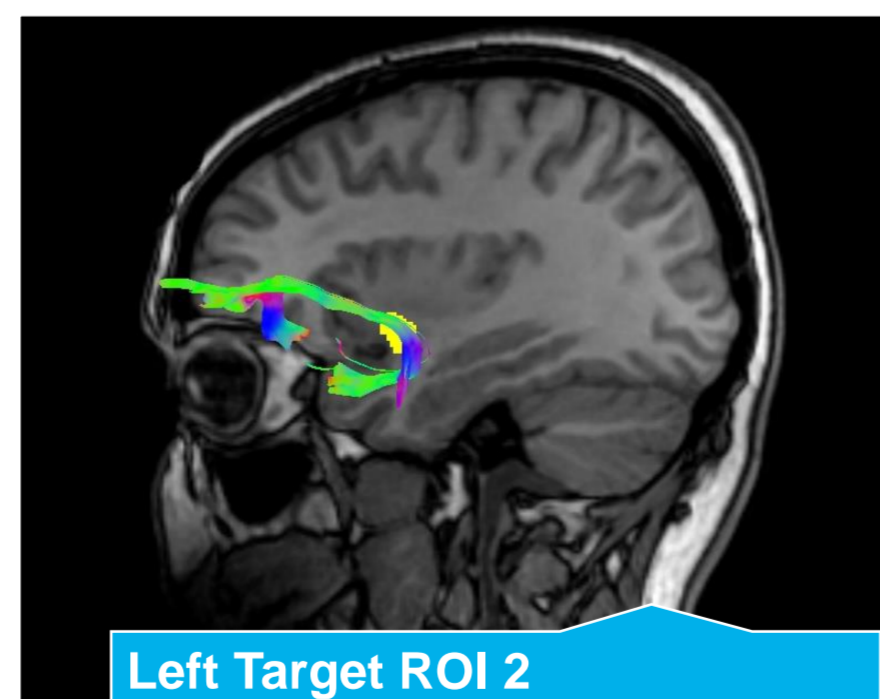
Regions Of Interest



Left Seed ROI
• White matter fibres running into the orbitofrontal cortex on an axial MRI slice



Left Target ROI 1
• Temporal lobe including the hippocampus on a coronal MRI slice



Left Target ROI 2
• White matter fibres running through the insula from the temporal lobe into orbitofrontal area on a sagittal slice

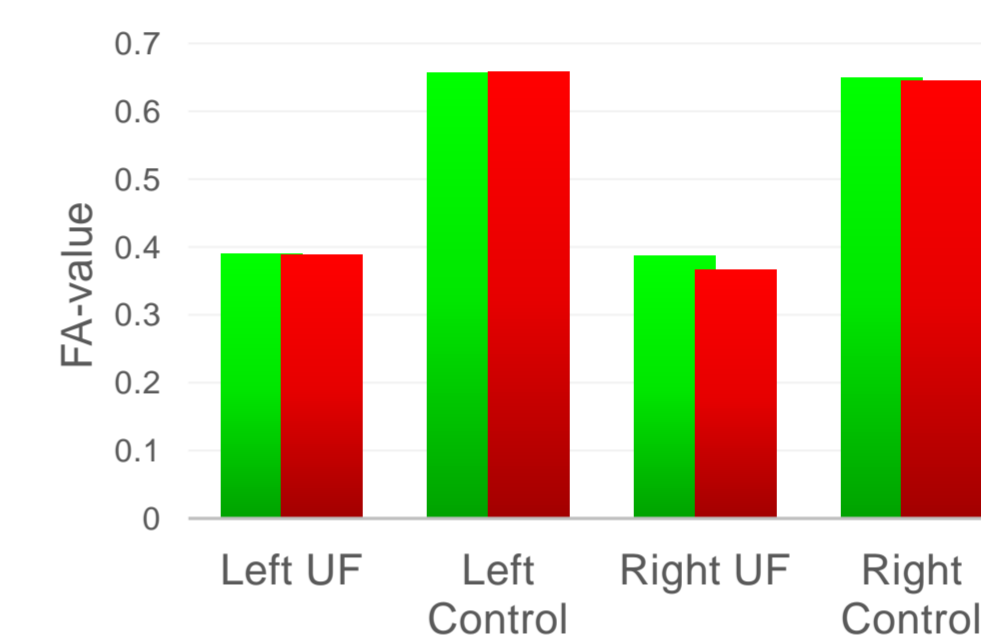


Left Control
• A tract that runs through two ROIs:
1. Spinal cord
2. Posterior limb of the internal capsule

Results

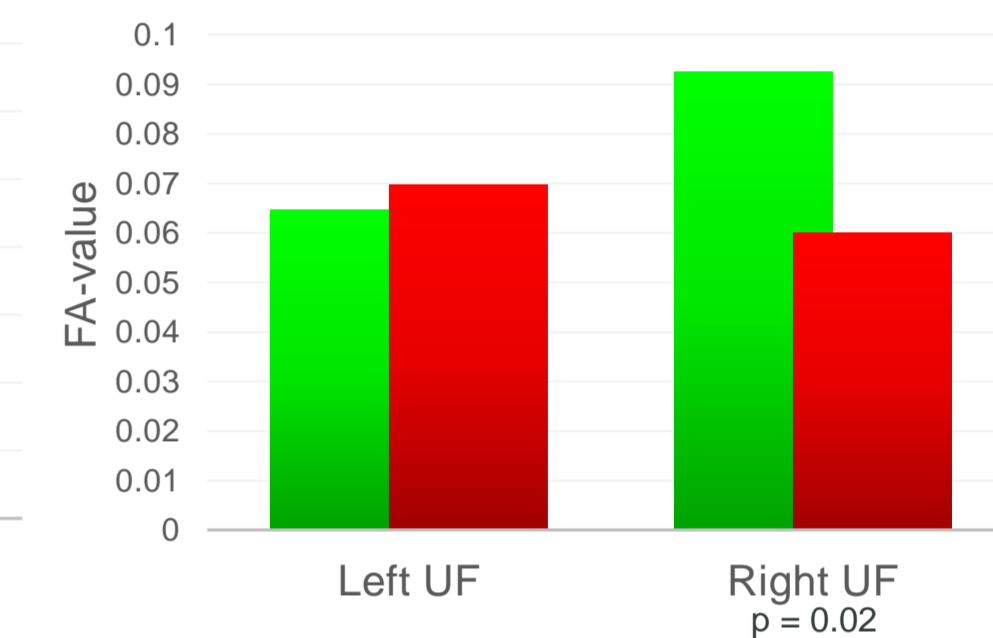
Mean deterministic FA-values by cohort

	Left UF	Left Control	Right UF	Right Control
Responders	0.390	0.657	0.387	0.649
Non-Responders	0.389	0.659	0.366	0.644



Mean probabilistic FA-values by cohort

	Left UF	Right UF
Responders	0.065	0.092
Non-Responders	0.069	0.060



Graph 1. This graph displays the FA-values obtained through deterministic tractography analysis. Here neuron density is calculated in respect to the exact number of fibres defined by the manually given ROIs.

Graph 2. This graph represents the probabilistic FA-values. Probabilistic tractography generates values for tracts that were poorly defined in the deterministic data, thus taking into account subjective and technical errors.

- We determined the **Fractional Anisotropy (FA)** of the tracts, which quantifies the degree of water diffusion within a given tract and thus reflects its fibre density¹
- The deterministic FA-values obtained for the UF and the control tract were very similar between responders and non-responders, indicating no significant difference in white matter integrity of the UF between the two cohorts (see Graph1)
- The probabilistic FA-values however did show a slight difference between the cohorts in the left UF and a **statistically significant** difference in the right UF (see Graph2)

Conclusion

- This pilot study indicates a possible role for specific brain tracts in depression
- Next steps are to conduct this study with a greater sample size, consideration of interobserver variability and other depression-linked tracts to validate our hypothesis
- In the future such studies may allow us to predict unsuccessful TMS outcome, so avoiding the risk of exacerbating depression in potential non-responders