

Focused ultrasound Neuromodulation for Parkinson's disease

Tom Gilbertson

Senior Clinical Lecturer

Honorary Consultant Neurologist

Ninewells Hospital & Medical School

University of Dundee

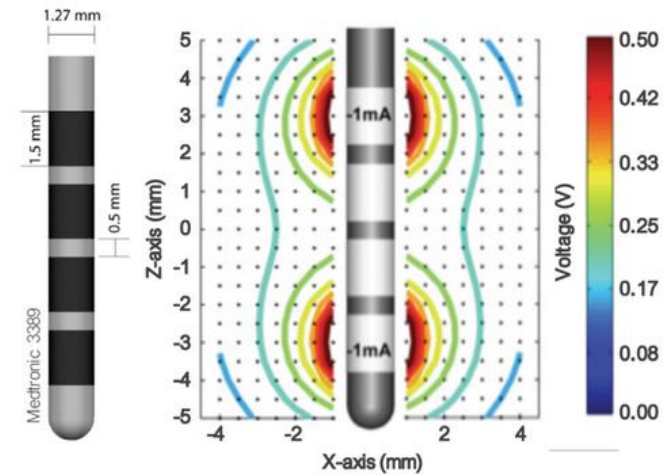
tgilbertson@dundee.ac.uk



Precision interfacing with the brain...Neuromodulation

The landscape of brain neuromodulation is advancing rapidly with neurotechnology

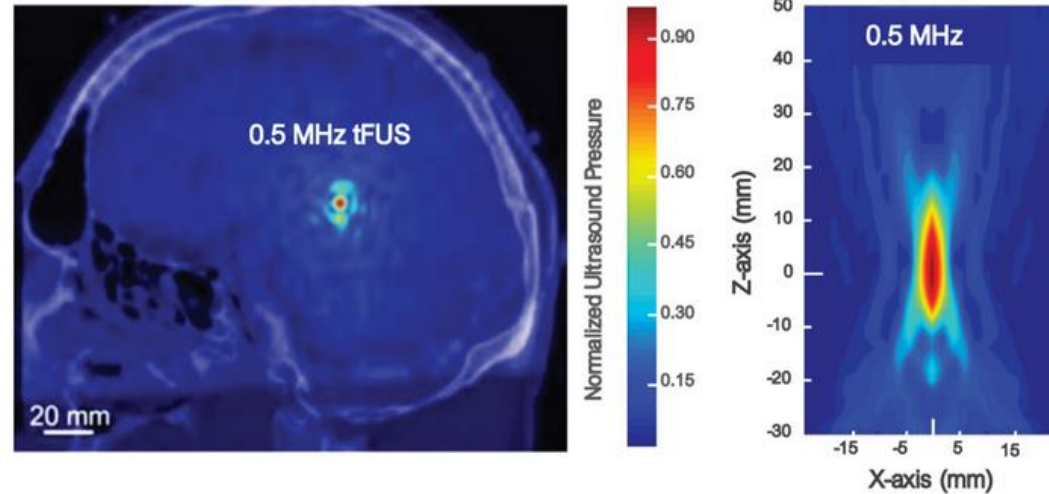
Invasive Neuromodulation



Deep Brain Stimulation (DBS)

+ Sub-millimetre precision
Clinical standard-of-care

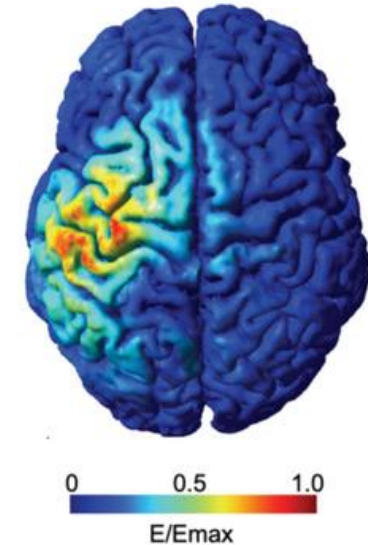
Non- Invasive Neuromodulation



Focused Ultrasound Neuromodulation (LIFU)

+ Sub- centimetre precision
Future clinical applications?

TMS



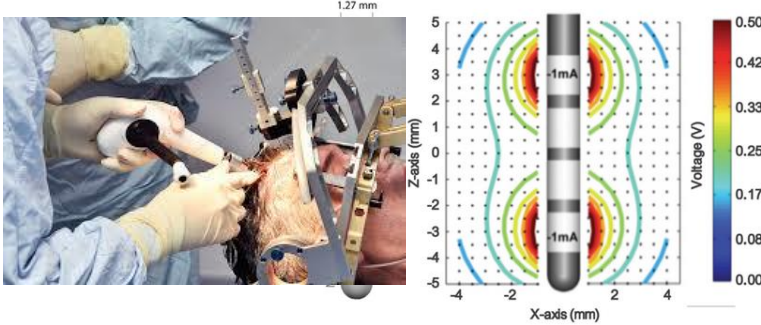
Transcranial
Magnetic
stimulation
(TMS)

>cm precision
No clinical role

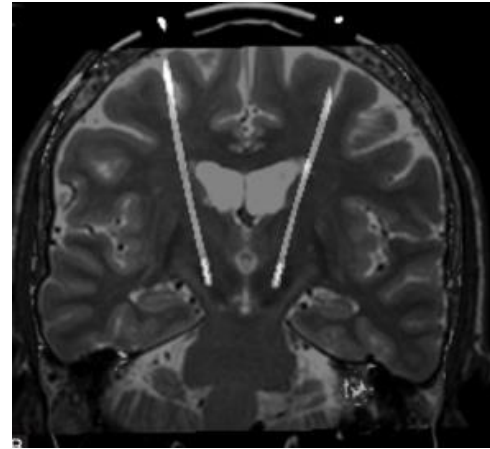
Precision neuromodulation in practice

Functional neurosurgery for Parkinson's

Deep Brain Stimulation



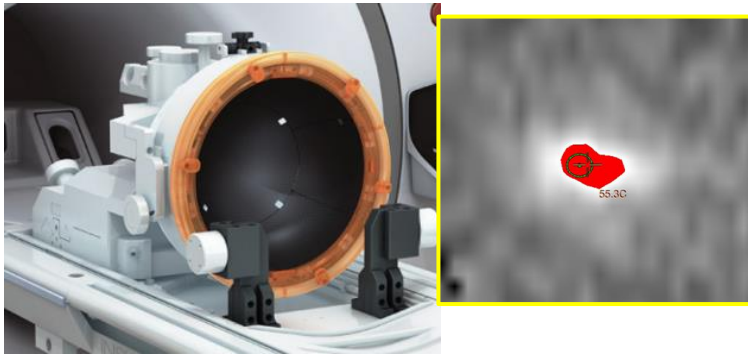
Electrical lesioning



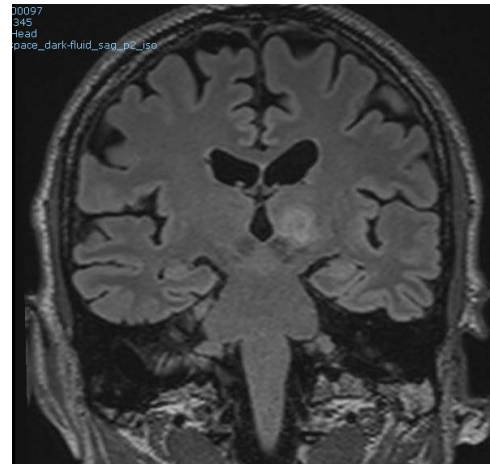
DBS Post op



Focused Ultrasound ablation



Thermal lesioning



Day 1 Pos-op Thalamotomy



Baseline

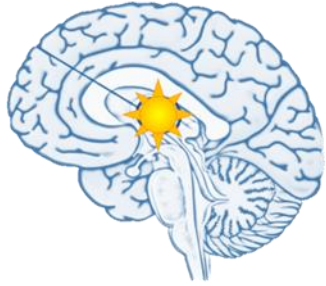


Day 1 post op (yesterday!)

1048-element
Phased array
Ultrasound

SUNRISE & PD012

Inclusion criteria and outcome measure



SUNRISE

Safety and efficacy of
thalamotomy by
Ultrasound for
Parkinson's disease



INSIGHTEC

PD012 Registry

ISRCTN17281700

Tremor Dominant Parkinson's disease¹

Tremor non-responsive to
levodopa (>600mg in 24hours)

Follow up 1,3,6 & 12 months

Outcome measures:-

UPDRS-III

CRST

PDQ-39



NCT04991831

Target enrolment **50** (Multicentre,
Europe & North America)

Follow up annually for 5 years

Outcome measures:-

UPDRS-III

CRST

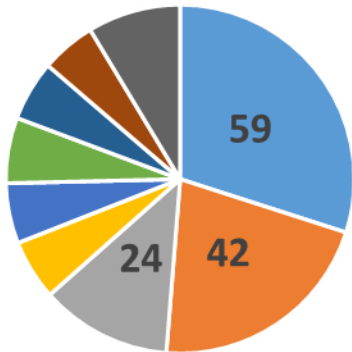
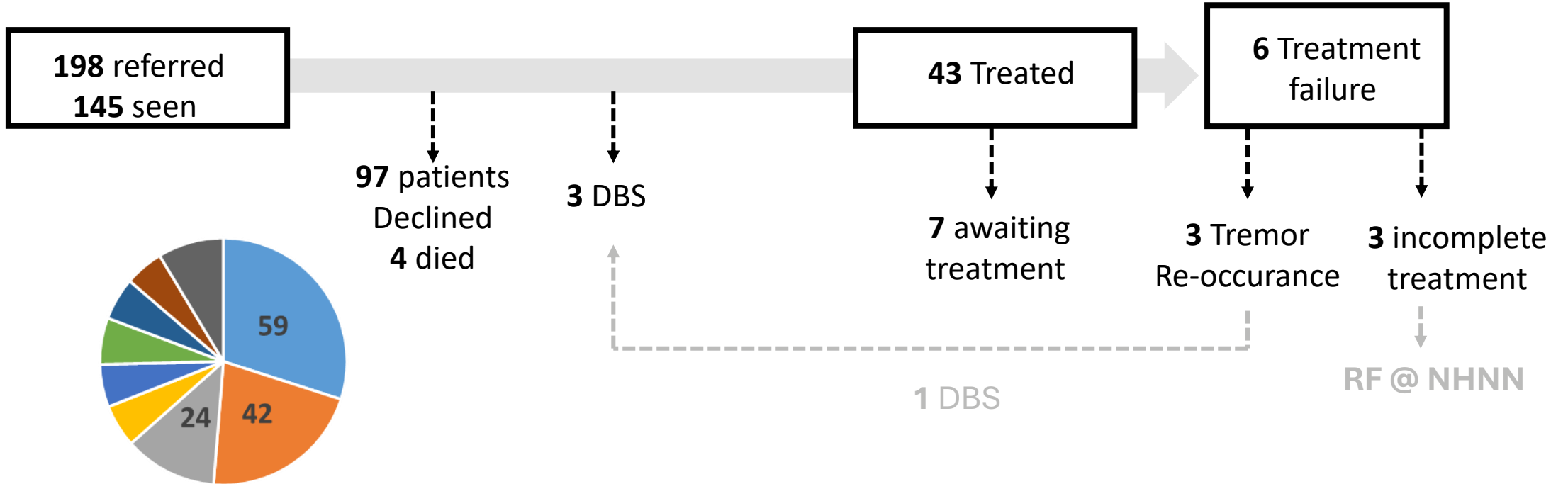
EQ-5D-5L, WPAI-GH (QoL)

¹Stebbins et. al., *Movement disorders* (2013)

First two years of experience in of MRgFUS thalamotomy in Essential Tremor

Addressing unmet burden of disease with neurotechnology

Minimum referral criteria: A) Diagnosis ET B) >2 medication trials C) Tremor impacting on QoL



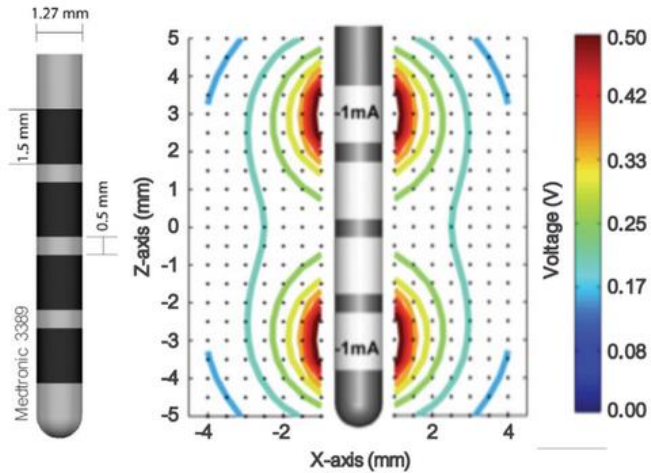
- NHS Tayside
- NHS GG&C
- NHS Lothian
- NHS Grampian
- NHS Forth Valley
- NHS Fife
- NHS Lanarkshire
- NHS Highland
- NHS Other

5-Fold increase in surgical treatment for ET in Scotland

? Unmet burden of disease versus novel treatment adoption

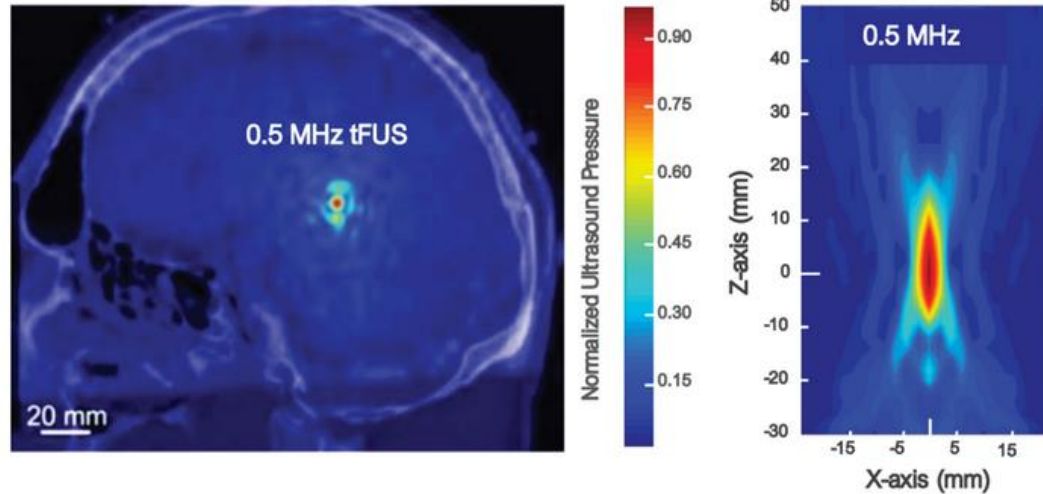
We need new targets for future non-invasive neuromodulation targets...
The landscape of brain neuromodulation is advancing rapidly with neurotechnology

Invasive Neuromodulation



Deep Brain Stimulation (DBS)
+ Sub-millimetre precision
Clinical standard-of-care

Non- Invasive Neuromodulation



Focused Ultrasound Neuromodulation (LIFU)
+ Sub- centmetre precision
Future clinical applications?

<https://www.aria.org.uk/>

Yaakub...Fourgan et. al., *Nature Communications* (2023)

What and Where of Clinical Apathy

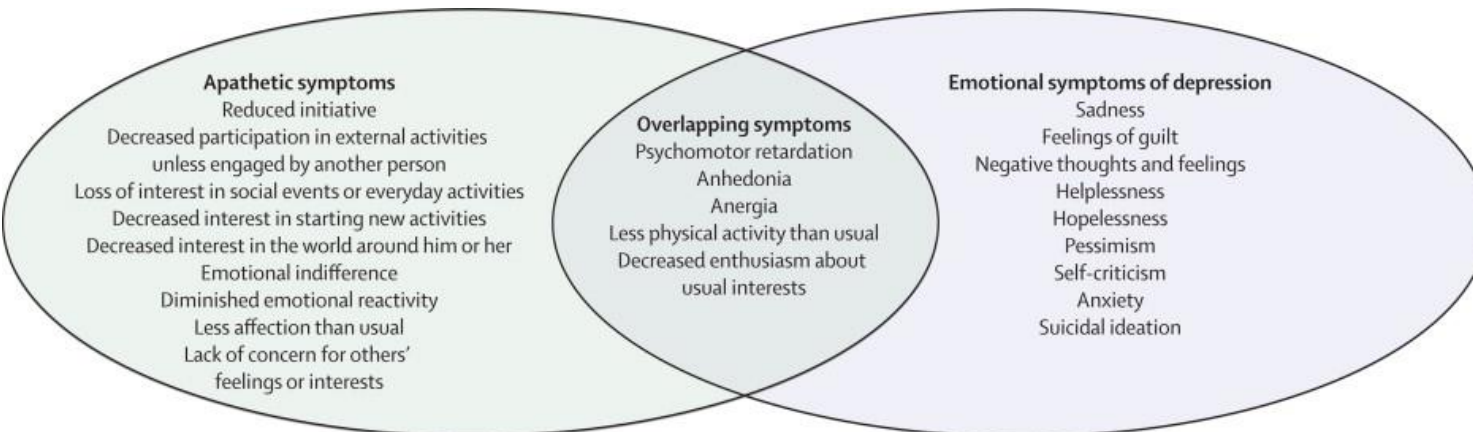
Framework for motivated behaviour

40% of PD *den Brok et. al., Mov Disorders (2015)*

Poor QoL OR **2.49** [1.49-4.15] *Benito-Leon et. al., Mov Dis (2012)*

PD Dementia risk HR **6.34** [2.32-11.6] *Fitts et. al., Parkin & Rel Dis (2015)*

Abolishes QoL from DBS *Martinez-Fernandez et. al, 2016 JNNP*



Pagonabarraga et. al., (2015), Lancet Neurology

Consensus criteria (2021)

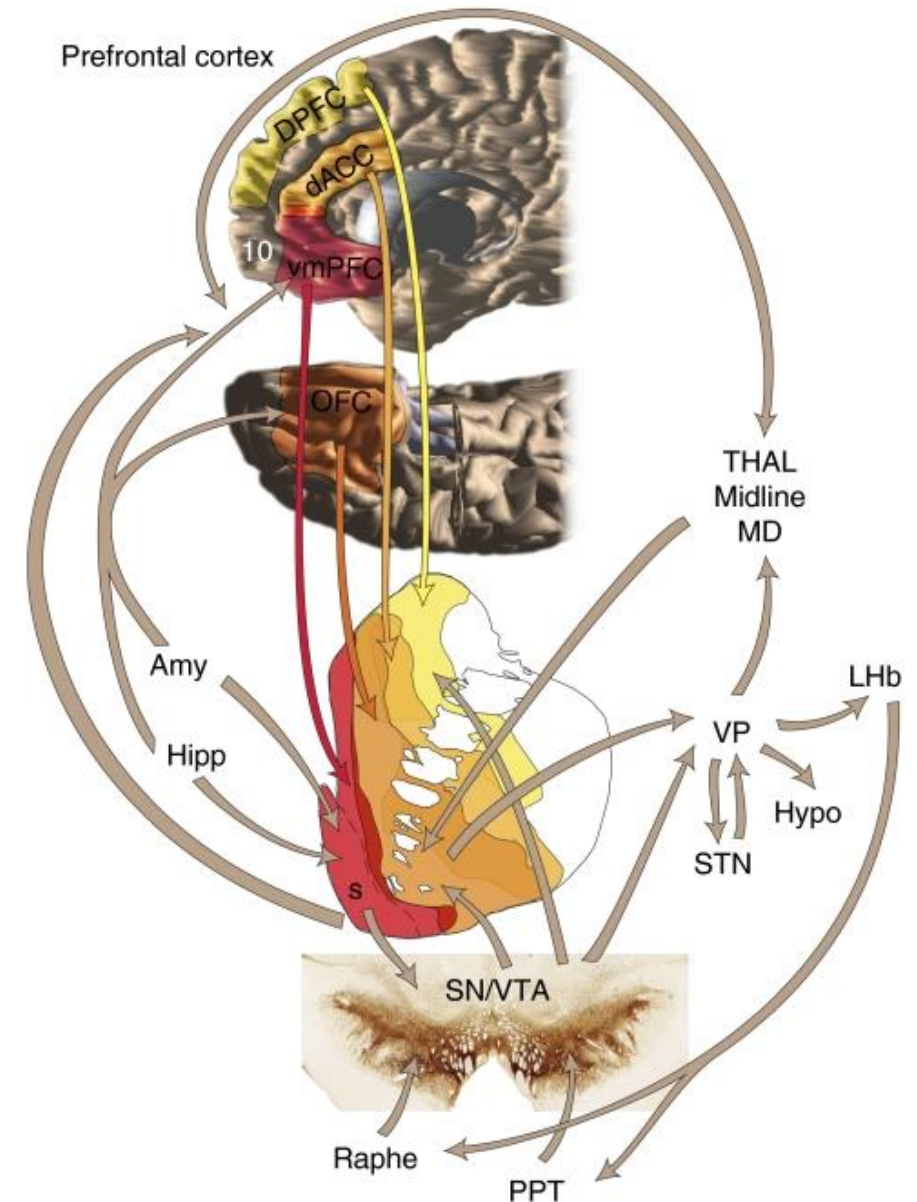
Reductions of ≥ 2 of the following:

Initiative

Interest

Emotional expression/responsiveness

Miller DS et. al., Alzheimer's & Dem(2021)

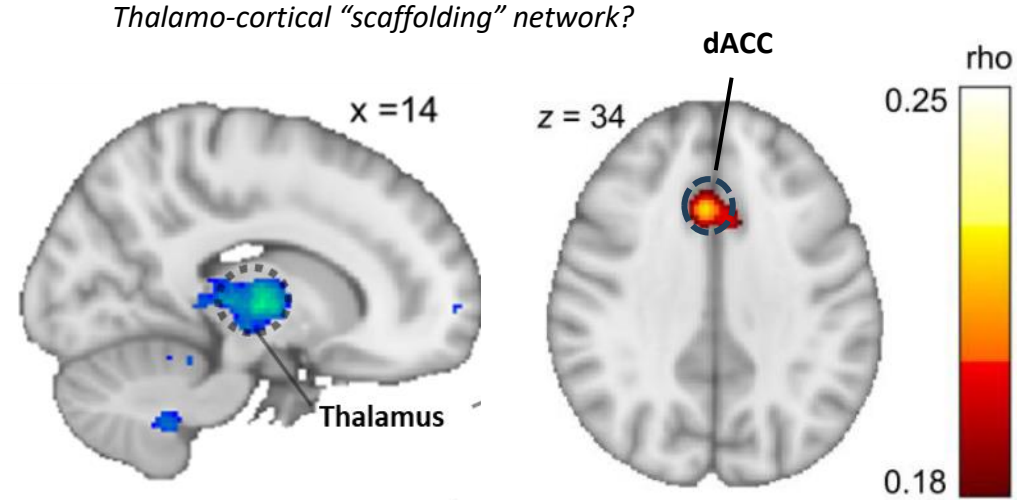
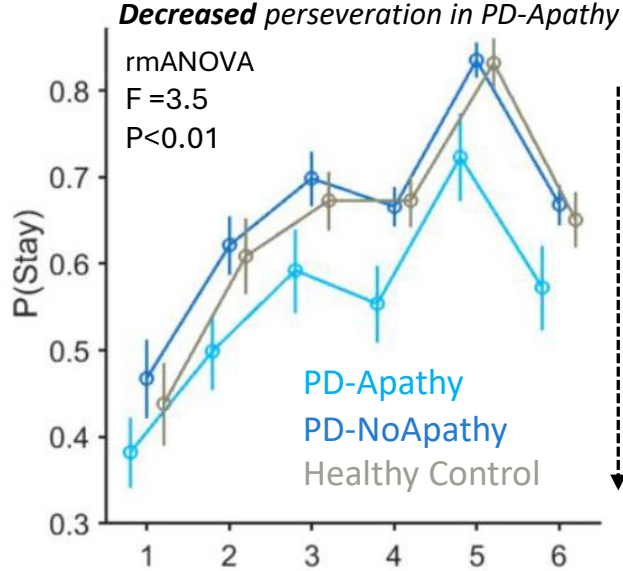
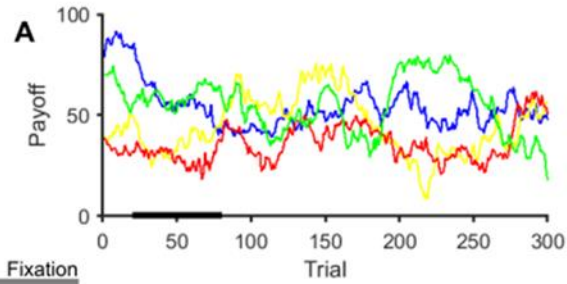


Haber & Knutson (2010) Neuropsychopharmacology

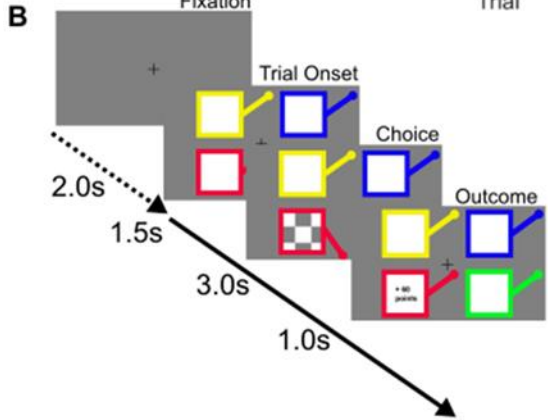
Using MRgFUS Thalamotomy to map thalamic contributions to non-motor PD symptoms

Implications for non-motor symptoms including apathy

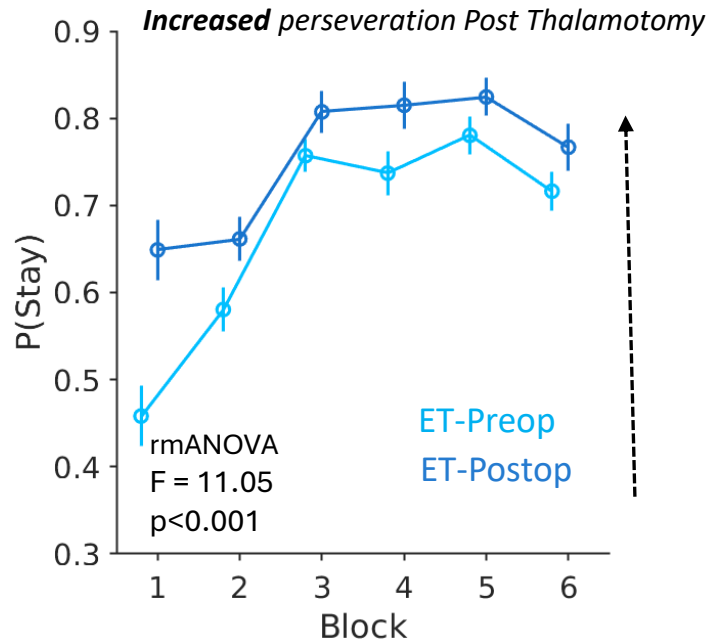
"Stock-market" task
4-armed restless bandit



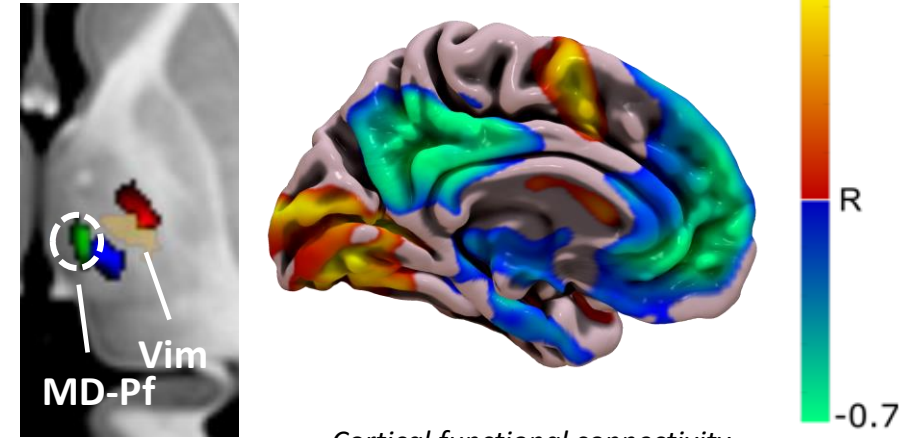
Gilmour et. al., (2024) Brain



Daw et. al, Nature 2006
Chakroun et. al., Elife 2020



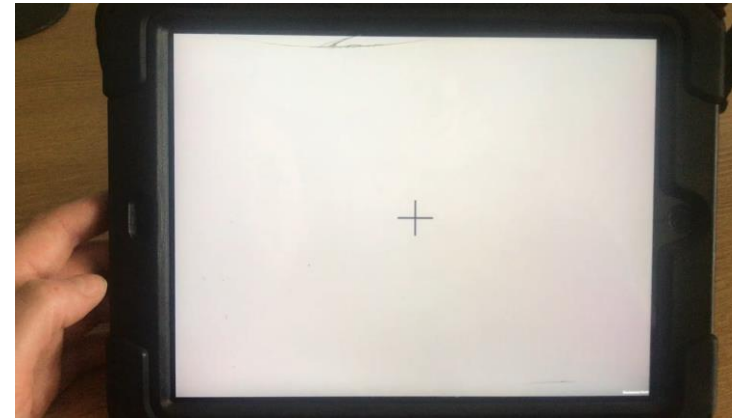
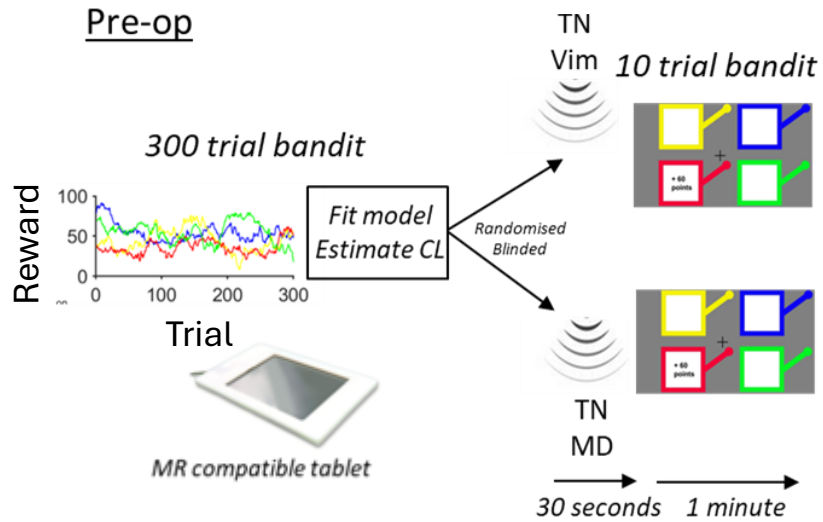
Thalamotomy lesion network mapping



Cortical functional connectivity
with MD-Pf

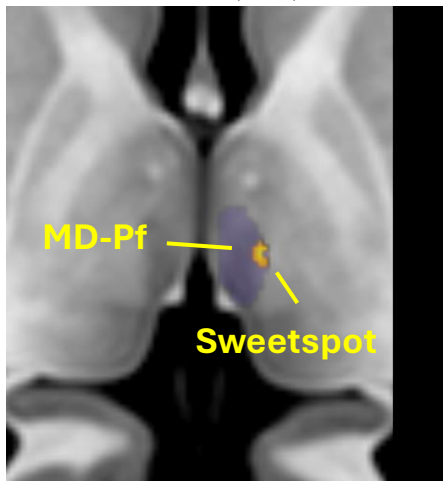
Mapping the function of the Mediodorsal thalamus with thermal neuromodulation (TN)

Exploring online effects with intra procedural cognitive testing

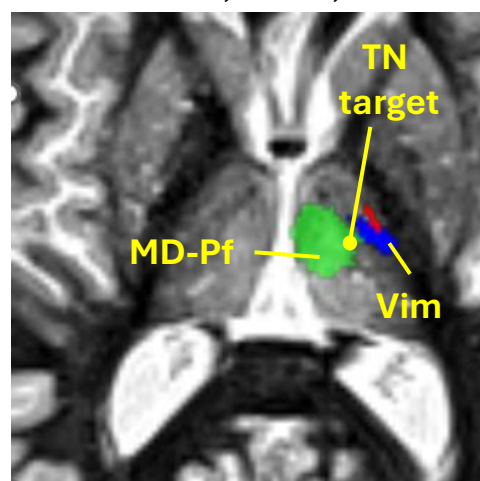


Courtesy of Dr Isla Barnard

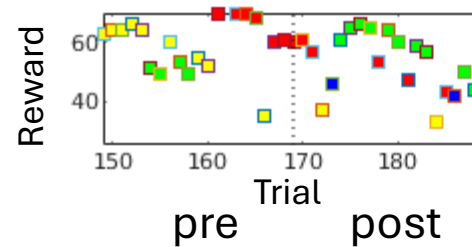
Group level co-ordinate
MNI = -7.9,-17,3



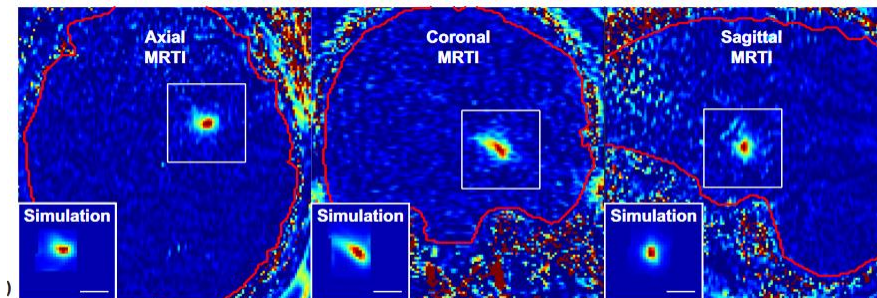
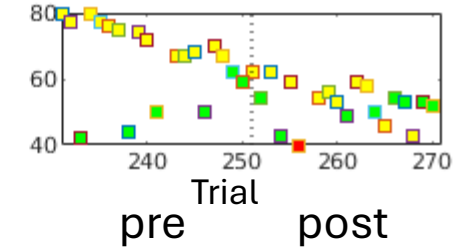
Patient co-ordinate
ML +7.6 mm, +7.3 AP, +3.96 SI



Sonicate MD



Sonicate Vim



TN Thermometry volumetric reconstruction

P(Stay) Voxel-wise Signed Rank
 $Z = 3.8, p < 0.05$ (FDR $q = 0.05$)

Thank you for listening...

Acknowledgements:-

Professor Douglas Steele

Mr Sonnie Khan

Dr Jen MacFarlane

Dr Steve Gandy

Baljit Jagpal

Tracy Brunton

Dr Graeme Mackenzie

Dr Isla Barnard

Dr Ed Newman

Dr Vicky Marshall

Mr Mike Canty

Dr Antonella Marcerollo

