Mapping Brain Circuit Targets for Neuromodulation

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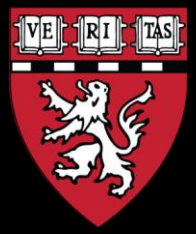
Professor of Neurology, Harvard Medical School
Director, Center for Brain Circuit Therapeutics
Raymond D. Adams Distinguished Chair in Neurology
Kaye Family Director of Psychiatric Brain Stimulation
Brigham and Women's Hospital

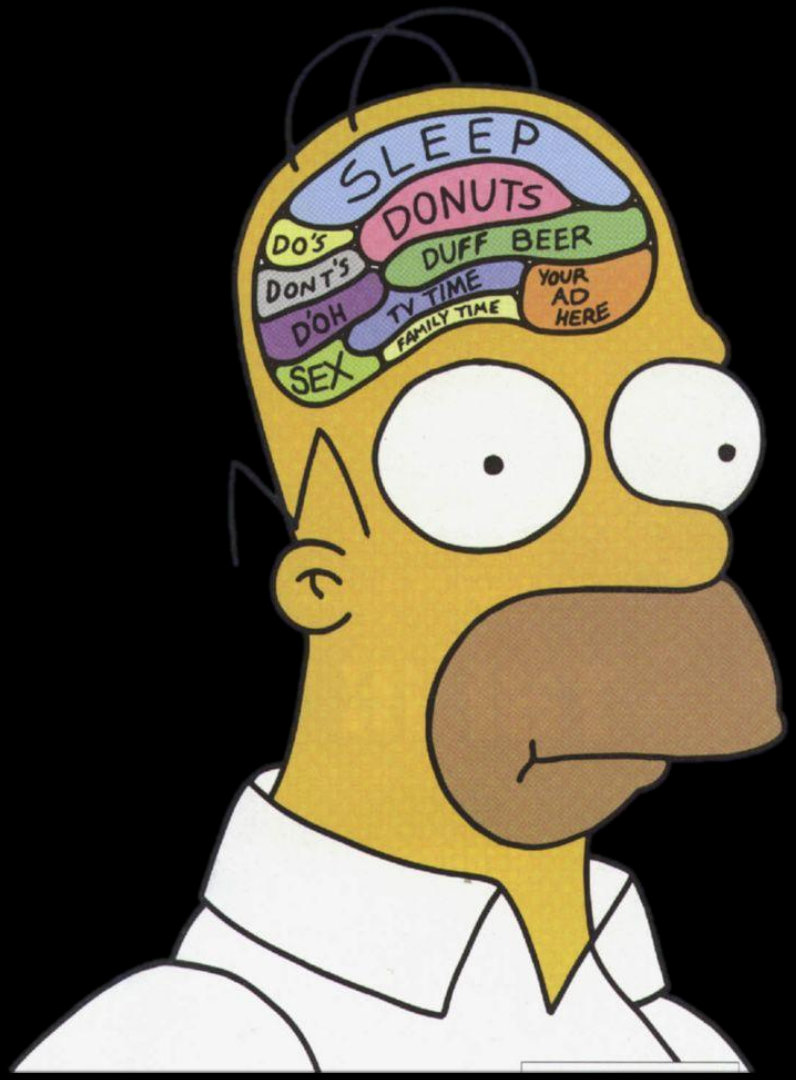


Disclosures

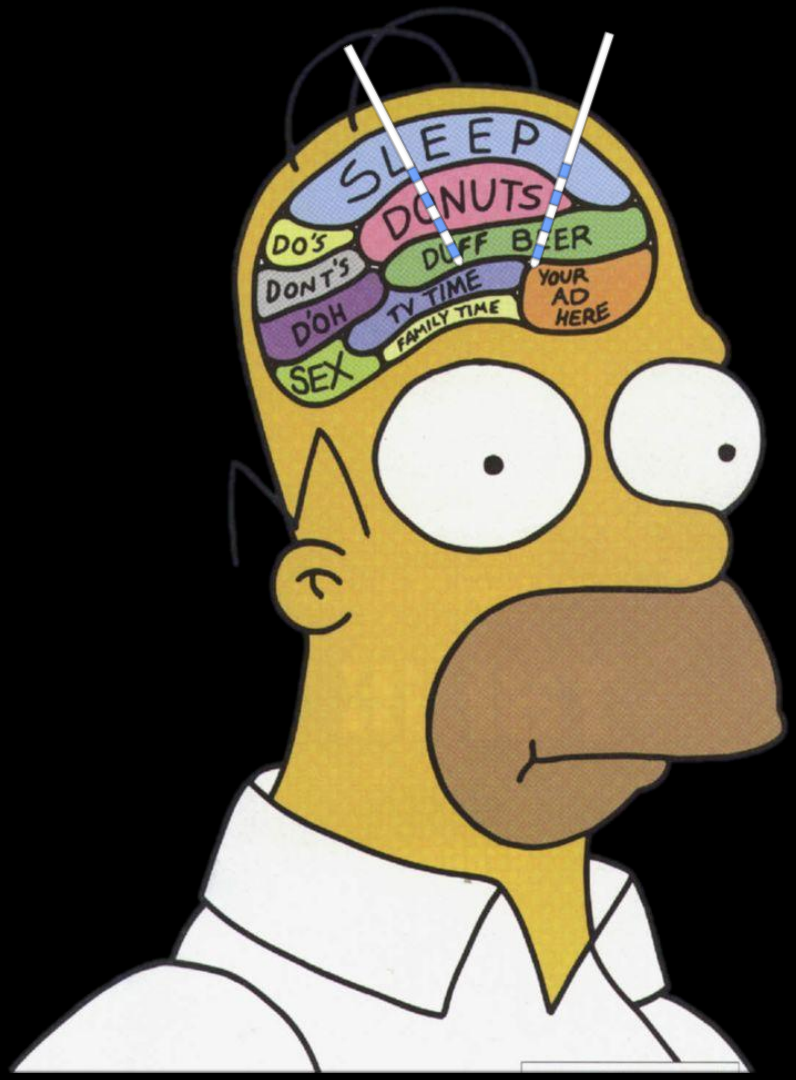
- Conflicts
  - Intellectual Property on using connectivity imaging to map lesions and guide neuromodulation
  - Consultant: Magnus Medical, Soterix, Abbott, Boston Scientific, Tal Medical, MDC Capital, Salma Health
  - May discuss non-FDA approved indications

- Funding
  - NIH: R01MH113929, R21MH126271, R21NS123813, R01NS127892, R01MH130666, UM1NS132358
  - Foundation: Kaye Family Research Endowment, the Ellison / Baszucki Family Foundation, Manley Family, Thomas May and Family, Once Upon a Time Foundation
  - Industry: Neuronetics, Boston Scientific

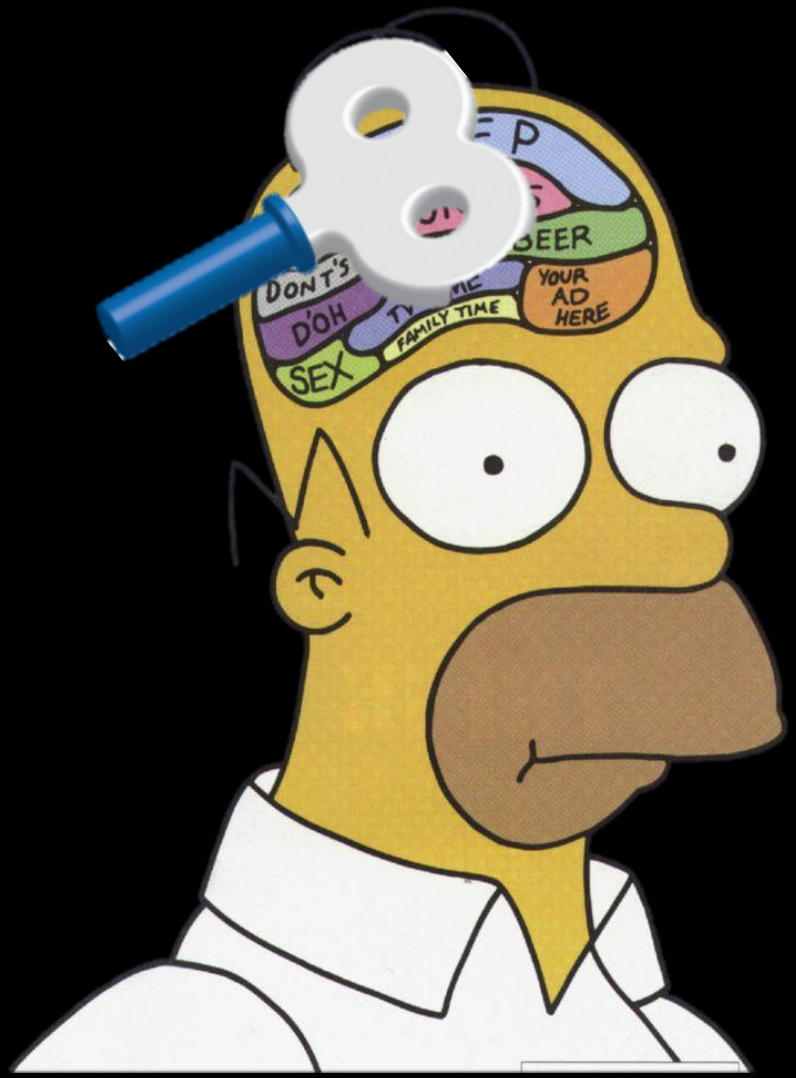
How do we identify a therapeutic target?



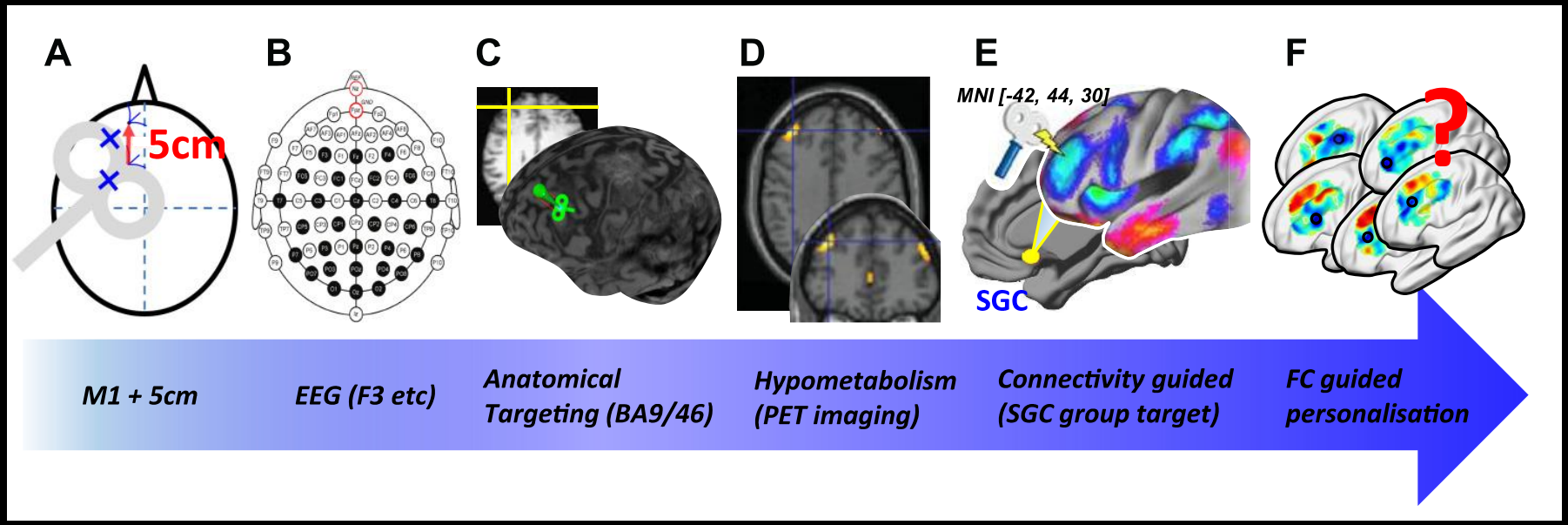
How do we identify a therapeutic target?



How do we identify a therapeutic target?



Targeting TMS in Depression



Cash et al. Biological Psychiatry 2020

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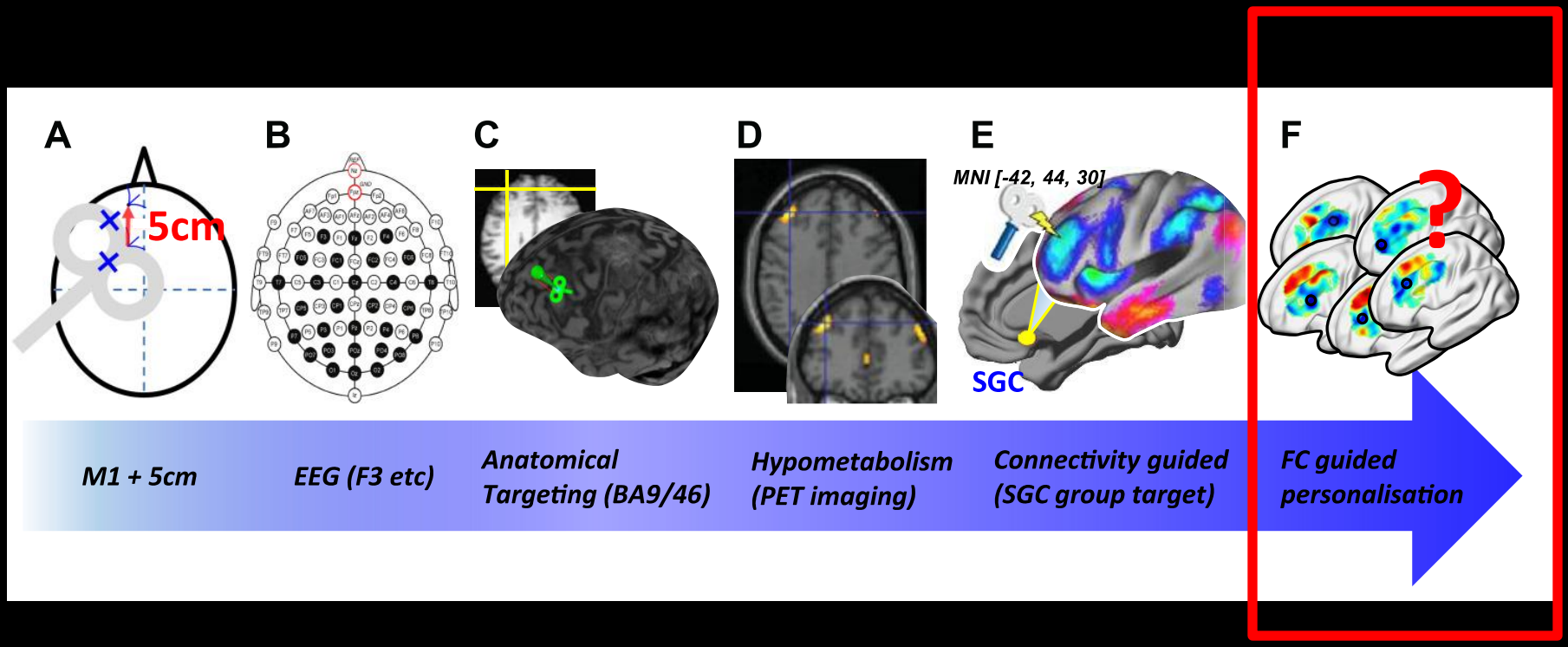

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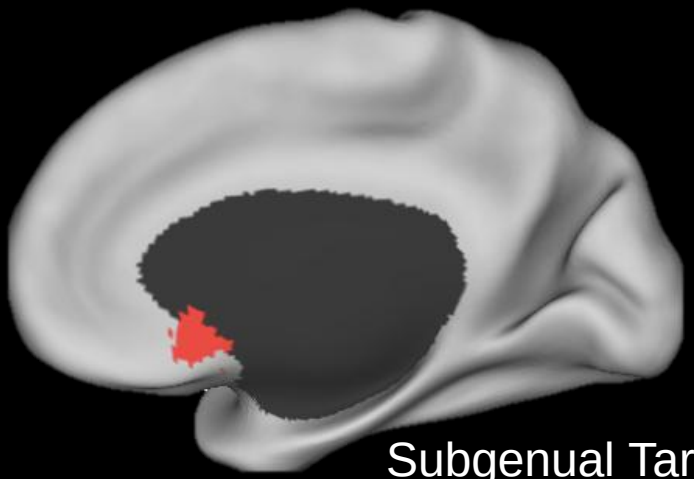
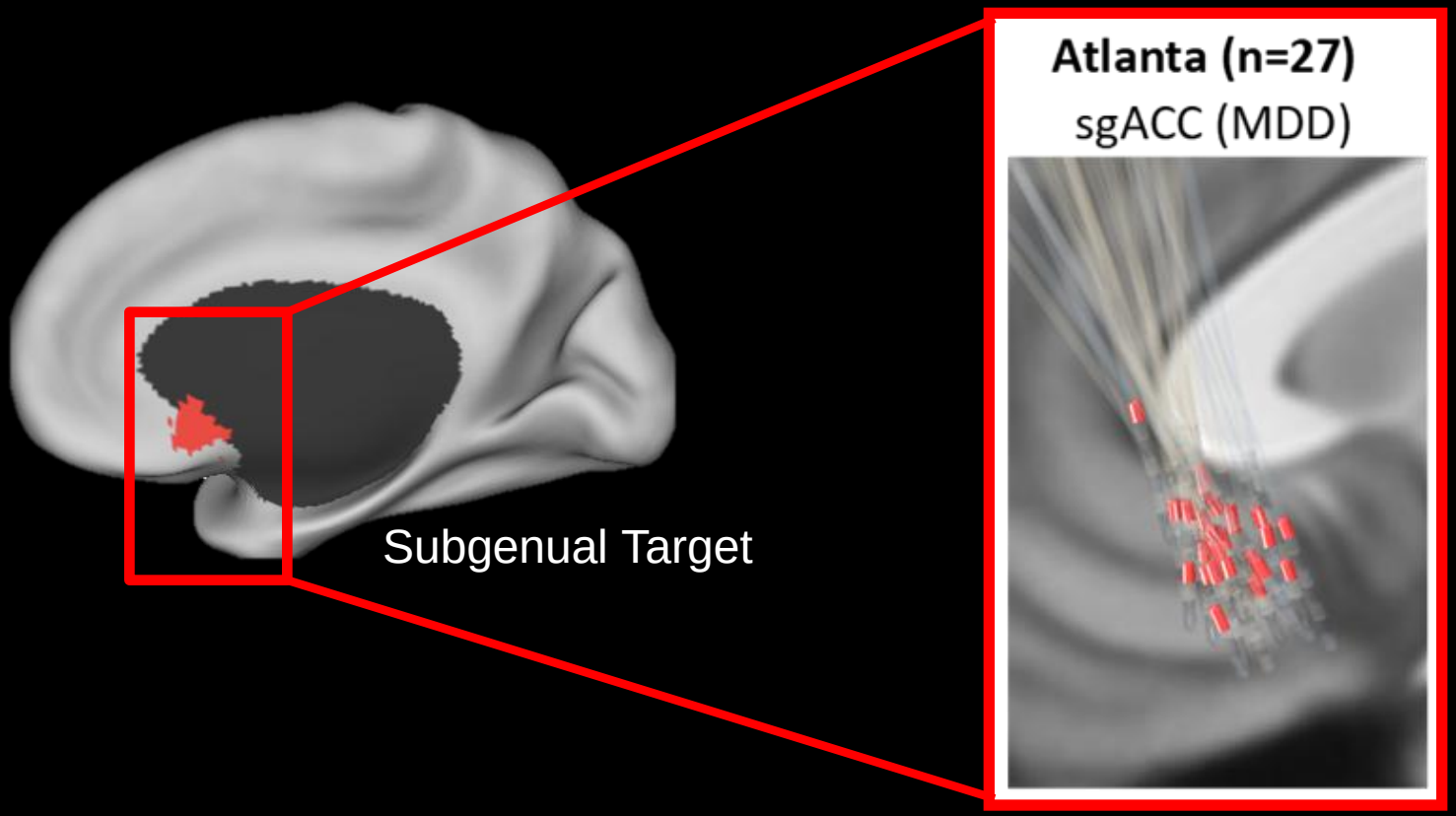


Subgenual Target

Fox et al. 2012 Biol Psych.



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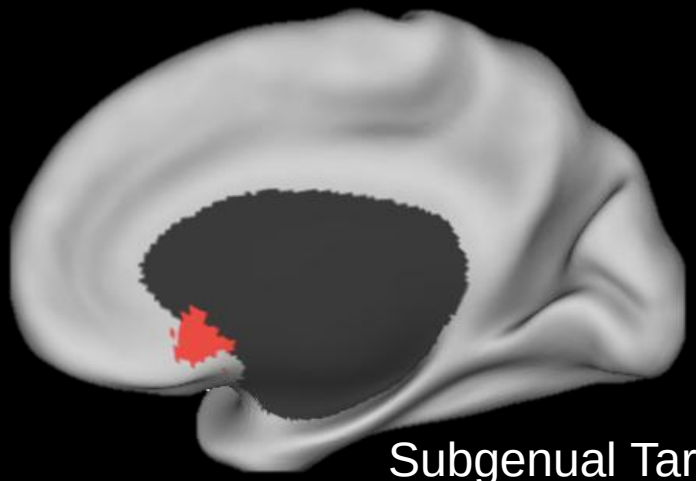

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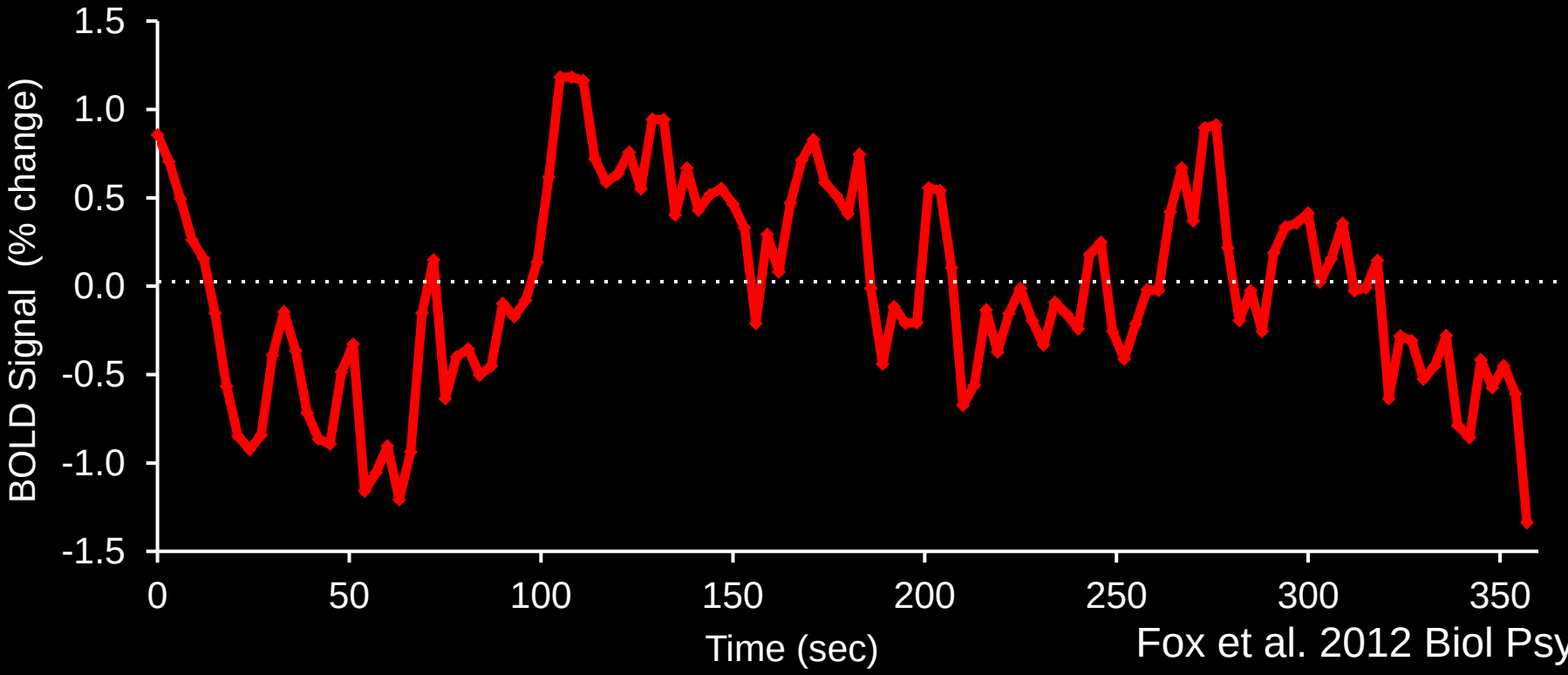

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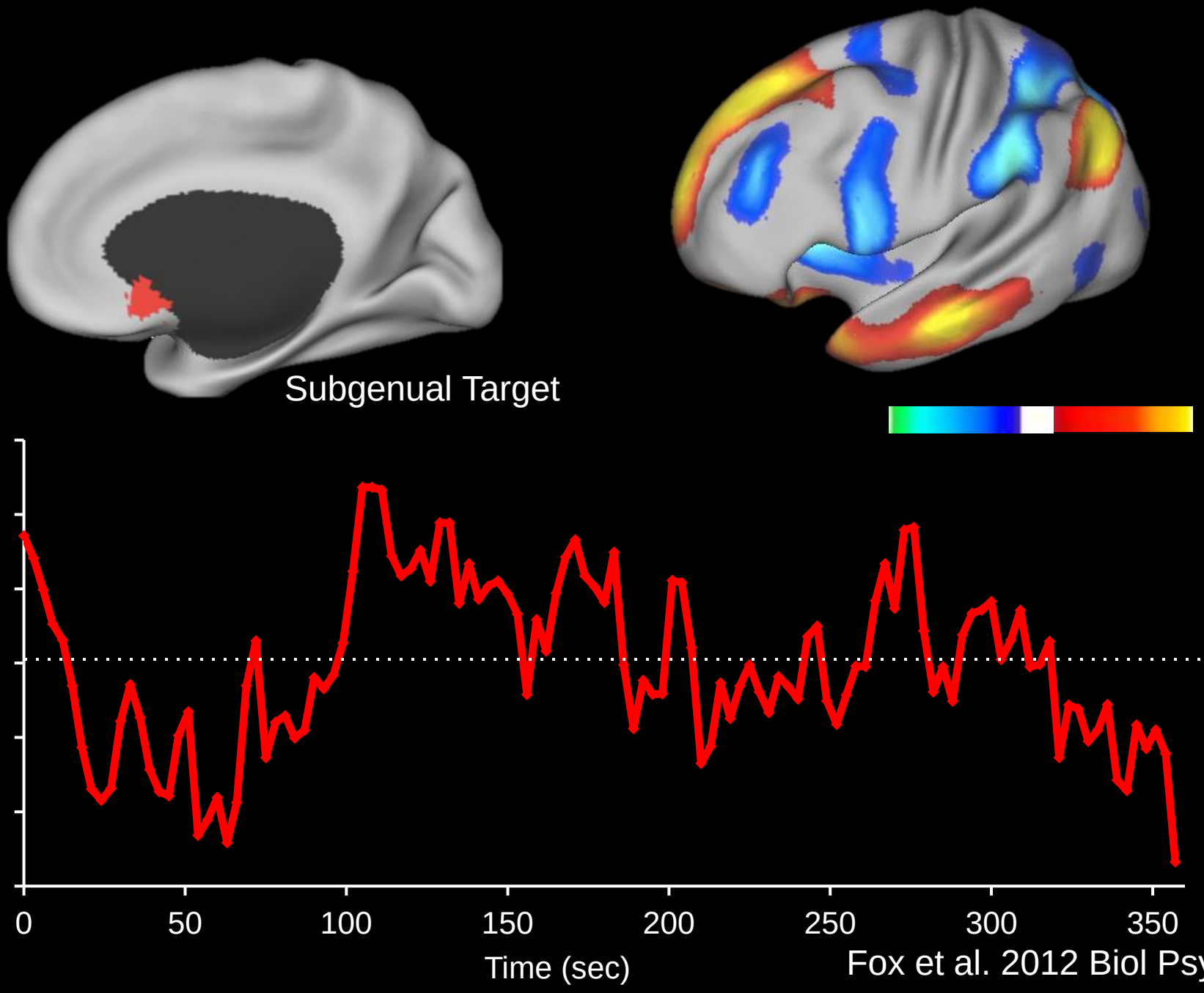
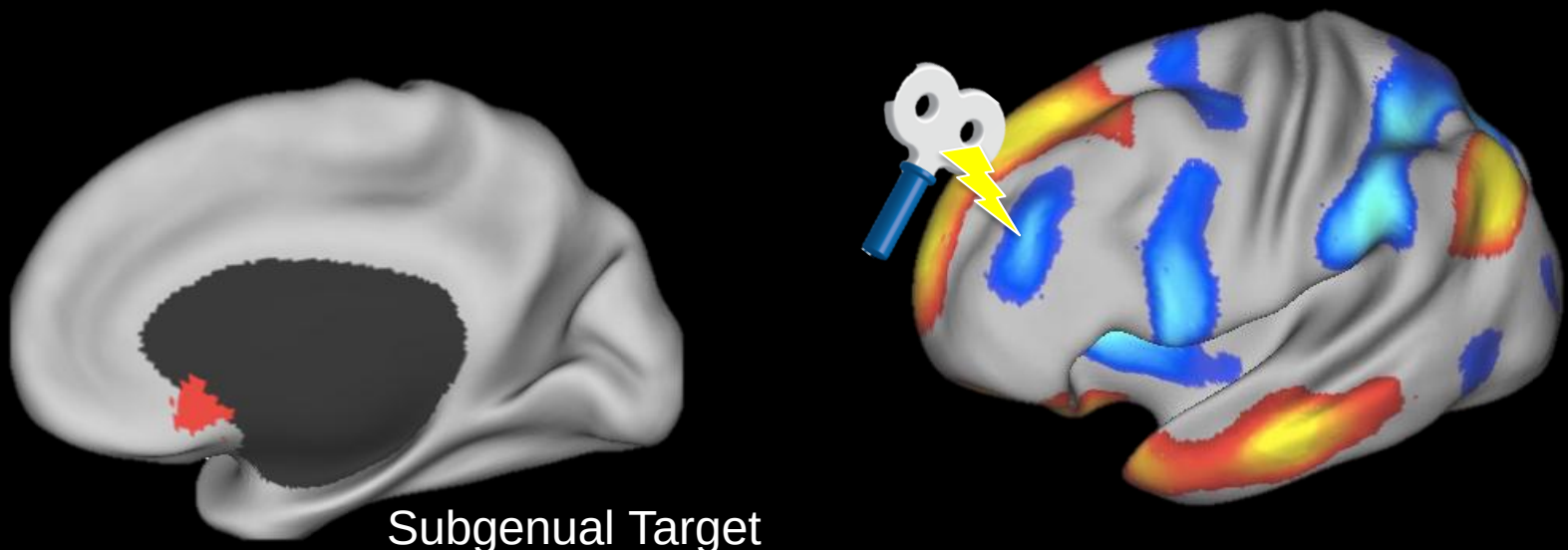

Subgenual Target
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
BOLD Signal (% change)
0
50
100
150
200
250
300
350
Time (sec)
Fox et al. 2012 Biol Psych.



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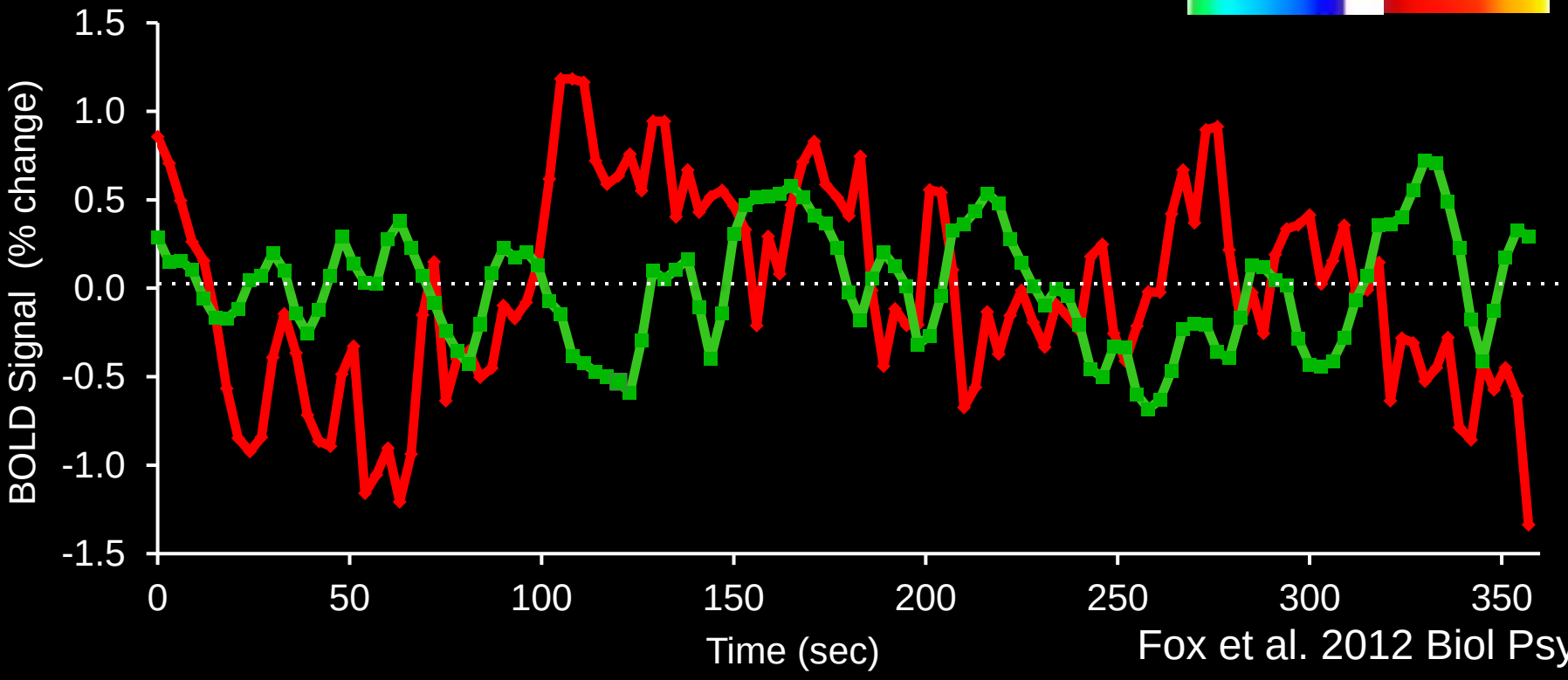

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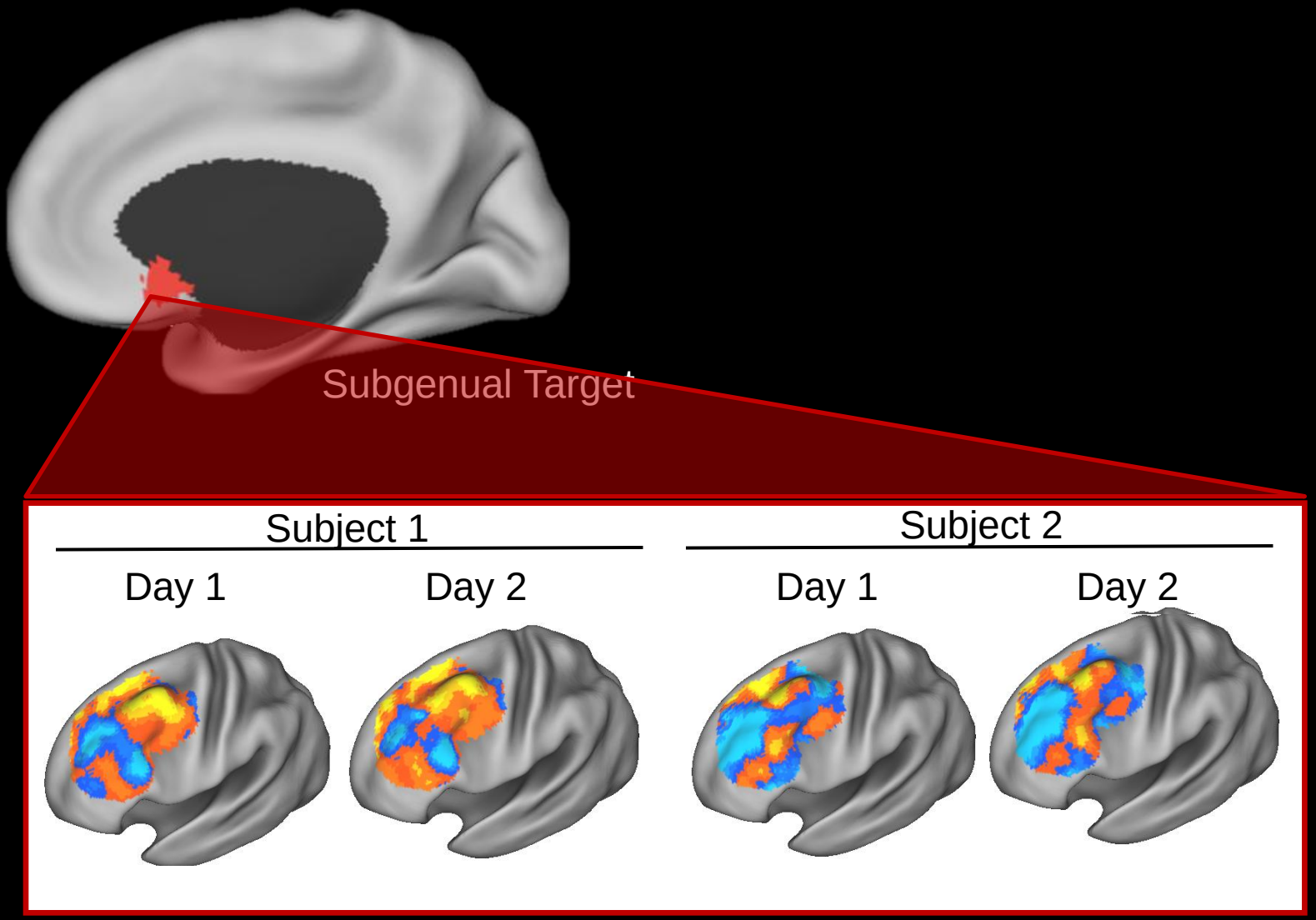
“Individualized” TMS Targets



Fox et al. 2013 Neuroimage

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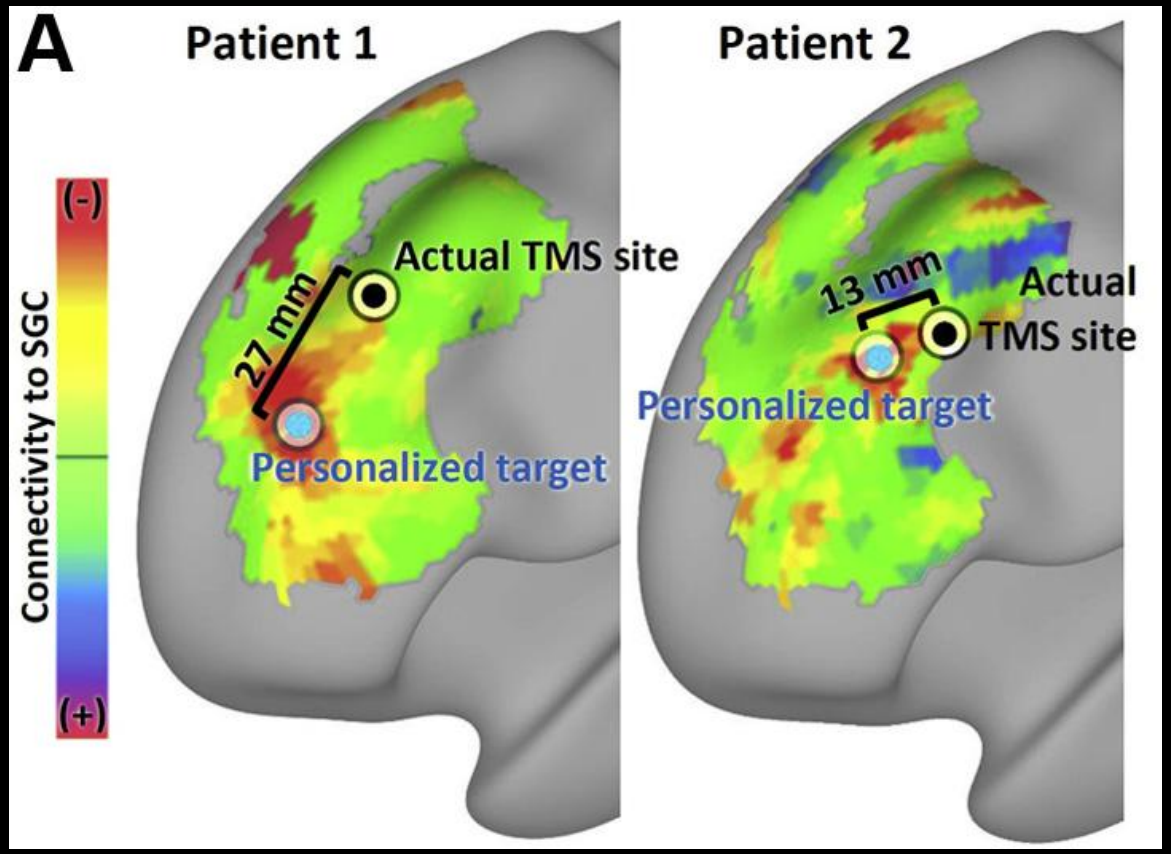

Siddiqi et al. 2021 Biological Psychiatry

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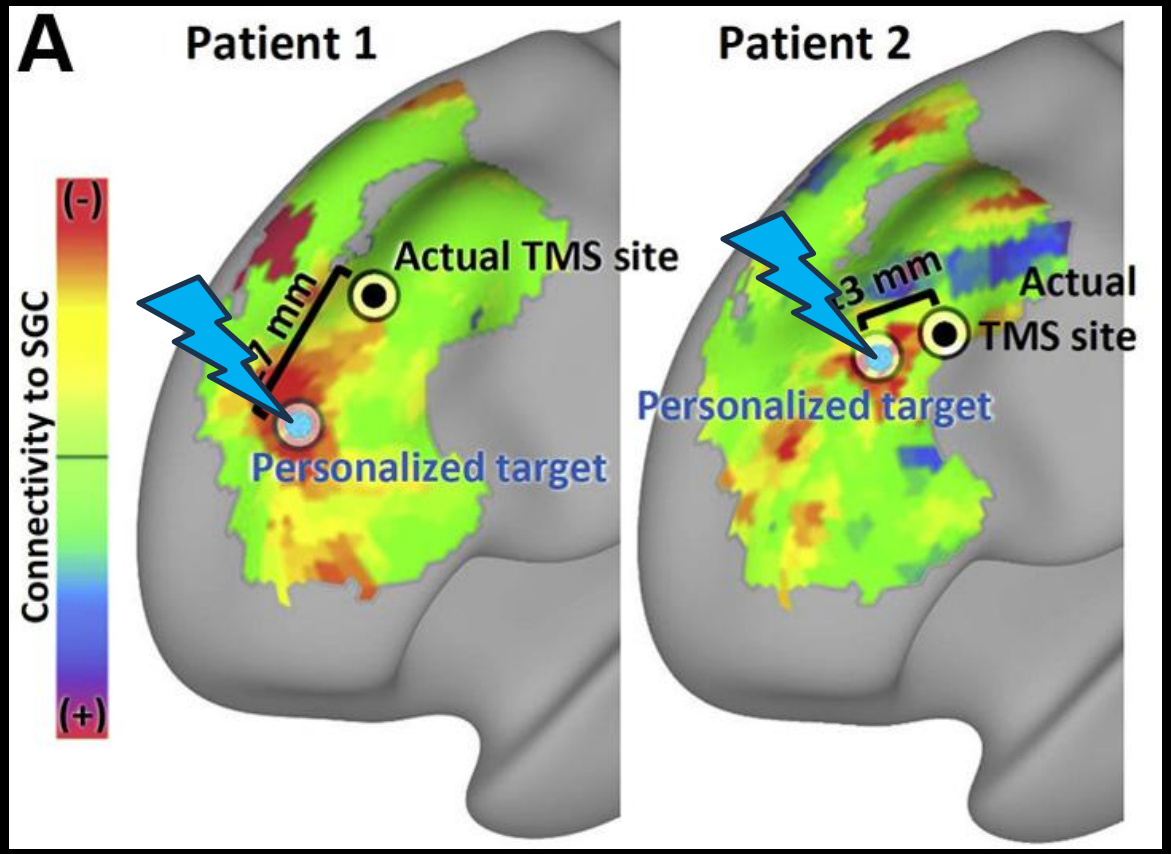
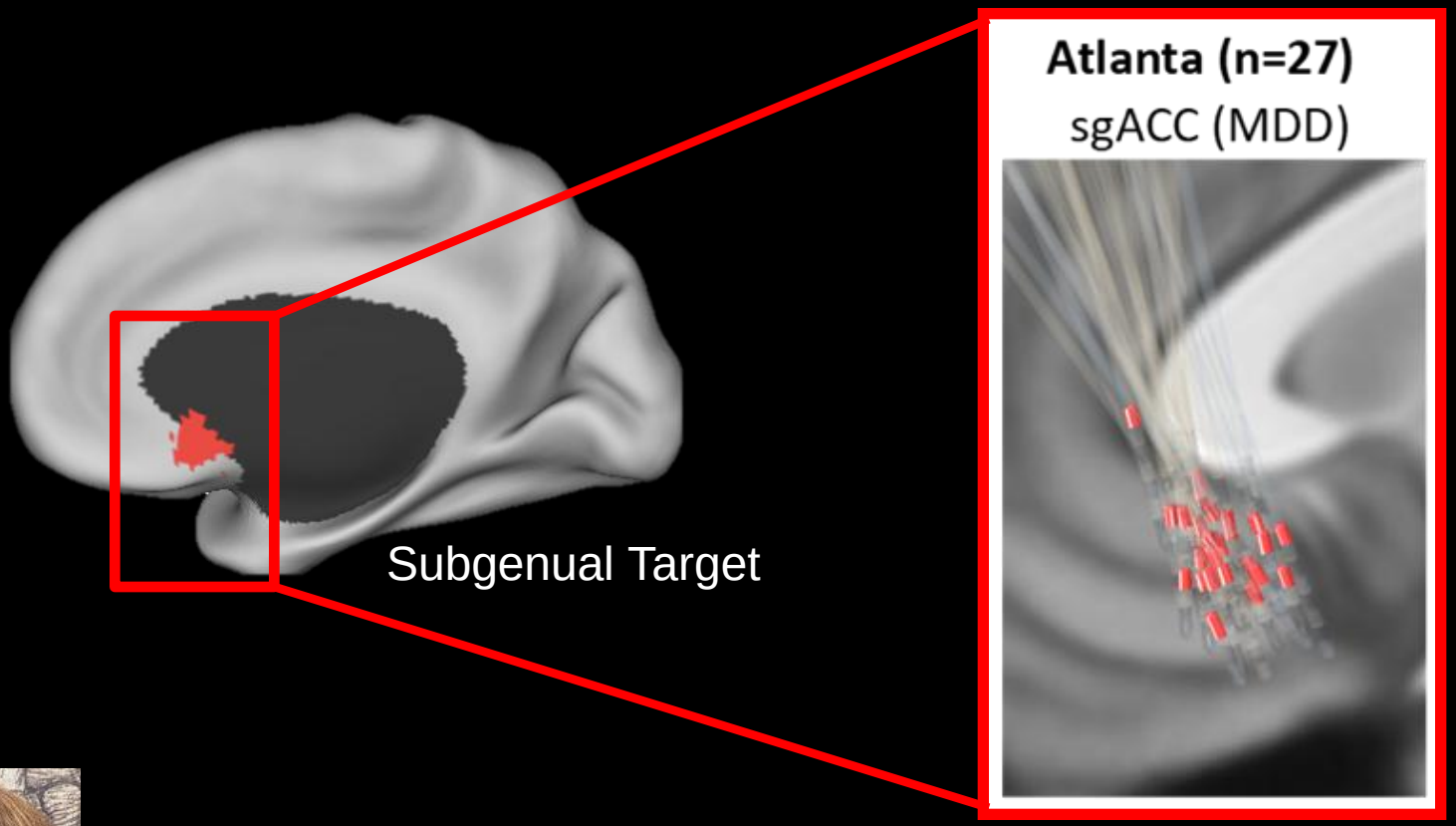


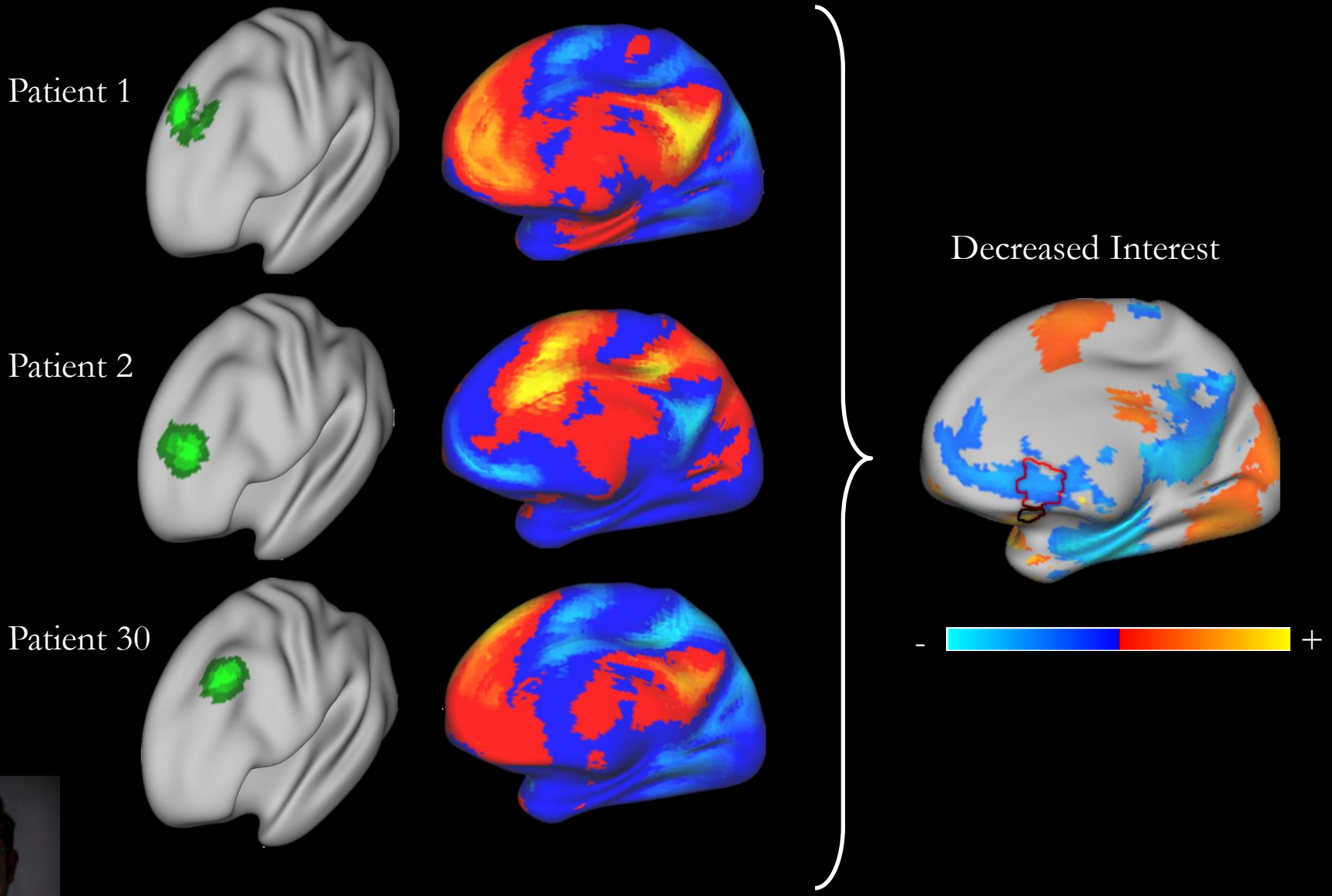
SAINT Neuromodulation System FDA approved 9/2022
Cole et al. 2020 AJP, Cole et al. 2021 AJP : >80% response rate

What if we're unsure of our target?



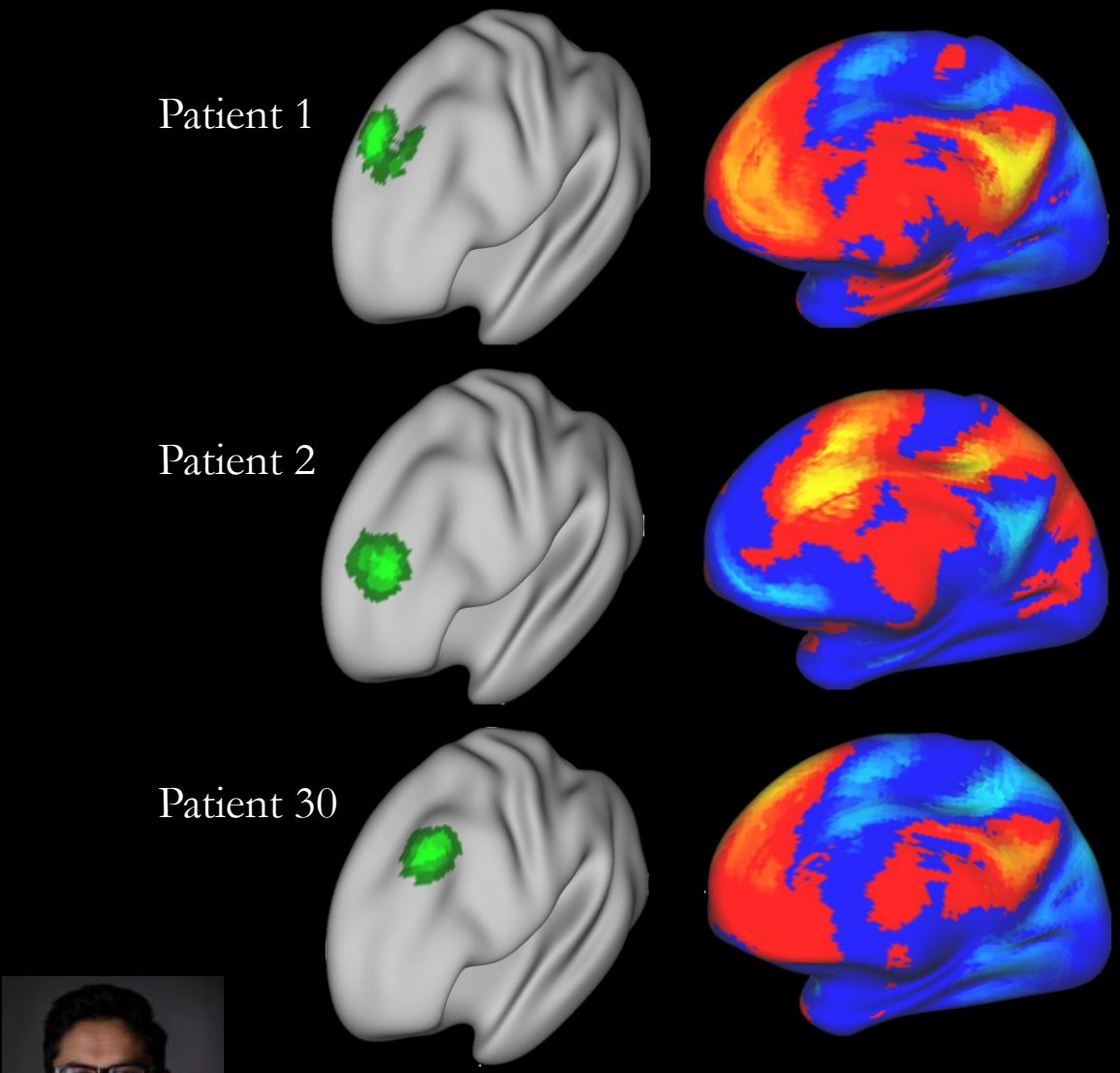
TMS Network Mapping

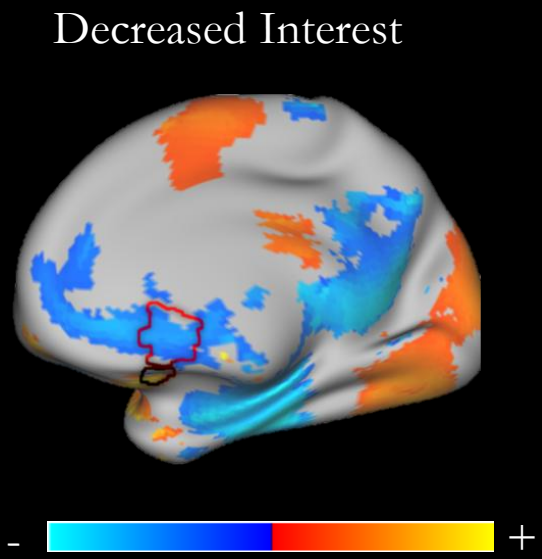
Siddiqi et al. 2020 Am. J. Psychiatry



Symptom-Specific TMS Targets?

Siddiqi et al. 2020 Am. J. Psychiatry





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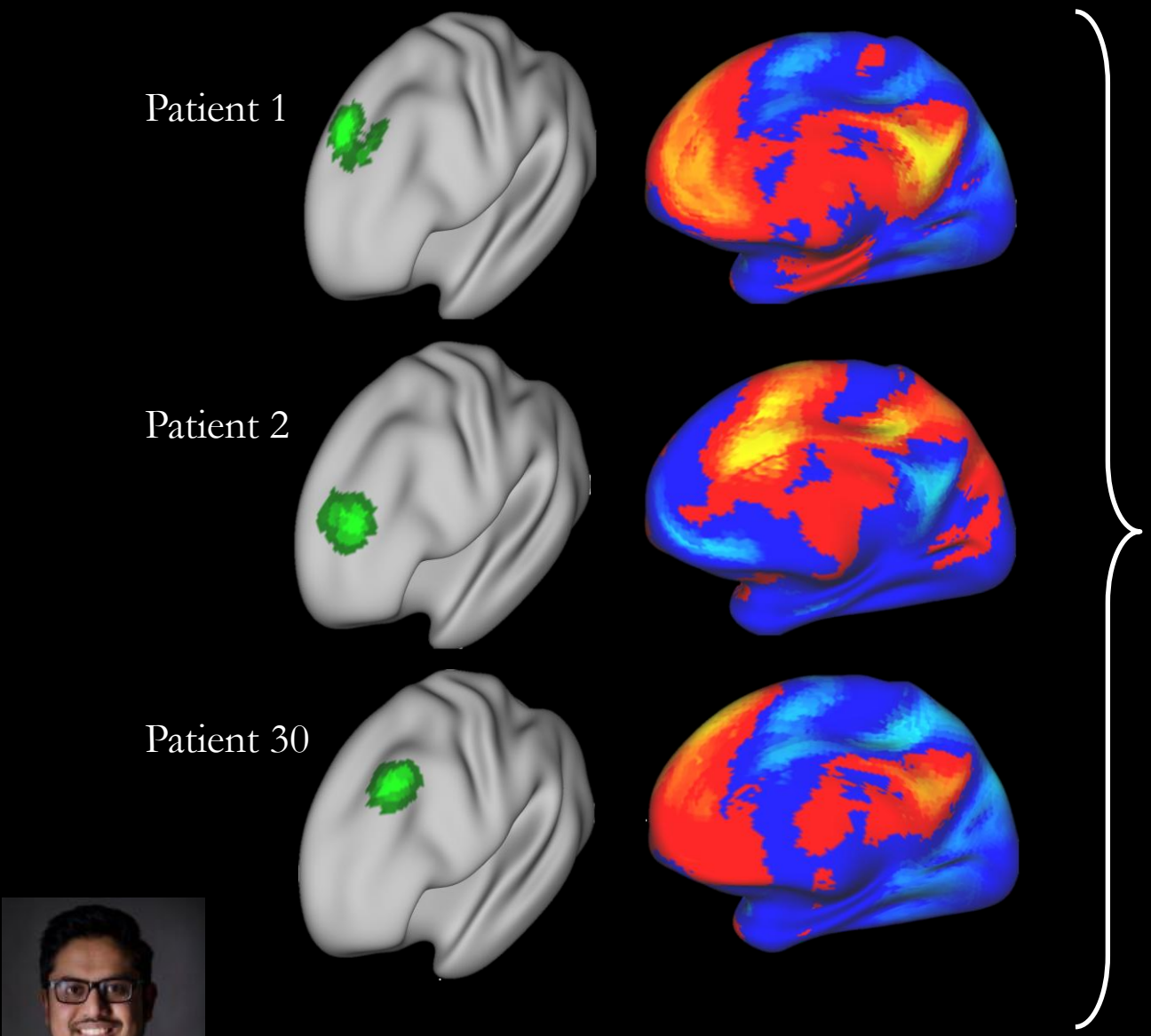
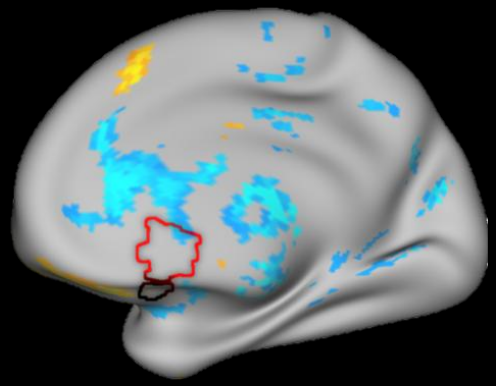
Siddiqi et al. 2020 Am. J. Psychiatry



Feelings of Failure



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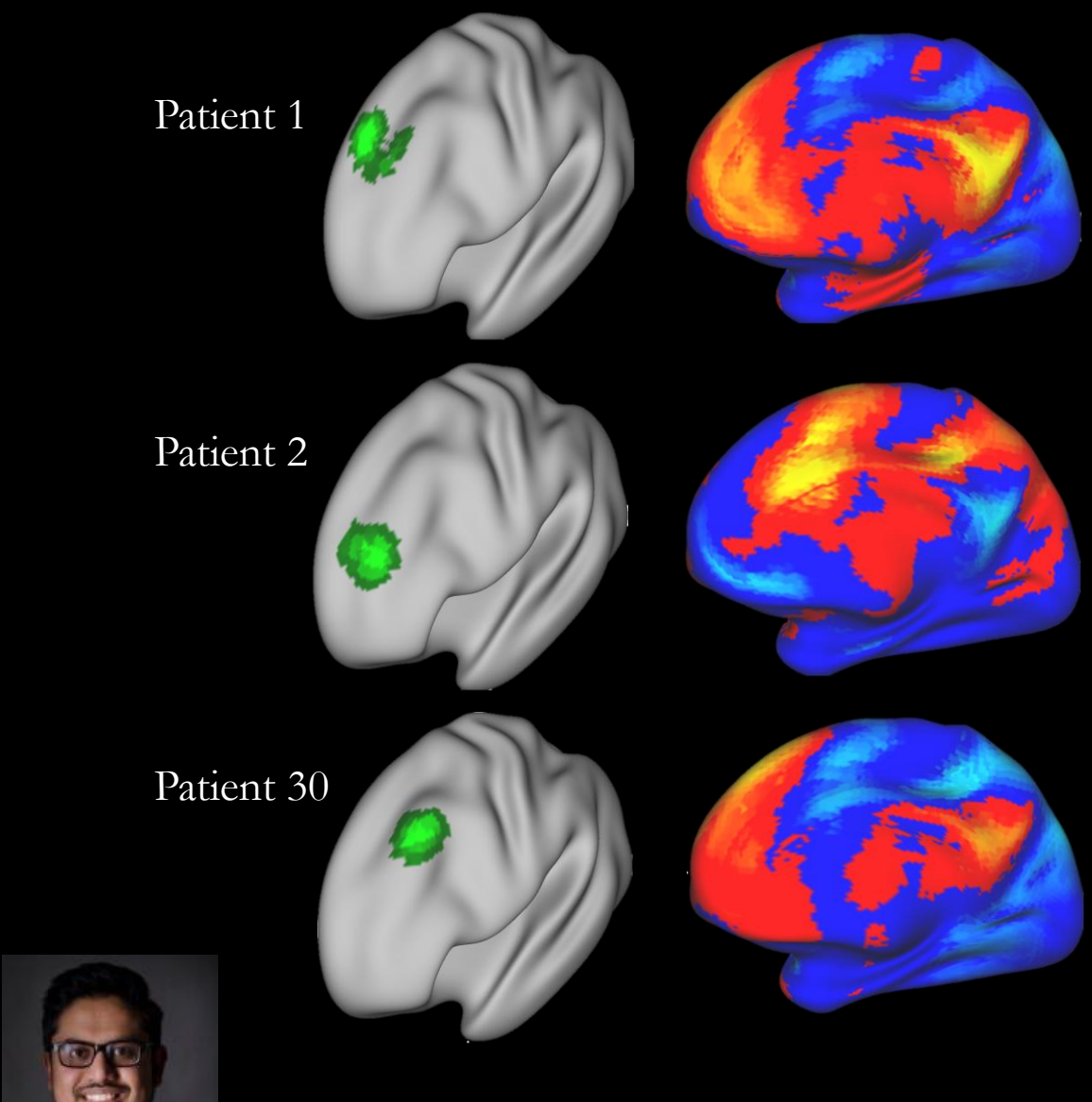

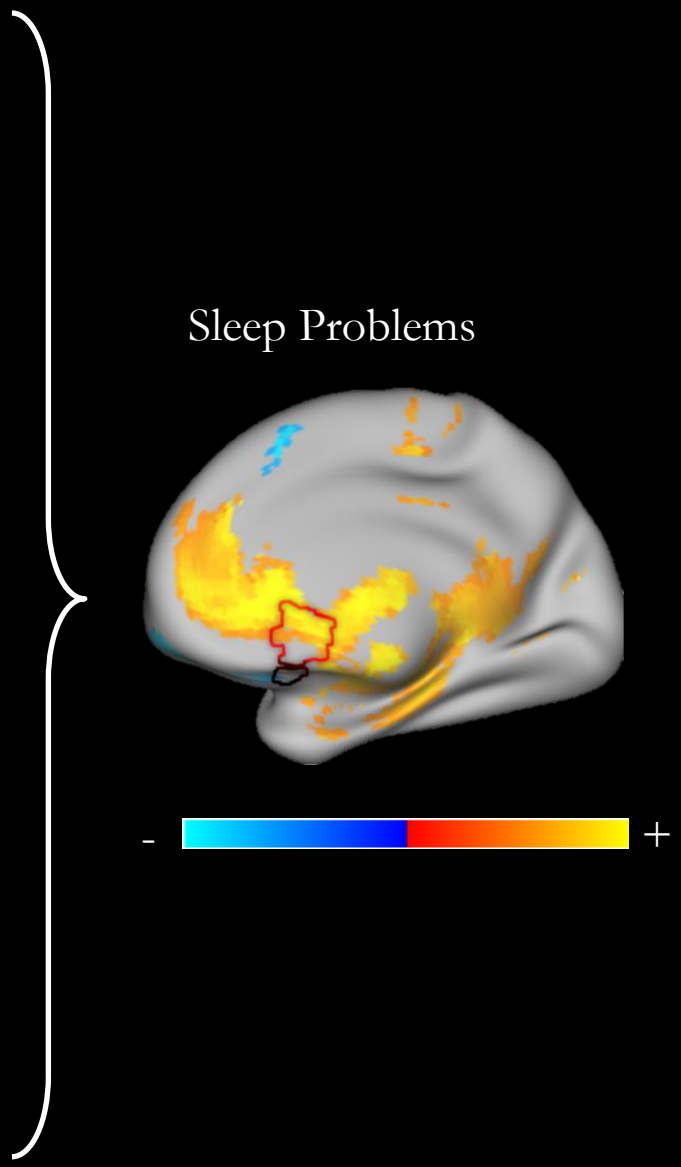

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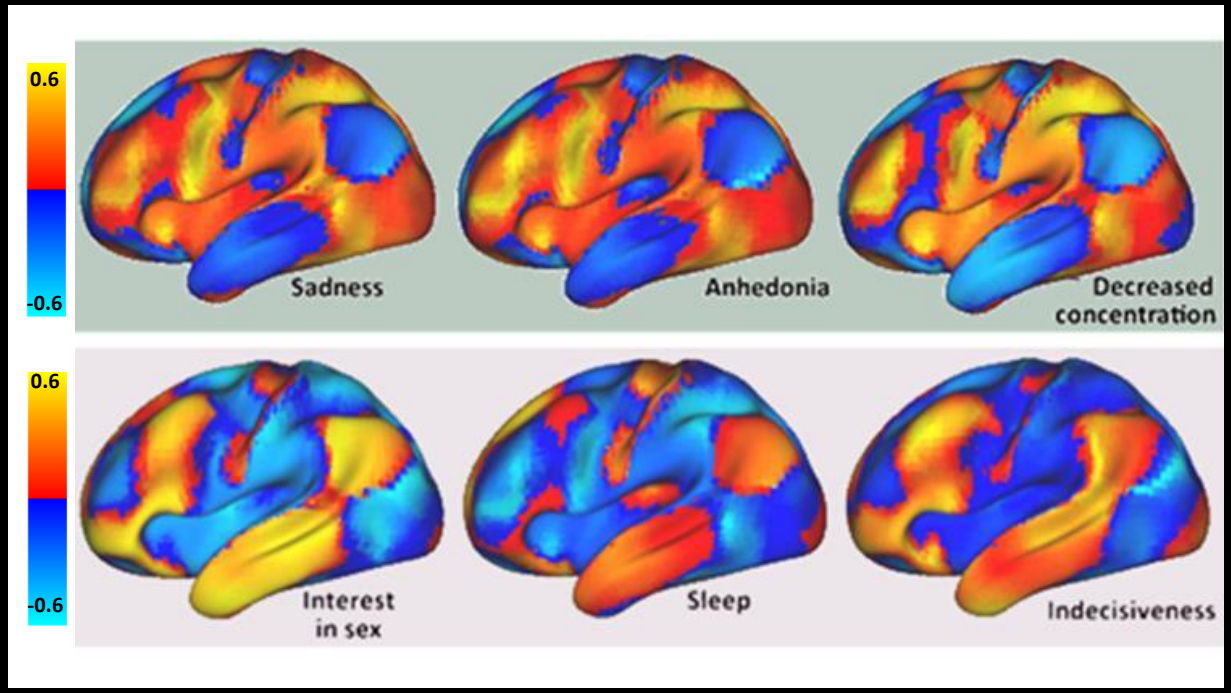

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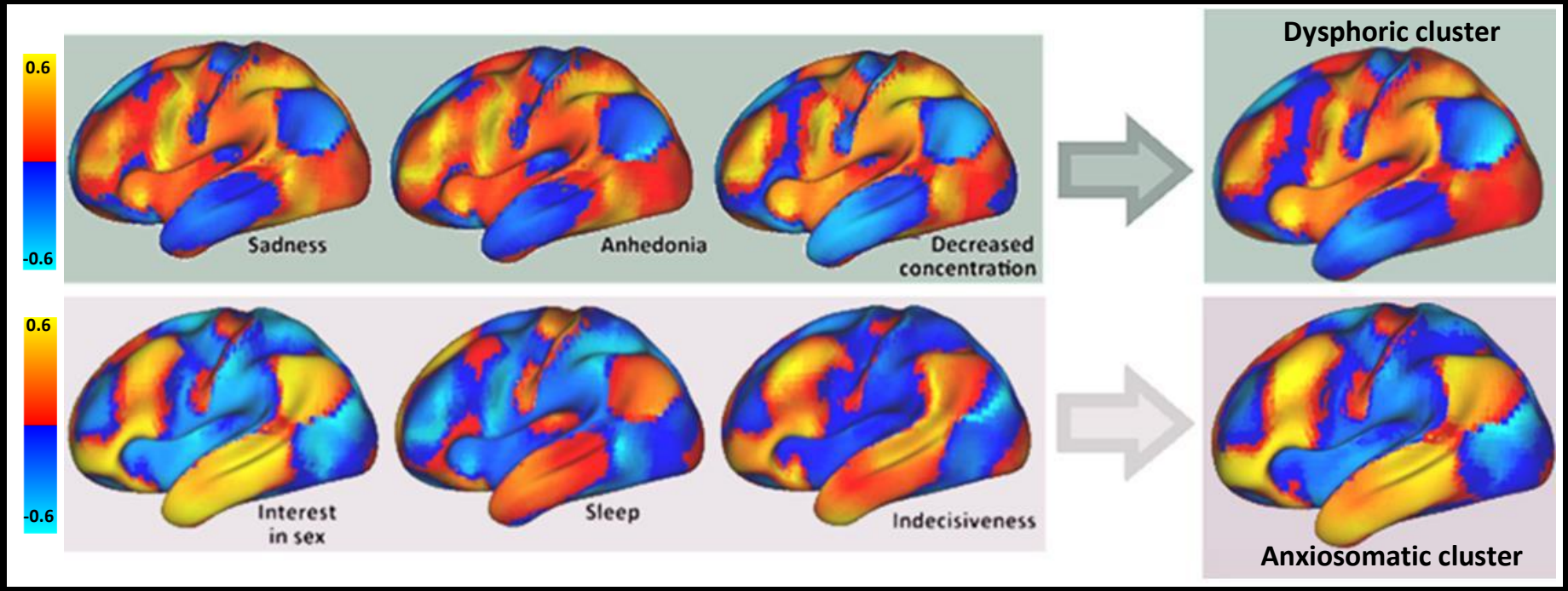

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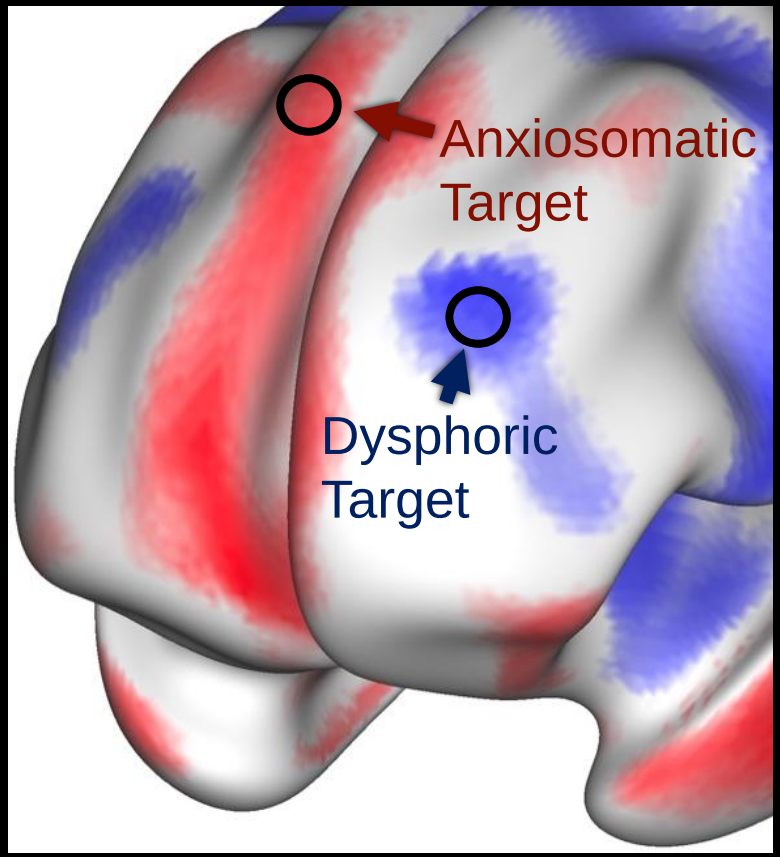
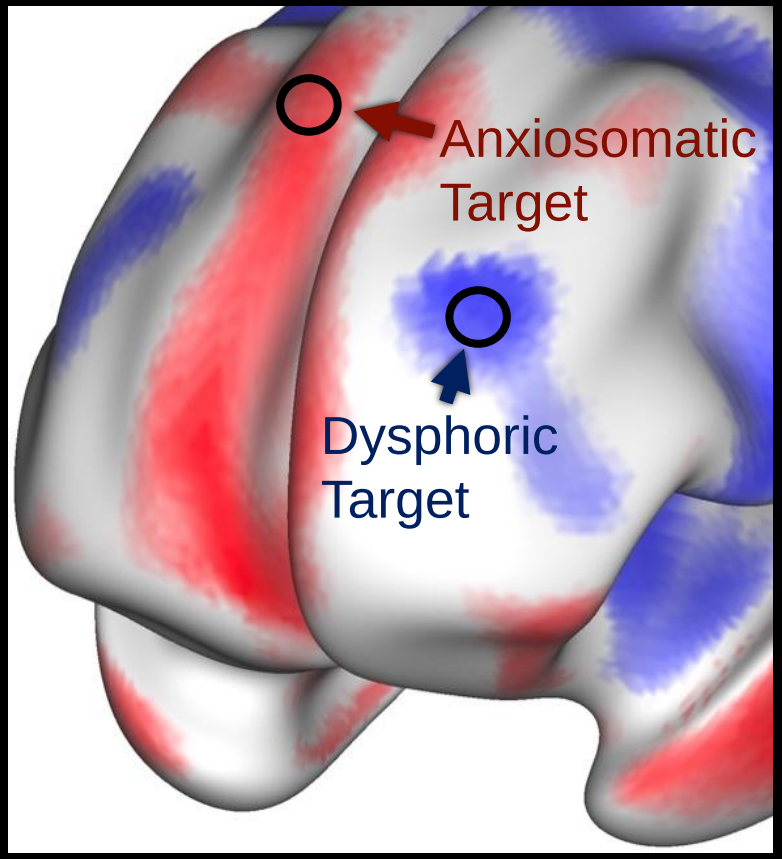
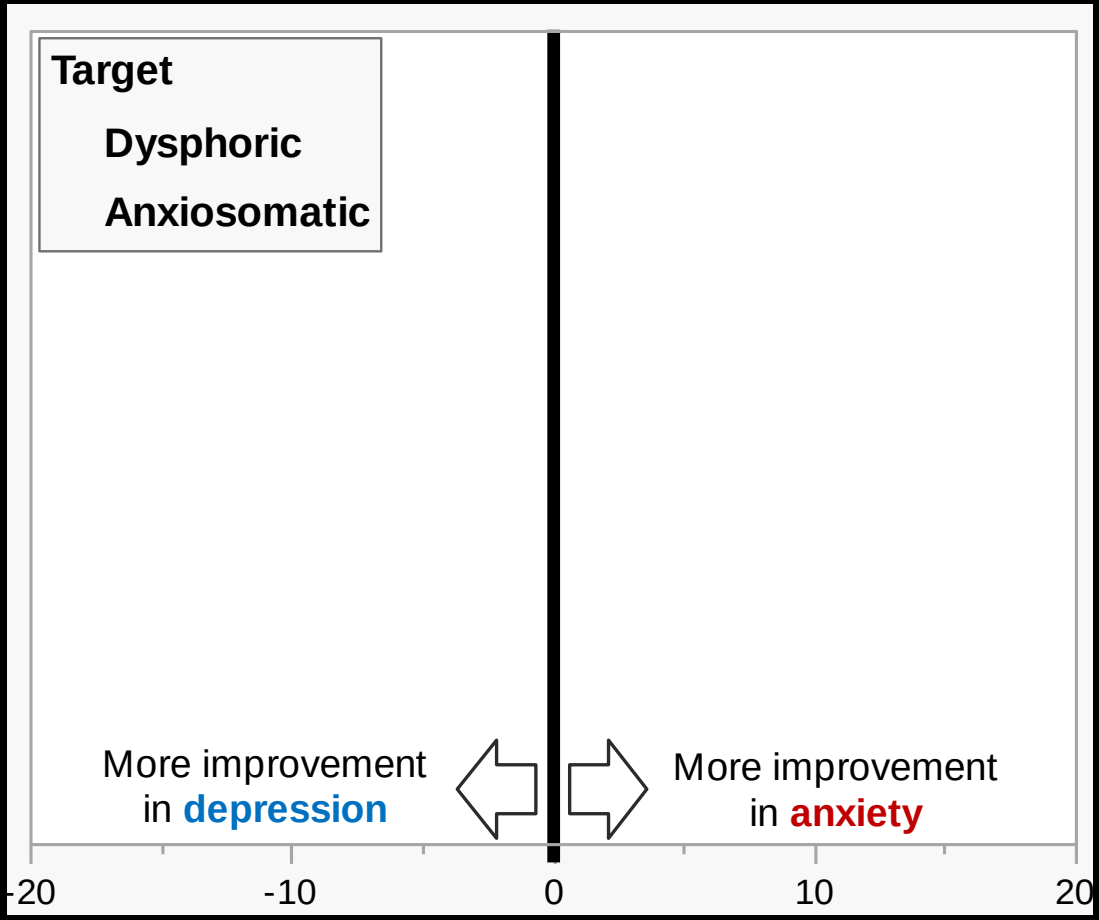


Taylor, Siddiqi et al., Submitted

Symptom-Specific TMS Targets?





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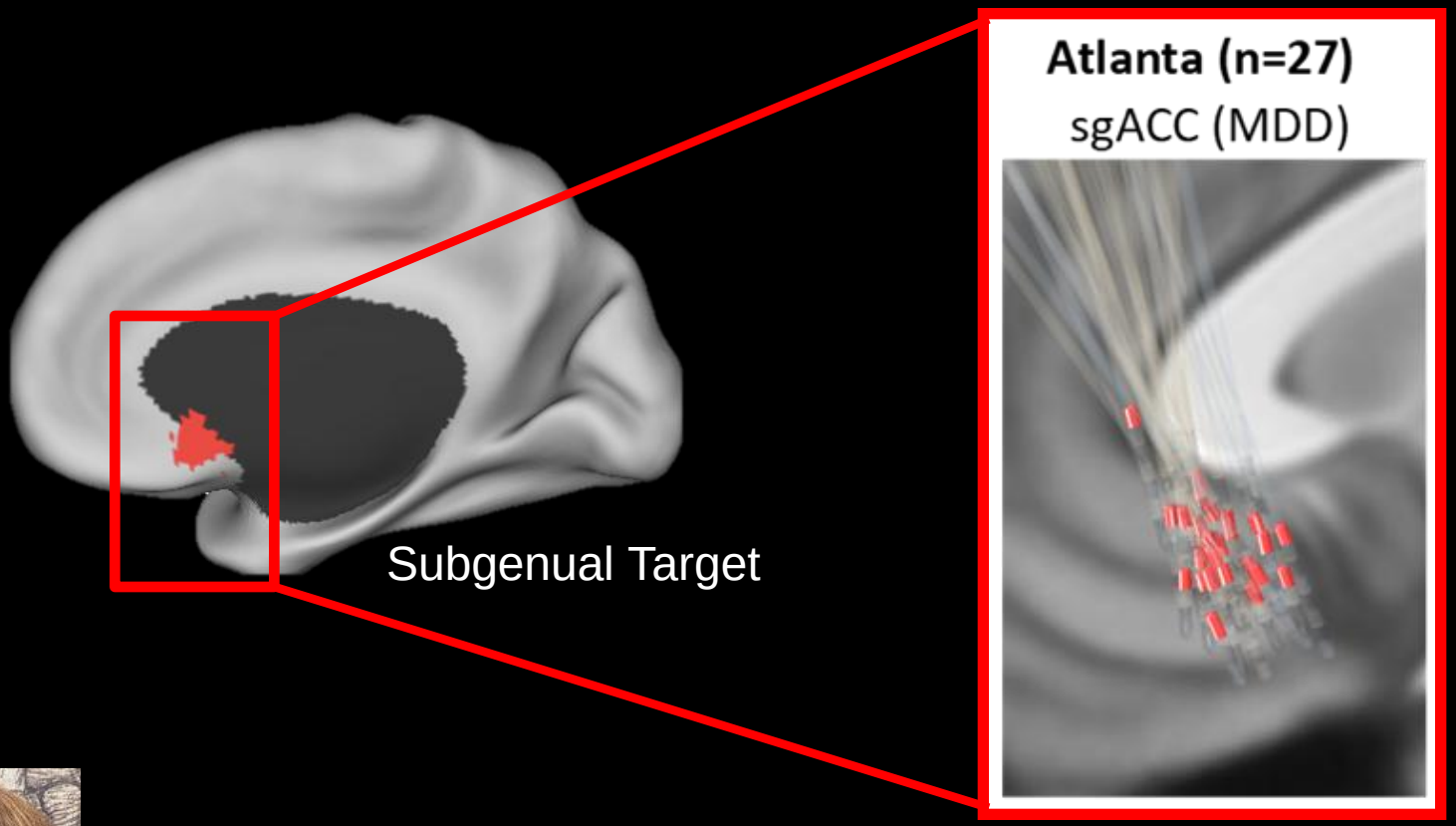
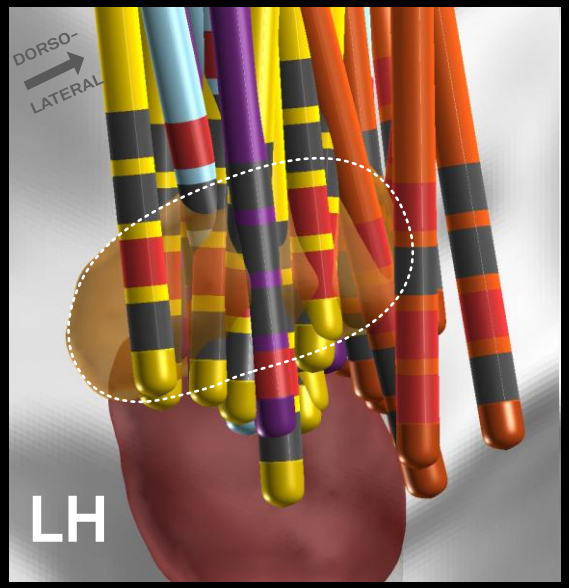
What if we're unsure of our target?



DBS Network Mapping

Stim. Site Variability



Horn et. al 2017 Annals of Neurology

DBS Network Mapping

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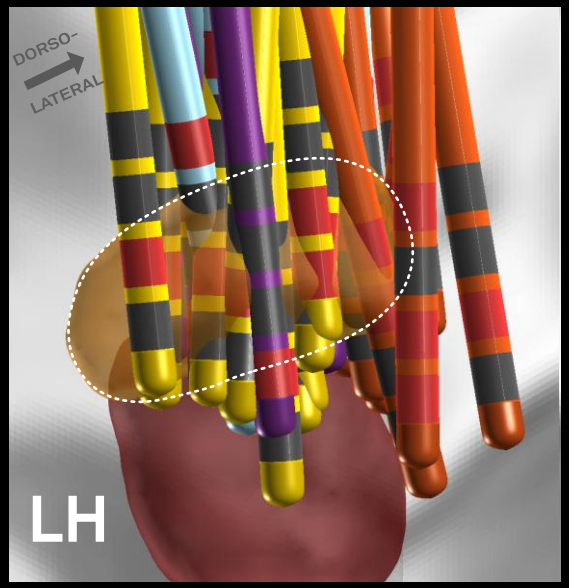
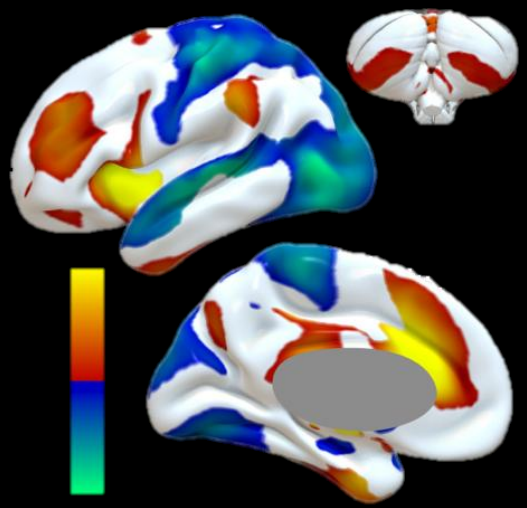


Important Connections



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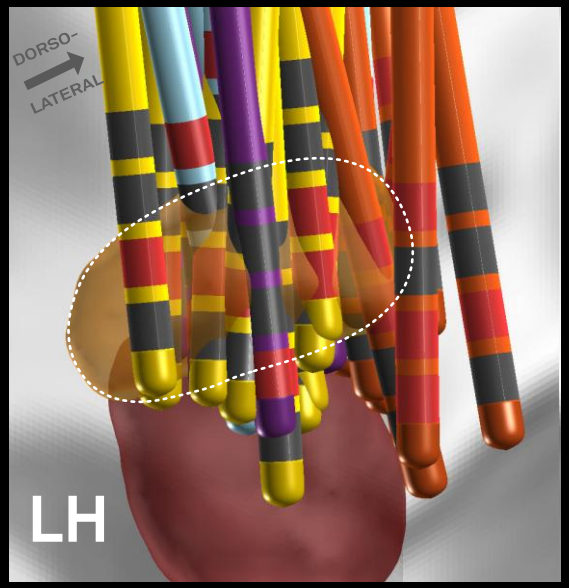

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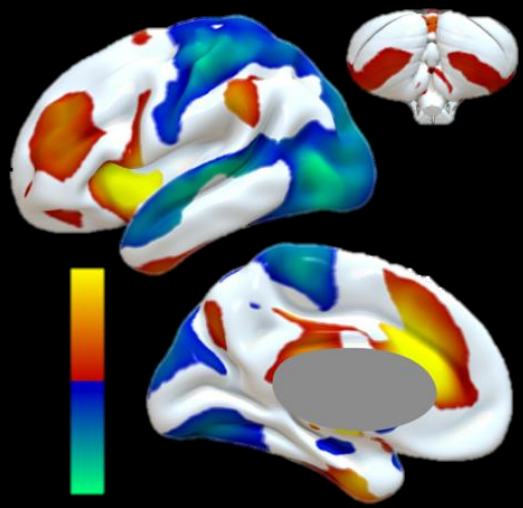
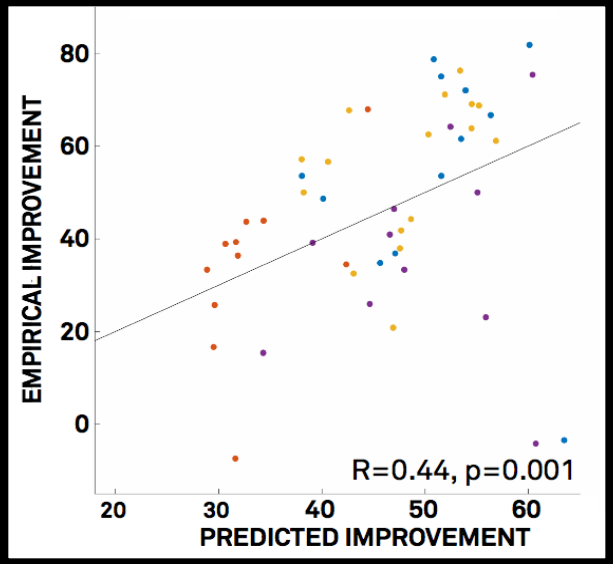


Response Prediction



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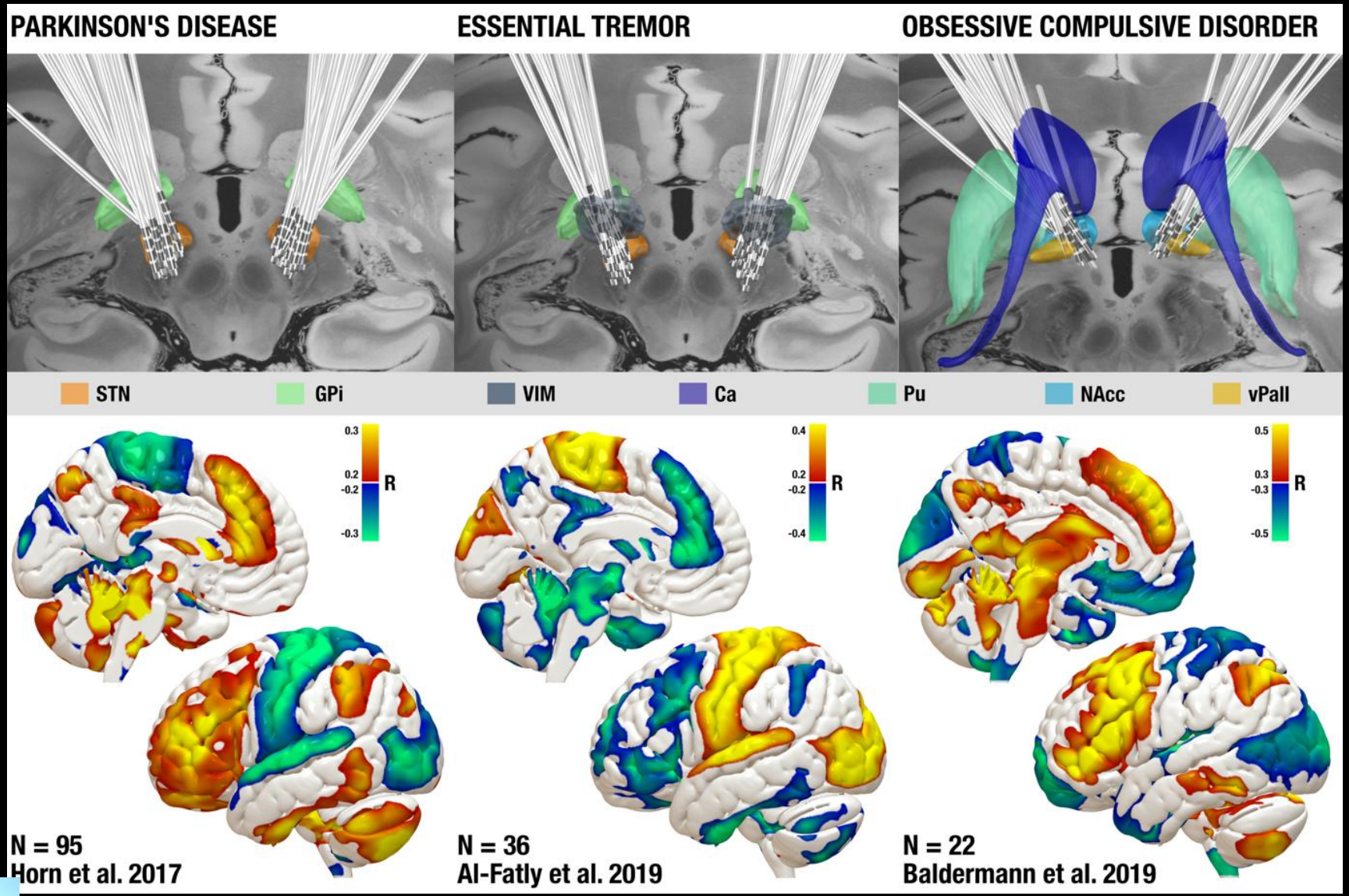
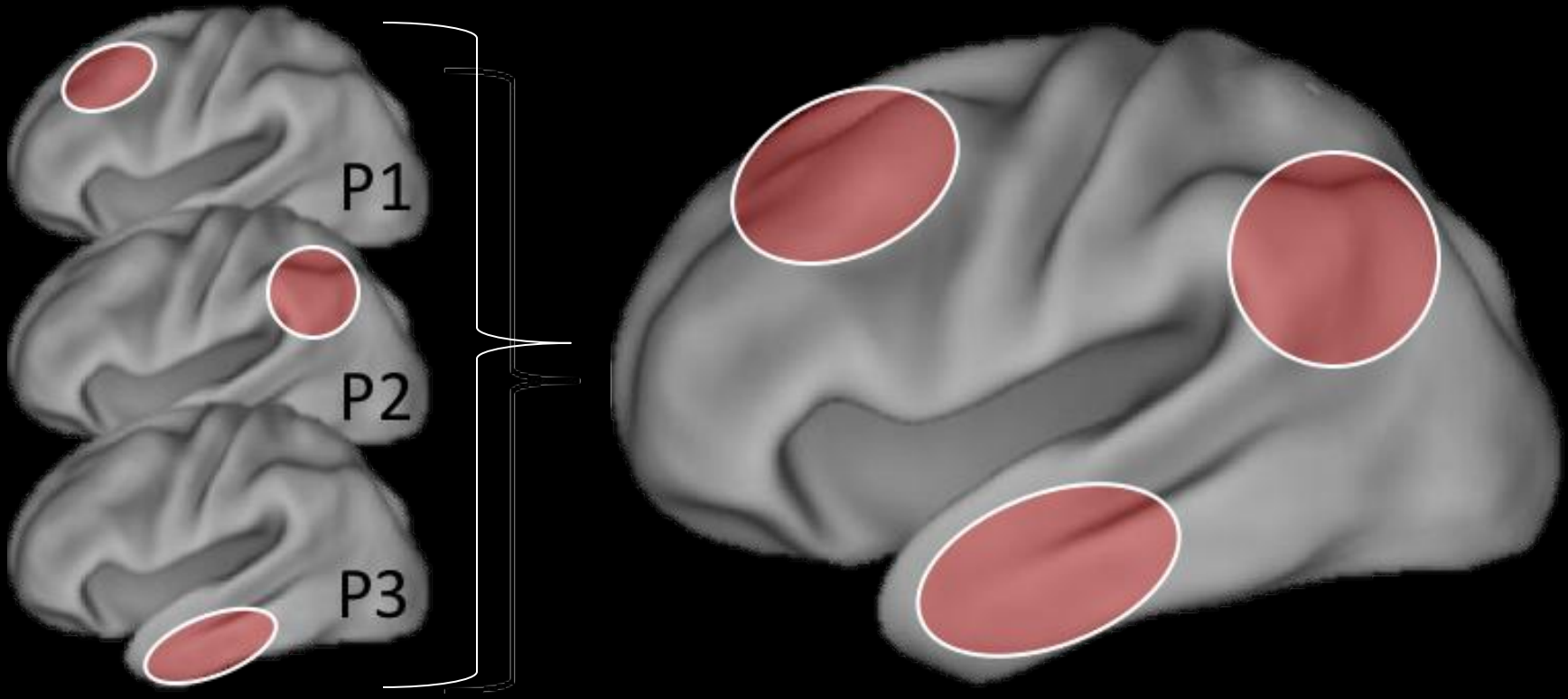


Review: Horn and Fox 2020 Neuroimage

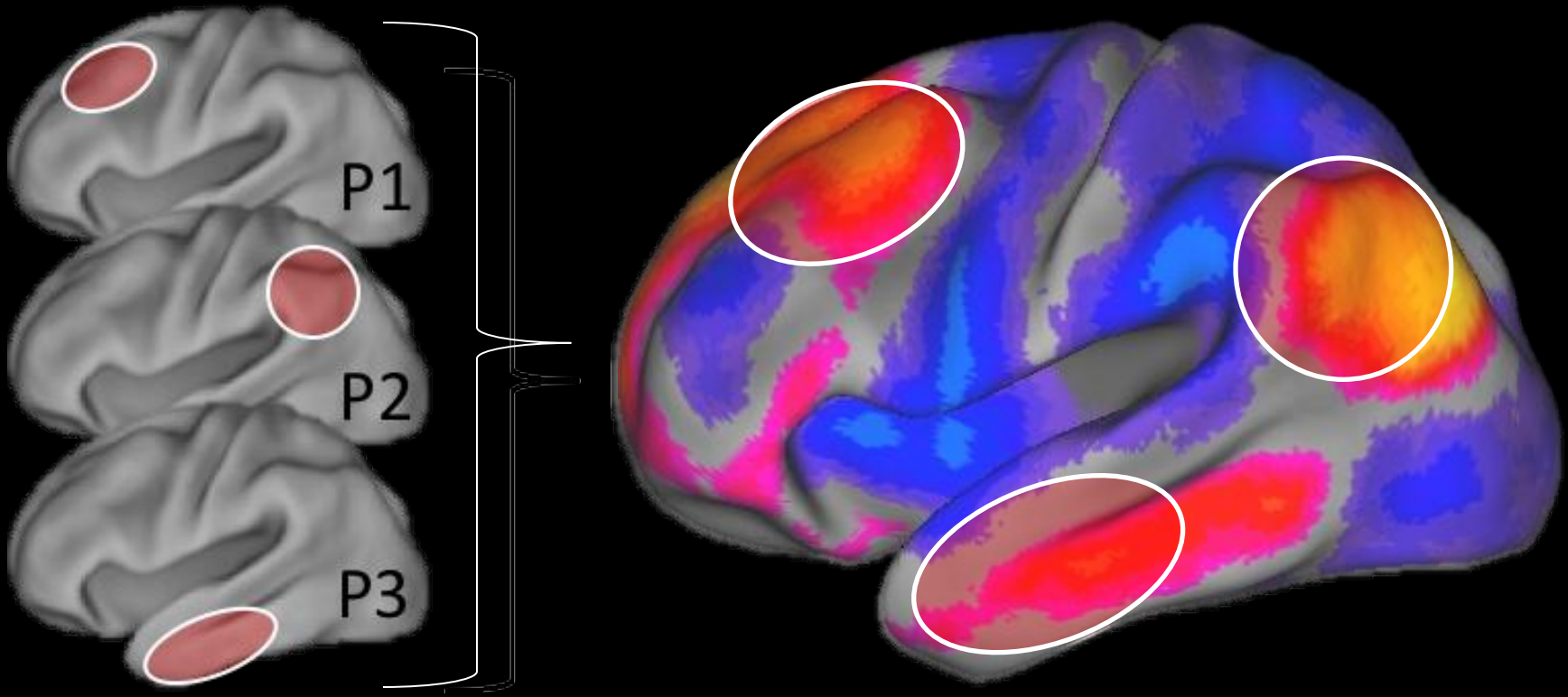
What if we’re (VERY) unsure of our target?

Lesion Localization



Review: Fox 2018 NEJM

Lesion “Network” Localization



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Lesion Network Mapping

Addiction Remission
Joutsa et al. 2022 Nature Medicine

Aggression
Peng et al. 2024 Biol. Psych

Alice in Wonderland Syndrome
Friedrich et al. 2024 Annl. of Neuro

Amnesia
Ferguson, Lim et al. 2019 Nature Comm.

Anosognosia
Kletenik et al. 2023 Annl. of Neurology

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Corp et al. 2019 Brain

Confabulation
Bateman et al. 2023 J. Neuropsych Clin. Neurosciences

Consciousness
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Freezing of Gait
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Taylor et al. 2023 Nature Hum. Behav

Post Traumatic Stress Disorder
Siddiqi et al. 2024 Nature Neurosci.

Religion / Spirituality
Ferguson et al. 2022 Bio Psych, Ferguson et al. 2024 PNAS

Stroke Severity
Bonkhoff et al. 2024 ACTN

Tics
Ganos et al. 2022 Brain

Tremor Relief
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Vertigo
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Reviews:
Fox 2018 NEJM, Joutsa et al. 2022 Cur. Opin. Neuro, Joutsa et al. 2023 Brain

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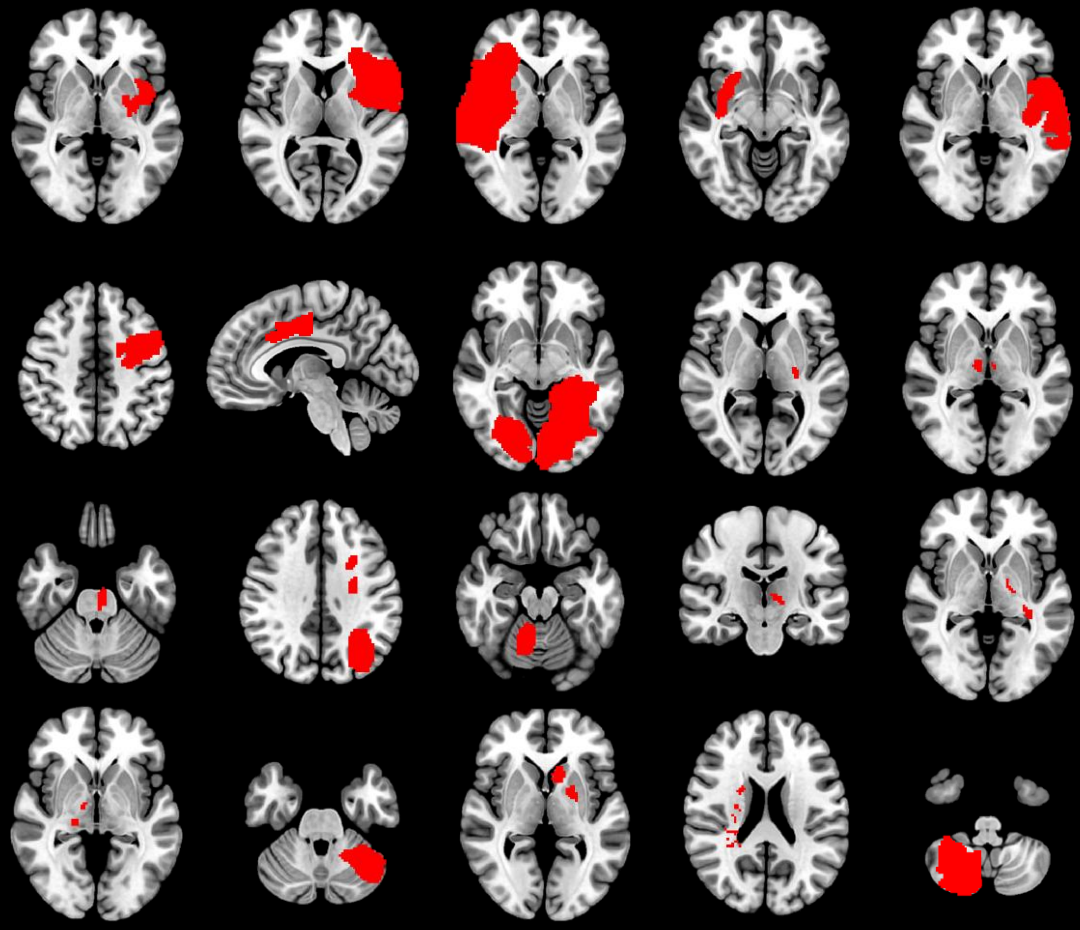
Addiction Remission



Joutsa, Moussawi, Siddiqi et al. 2022 Nature Medicine

Addiction Remission

Remission

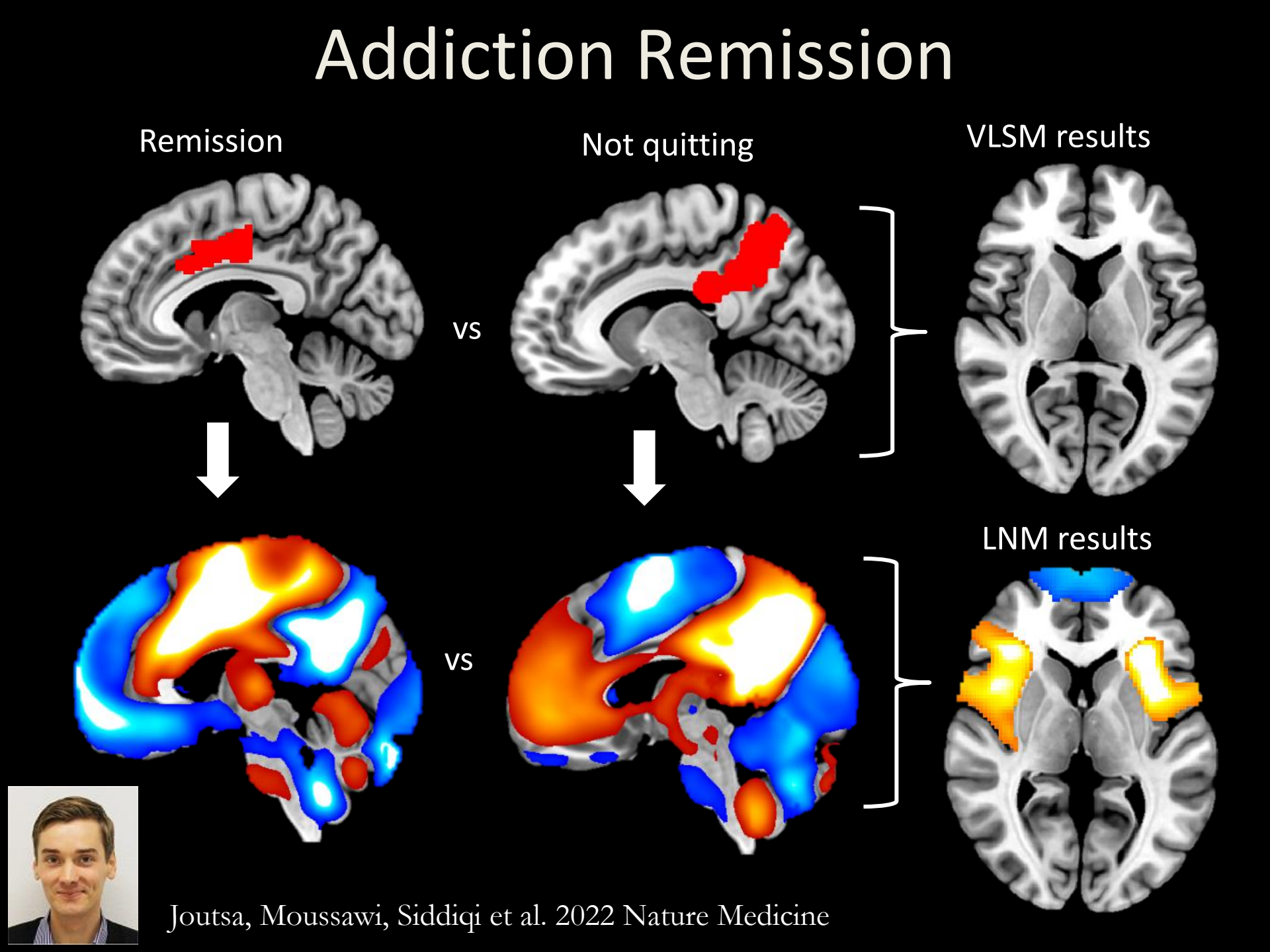
vs

Not quitting

VLSM results

Joutsa, Moussawi, Siddiqi et al. 2022 Nature Medicine

Addiction Remission



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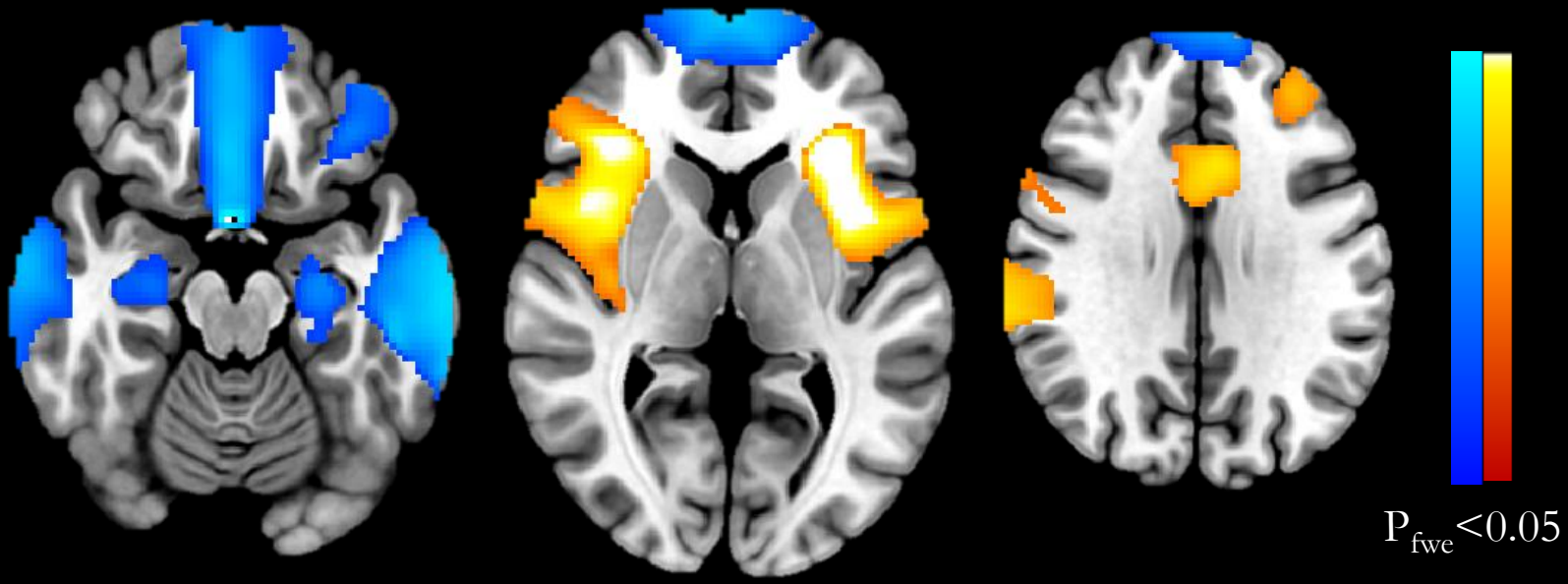

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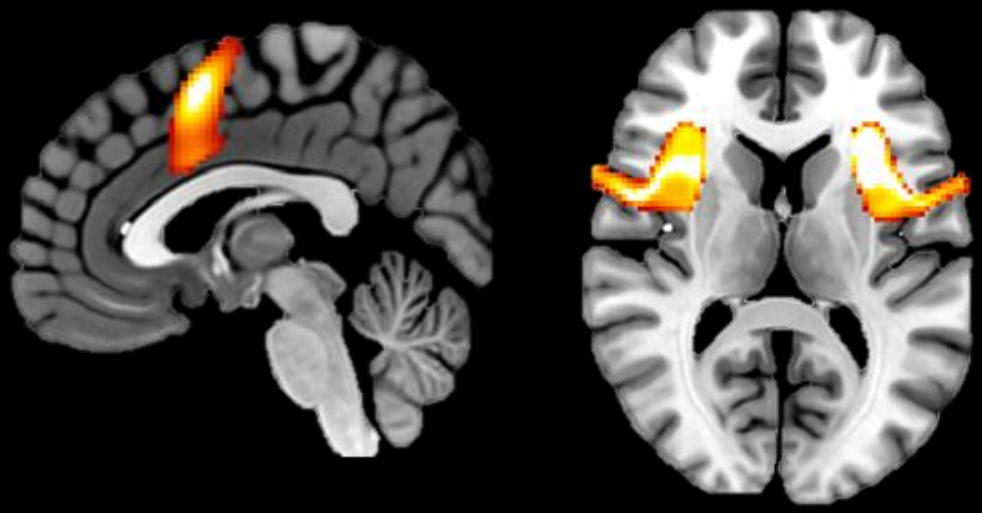
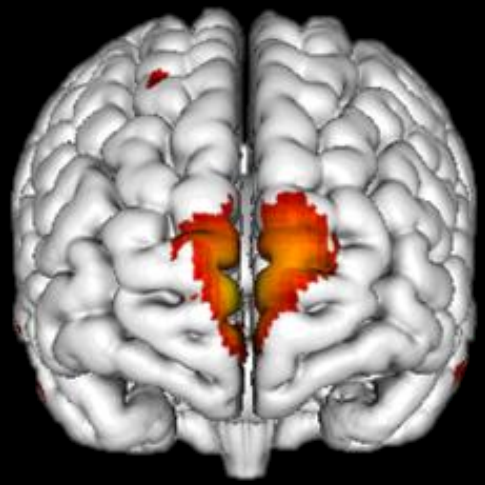
Addiction Remission Targets

Lesion / DBS Targets

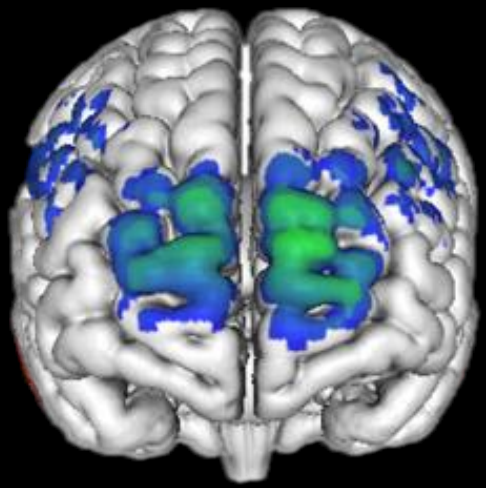


Joutsa, Moussawi, Siddiqi et al. 2022 Nature Medicine

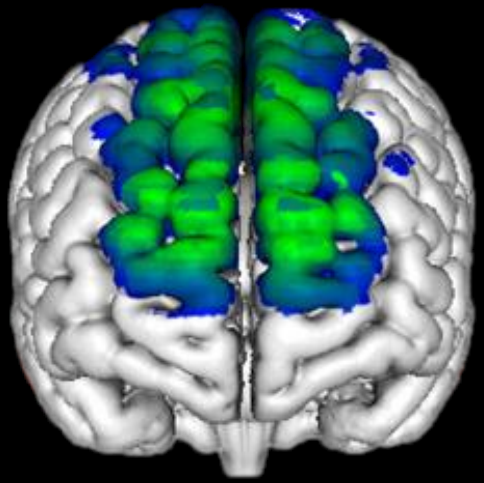
Addiction Remission Targets



TMS Target



Smoking (H4 Coil)



Alcoholism (H7 Coil)

Electric Field Intensity

% of max

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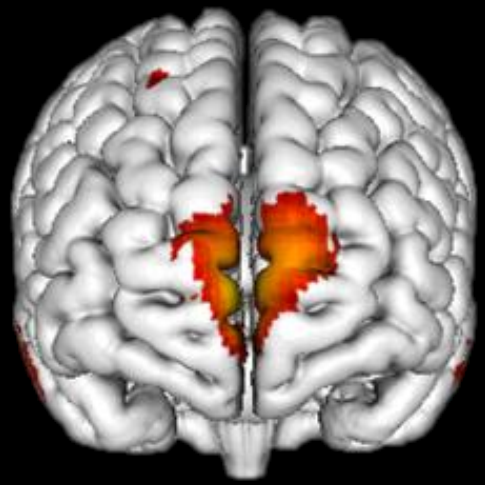
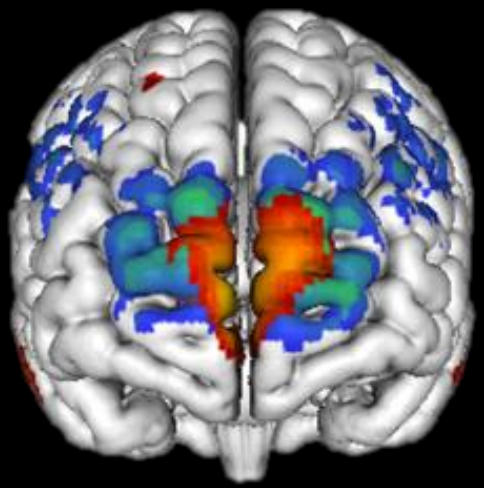
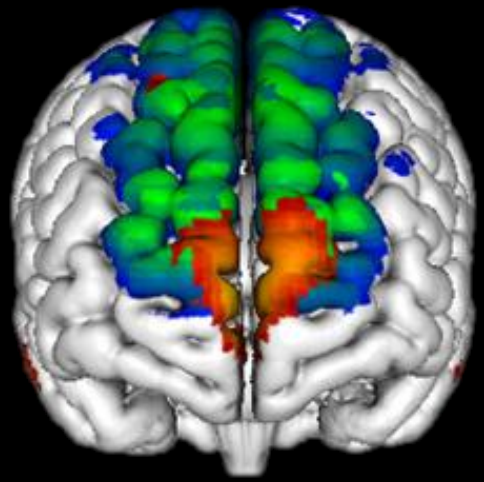
Addiction Remission Targets



TMS Target



Smoking (H4 Coil)



Alcoholism (H7 Coil)

Electric Field Intensity

Joutsa, Moussawi, Siddiqi et al. 2022 Nature Medicine

Lesion Network Mapping

Addiction Remission
Joutsa et al. 2022 Nature Medicine

Aggression
Peng et al. 2024 Biol. Psych

Alice in Wonderland Syndrome
Friedrich et al. 2024 Annl. of Neuro

Amnesia
Ferguson, Lim et al. 2019 Nature Comm.

Anosognosia
Kletenik et al. 2023 Annl. of Neurology

Aphasia
Boes et al. 2015 Brain

Blindsight
Kletenik et al. 2022 Annl. of Neurology

Cervical Dystonia
Corp et al. 2019 Brain

Confabulation
Bateman et al. 2023 J. Neuropsych Clin. Neurosciences

Consciousness
Fischer et al. 2016 Neurology, Snider et al. 2020 HBM

Criminality
Darby et al. 2018 PNAS

Delusions
Darby et al. 2017 Brain

Depression
Padmanabhan et al. 2019 Biol. Psych, Siddiqi et al. 2021 NHB

Emotion Regulation
Jiang et al. 2023 Biol. Psych

Epilepsy
Schaper et al. 2023 JAMA Neurology

Freezing of Gait
Fasano et al. 2017 Annl. of Neurology

Free Will
Darby et al. 2018 PNAS

Facial Recognition
Cohen et al. 2019 Brain

Hallucinations
Boes et al. 2015 Brain, Kim et al. 2021 Mol Psych

Hemichorea
Laganiere et al. 2016 Neurology

Holmes Tremor
Joutsa et al. 2019 Annl. Neurology

Infantile Spasms
Cohen et al. 2021 Annl. Neurology

Mania
Cotovio, Talmasov et al. 2020 JCI

Pain
Boes et al. 2015 Brain, Kim 2022 Annl. of Neurology

Parkinsonism
Joutsa et al. 2018 Brain

Psychiatric Comorbidity
Taylor et al. 2023 Nature Hum. Behav

Post Traumatic Stress Disorder
Siddiqi et al. 2024 Nature Neurosci.

Religion / Spirituality
Ferguson et al. 2022 Bio Psych, Ferguson et al. 2024 PNAS

Stroke Severity
Bonkhoff et al. 2024 ACTN

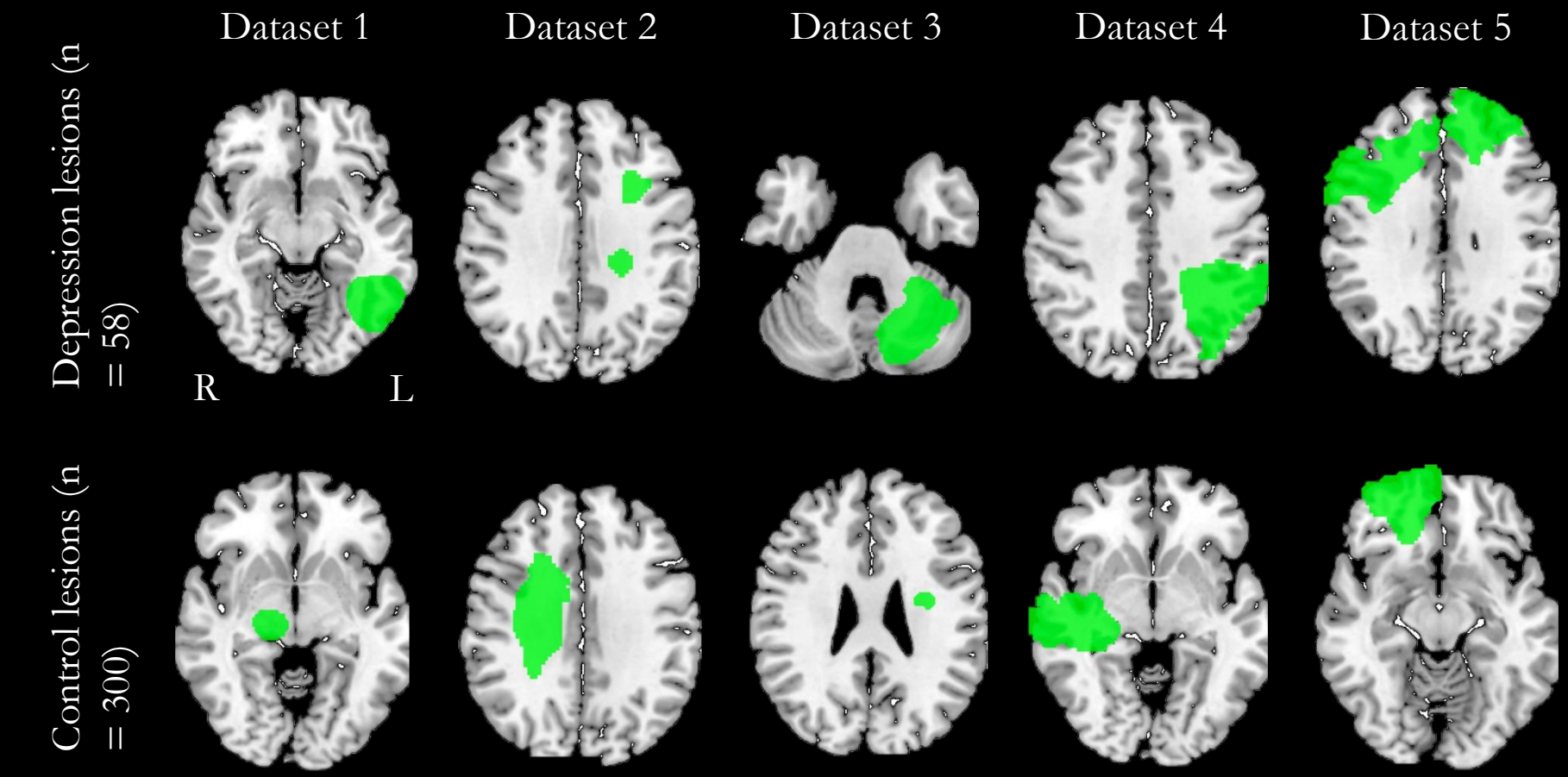
Tics
Ganos et al. 2022 Brain

Tremor Relief
Joutsa et al. 2018 Annl. of Neurology

Vertigo
Li et al. 2023 Brain Comm.

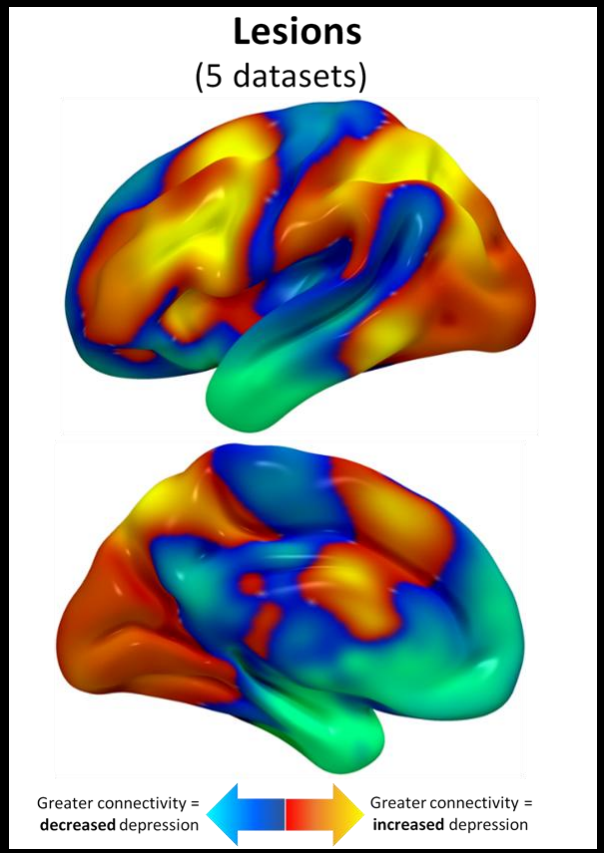
Reviews:
Fox 2018 NEJM, Joutsa et al. 2022 Cur. Opin. Neuro, Joutsa et al. 2023 Brain

Lesion mapping of depression (n = 461)



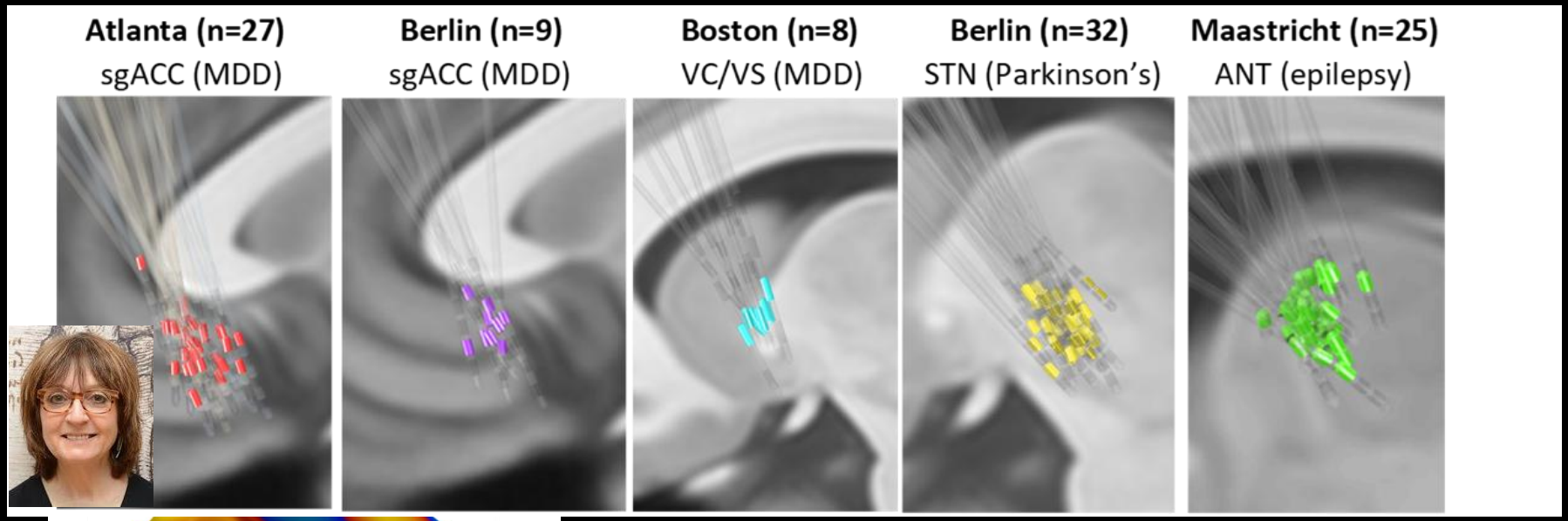
Padmanabhan, et al. 2019 Biological Psychiatry

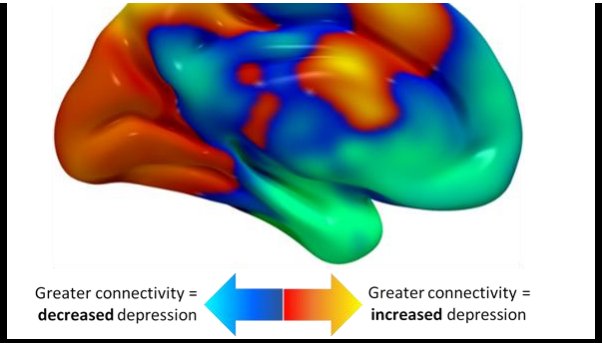
Convergent Depression Circuit



Siddiqi et al. 2021 Nature Hum Behav; Siddiqi et al. 2022 Nature Rev Neuros.

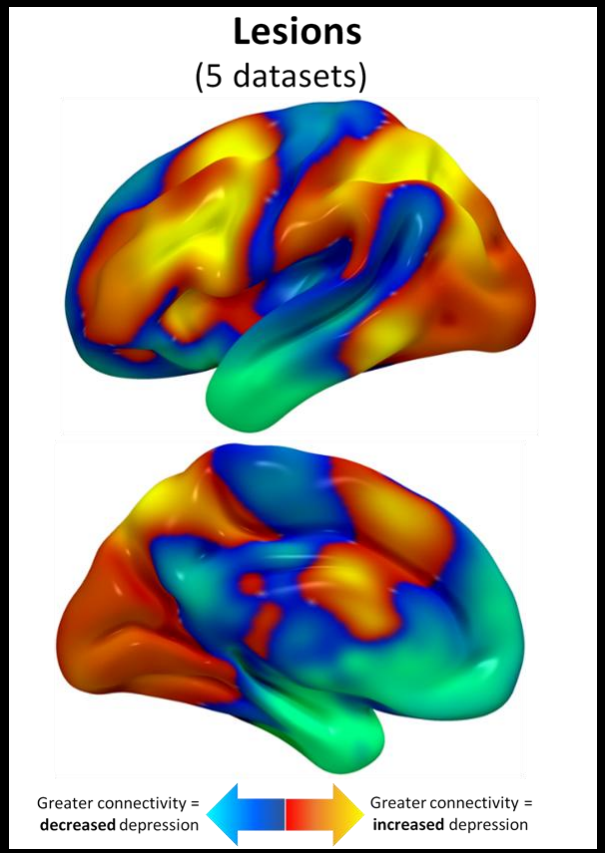
Convergent Depression Circuit

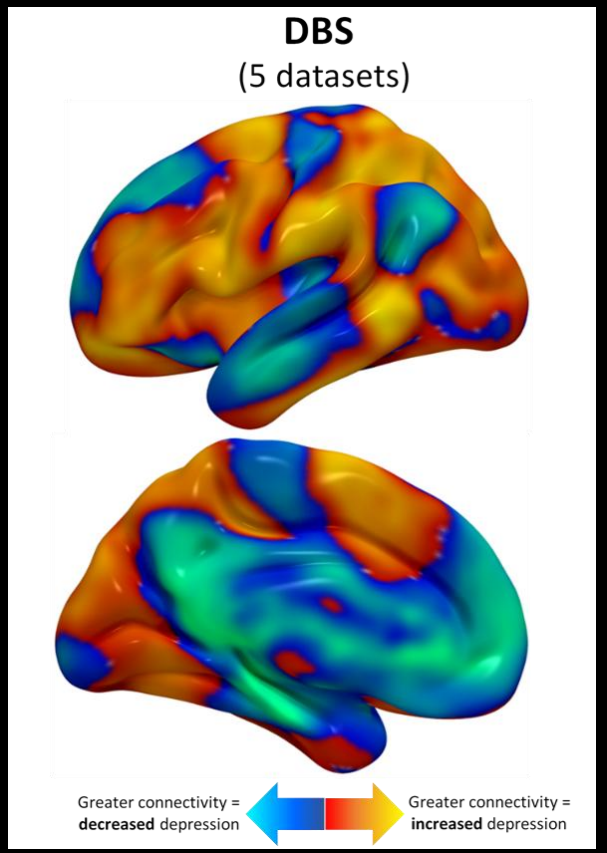




Siddiqi et al. 2021 Nature Hum Behav; Siddiqi et al. 2022 Nature Rev Neuros.

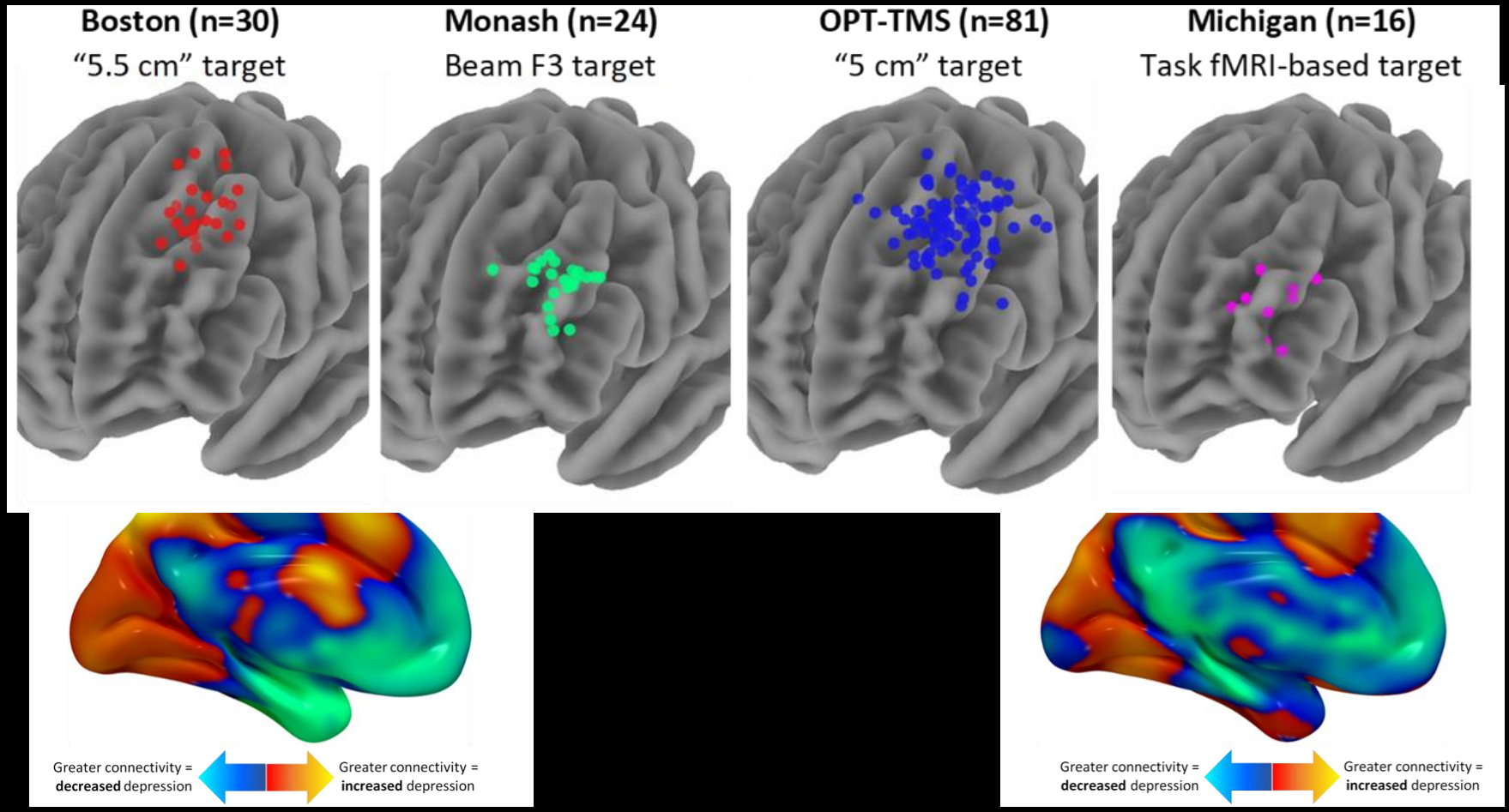
Convergent Depression Circuit





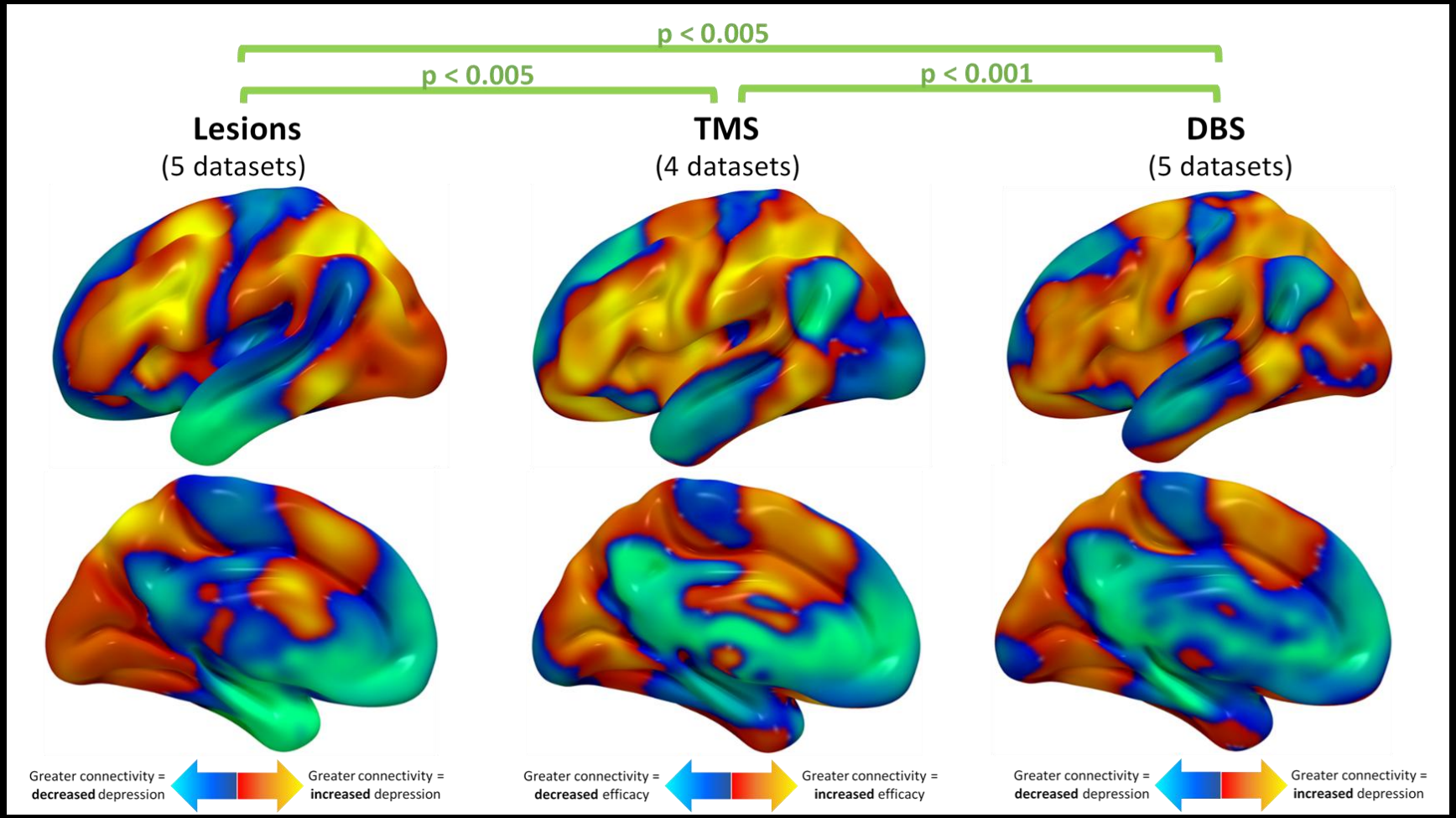
Siddiqi et al. 2021 Nature Hum Behav; Siddiqi et al. 2022 Nature Rev Neuros.

Convergent Depression Circuit



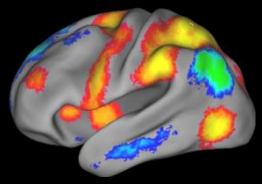
Siddiqi et al. 2021 Nature Hum Behav; Siddiqi et al. 2022 Nature Rev Neuros.

Convergent Depression Circuit



Siddiqi et al. 2021 Nature Hum Behav; Siddiqi et al. 2022 Nature Rev Neuros.

Conclusions



- Neuromodulation effects propagate beyond the target region to modulate brain circuits
- The human connectome can be used to map neuromodulation effects onto brain circuits
- These brain circuits may provide improved targets for neuromodulation treatments

Center for
BRAIN CIRCUIT THERAPEUTICS

BWH

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AND SOOO MANY OTHERS

Questions?

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https://www.brighamandwomens.org/neurosciences-center/center-for-brain-circuit-therapeutics