Brain Circuit Therapeutics

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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

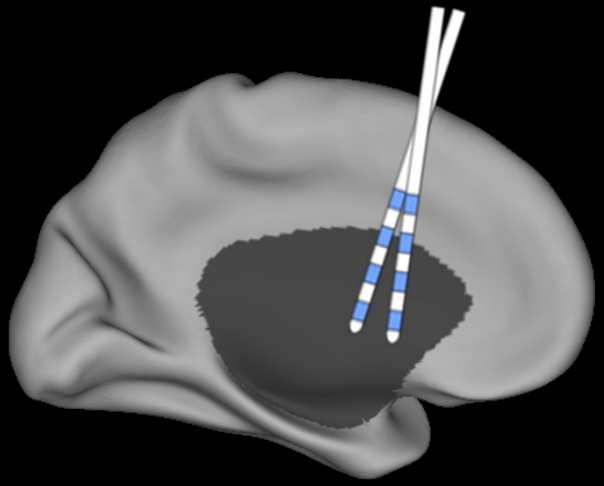
Disclosures

- Conflicts
  - Intellectual Property on using connectivity imaging to map lesions and guide neuromodulation
  - Consultant: Magnus Medical, Soterix, Abbott, Boston Scientific, Tal Medical
  - 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
  - Industry: Neuronetics, Boston Scientific

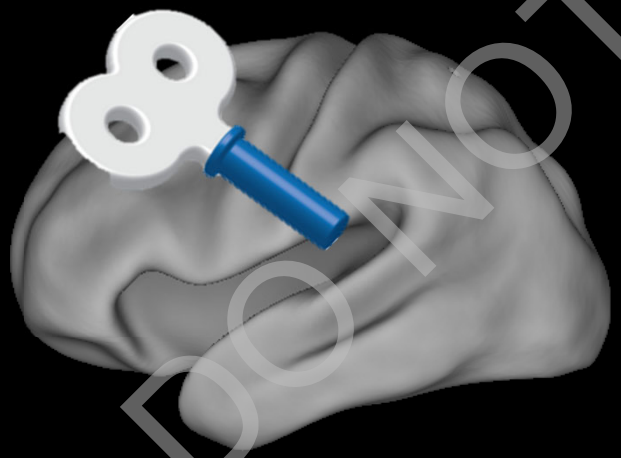
Therapeutic Neuromodulation

Deep Brain Stimulation (DBS)



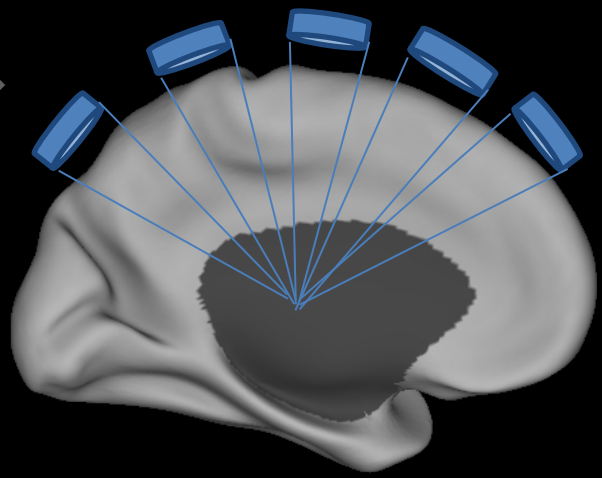
- FDA approved for Parkinson's, essential tremor, epilepsy, dystonia, OCD

Transcranial Magnetic Stimulation (TMS)



- FDA approved for depression, OCD, migraine, smoking addiction

Focused Ultrasound (FUS)



- FDA approved for tremor

How do we identify a therapeutic target?

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Therapeutic Neuromodulation

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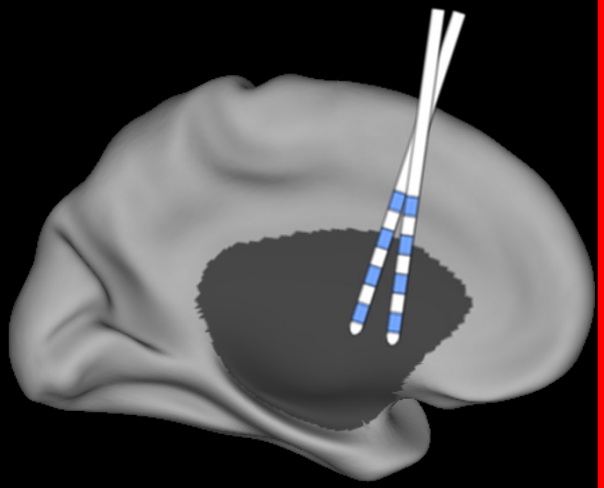

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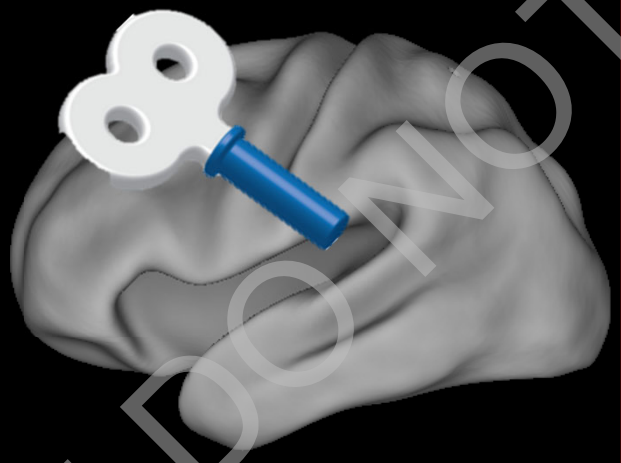

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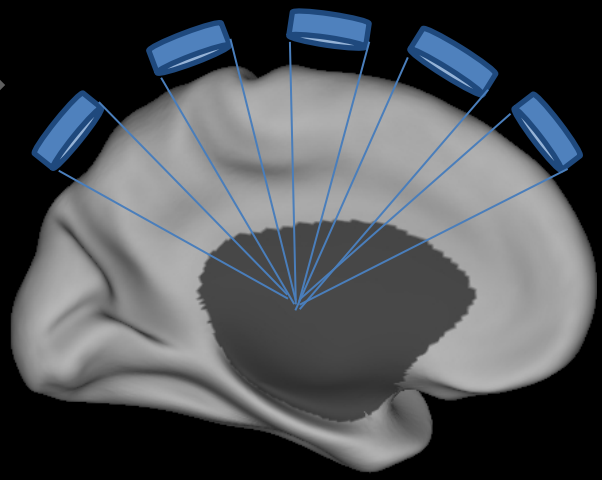

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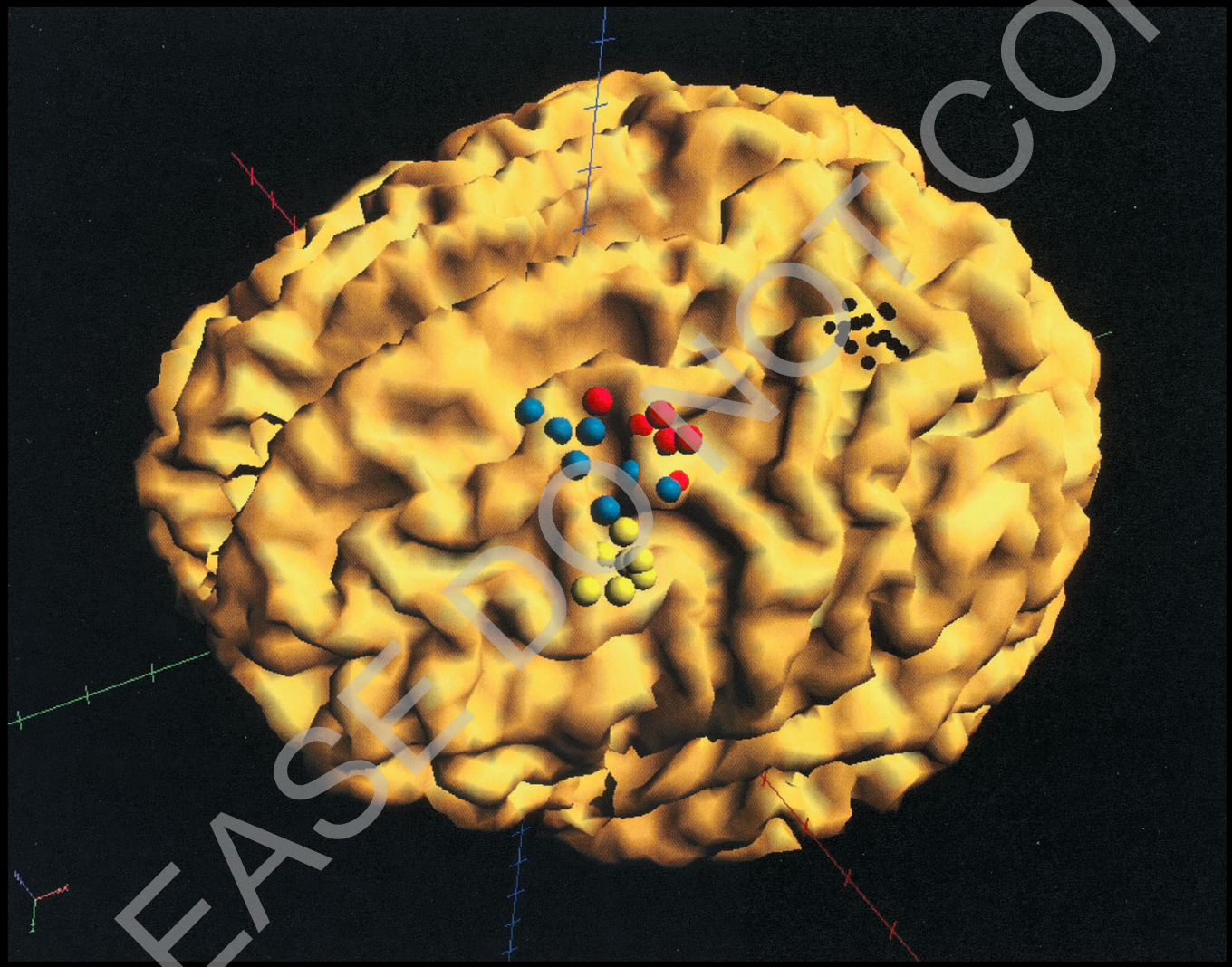
Targeting TMS in Depression: The 5 cm method



Herwig et al. 2001 BIOL PSYCHIATRY 50:58–61

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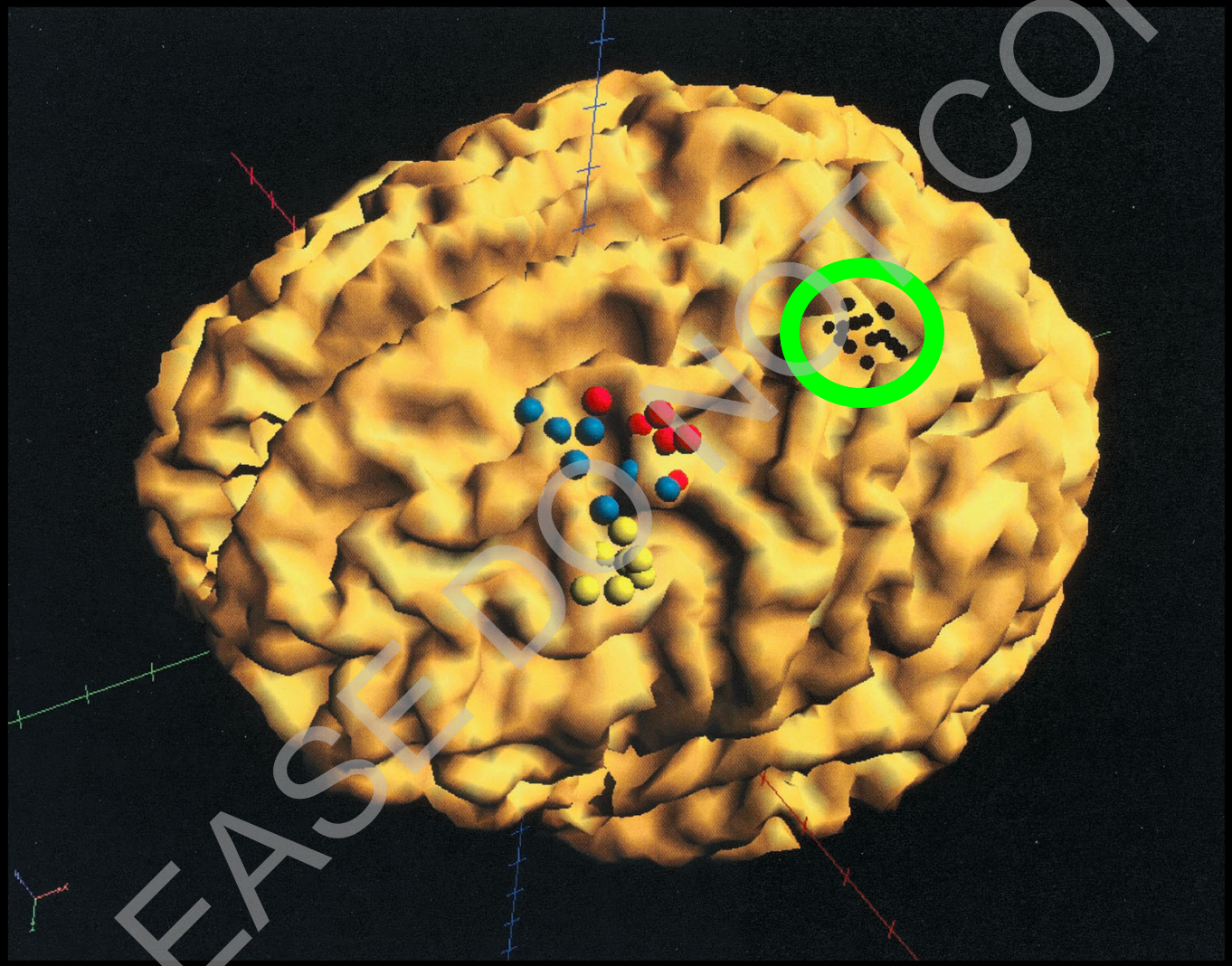

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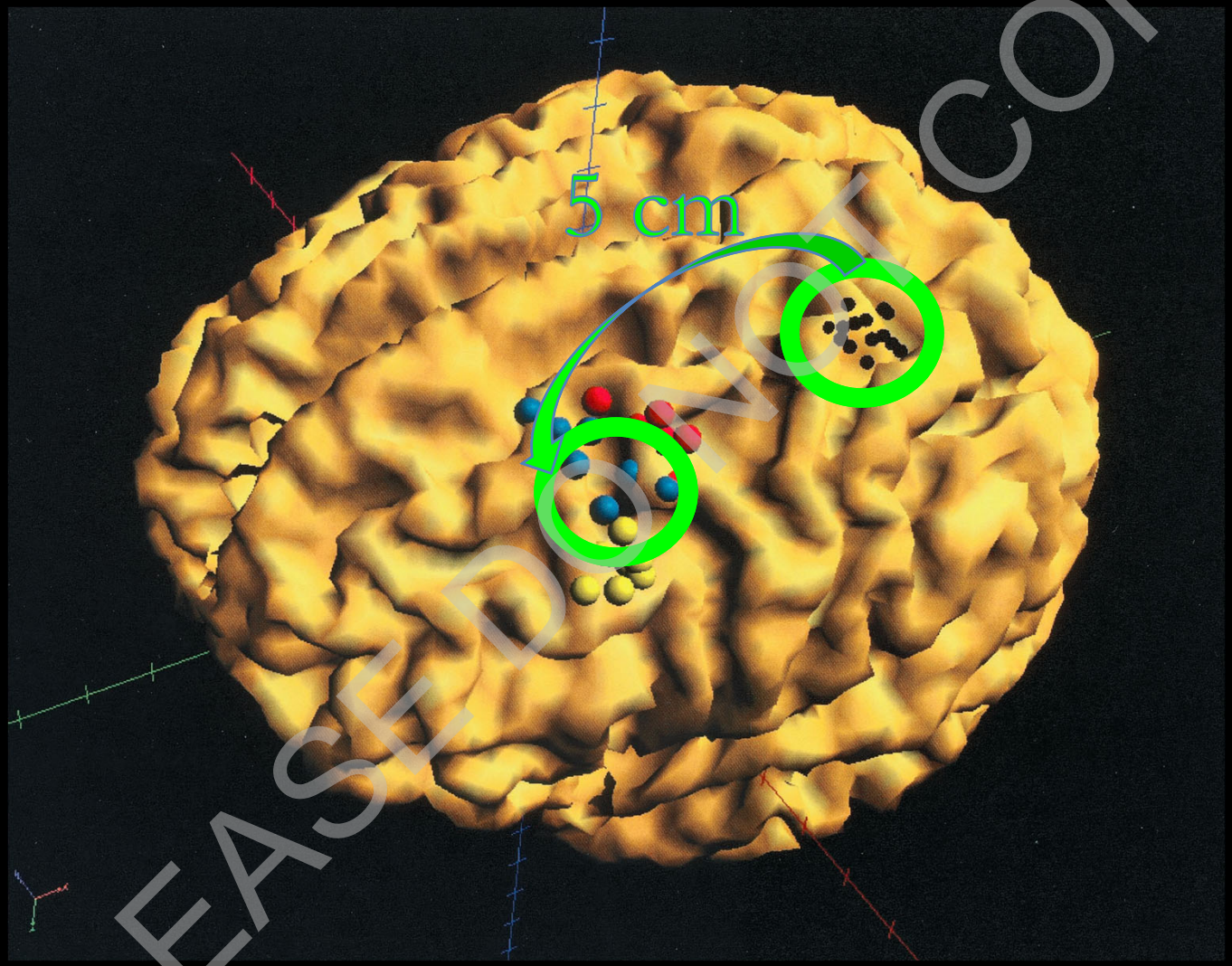

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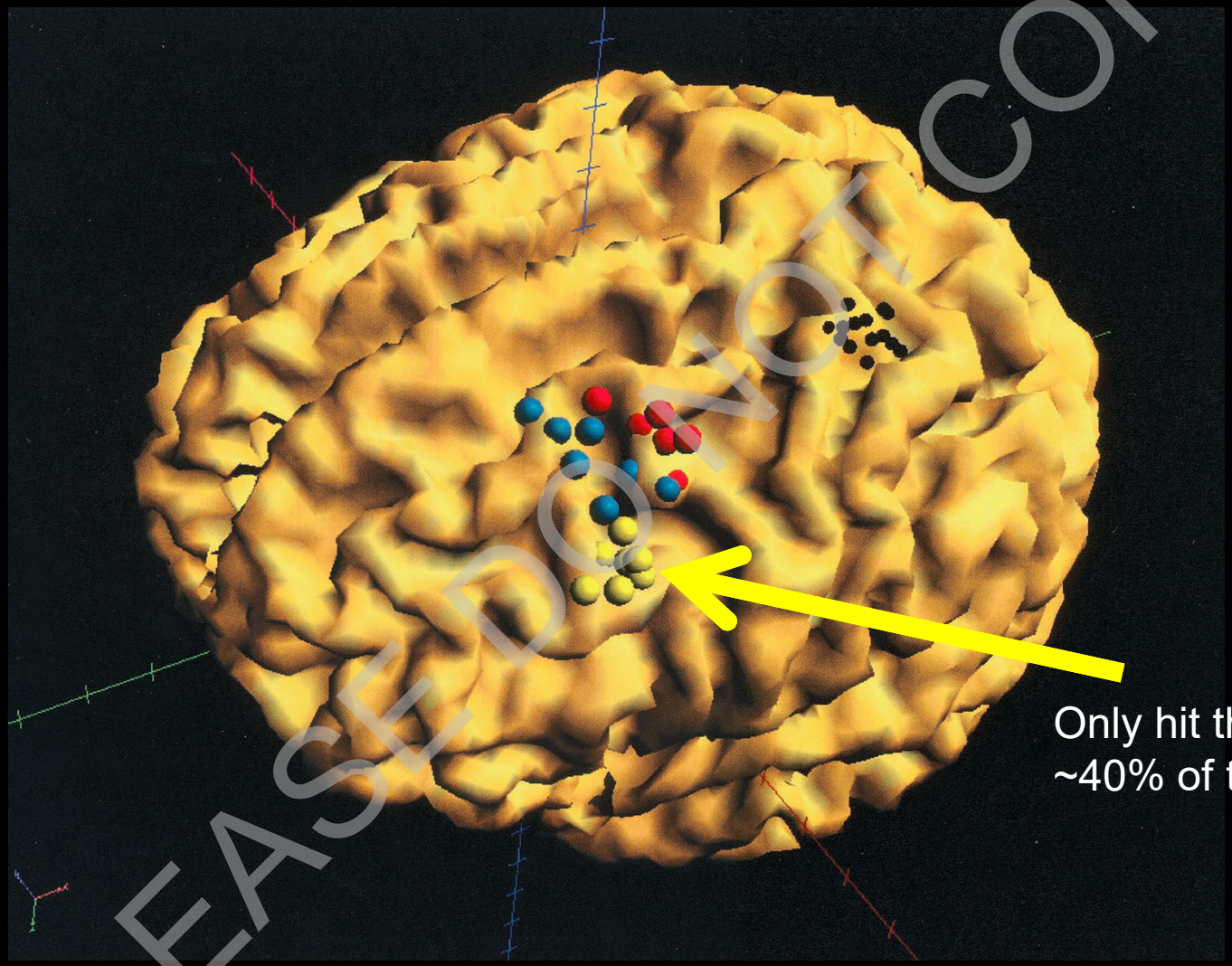

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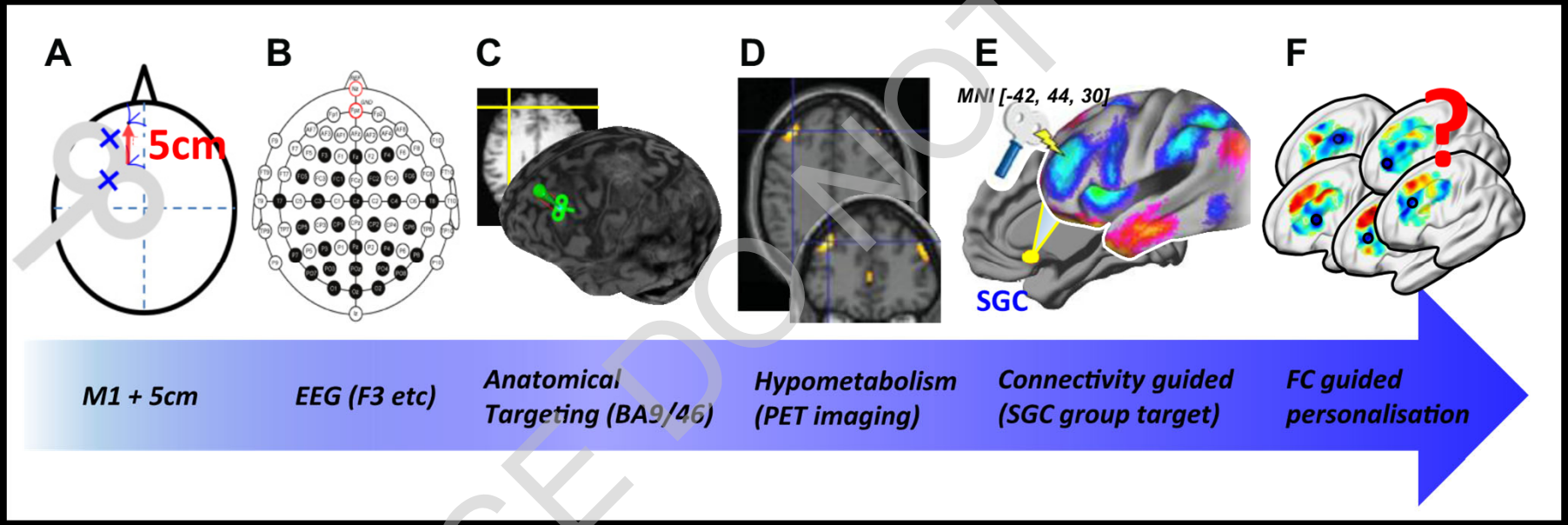

Cash et al. Biological Psychiatry 2020

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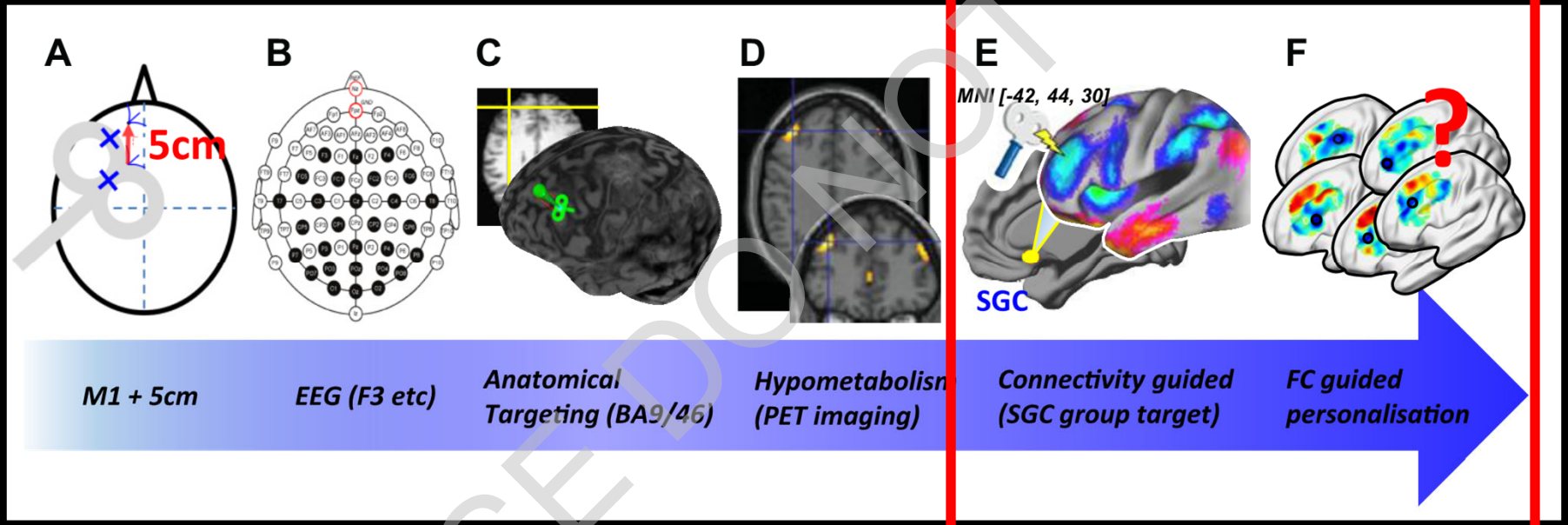

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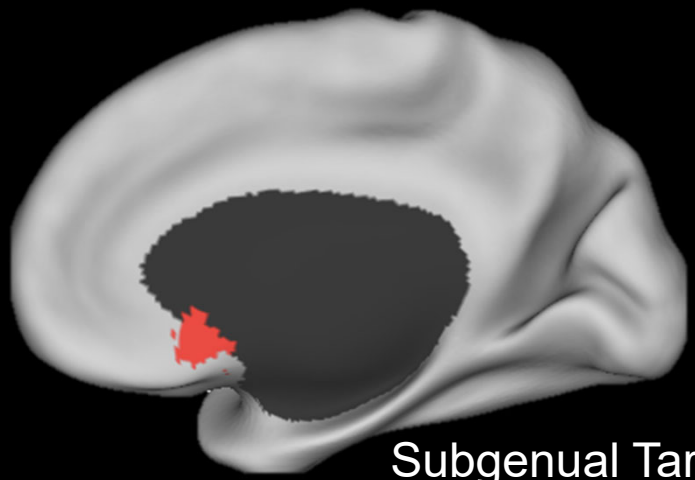
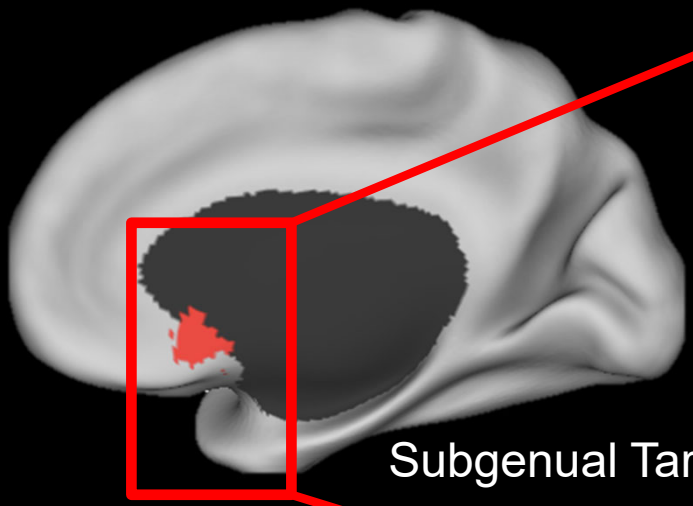
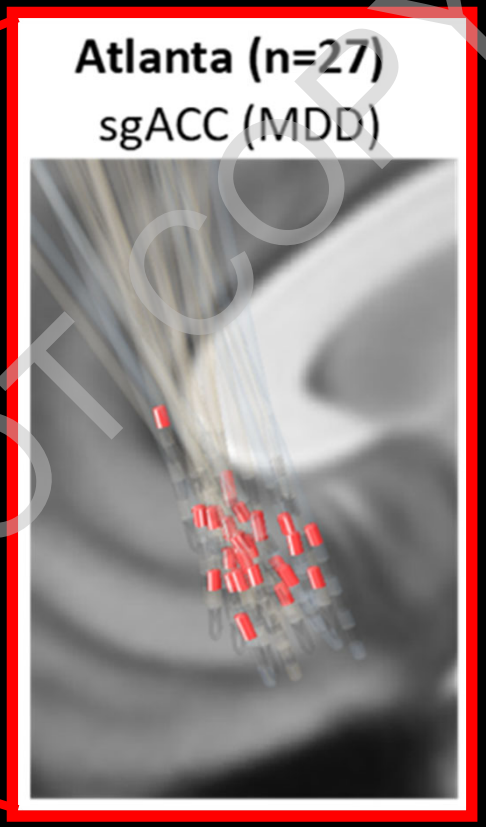


Subgenual Target

Fox et al. 2012 Biol Psych.





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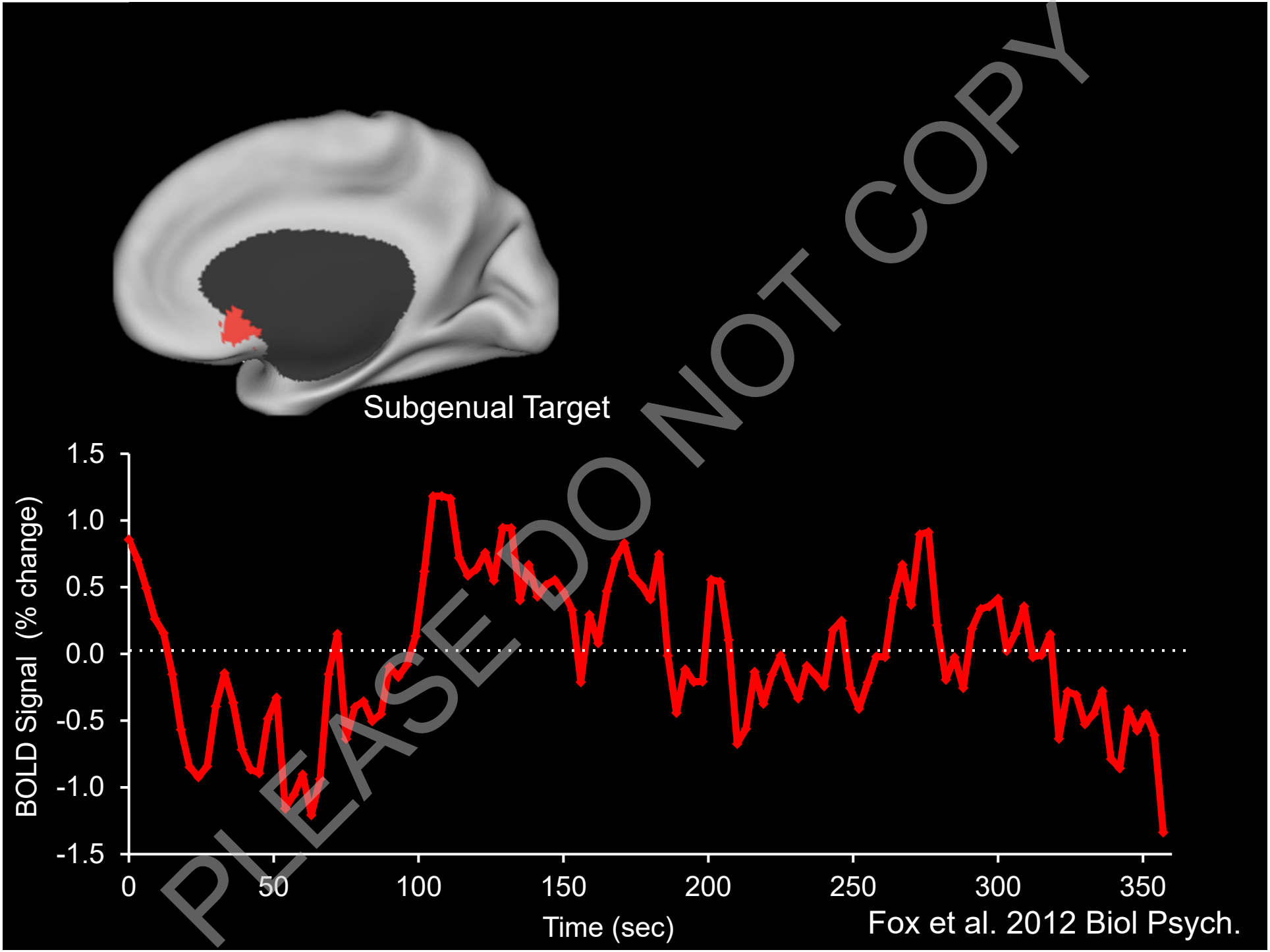
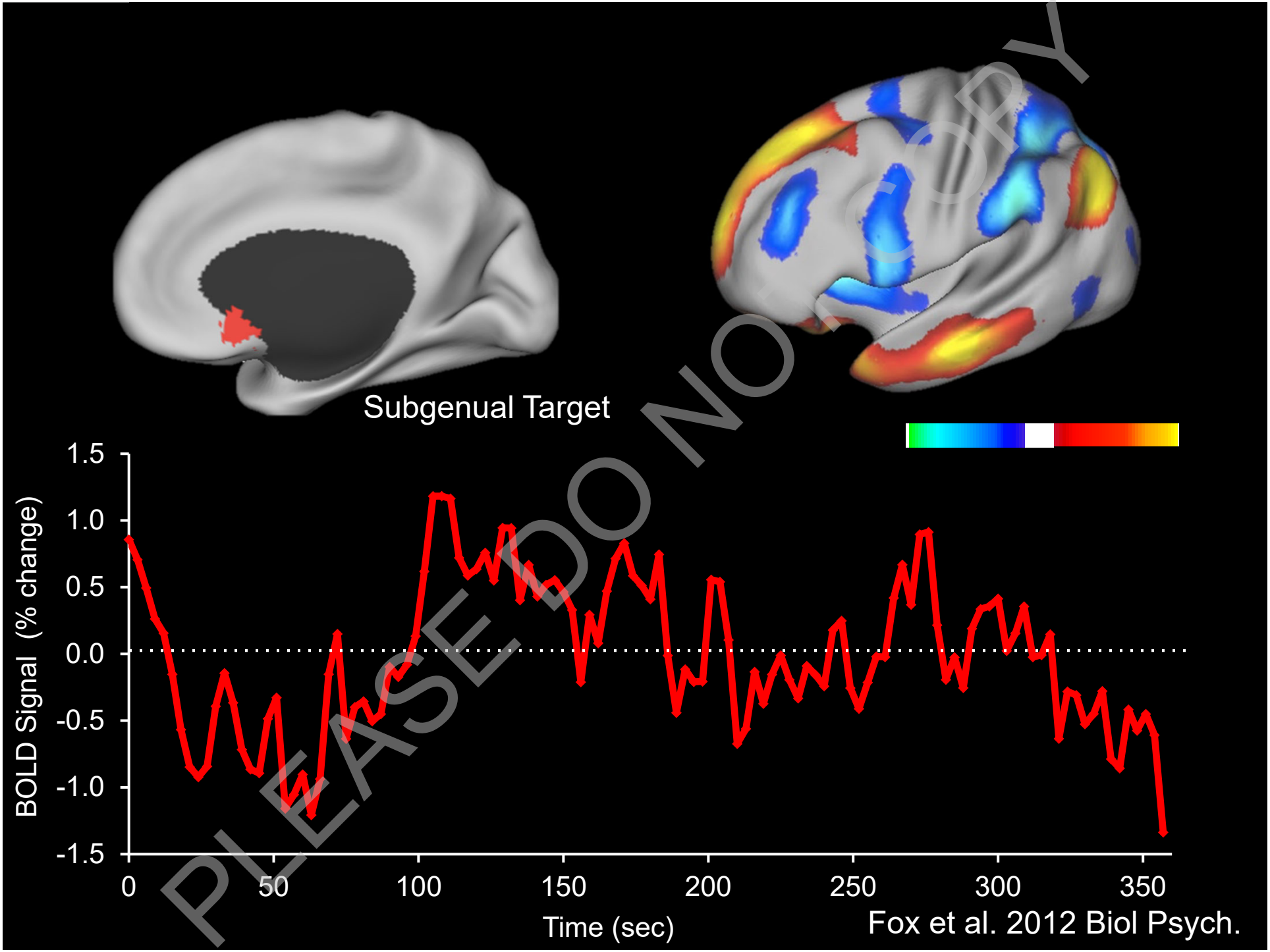
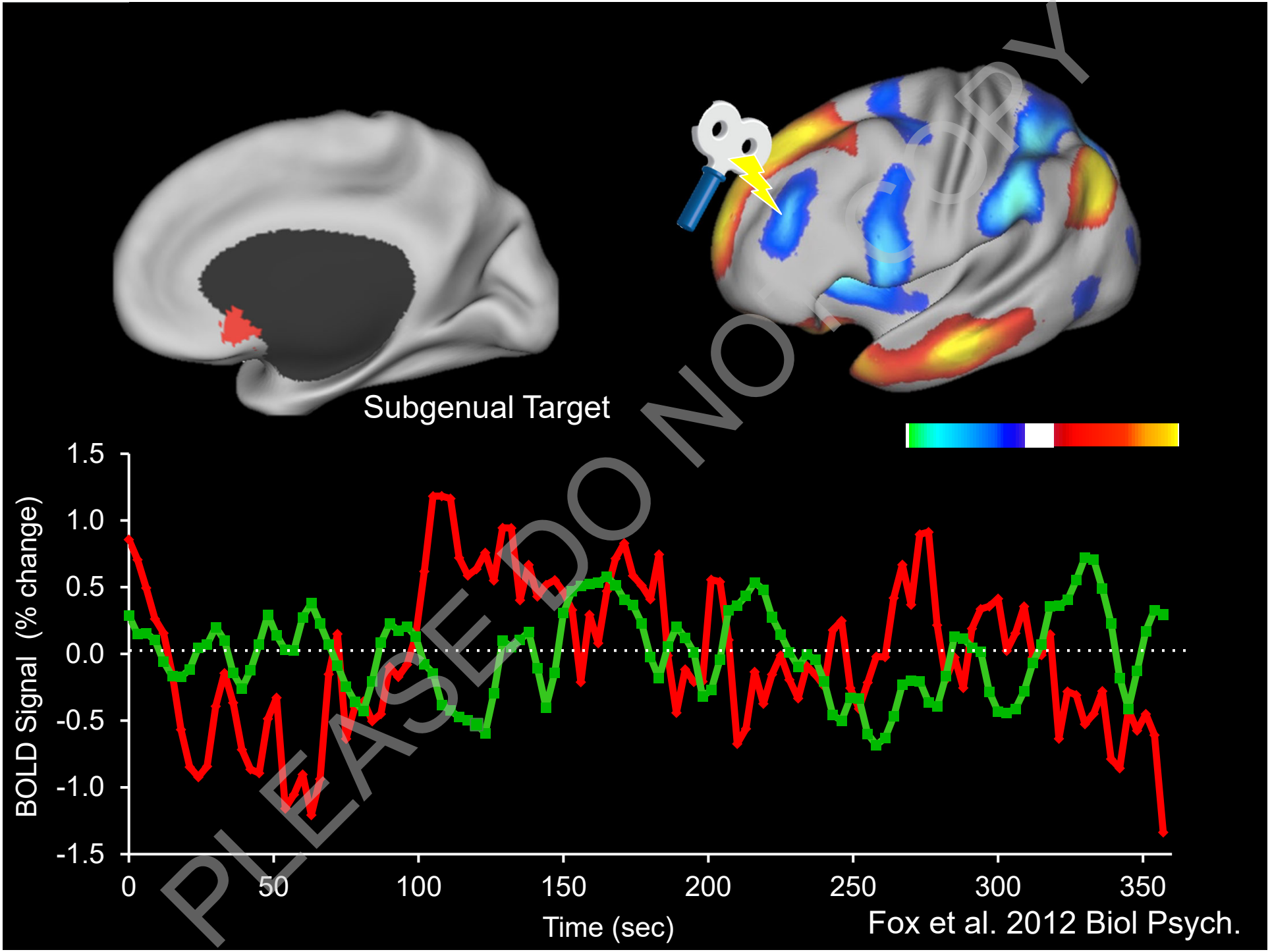
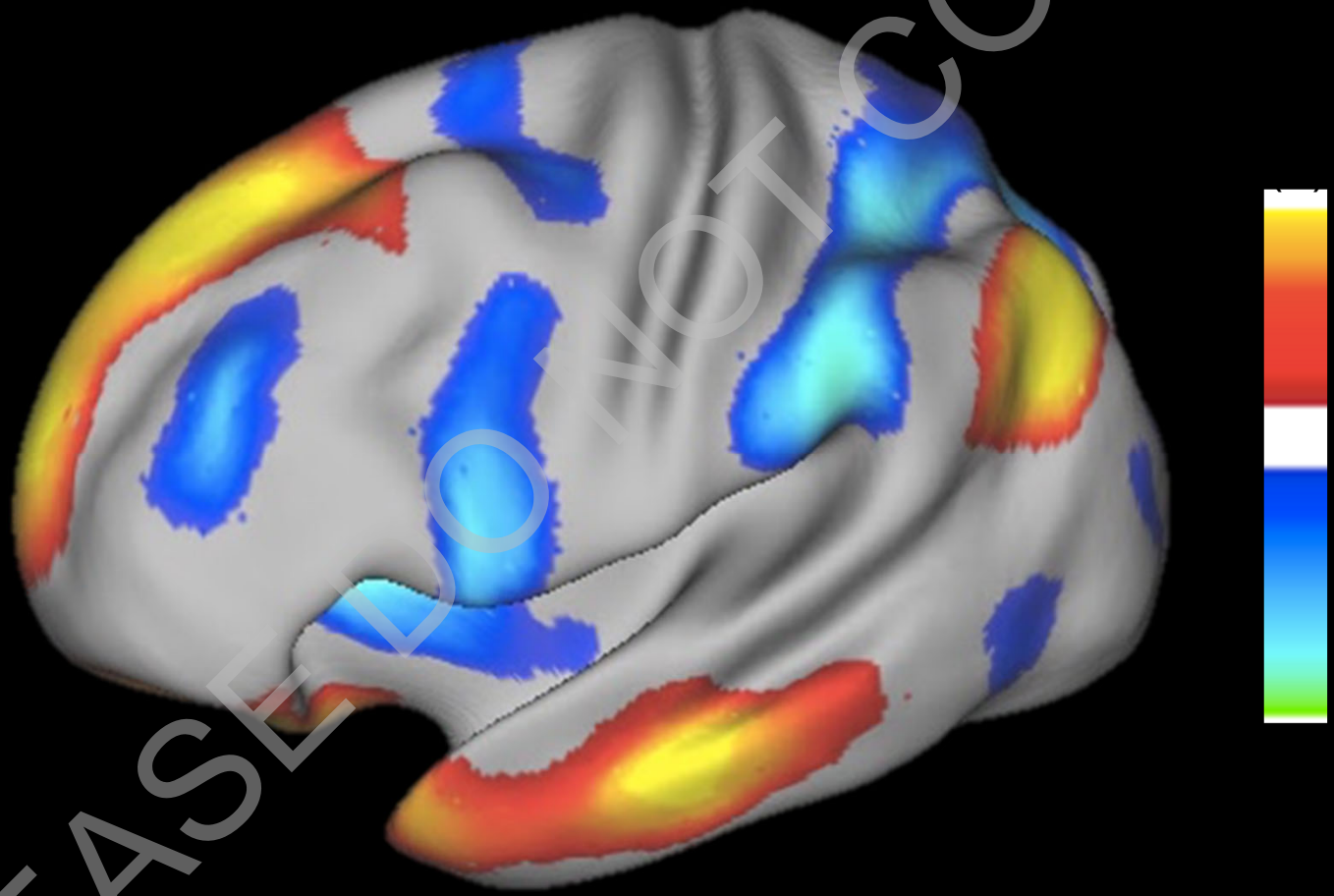






Can subgenual connectivity guide stimulation?



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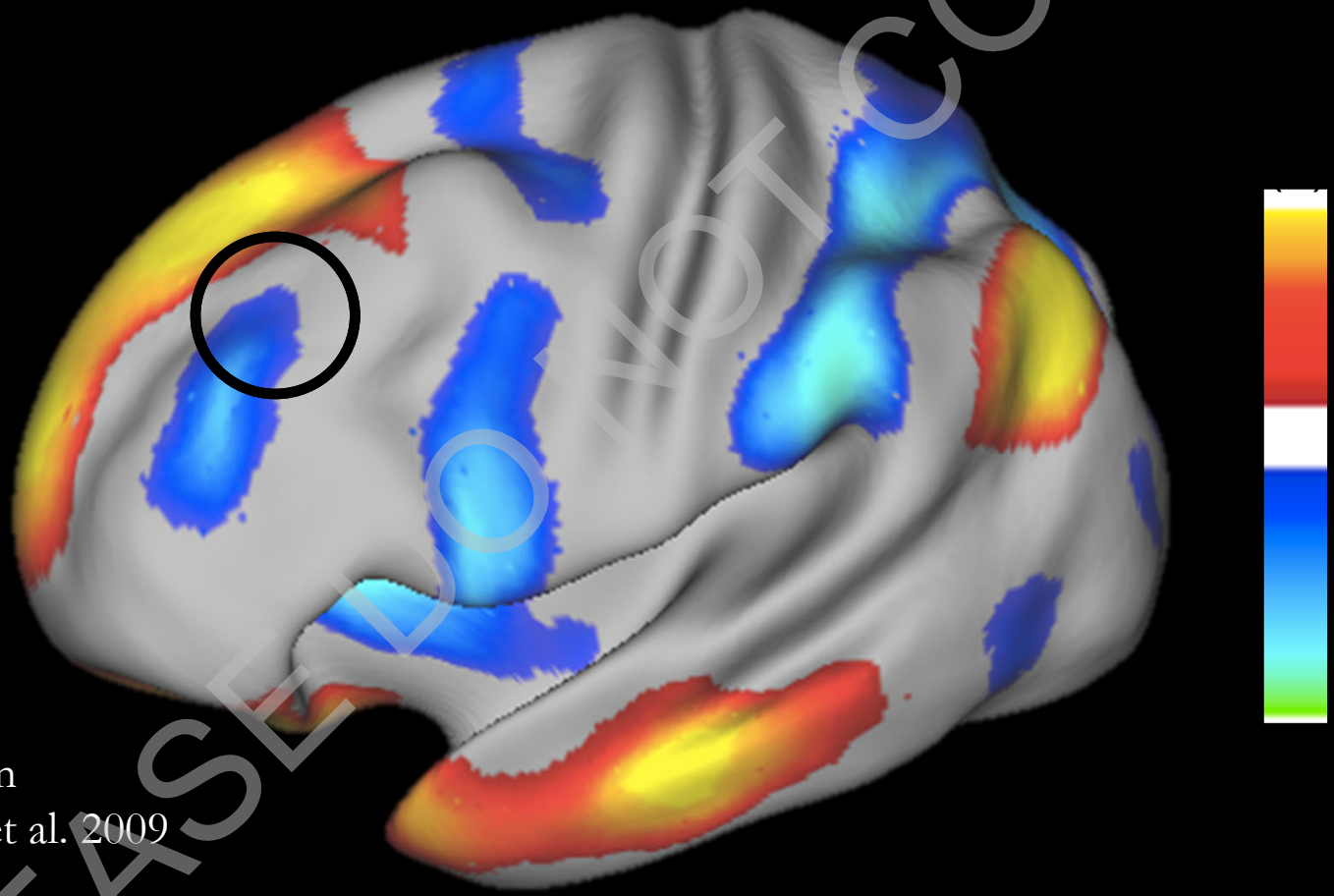

Targets from
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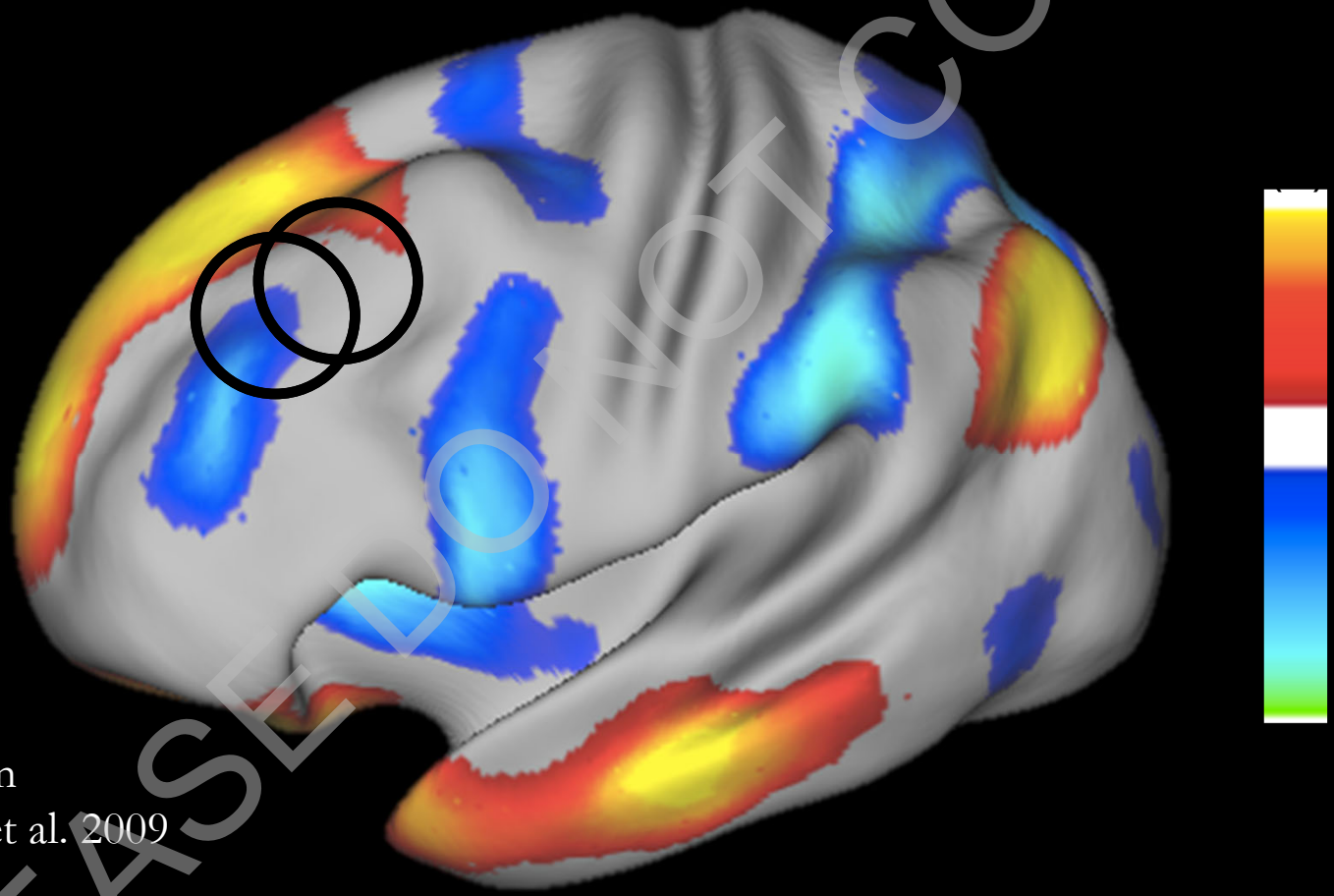

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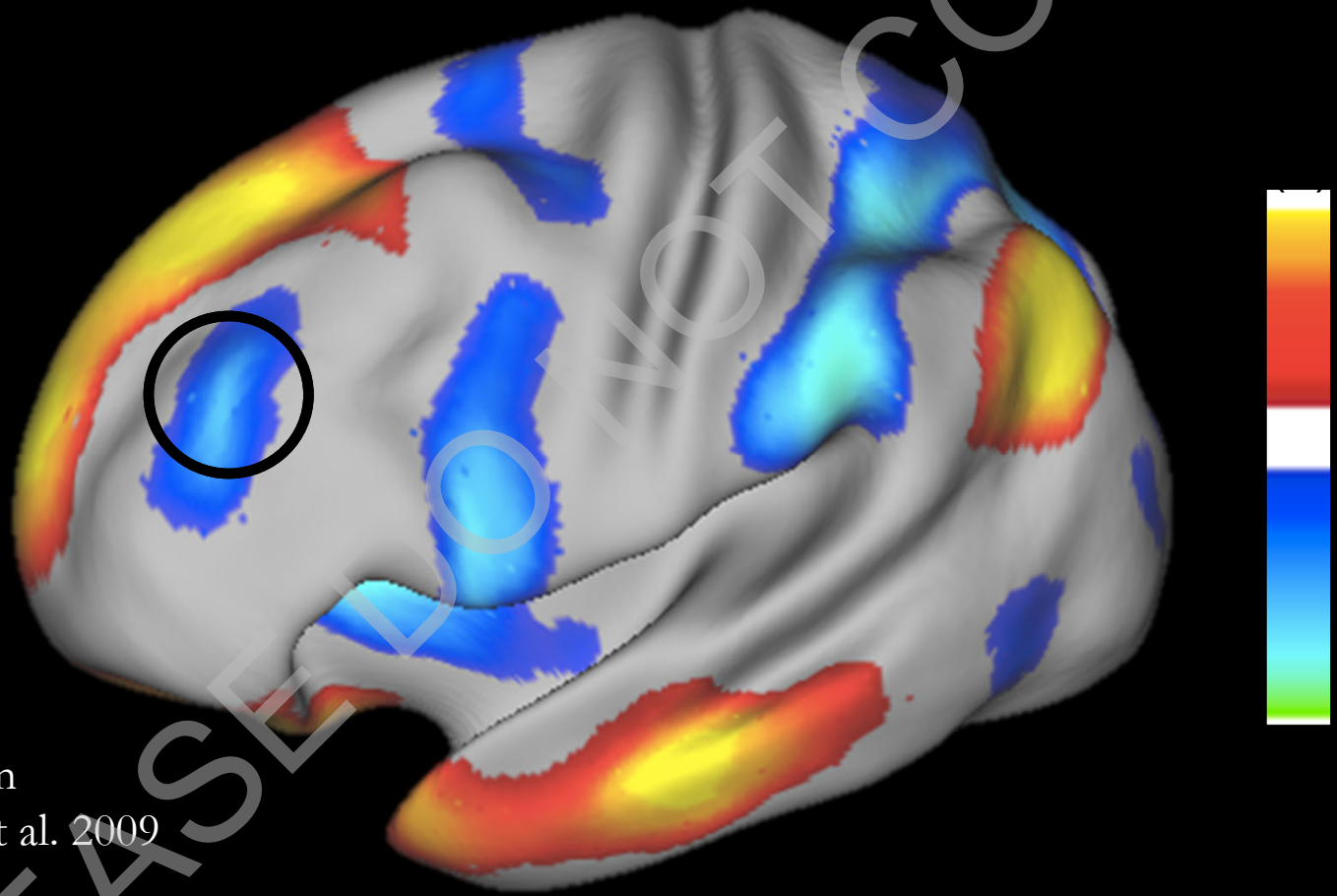

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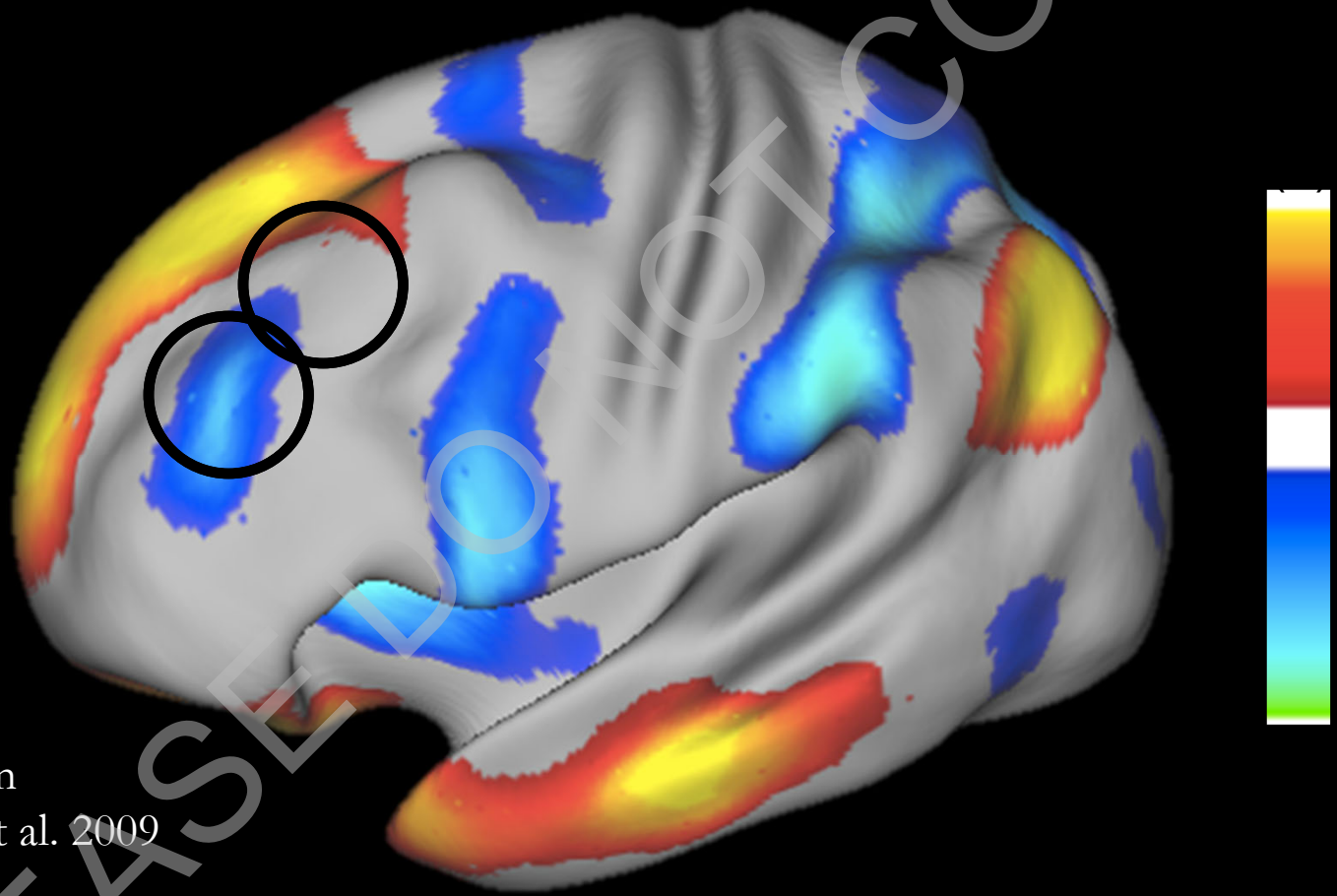

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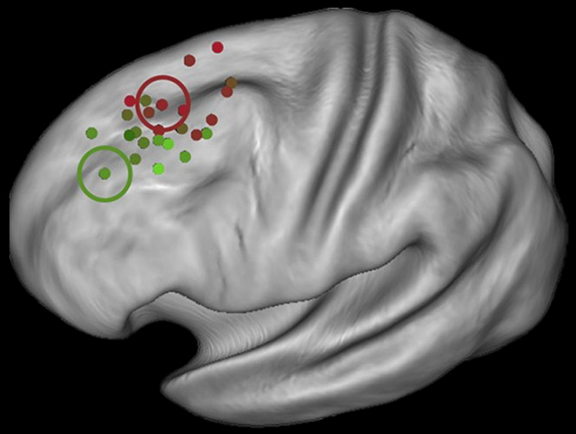
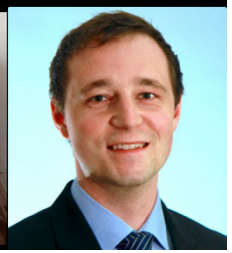
TMS Network Mapping

Stim. Site Variability



Weigand, Horn et al. 2018 Bio. Psych



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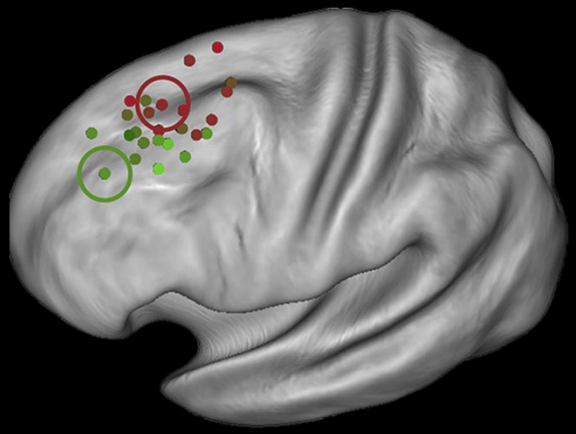
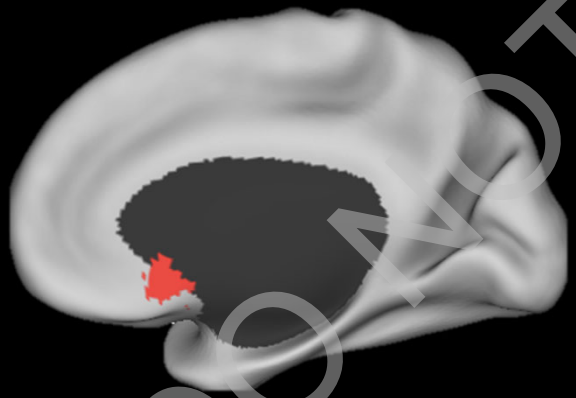


Important Connections



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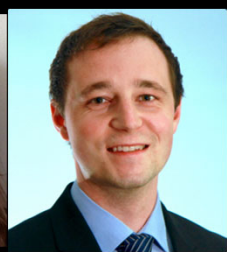

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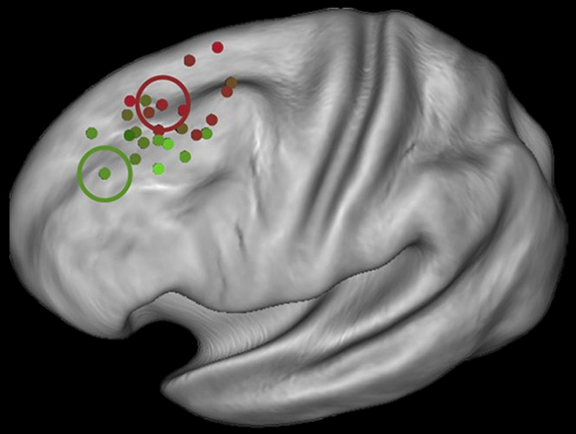

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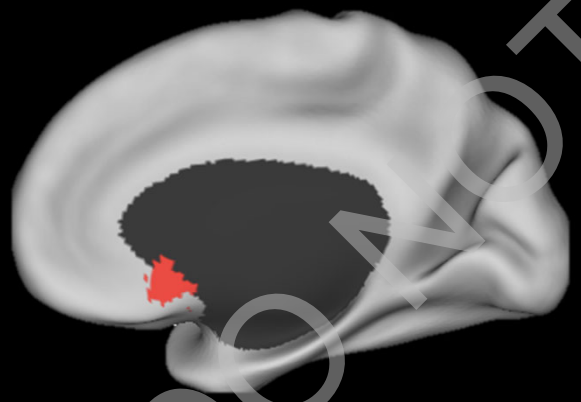
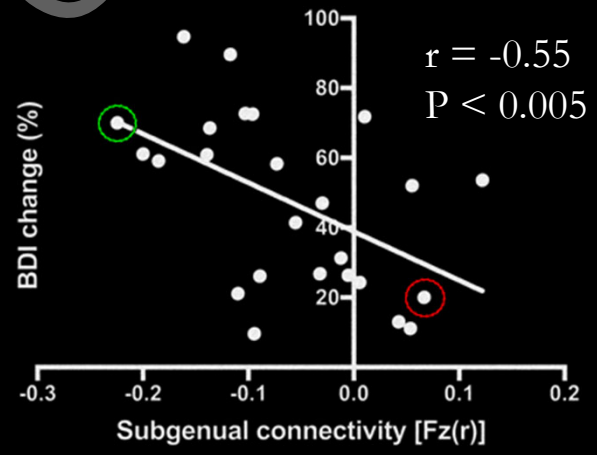


Response Prediction



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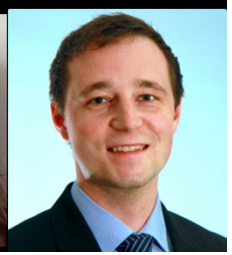

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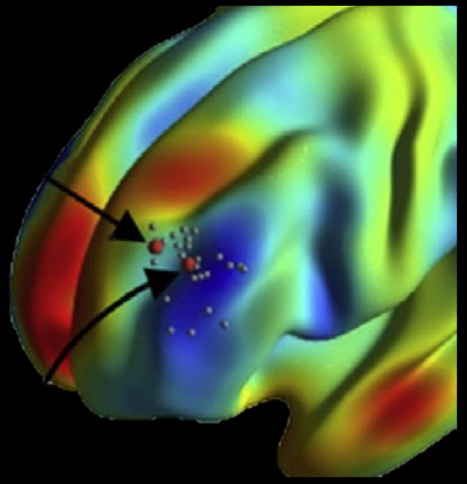

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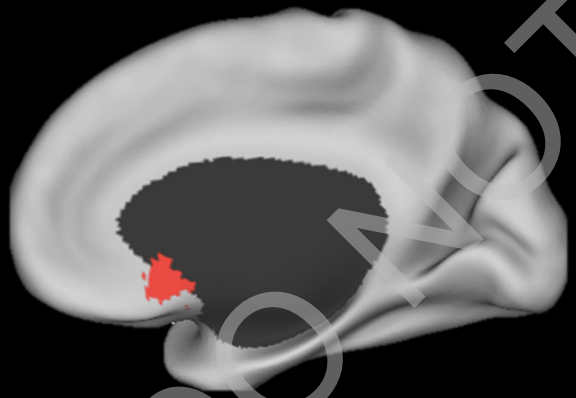

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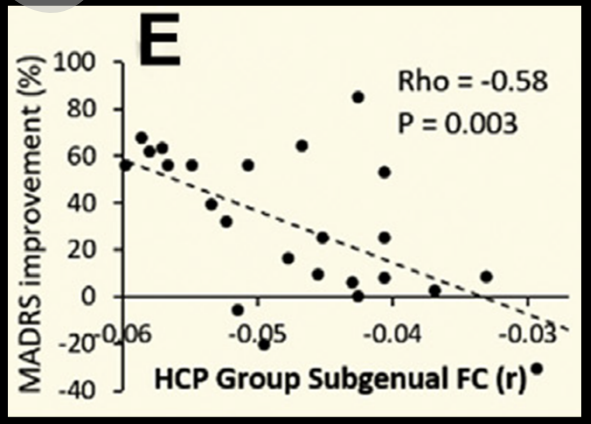
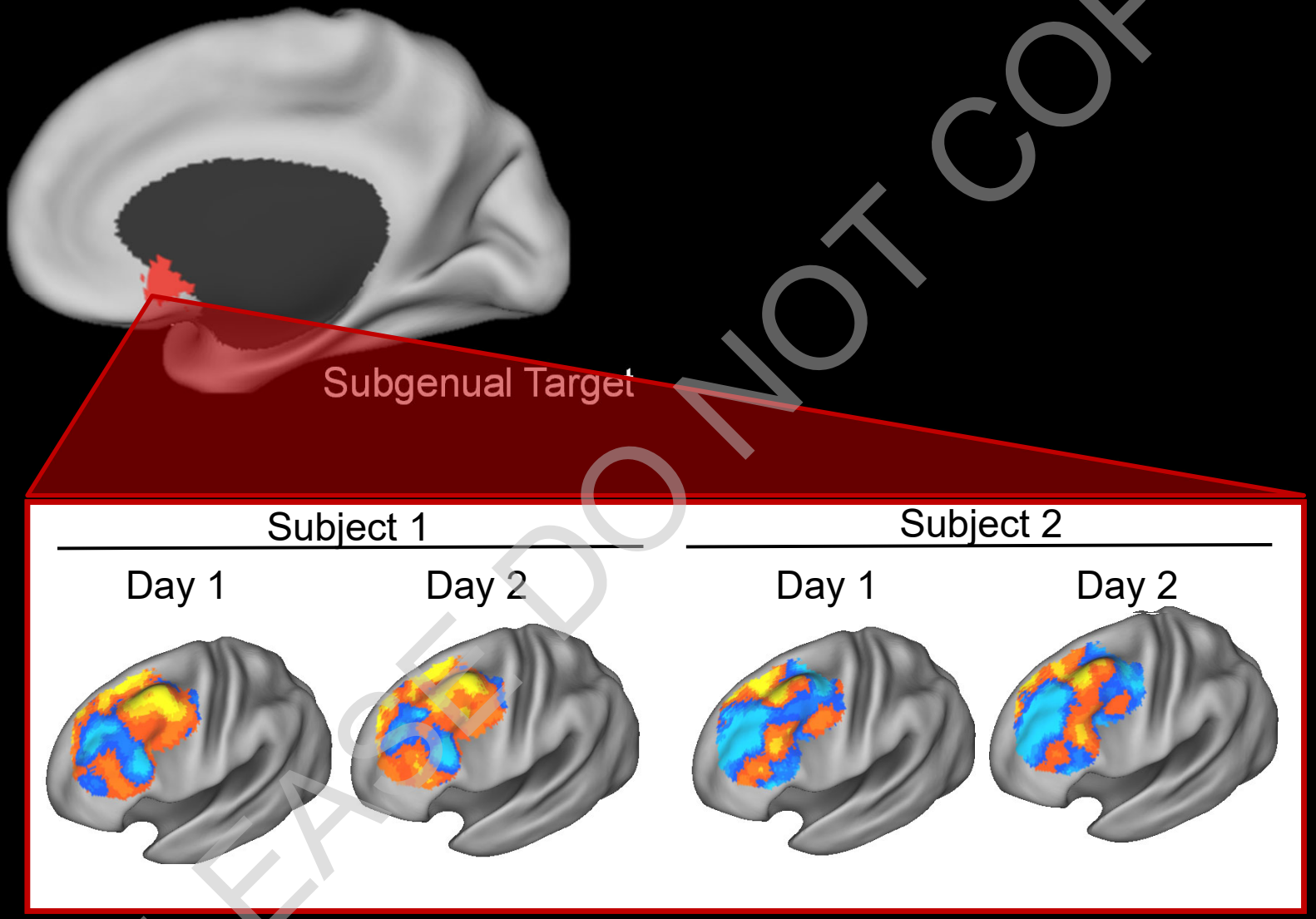


Cash et al. 2019, 2020 Biological Psychiatry

“Individualized” TMS Targets



Fox et al. 2013 Neuroimage

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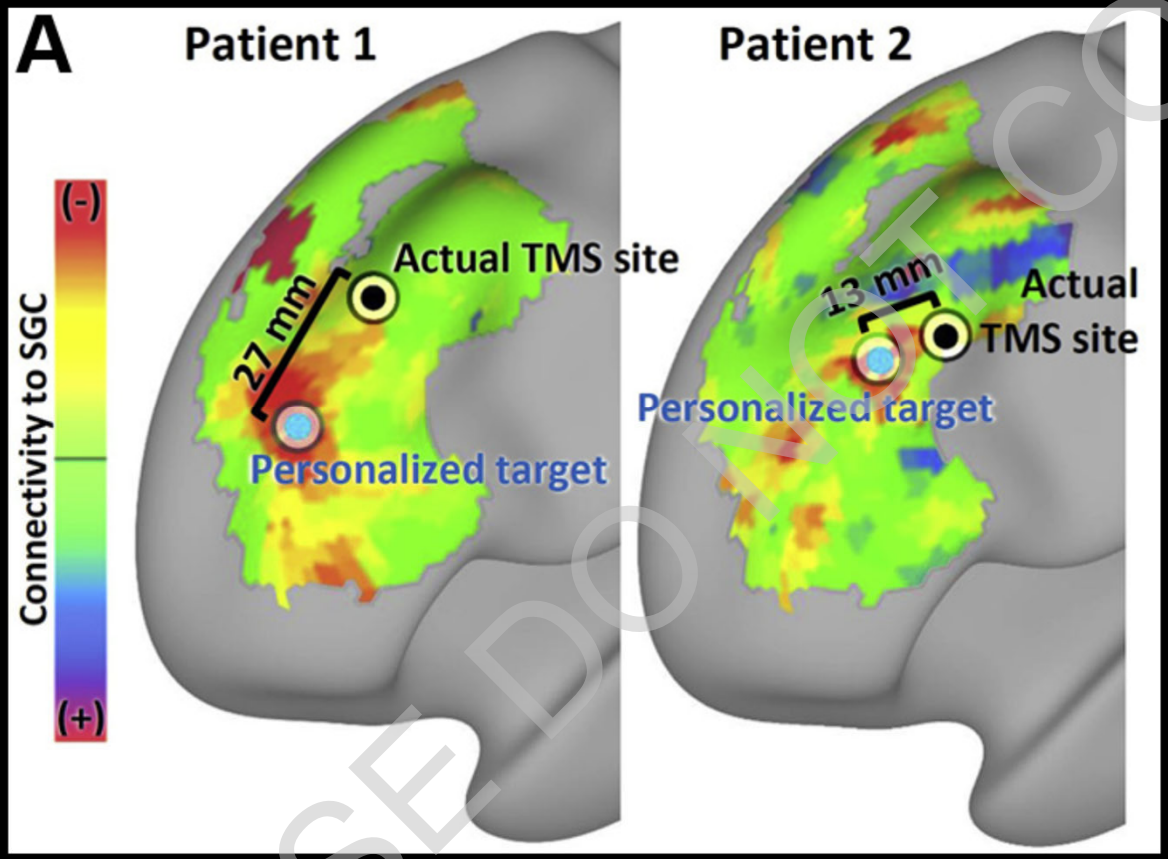

Siddiqi et al. 2021 Biological Psychiatry

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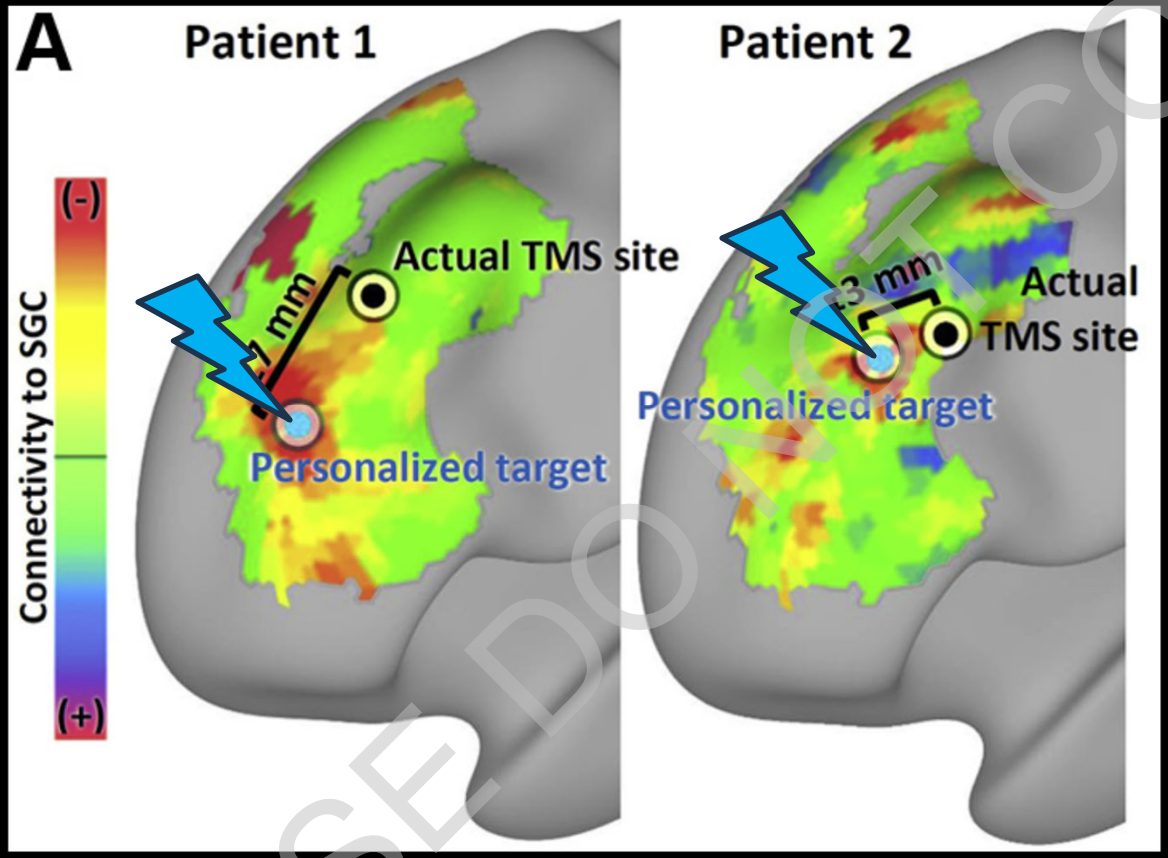
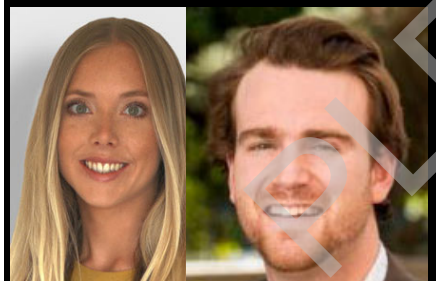
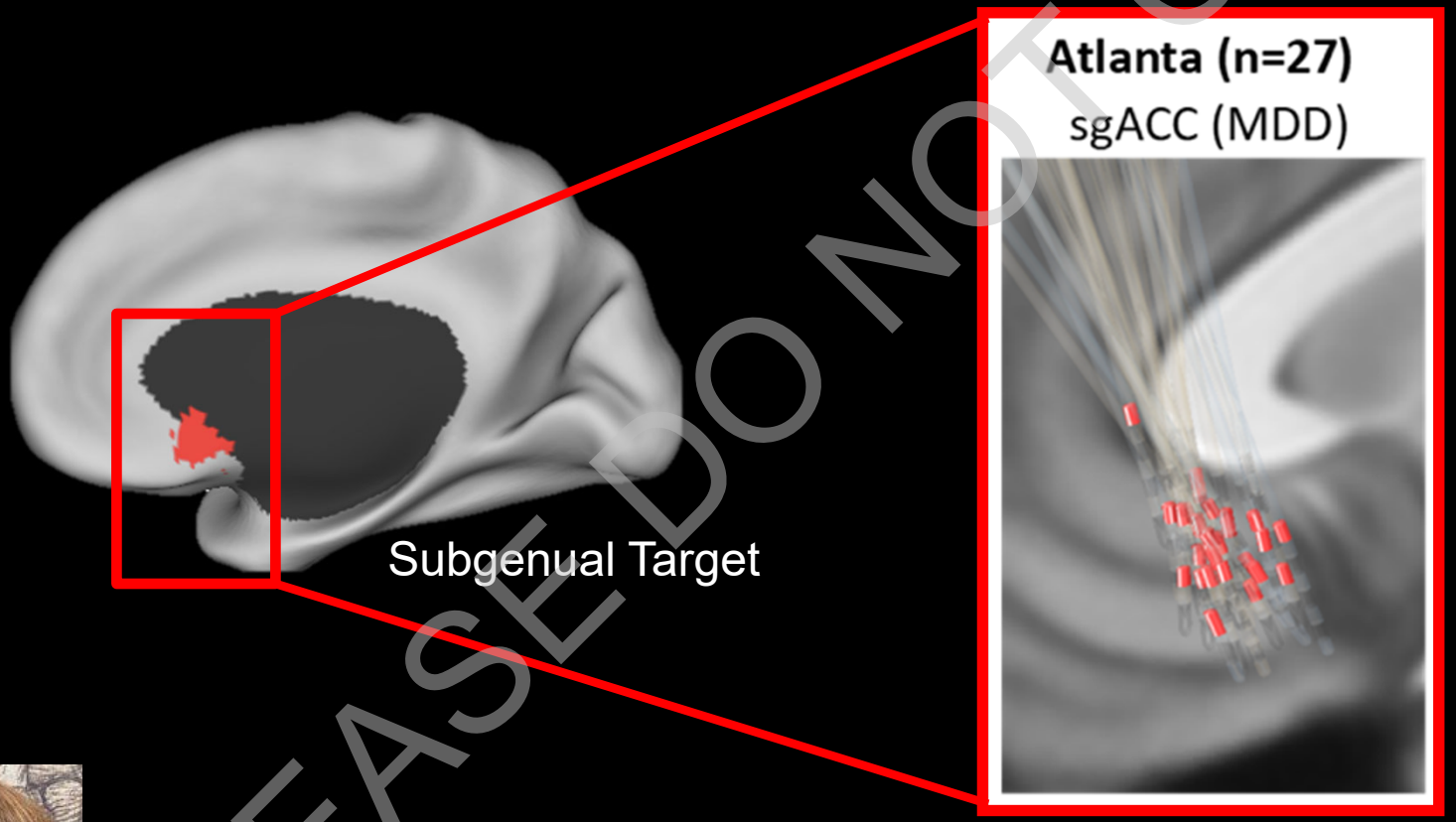




SAINT Neuromodulation System FDA approved 9/2022
Cole et al. 2020 AJP, Cole et al. 2021 AJP : >80% response rate

What if we're unsure of our target?



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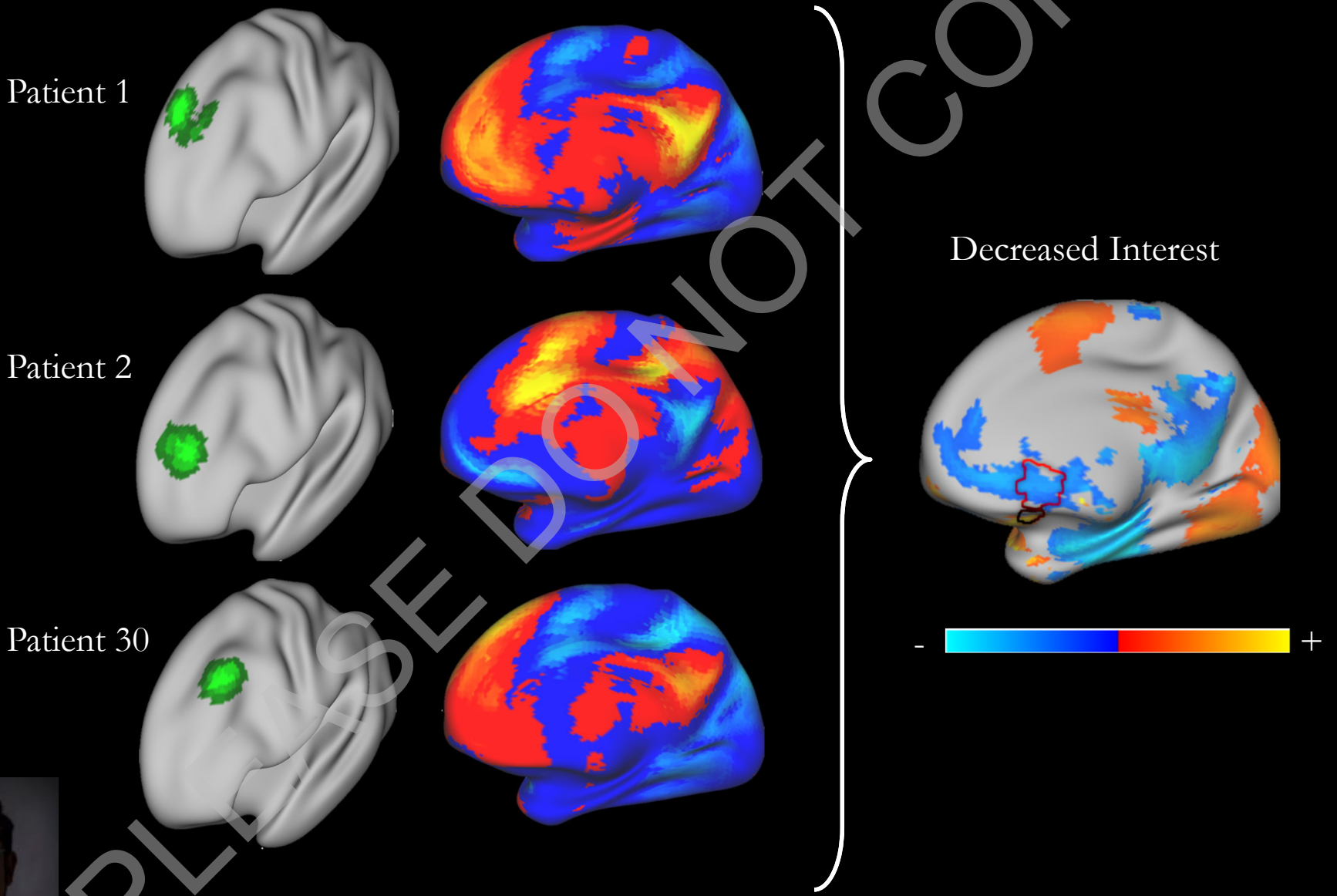
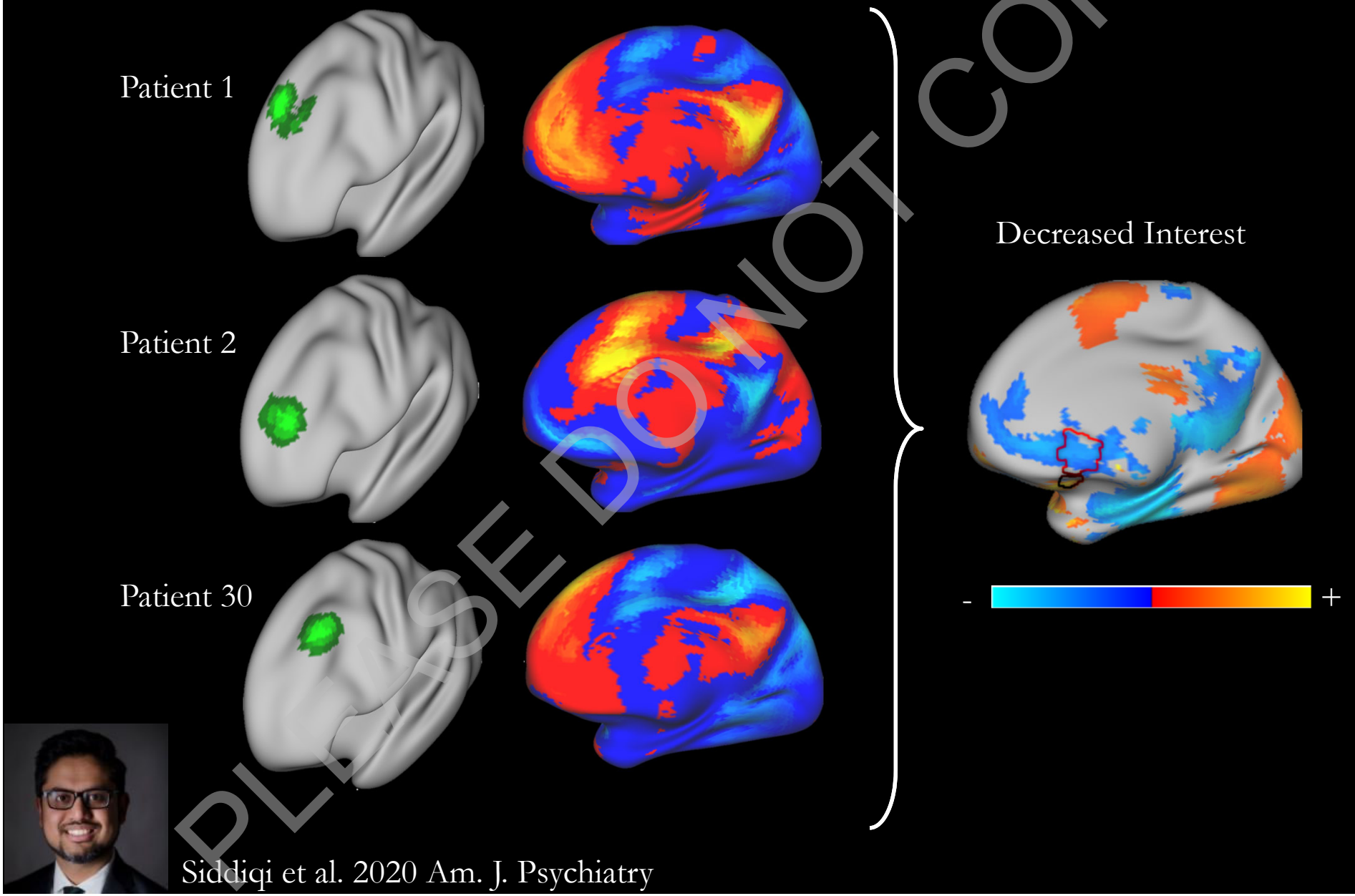


Siddiqi et al. 2020 Am. J. Psychiatry

Symptom-Specific TMS Targets?



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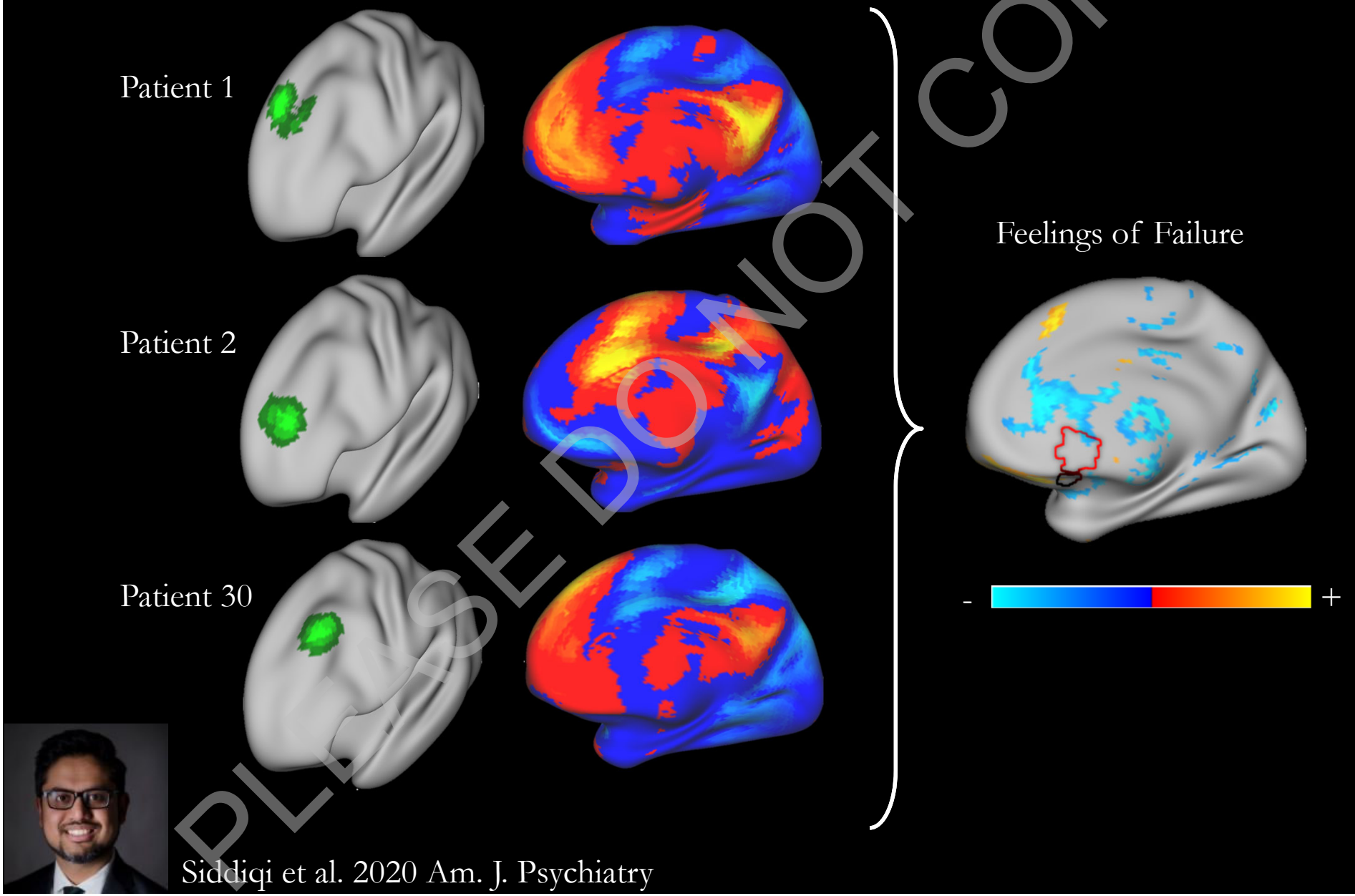

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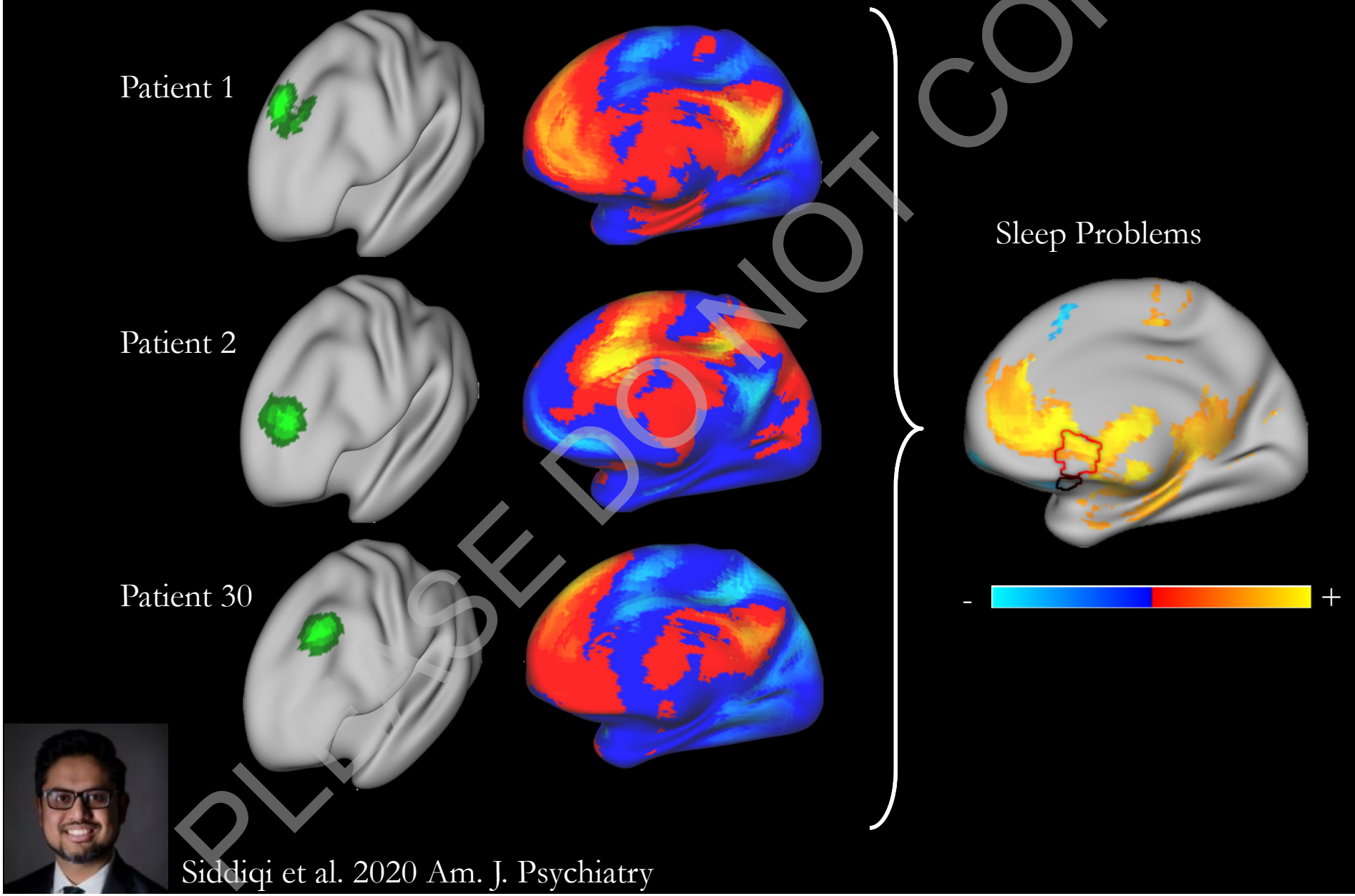

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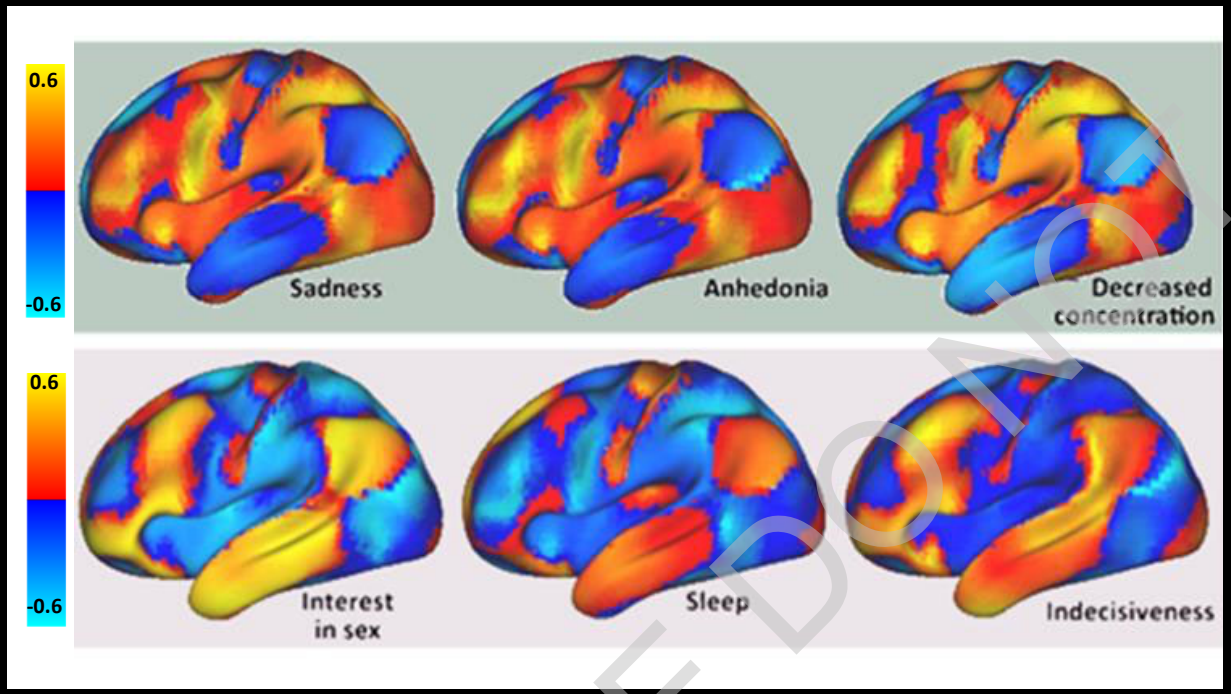

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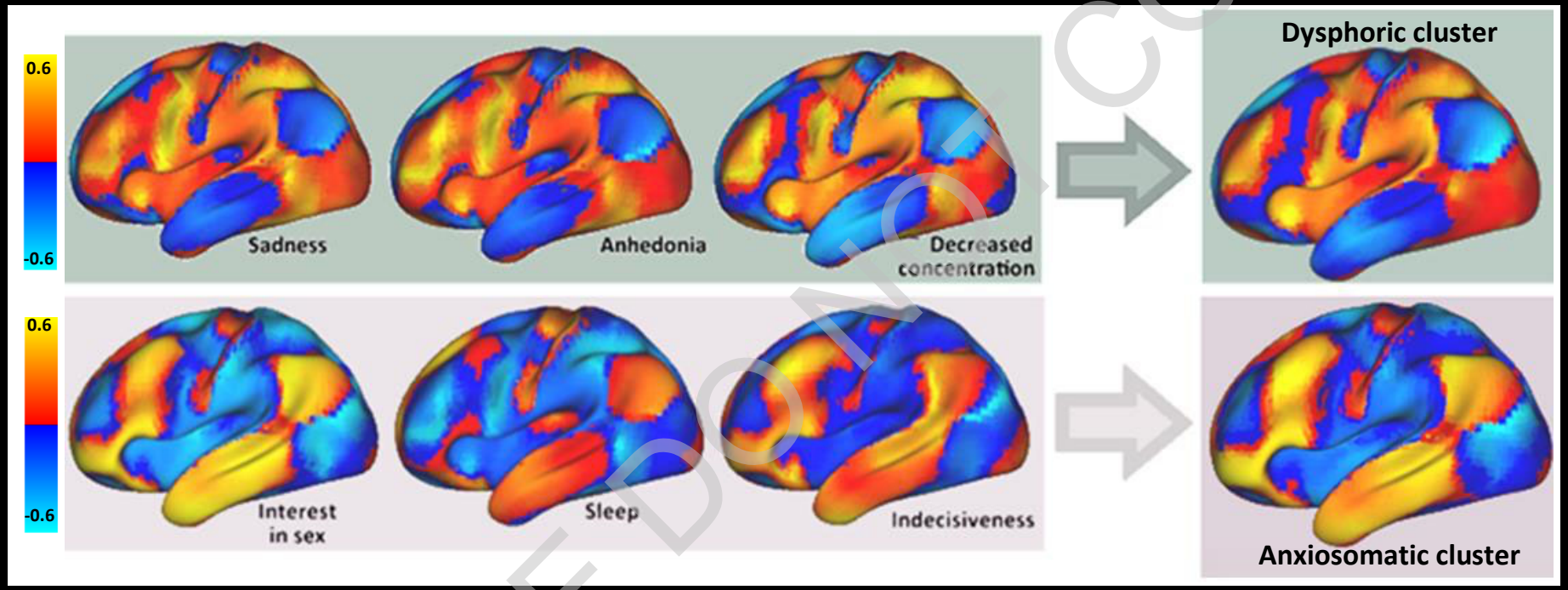

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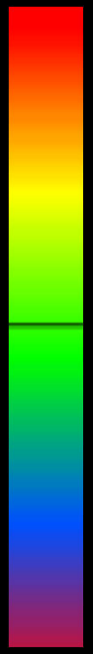
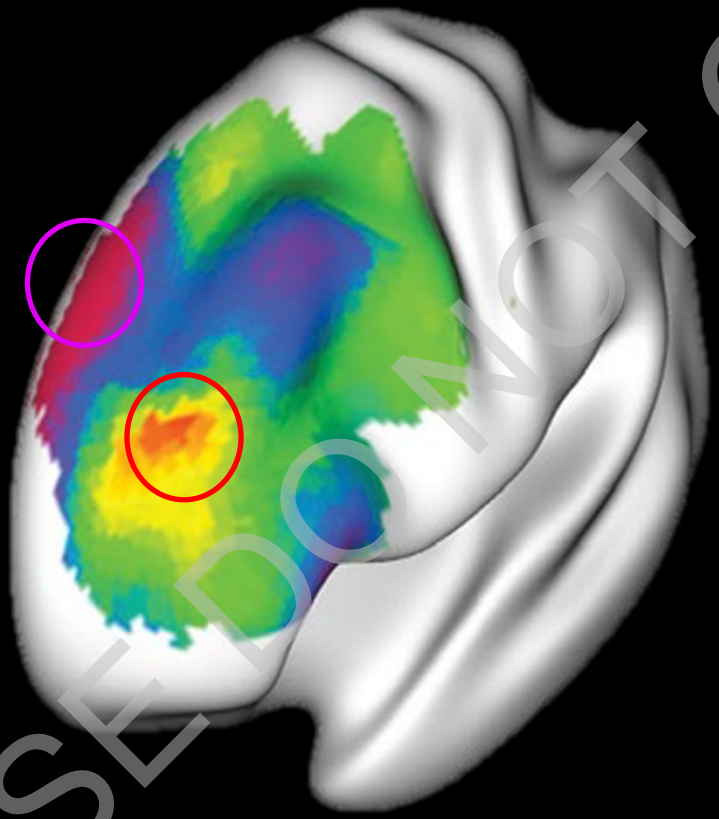
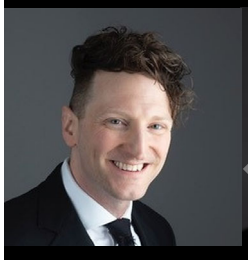
Symptom-Specific TMS Targets?

Dysphoric



Anxiosomatic





Taylor, Siddiqi et al., Under Preparation

Symptom-Specific TMS Targets?

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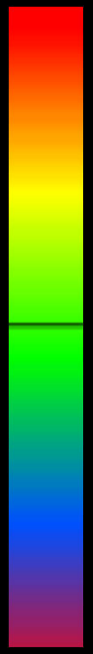

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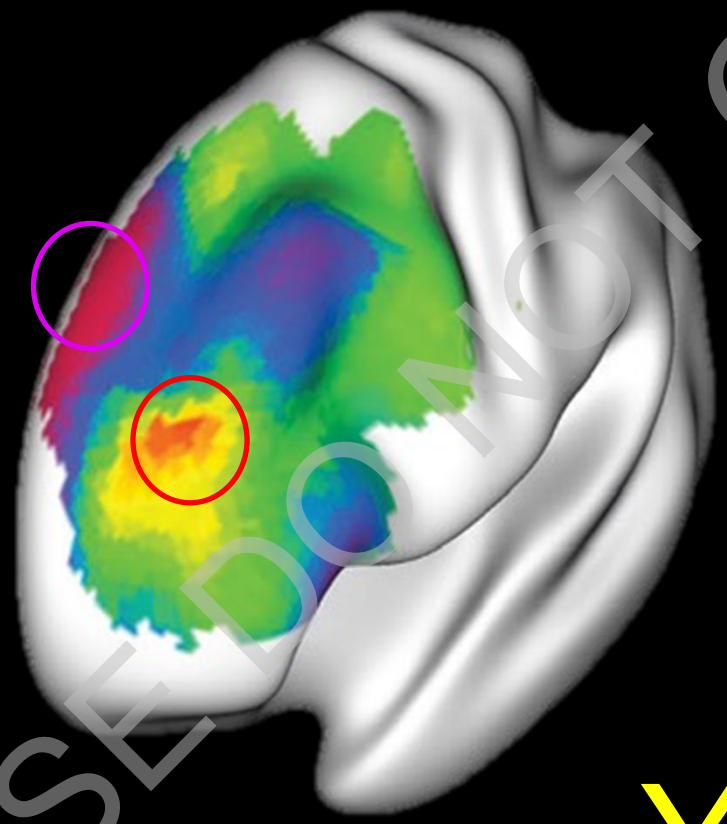
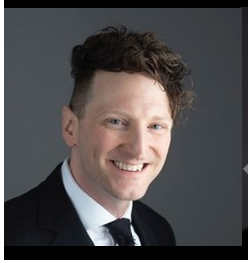
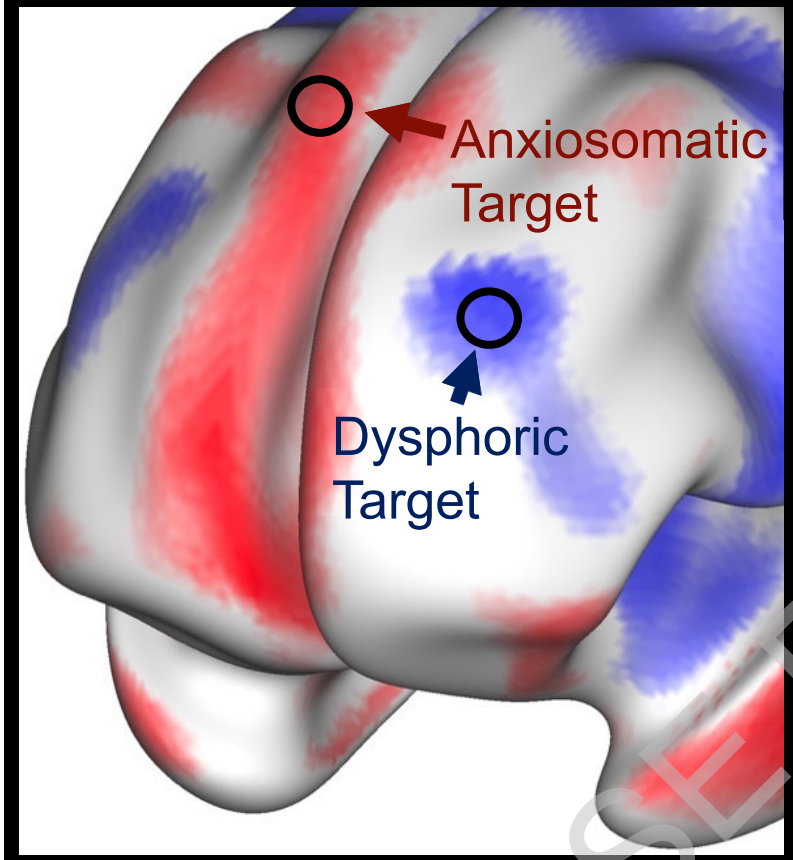


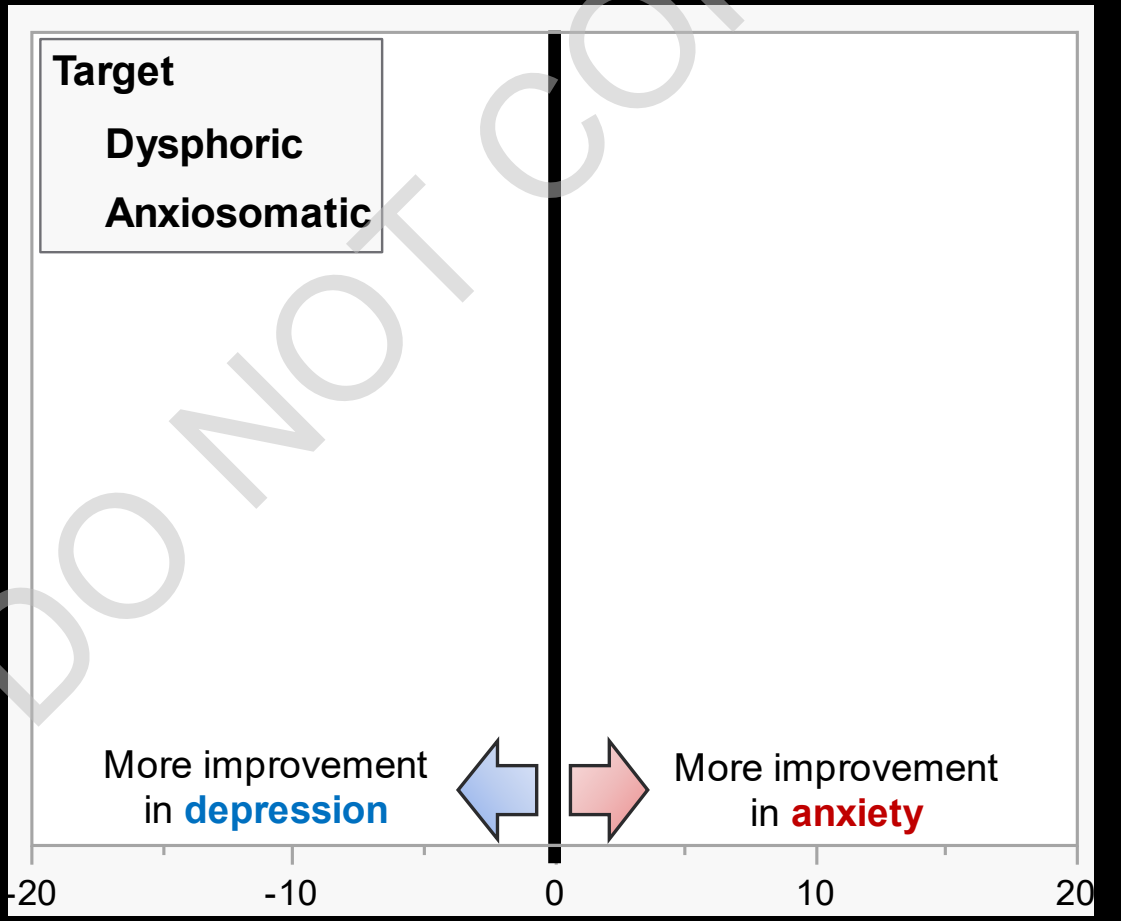
YES!

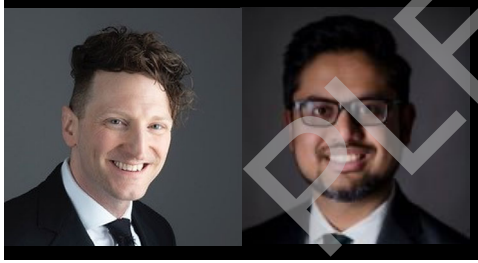


Taylor, Siddiqi et al., Under Preparation

Symptom-Specific TMS Targets?

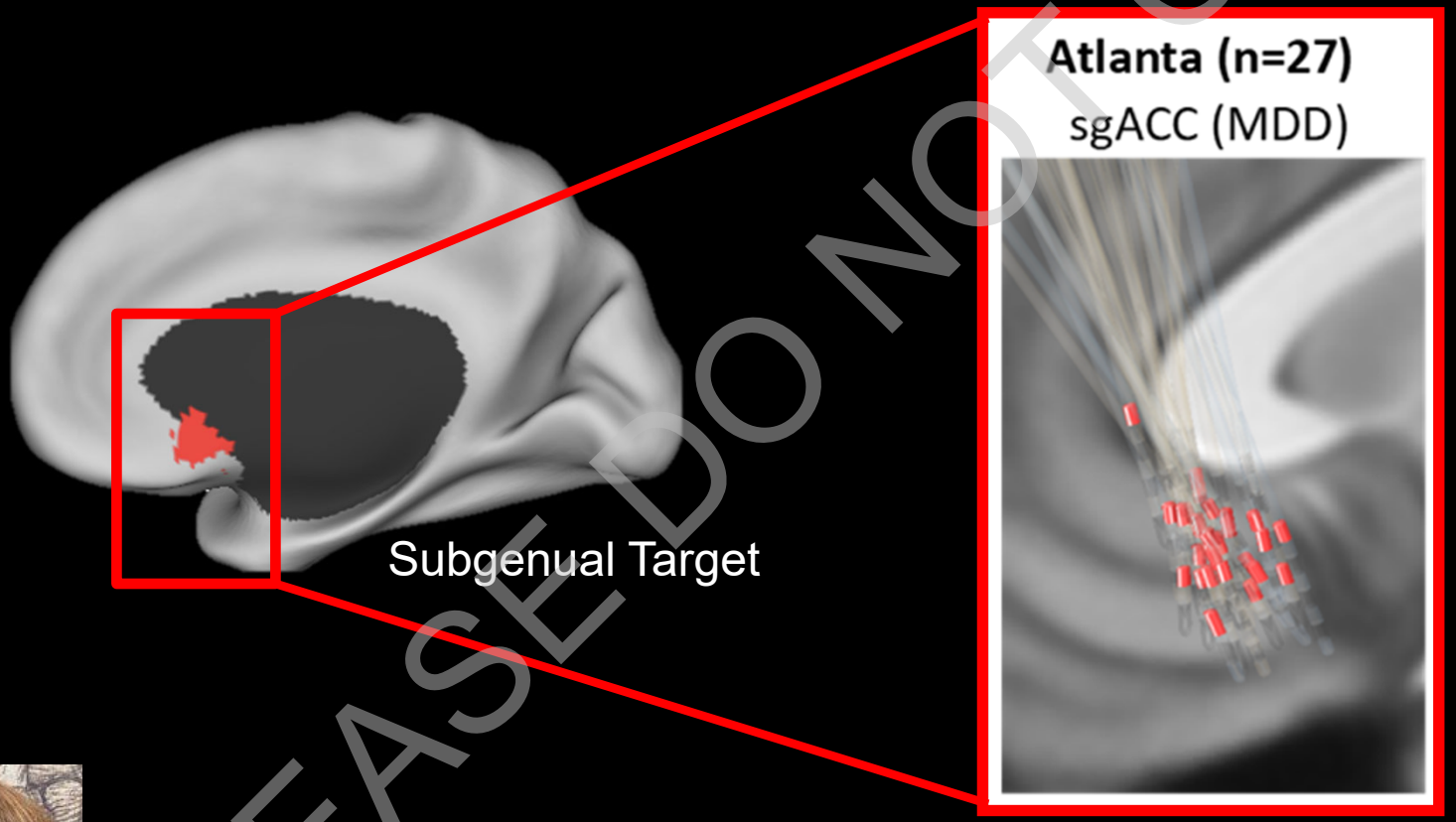






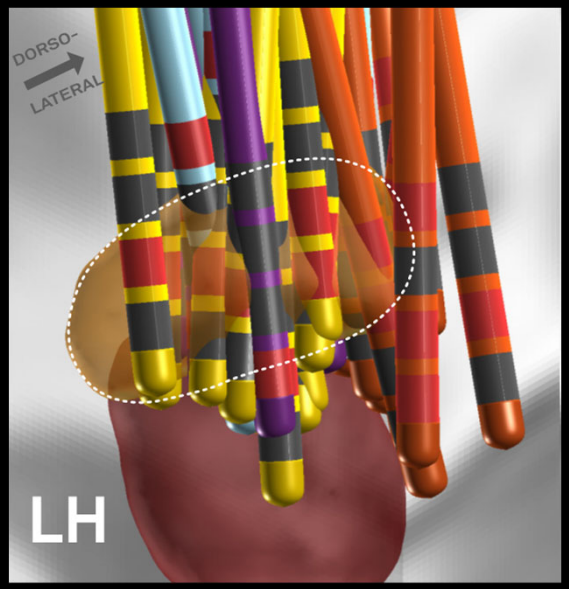
Taylor, Siddiqi et al., Submitted

What if we're unsure of our target?



DBS Network Mapping

Stim. Site Variability



Horn et. al 2017 Annals of Neurology

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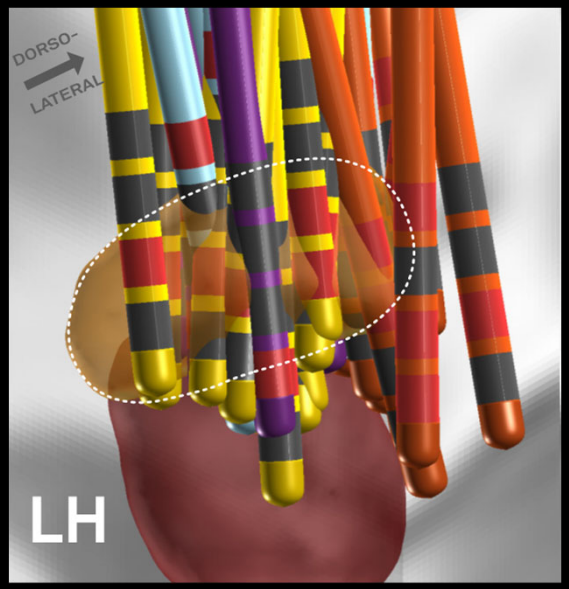
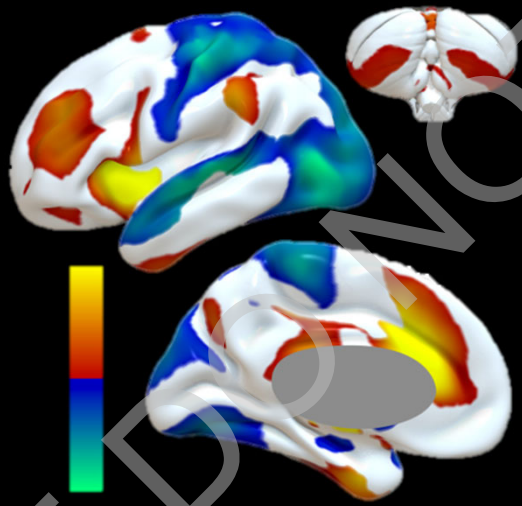


Important Connections



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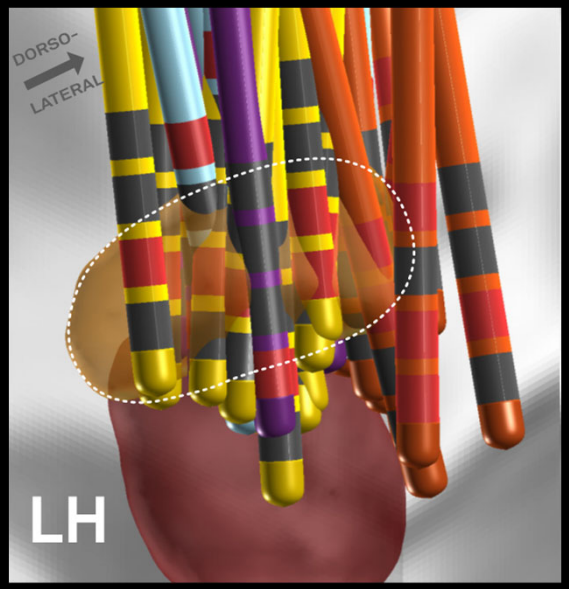

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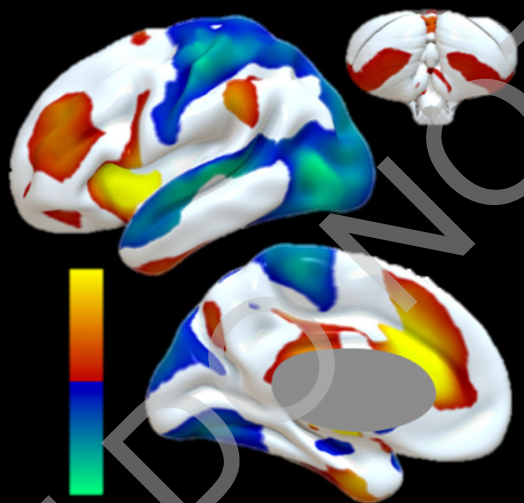
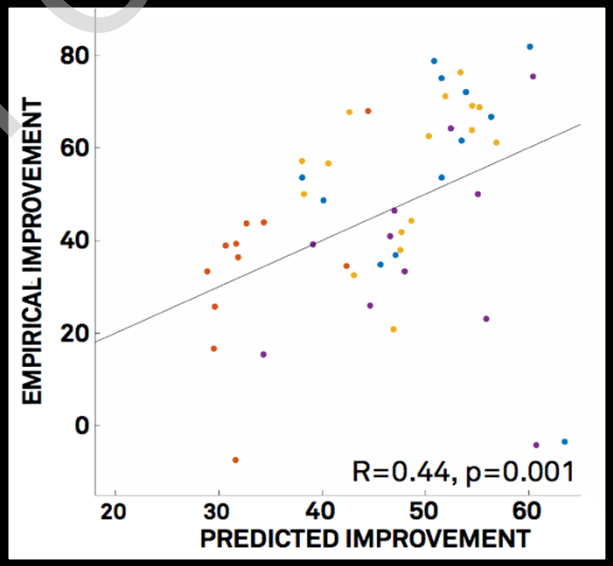


Response Prediction



Horn et. al 2017 Annals of Neurology

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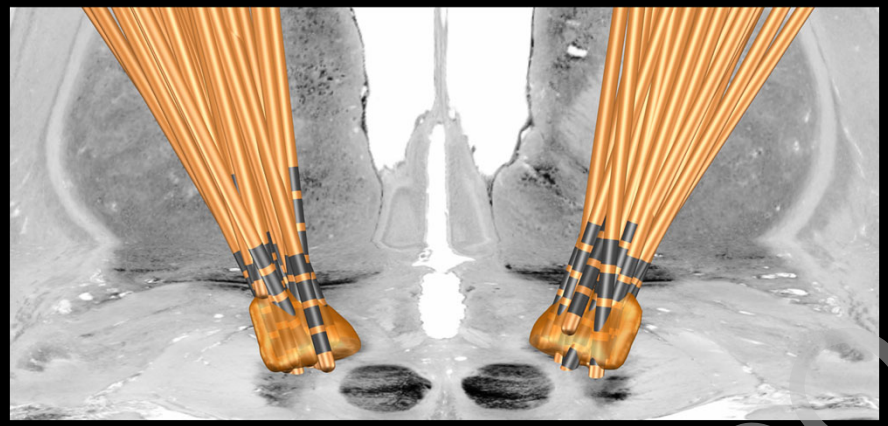
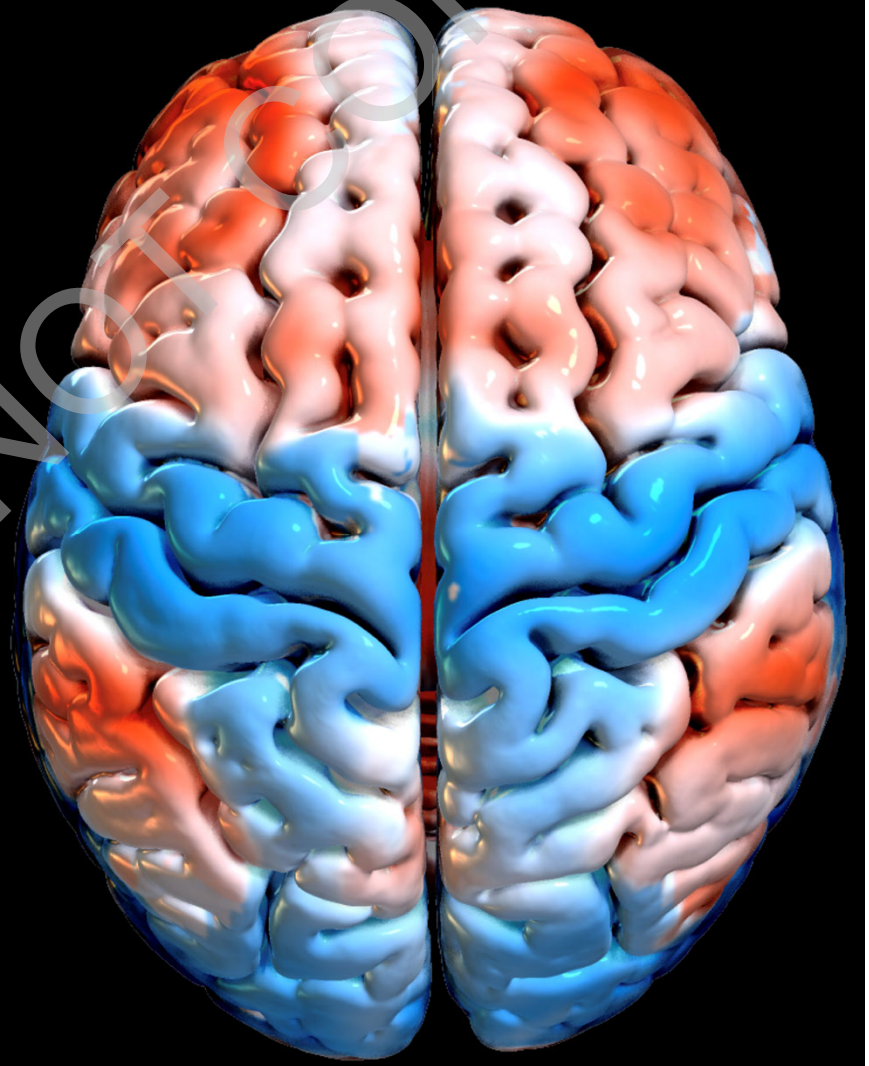
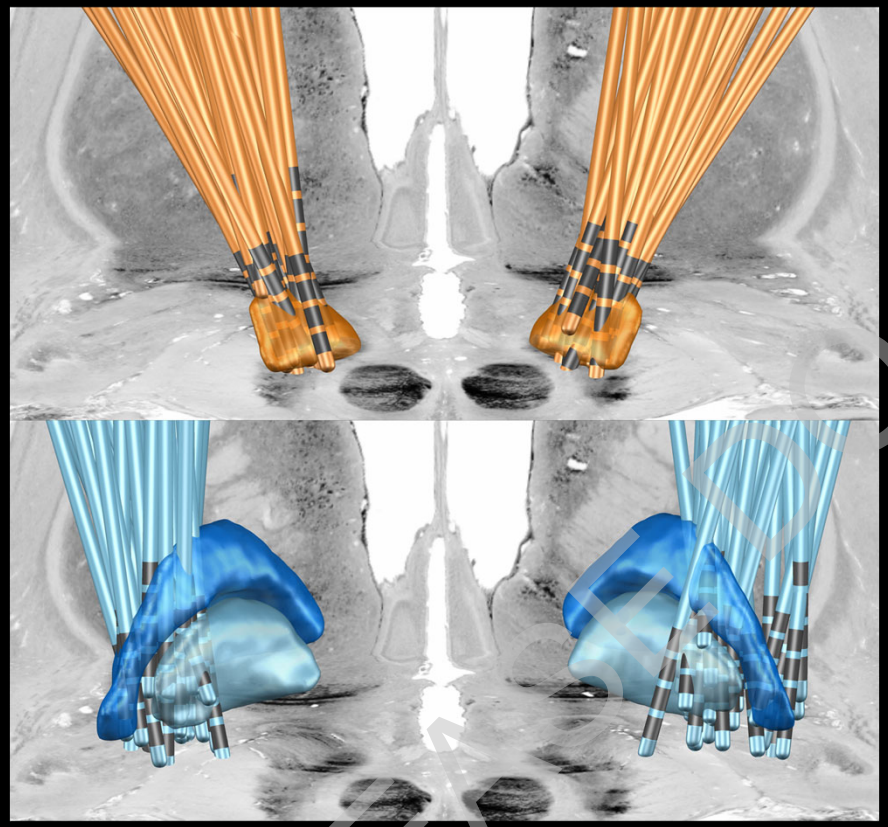
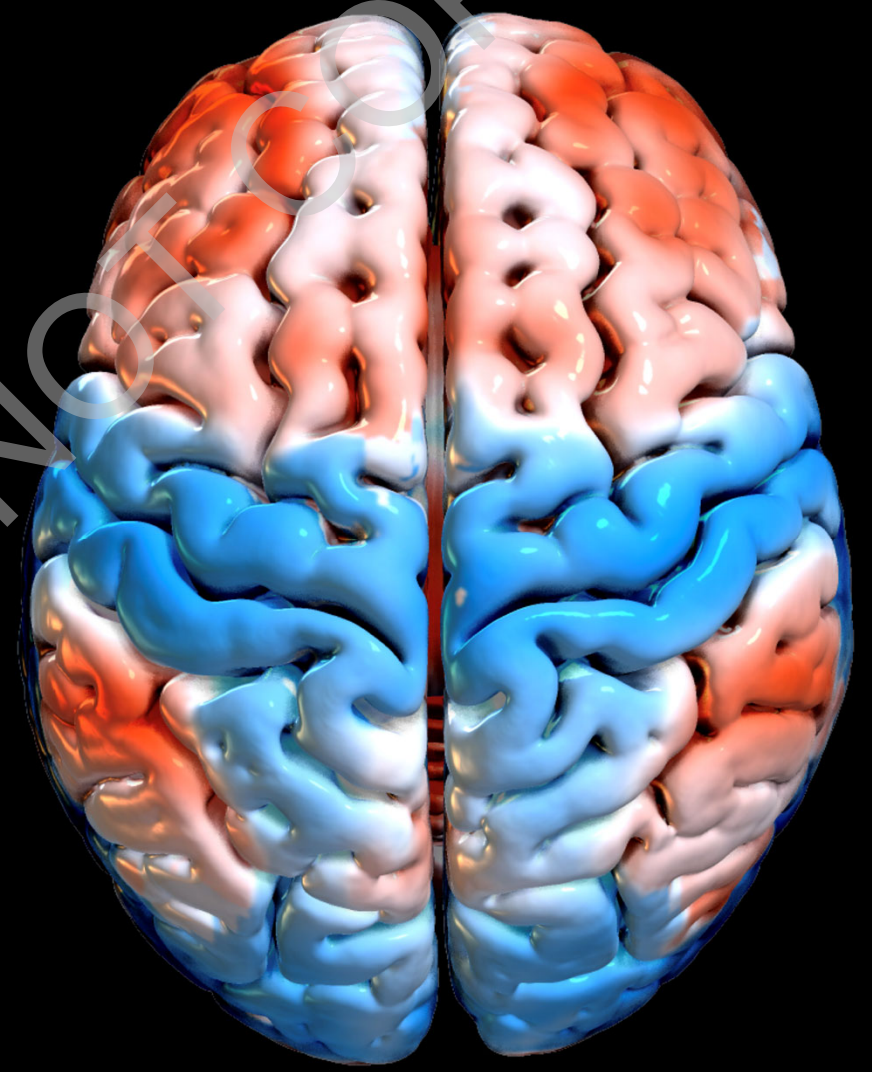




Horn et al., 2017. Annals of Neurology

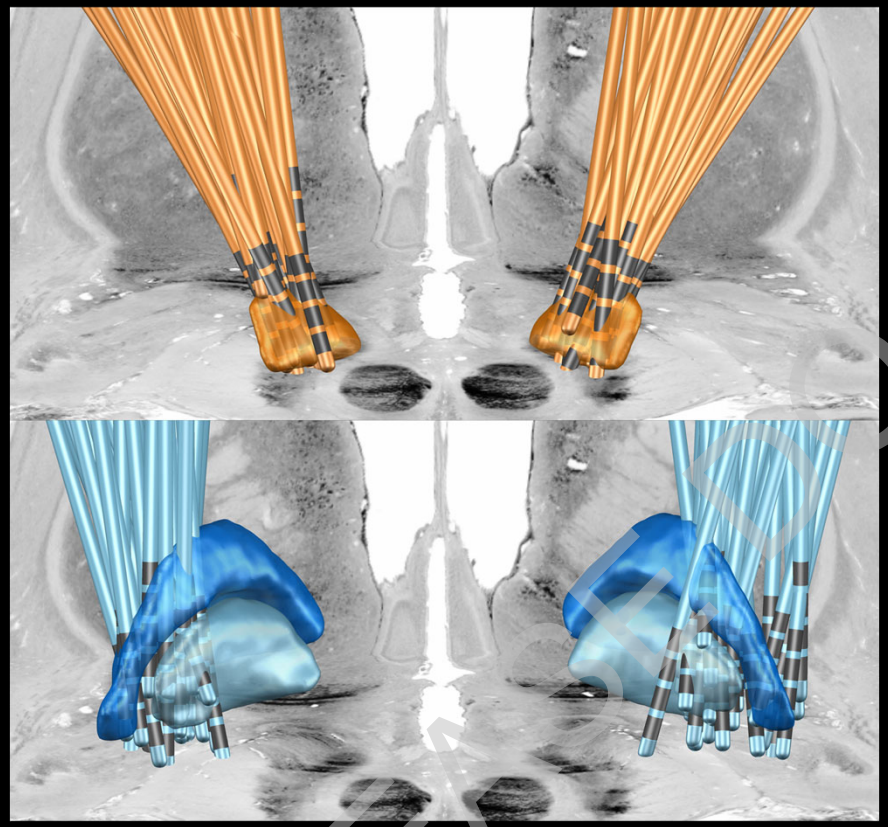
DBS Network Mapping

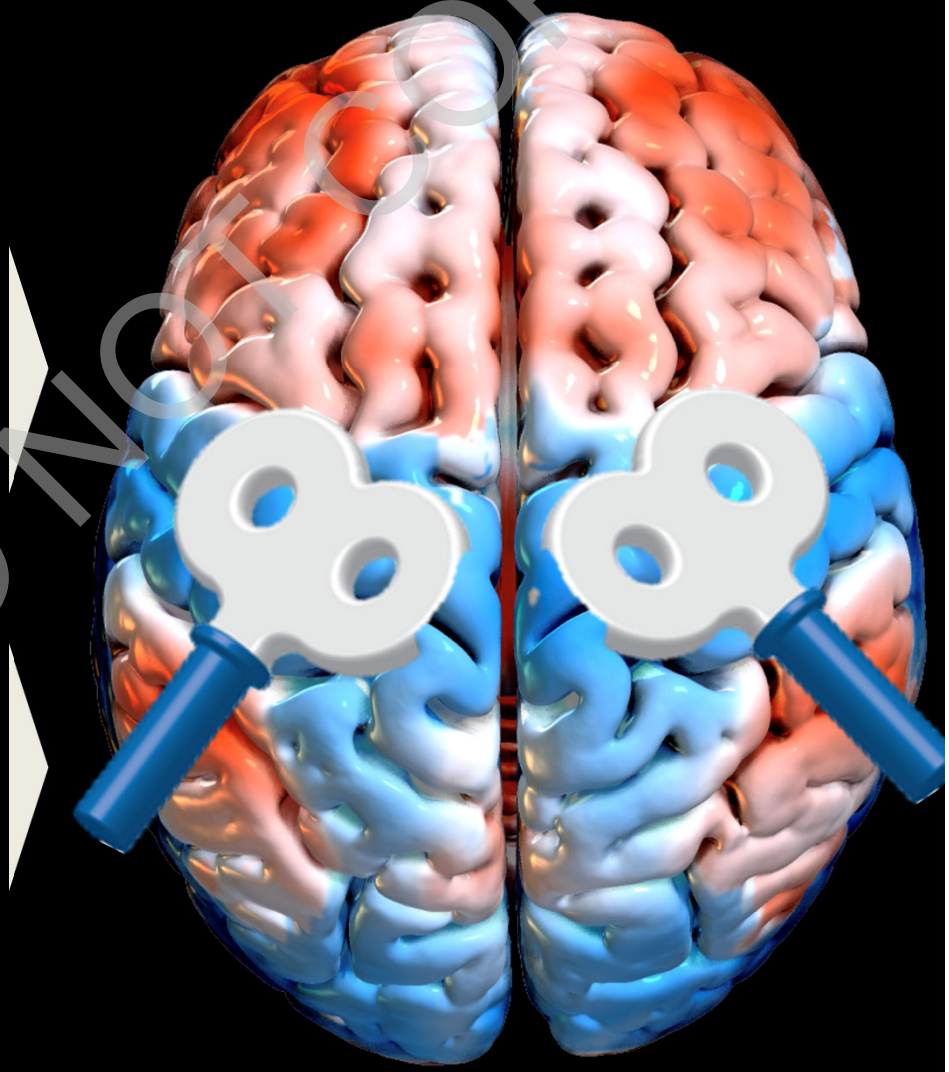




Horn et al., 2017. Annals of Neurology; Sobesky et al., 2022. Brain

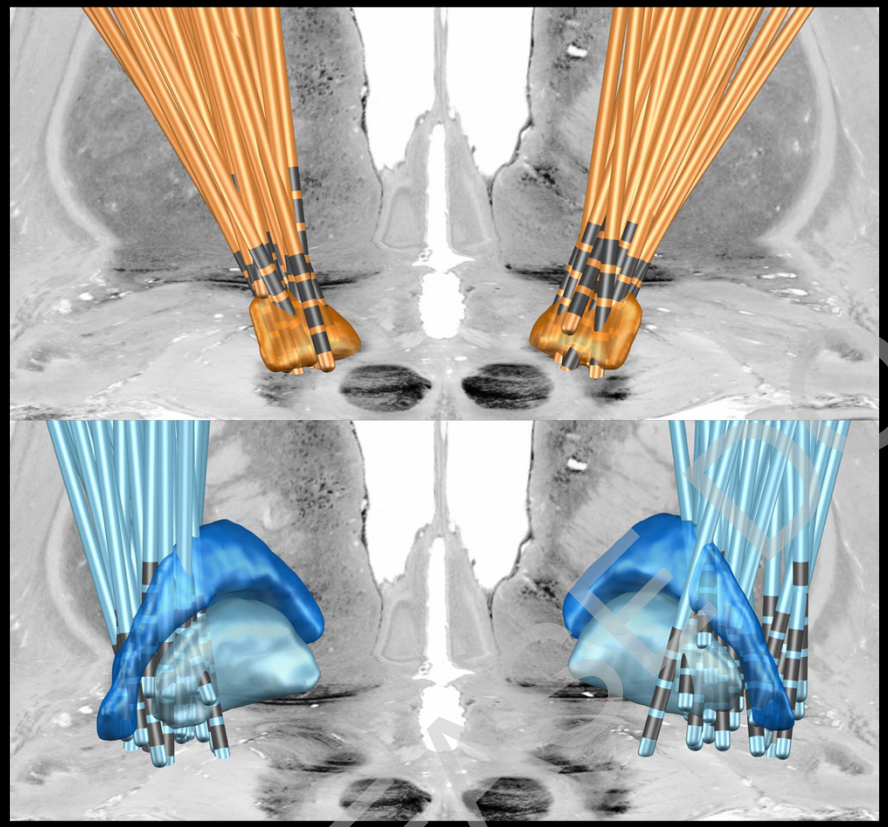
DBS Network Mapping

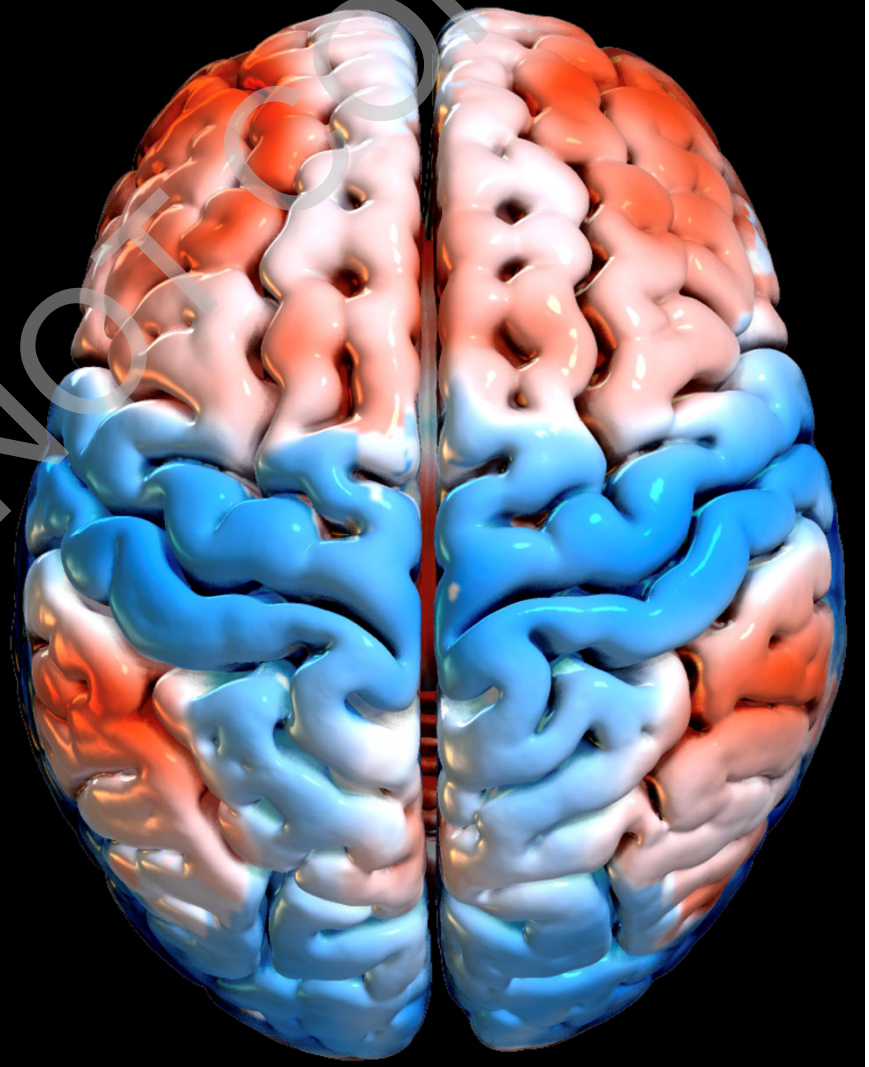




Brys, Fox, et al. 2017 Neurology

DBS Network Mapping





Brys, Fox, et al. 2017 Neurology

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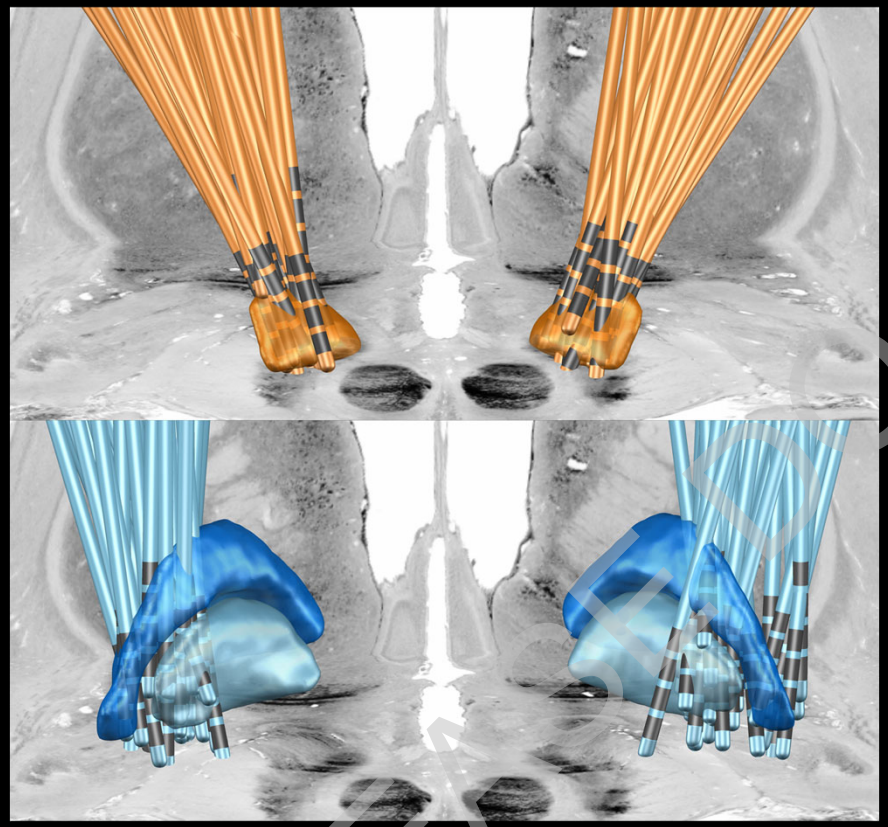
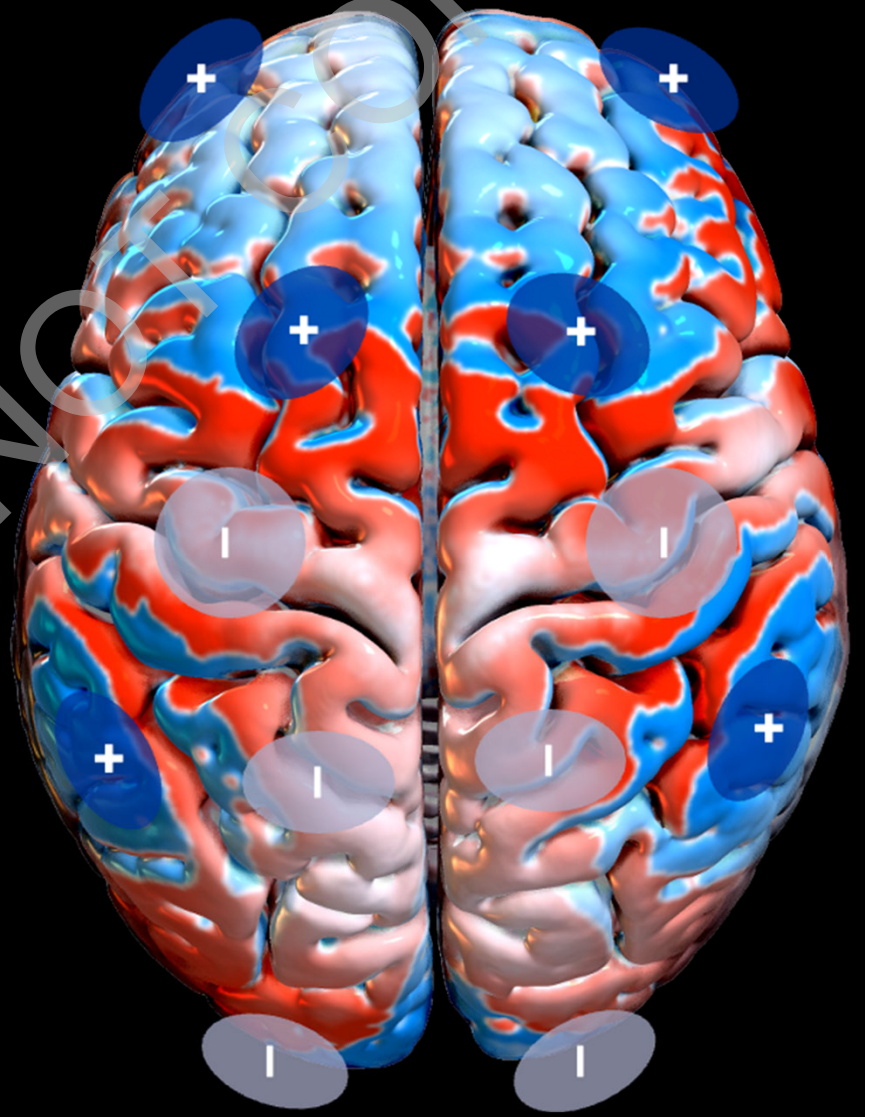
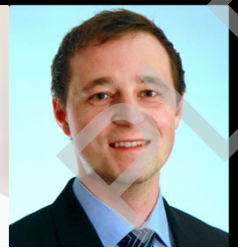
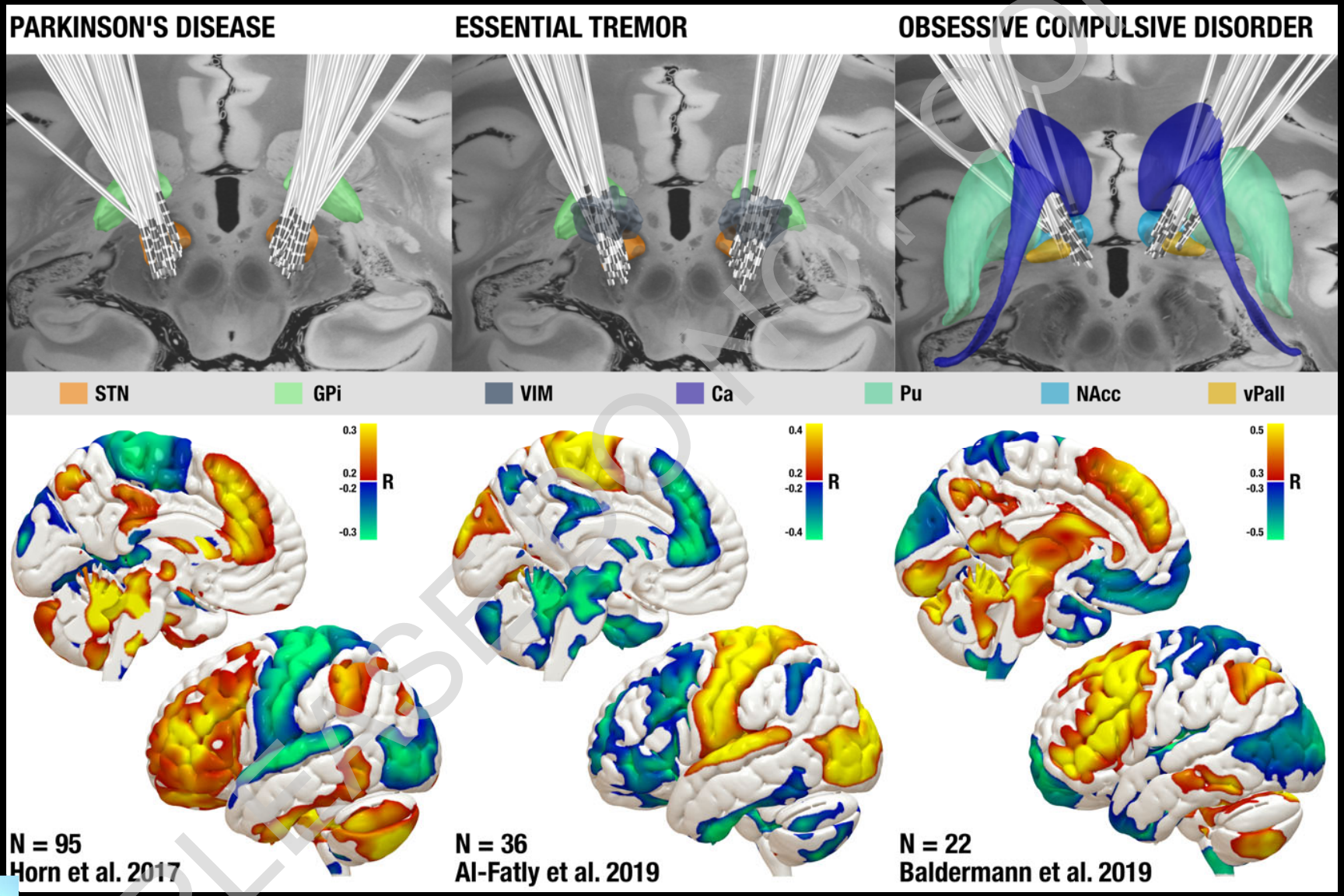






Goede, Horn et al., 2024
Movement Disorders

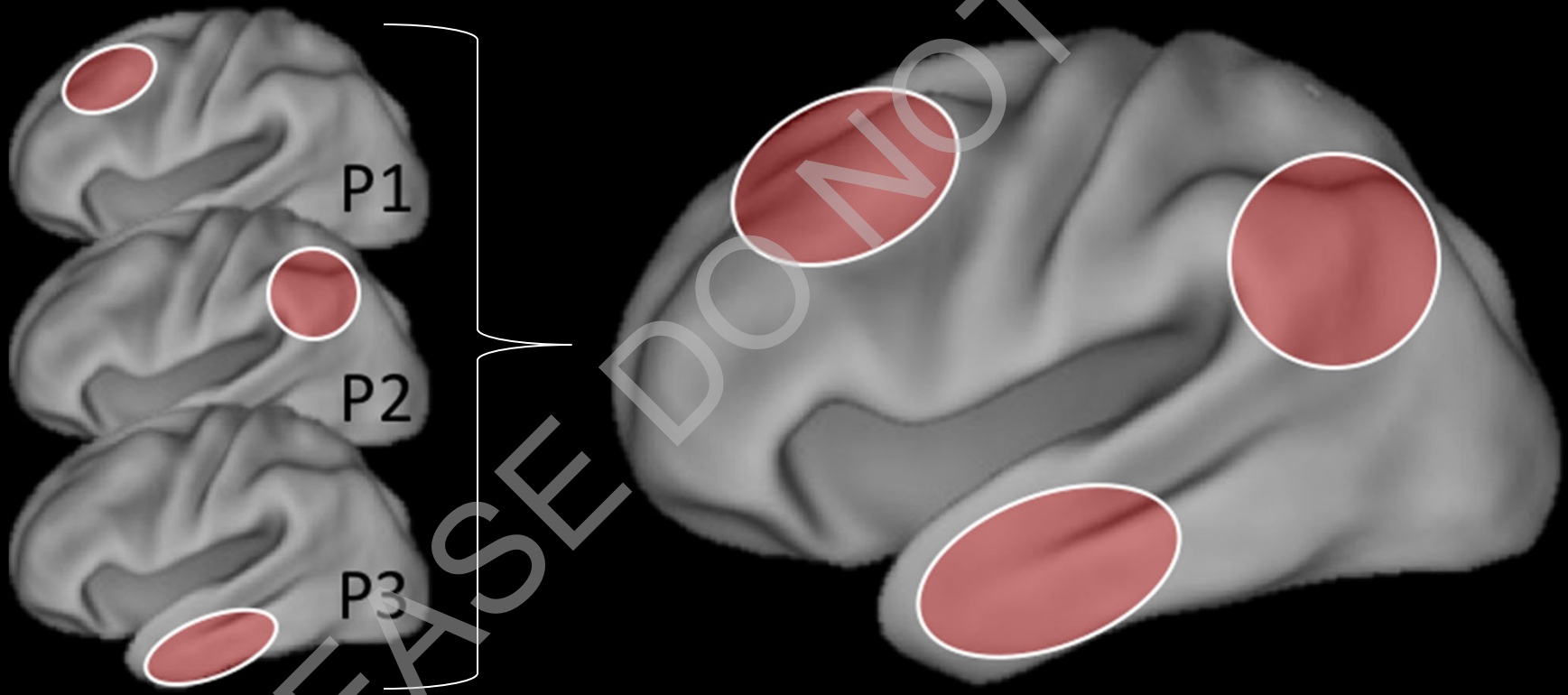
DBS Network Mapping



Review: Horn and Fox 2020 Neuroimage

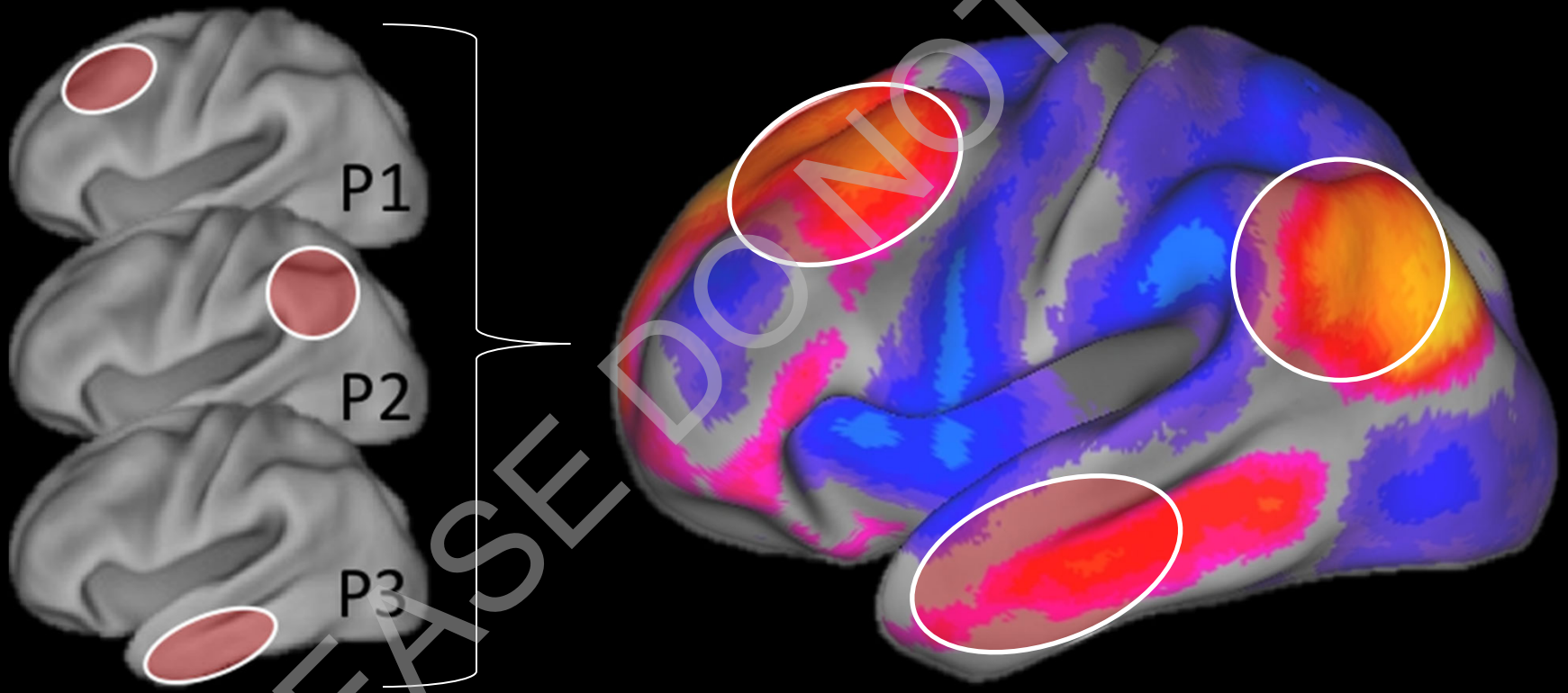
What if we're (VERY) unsure of our target?

Lesion Localization

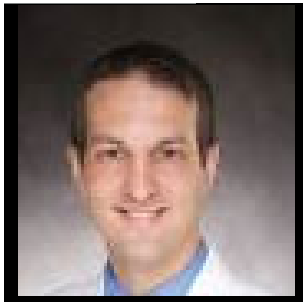


Review: Fox 2018 NEJM

Lesion “Network” Localization



Review: Fox 2018 NEJM

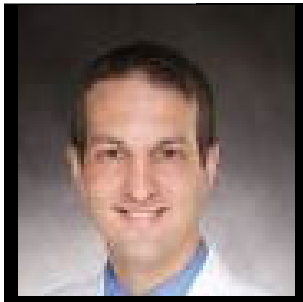


Lesion Network Mapping

> 40 symptoms
> 50 papers
> 8 groups

Motor and speech disorders		Nonmotor symptoms		Behavioral changes	
Akinetic mutism	*Darby, 2018*	Amnesia	*Ferguson, 2019*	Criminality	*Darby, 2018*
Alien limb	*Darby, 2018*	Anosognosia for hemiplegia	*Klingbeil, 2020*	Mind wandering	*Philippi, 2021*
Aphasia	*Wawrzyniak, 2022*	Autoscopic phenomena	*Blondiaux, 2021*	Pedophilia	*Scarpazza, 2021*
	Boes, 2015	Blindsight	*Kletenik, 2022*	Spirituality and religiosity	*Ferguson, 2021*
Central hypoventilation syndrome	*Prabhakar, 2020*	Bodily awareness disorders	*Herbet, 2019*		
Cervical dystonia	*Corp, 2019*	Bodily self-consciousness failure	*Wawrzyniak, 2018*		
Falling risk	*Crockett, 2022*	Cerebellar cognitive affective syndrome	*Albazron, 2019*		
Foreign accent syndrome	*Higashiyama, 2021*	Cognitive impairment	*Reber, 2021*		
Freezing of gait	*Fasano, 2017*		*Crockett, 2021*		
Infantile spasms	*Cohen, 2021*	Coma	*Fischer, 2016*		
Hemichorea	*Laganiere, 2016*	Decision-making impairment	*Sutterer, 2016*		
Holmes' tremor	*Joutsa, 2019*	Delusional misidentification	*Darby, 2017*	**Improvement of symptoms**	
Parkinsonism	*Joutsa, 2018*	Depression	*Padmanabhan, 2019*	Addiction remission	*Joutsa, 2022*
Poststroke motor outcomes	*Lee, 2020*	Epilepsy	*Bdaiwi, 2021*	Essential tremor improvement	*Joutsa, 2018*
Poststroke sensorimotor outcomes	*Jimenez-Marin, 2021*		*Mansouri, 2020*		
Step length asymmetry	*Kyeong, 2021*	Executive function impairment	*Hwang, 2020*		
Poststroke functional outcomes[a]	*Bowren, 2022*	Hallucinations	*Boes, 2015*		
	Cohen, 2021		*Kim, 2021*		
	Pini, 2021	Loss of consciousness	*Snider, 2020*		
	Salvalaggio, 2020	Mania	*Cotovio, 2020*		
Tics	*Ganos, 2022*		*Lee, 2019*		
		Pain	*Boes, 2015*		
			Elias, 2020		
		Pathological laughter and crying	*Klingbeil, 2021*		
		Prosopagnosia	*Cohen, 2019*		
		Spatial delusions	*Alves, 2021*		

Review: Joutsa 2022 Cur. Opin. Neuro



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Review: Joutsa 2022 Cur. Opin. Neuro

Lesion Network Mapping

Addiction Remission
Joutsa et al. 2022 Nature Medicine

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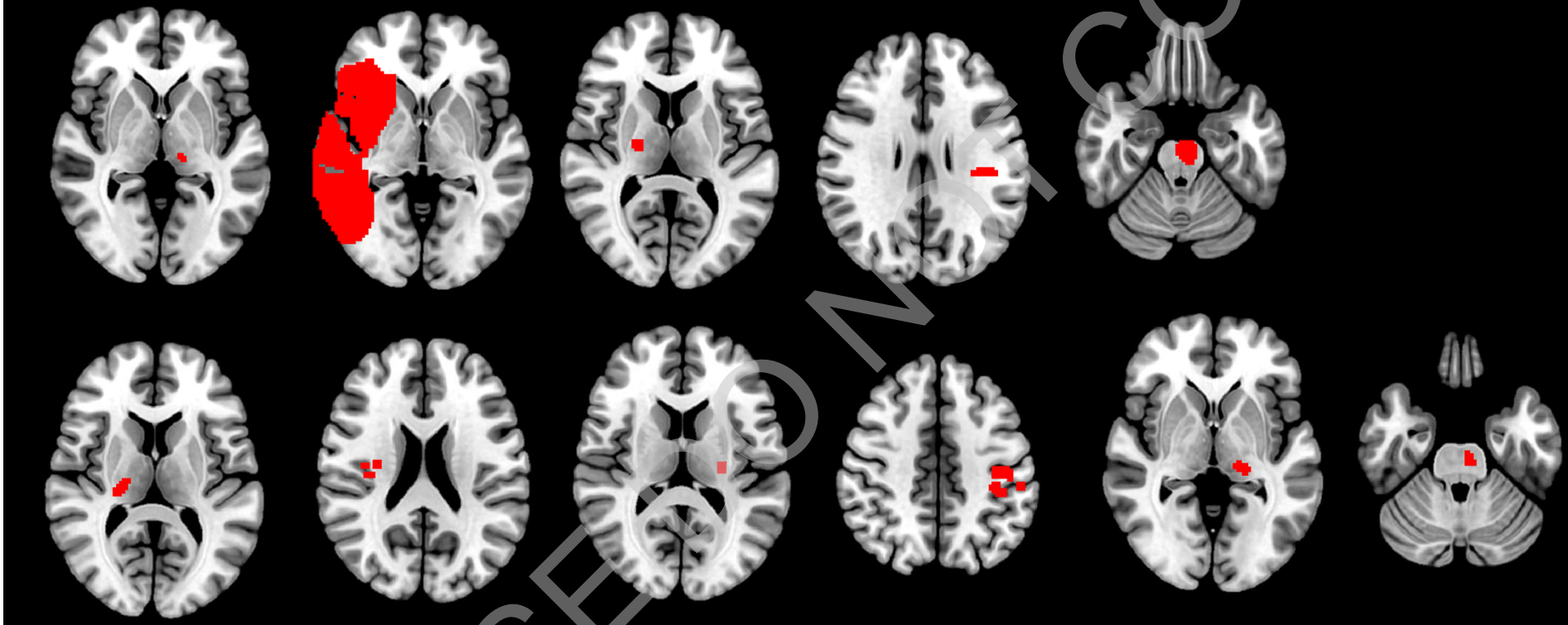
New Approach for Finding Targets



Joutsa, Shih et al. 2018 Annals of Neurology

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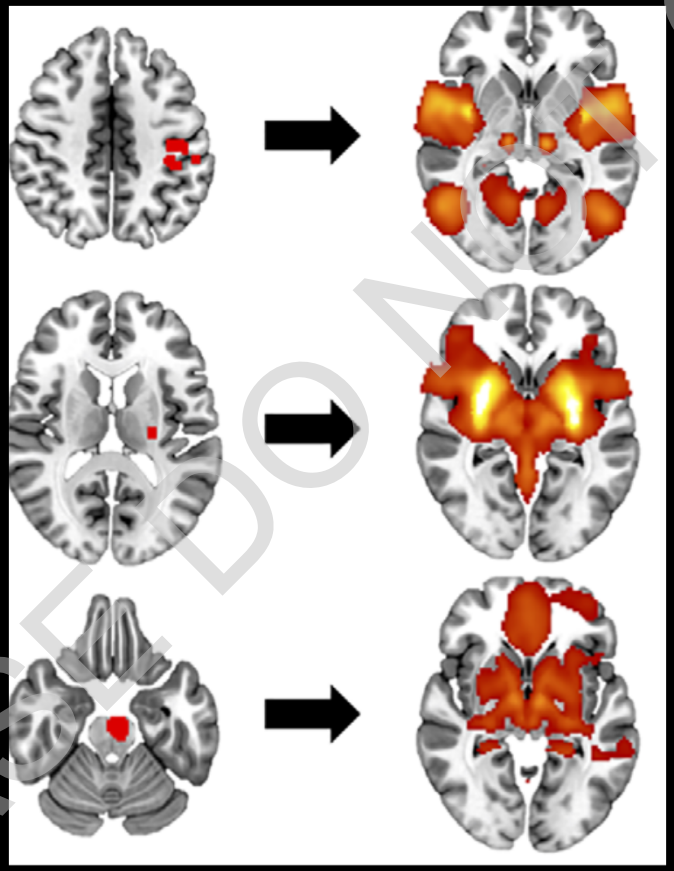

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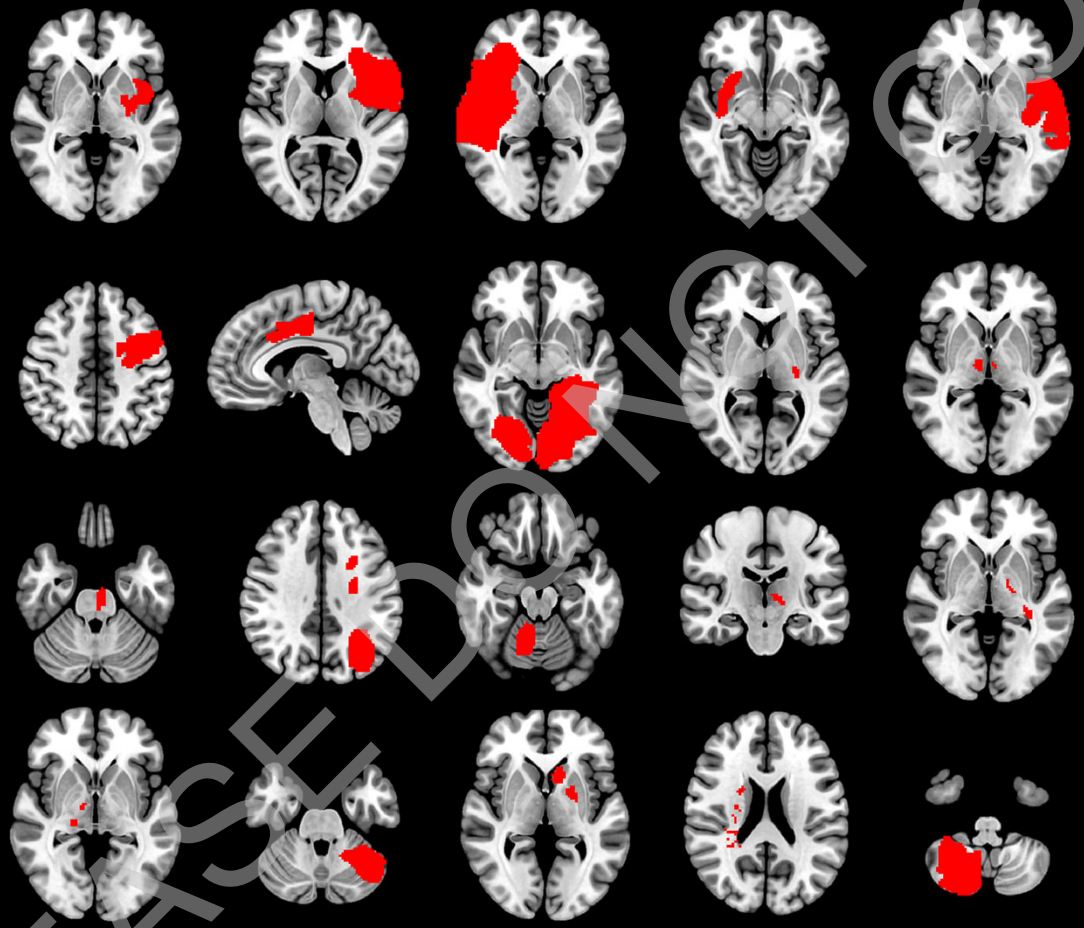
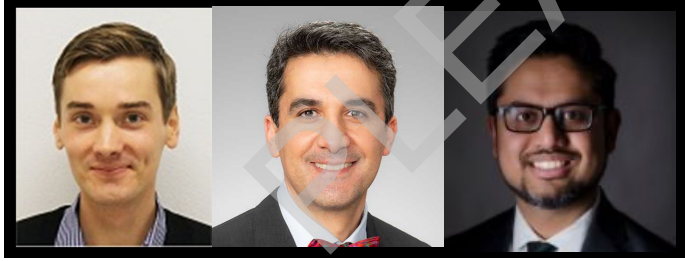




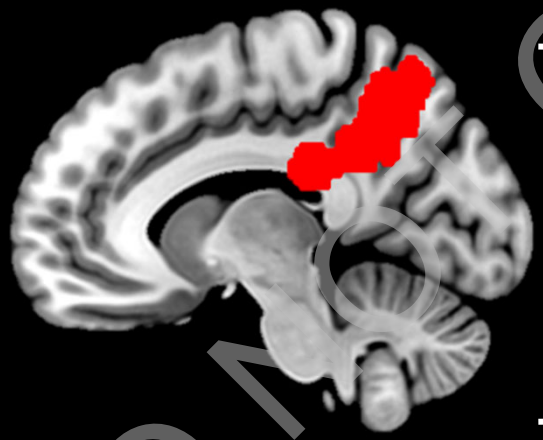
Joutsa, Moussawi, Siddiqi et al. 2022 Nature Medicine

Addiction Remission

Remission

vs

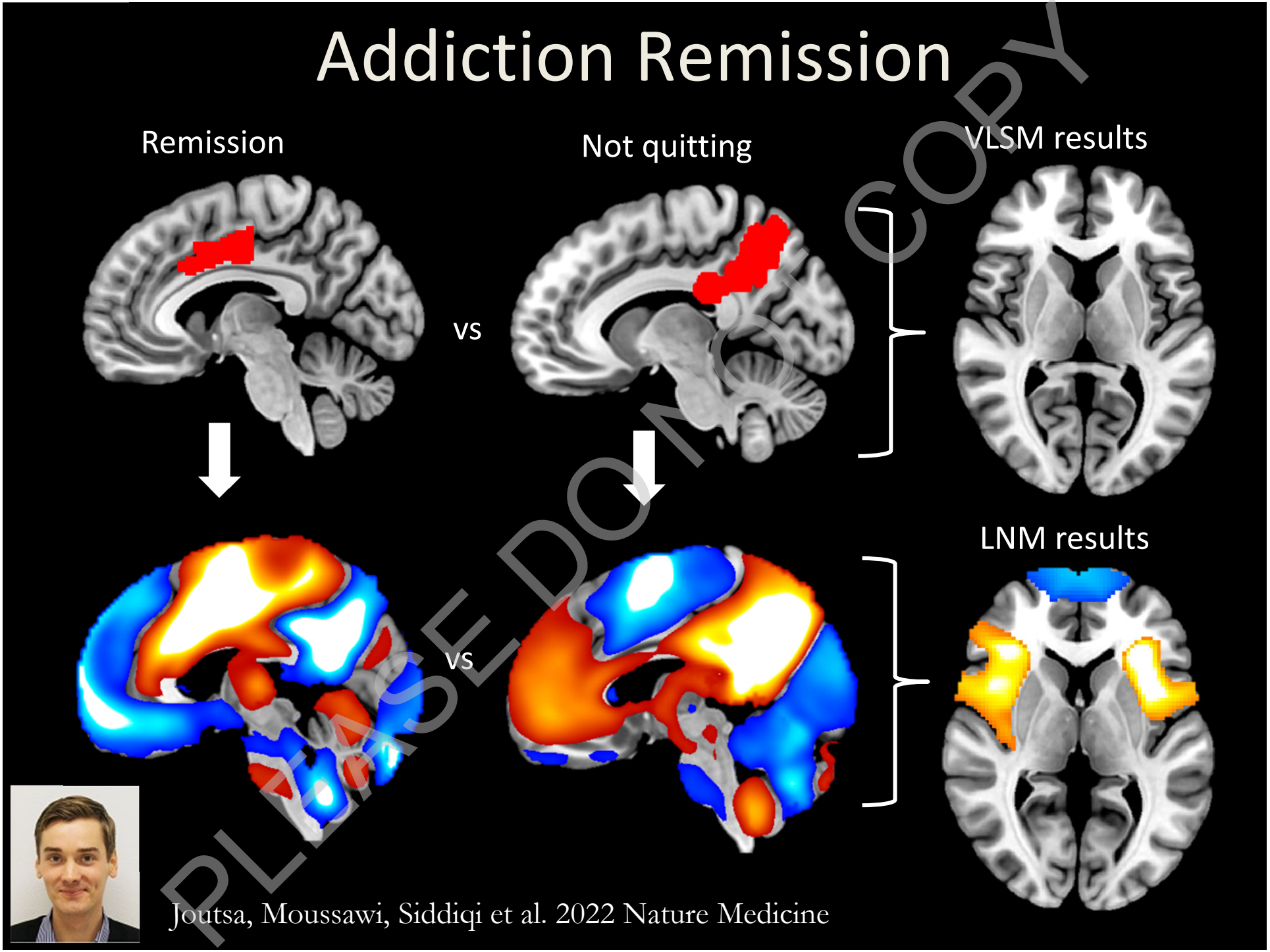
Not quitting



VLSM results

Joutsa, Moussawi, Siddiqi et al. 2022 Nature Medicine

Addiction Remission



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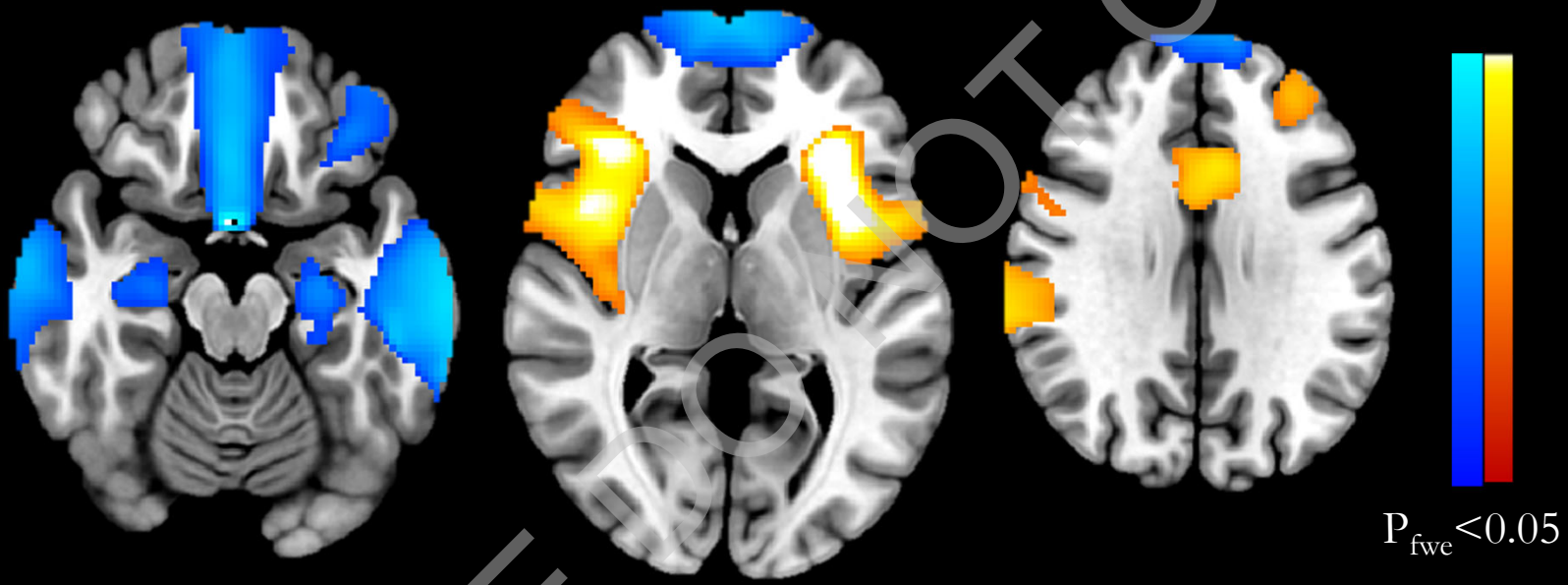

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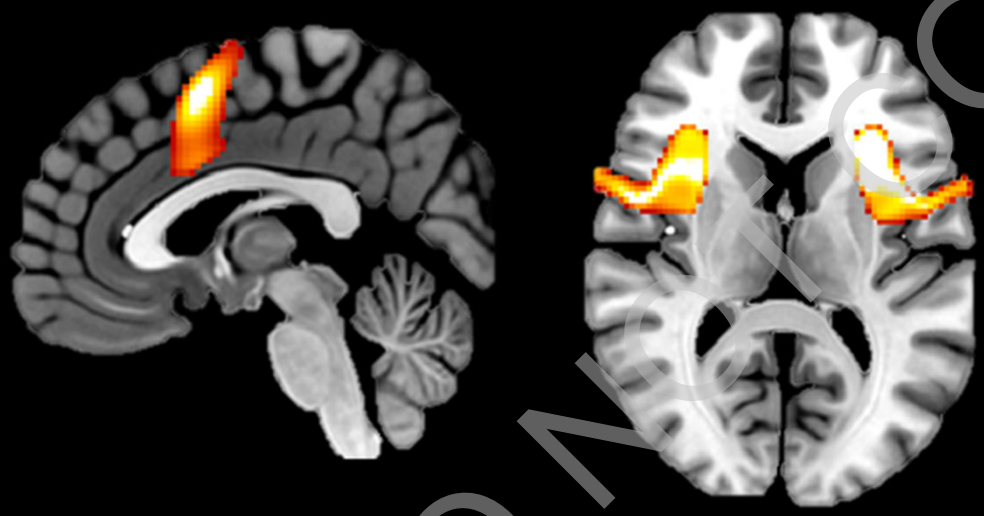
Addiction Remission Targets

Lesion / DBS Targets



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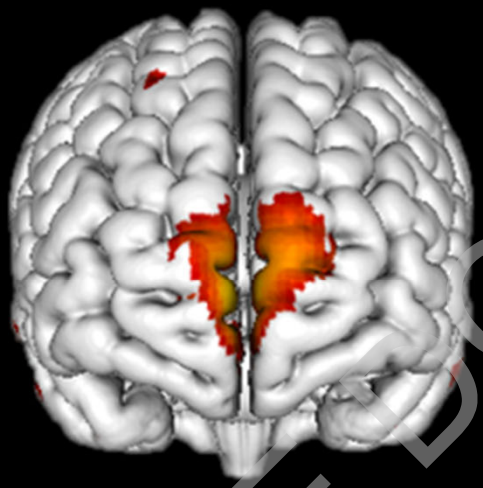

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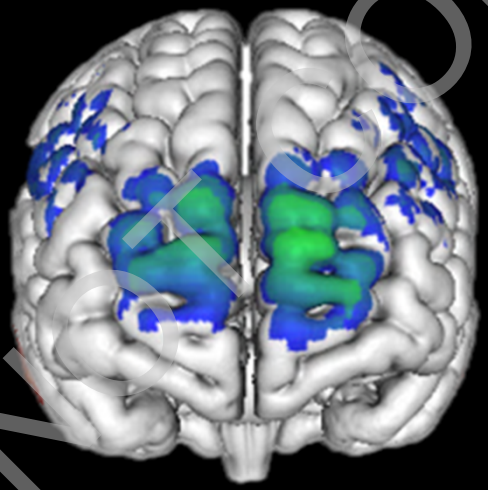
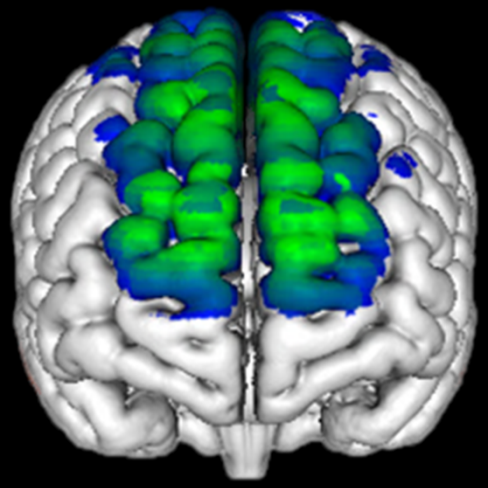


Smoking (H4 Coil)



Alcoholism (H7 Coil)

Electric Field Intensity

% of max

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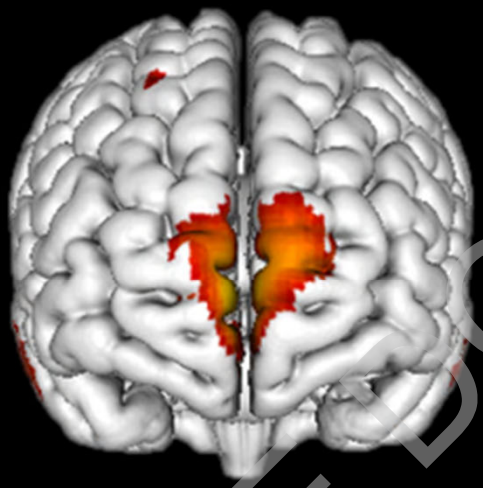
Addiction Remission Targets



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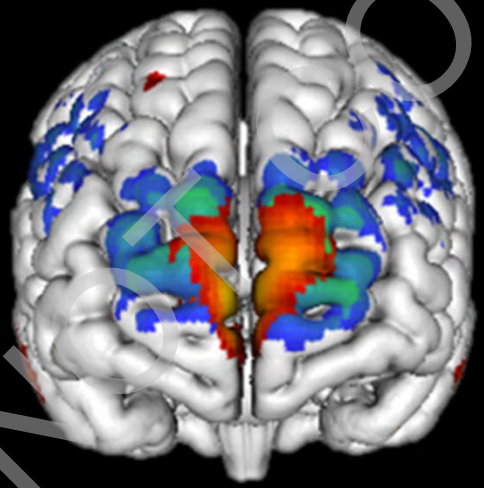

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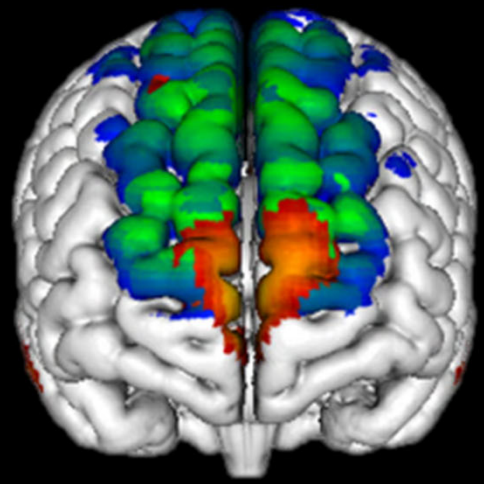

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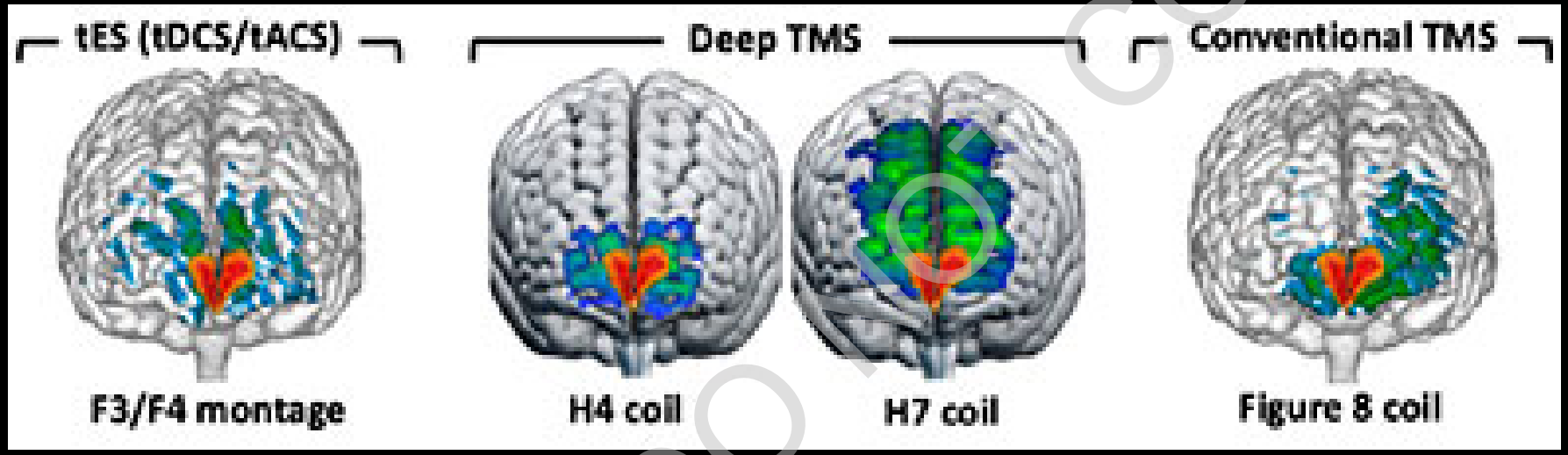
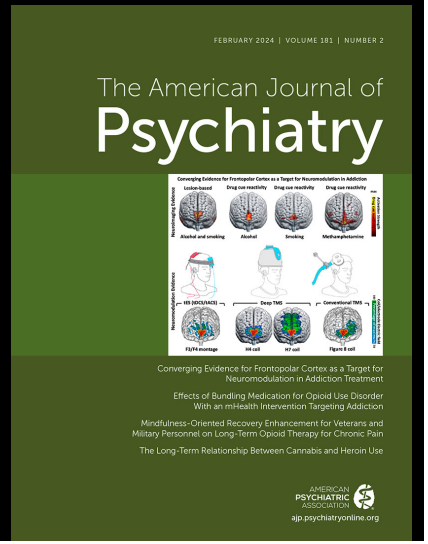


Soleimani.. Ekhtiari et al. 2024
American Journal of Psychiatry



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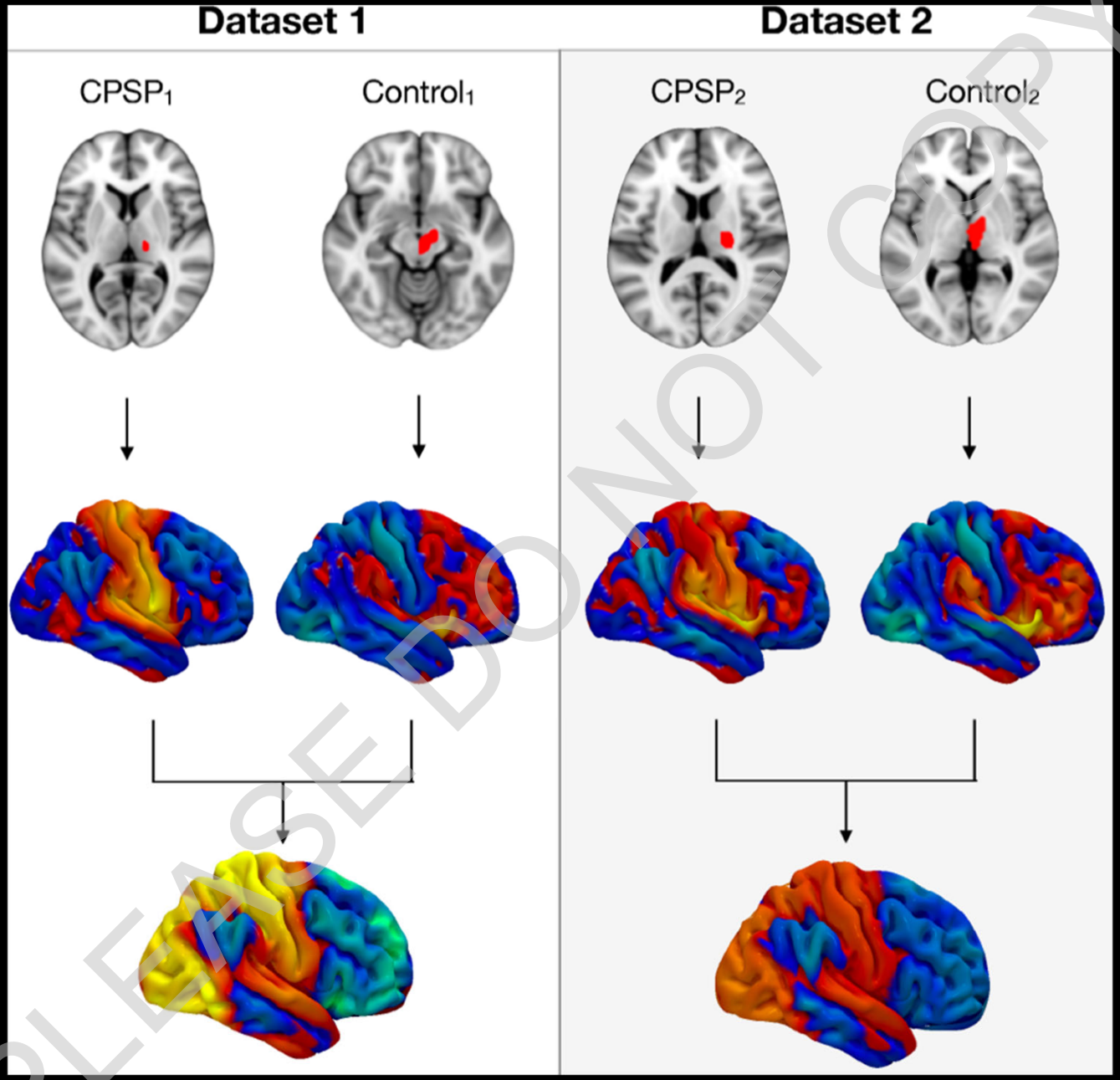
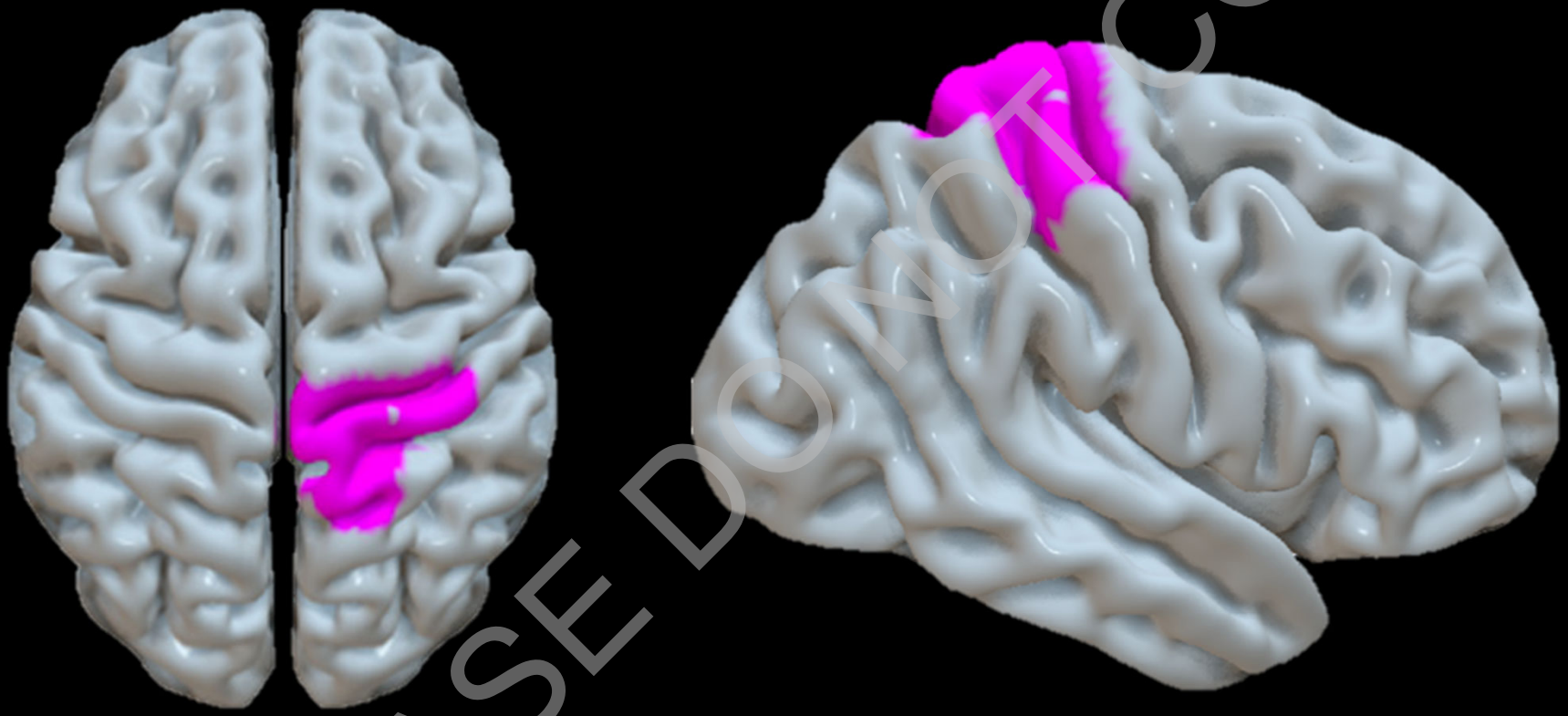


Kim et al. 2022 Annals of Neurology

Neuropathic Pain



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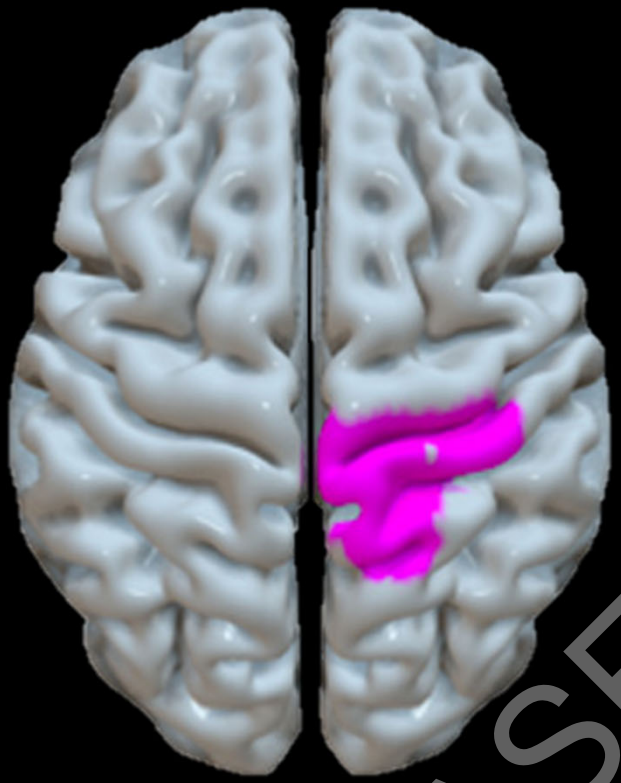

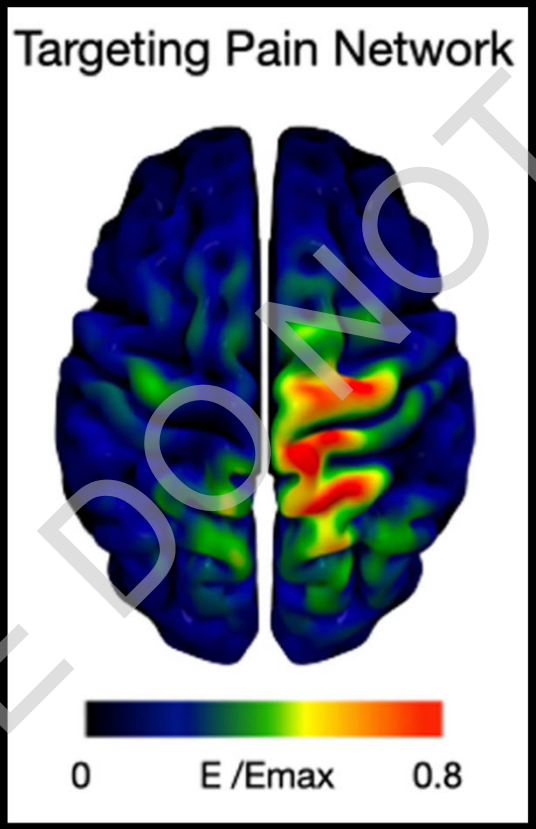

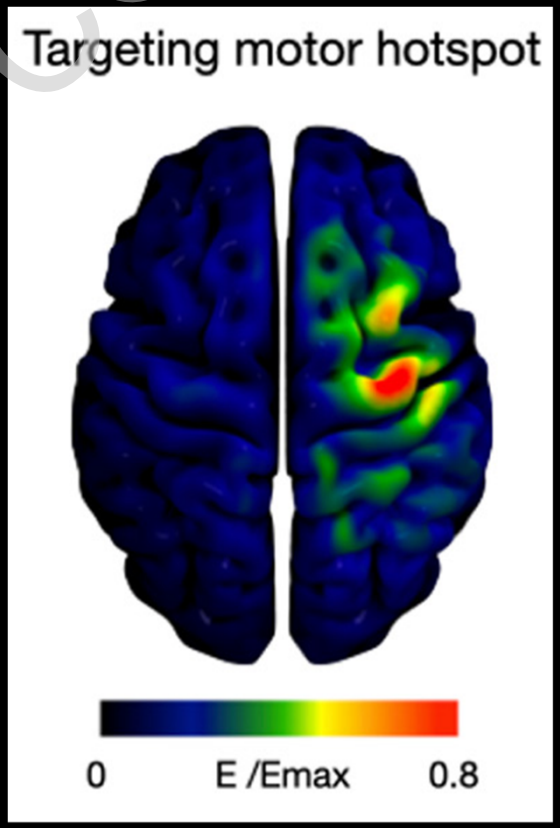

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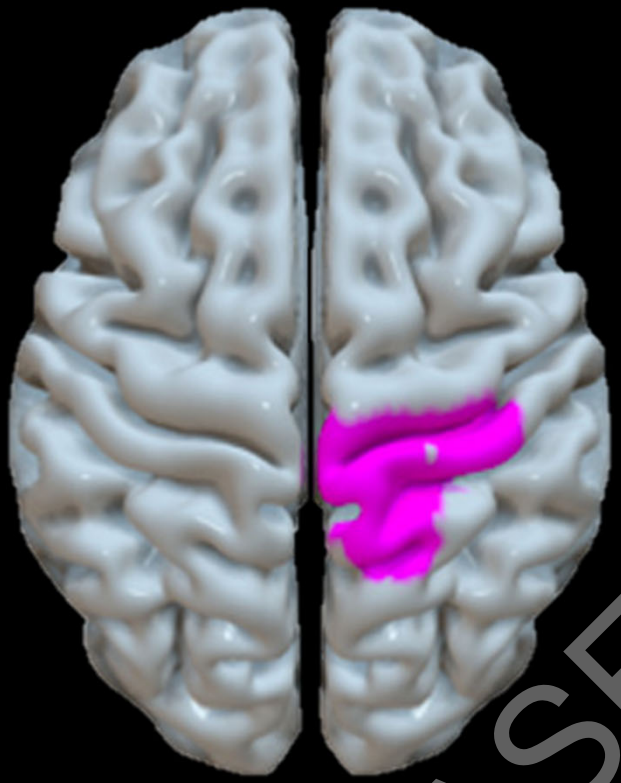

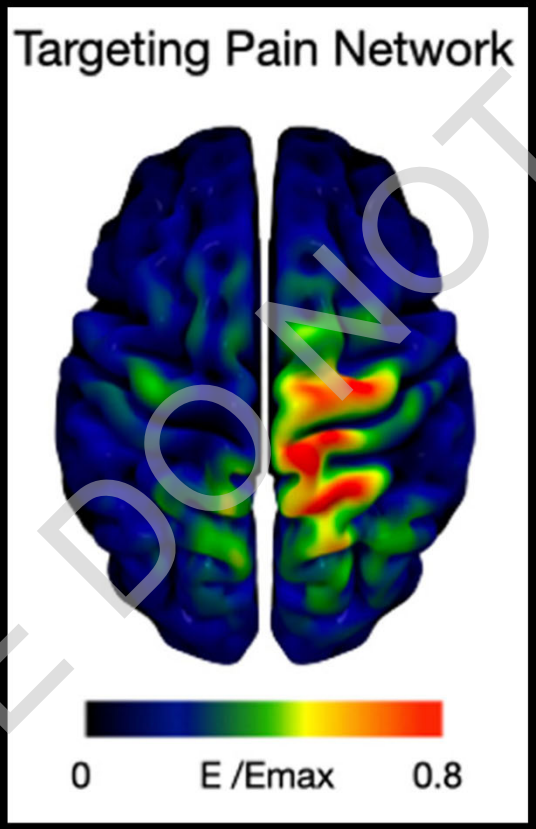

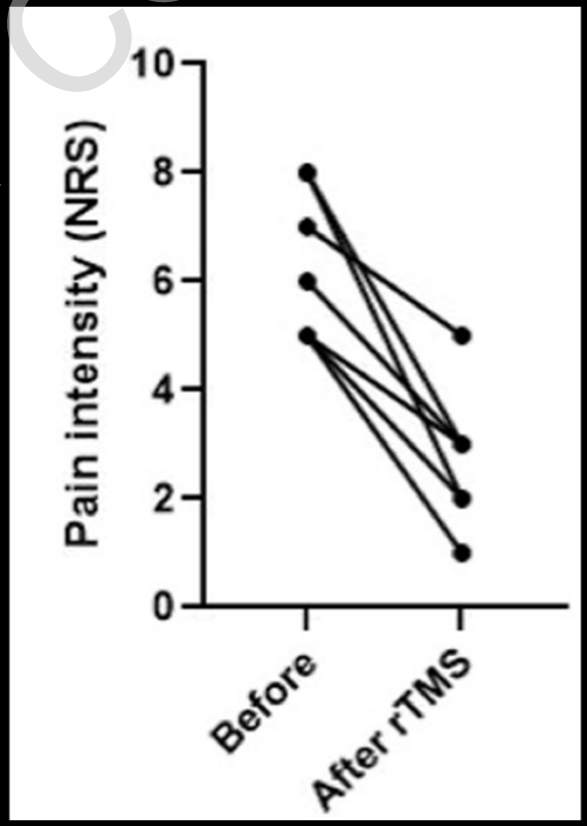

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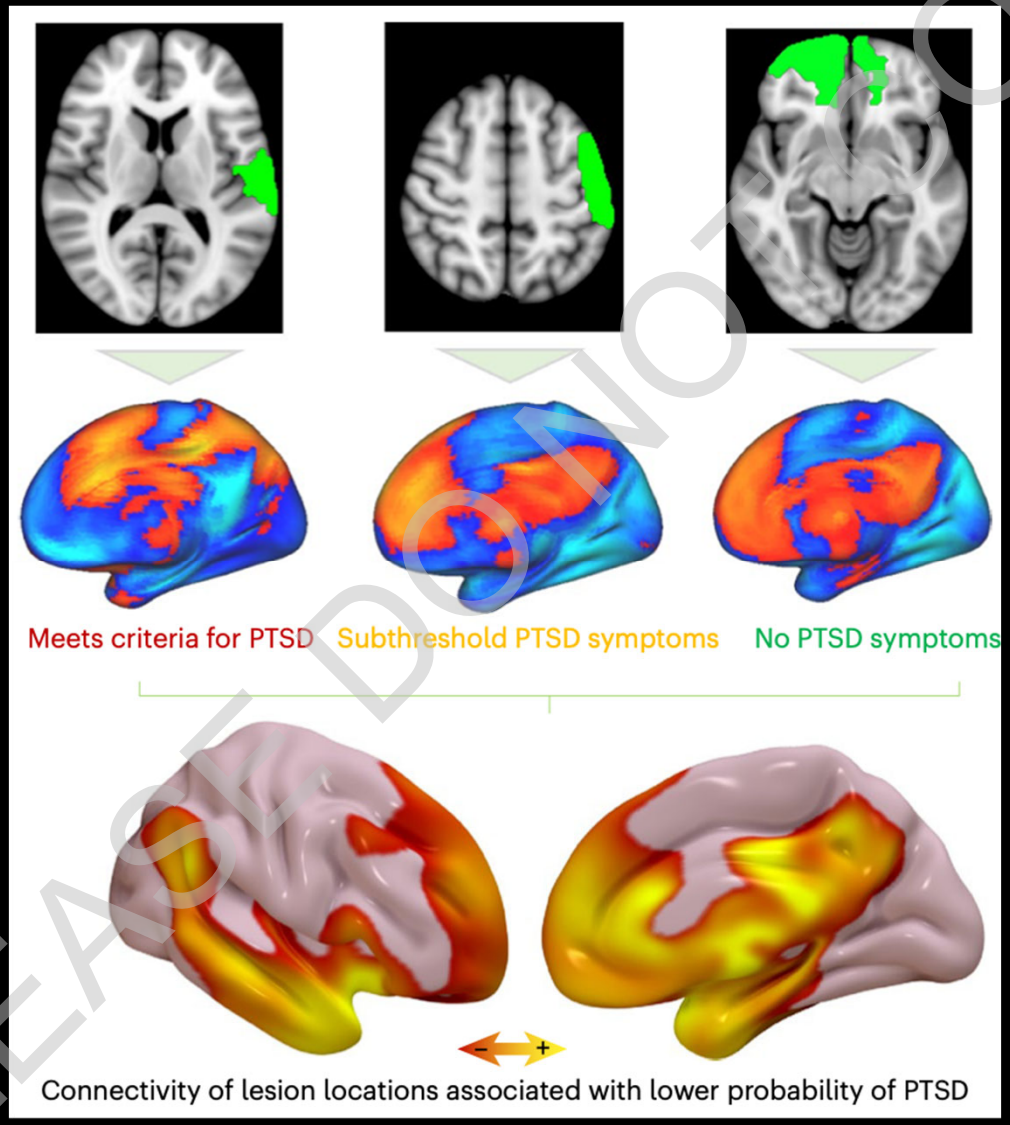
PTSD: Lesion Network Mapping



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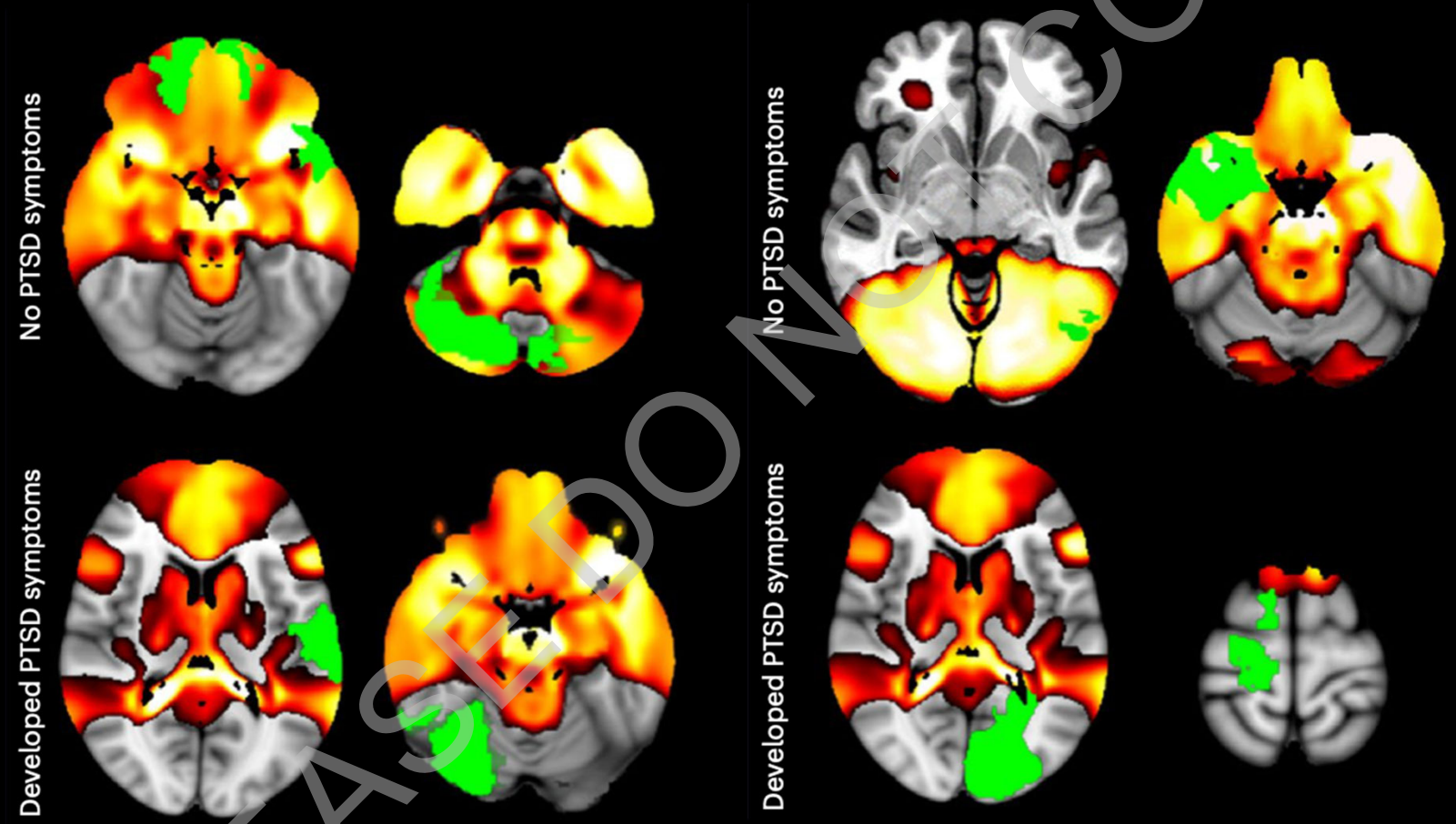

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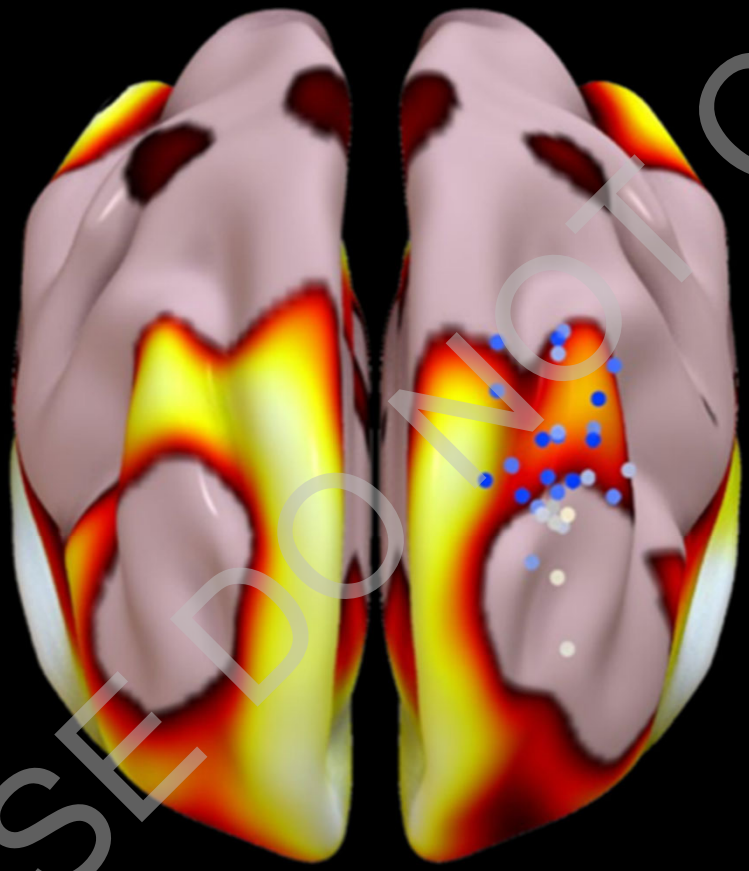
PTSD: TMS Targets



Anxiosomatic Symptom Benefit — Dysphoric Symptom Benefit

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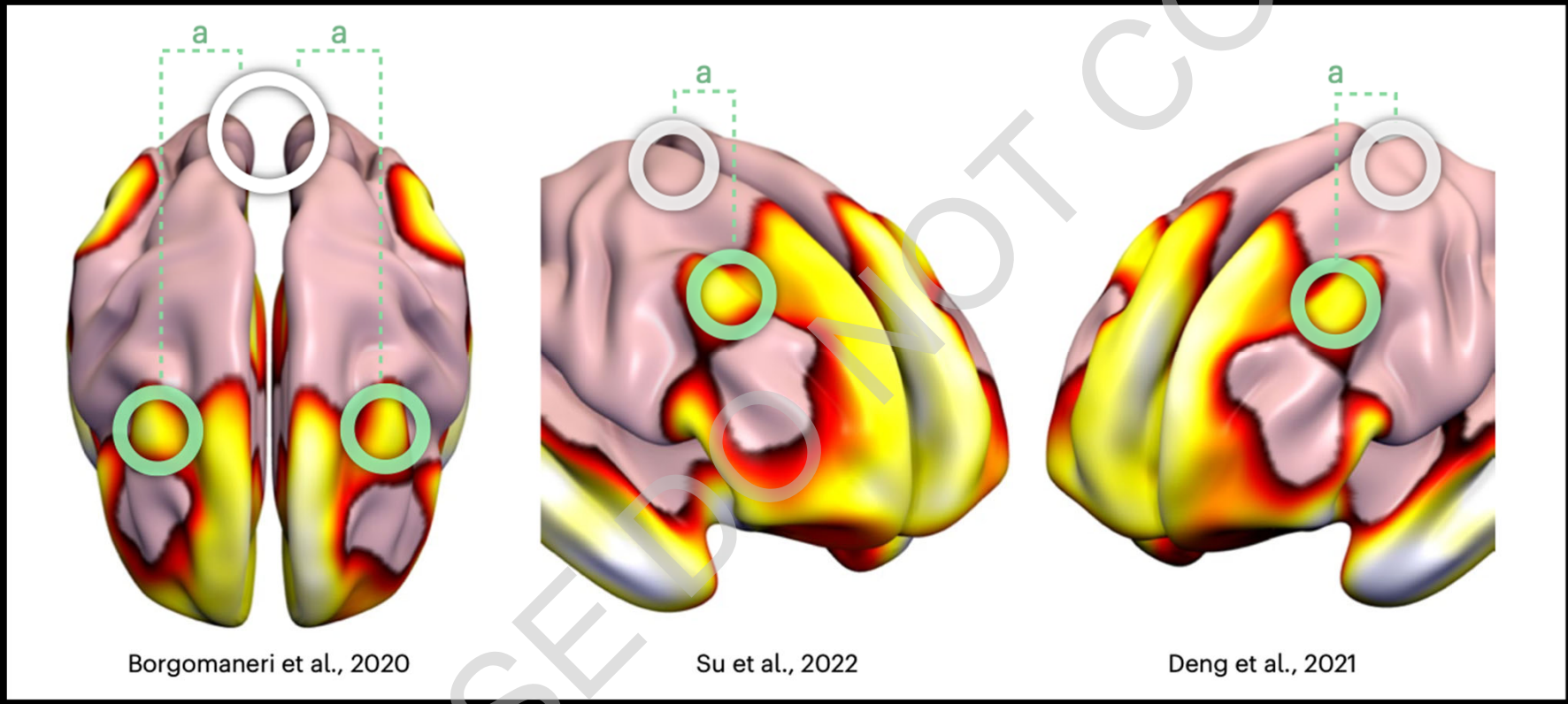

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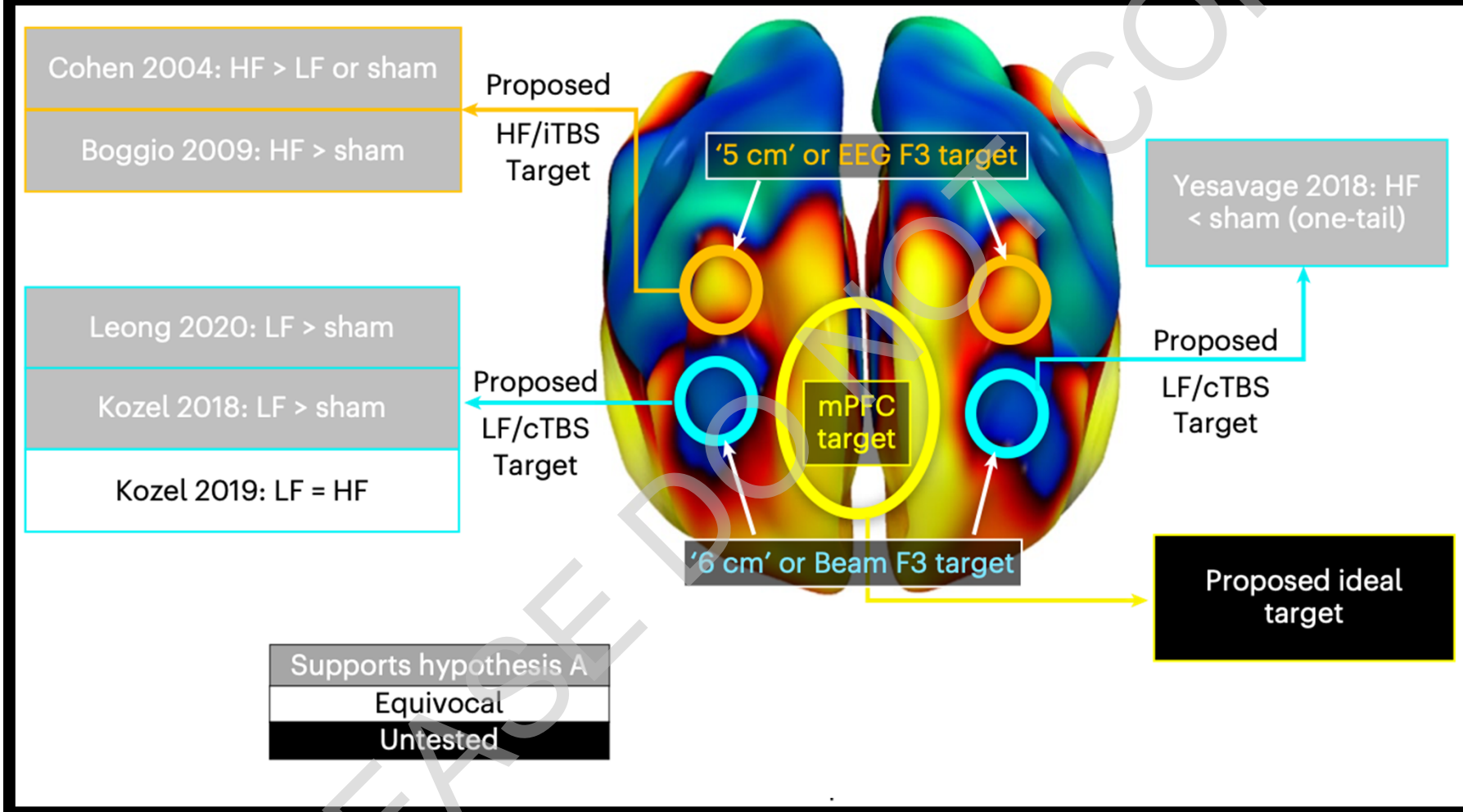

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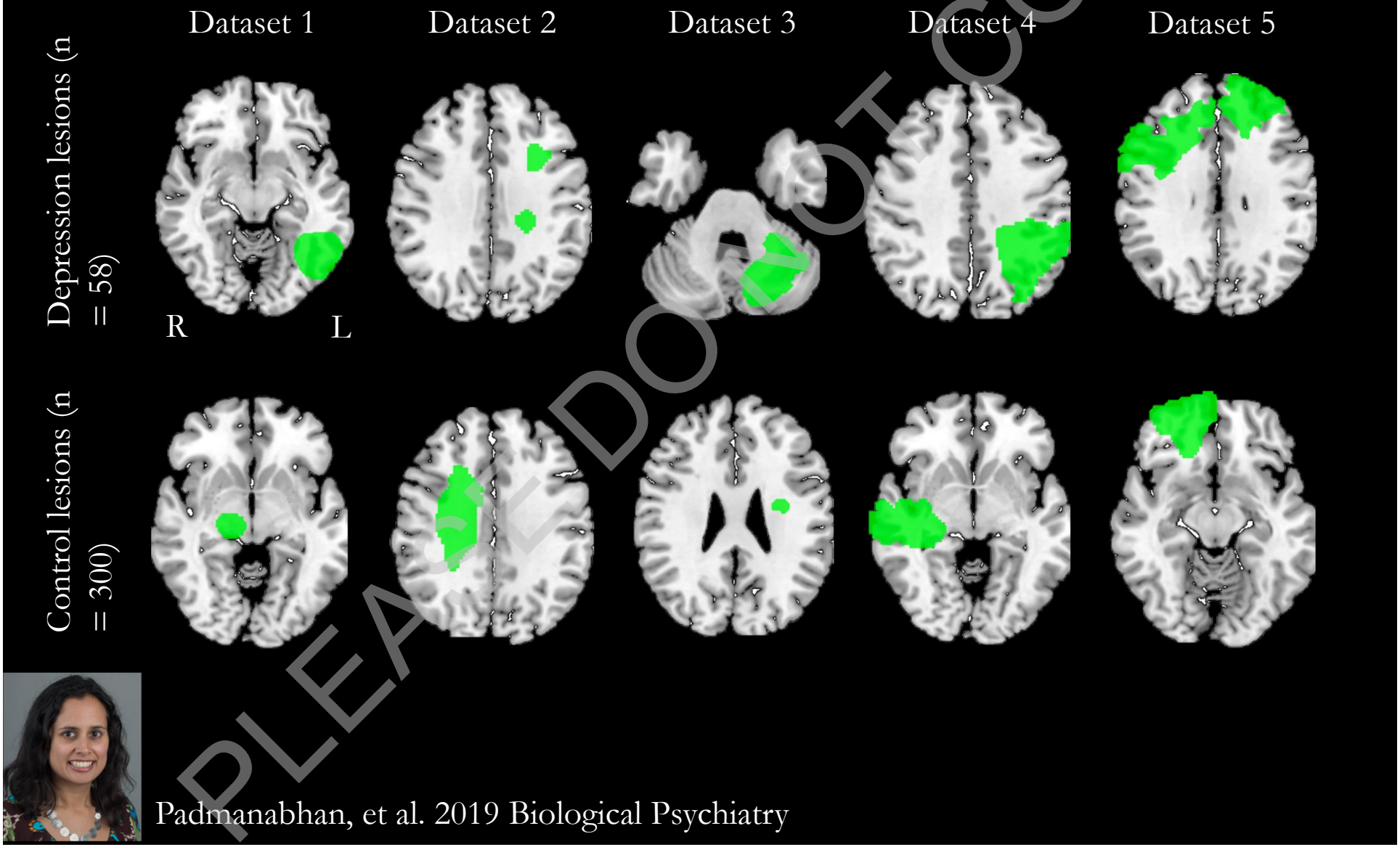
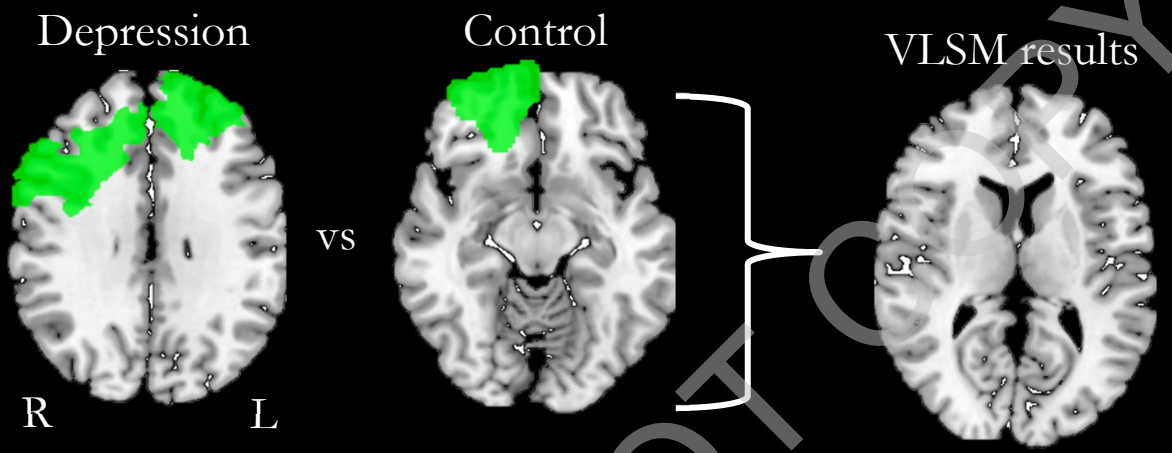
Lesion mapping of depression (n = 461)



Padmanabhan, et al. 2019 Biological Psychiatry



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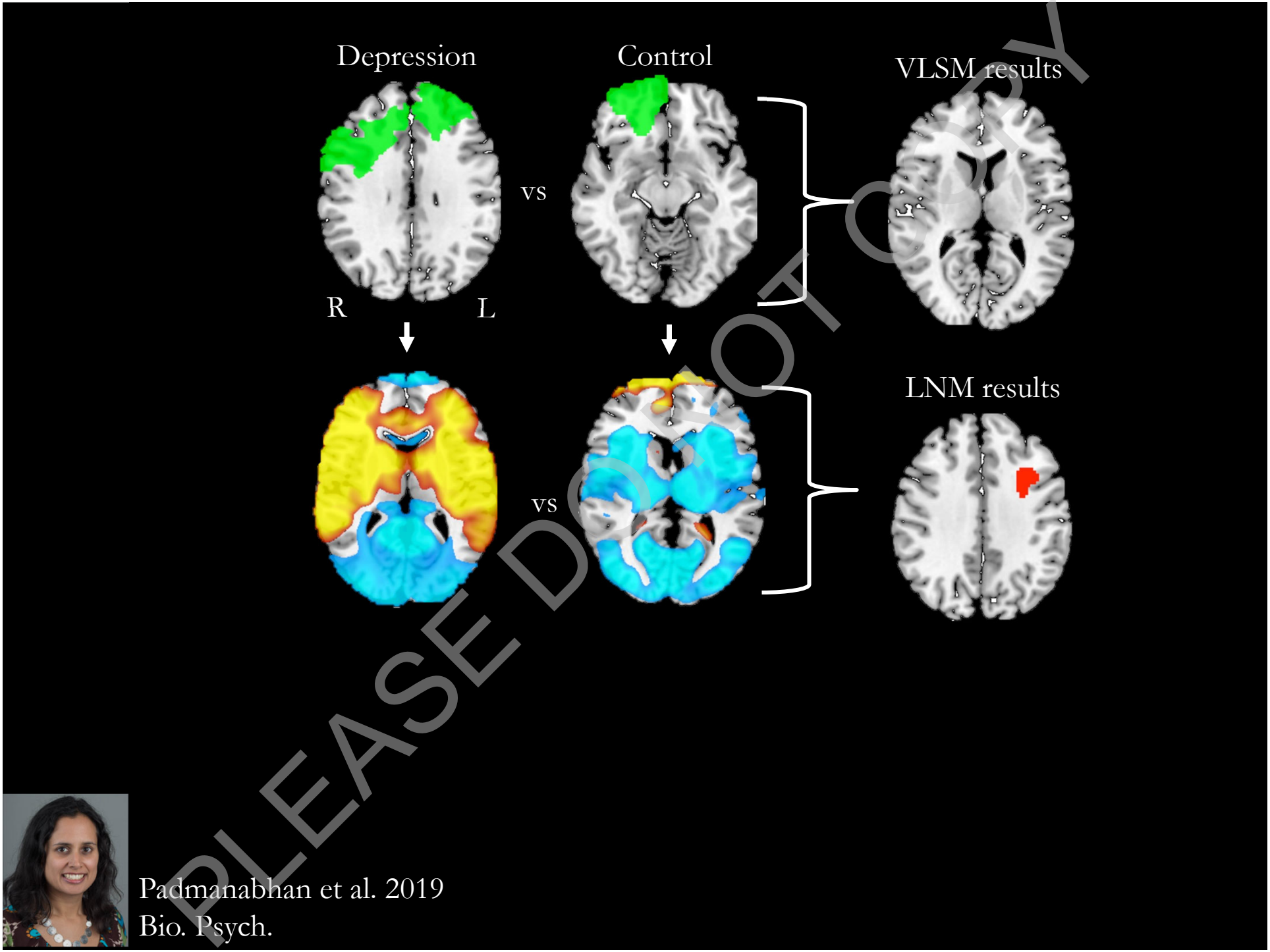

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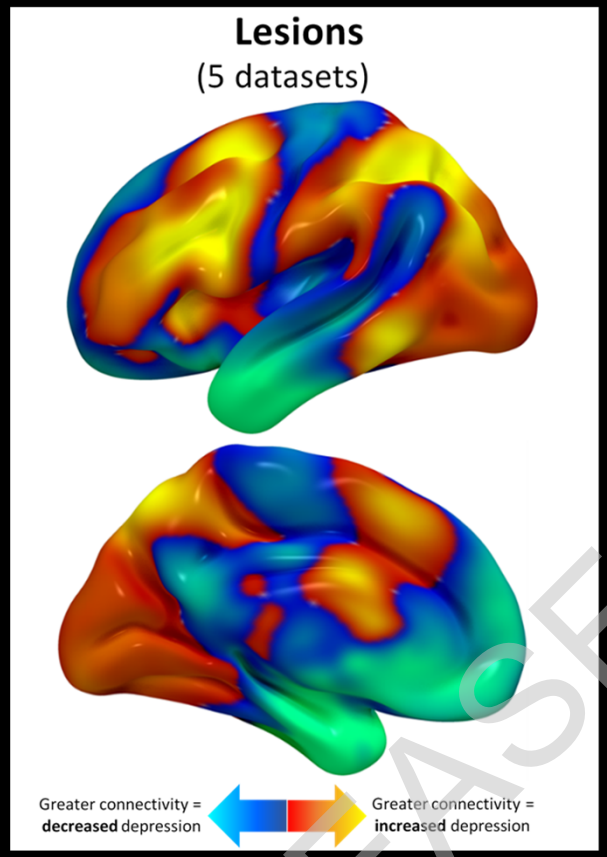
Convergent Depression Circuit



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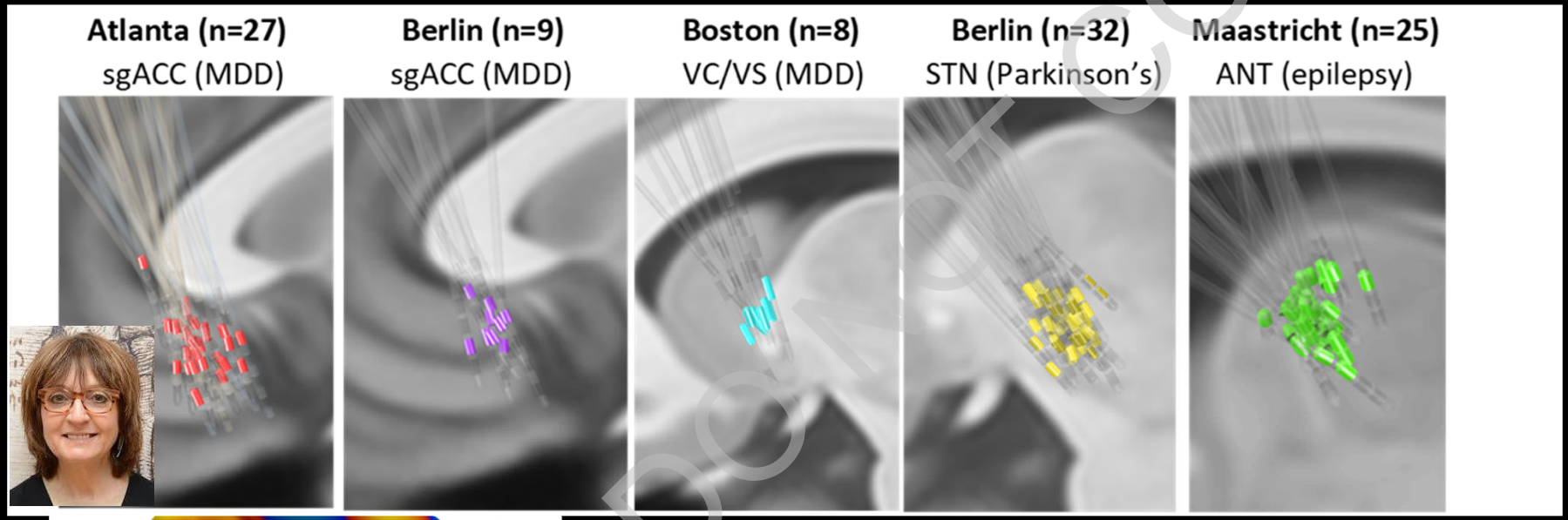

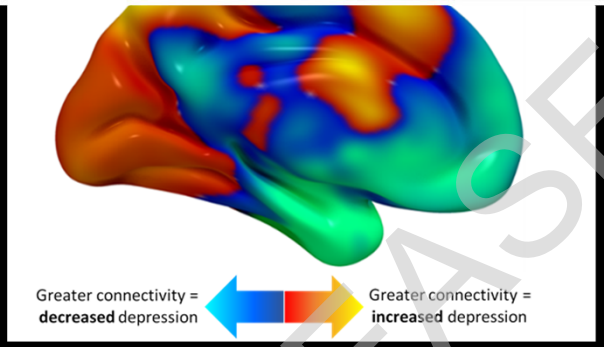

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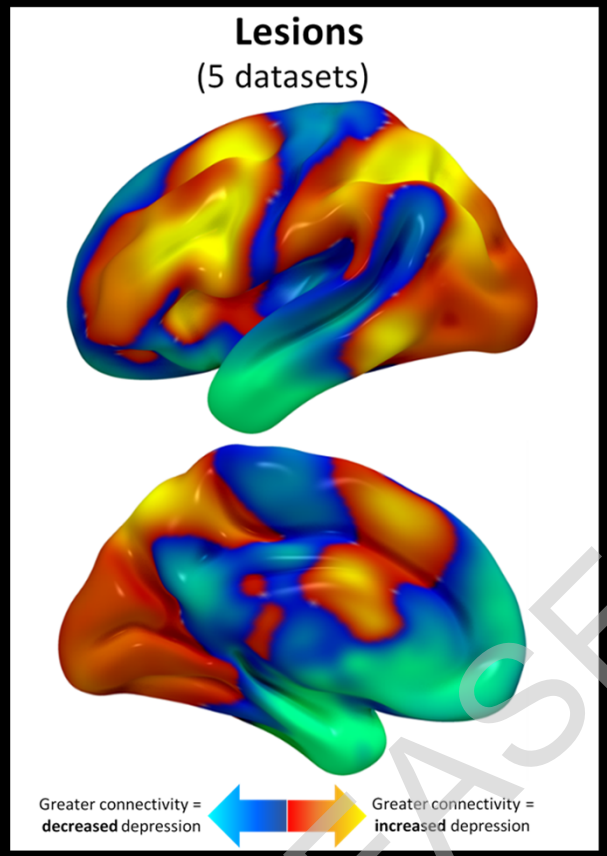

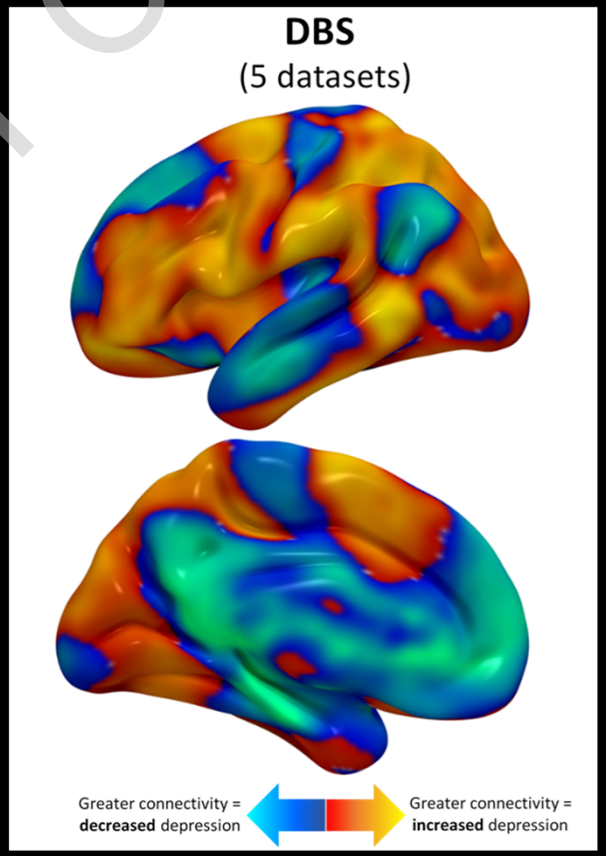

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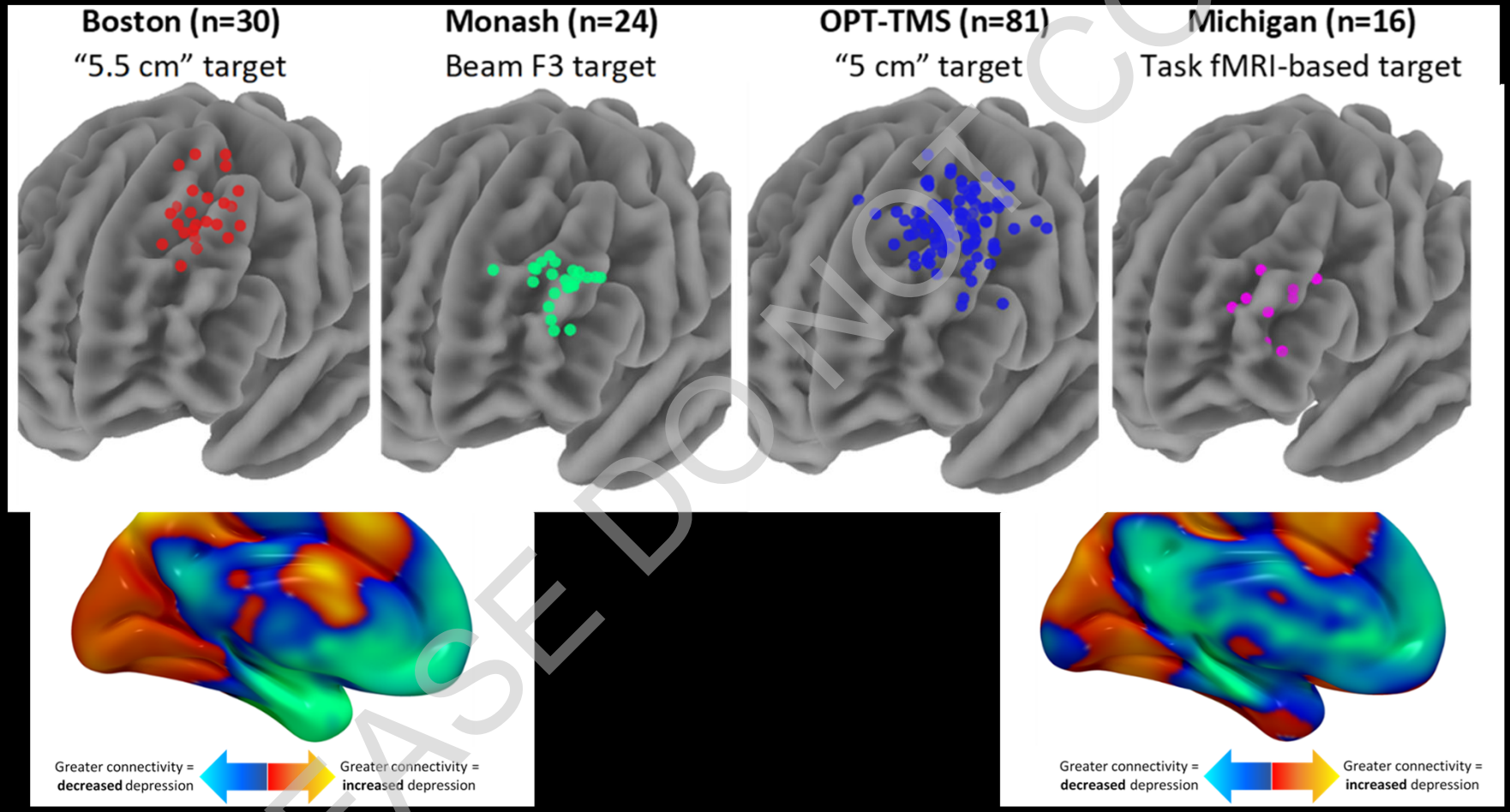

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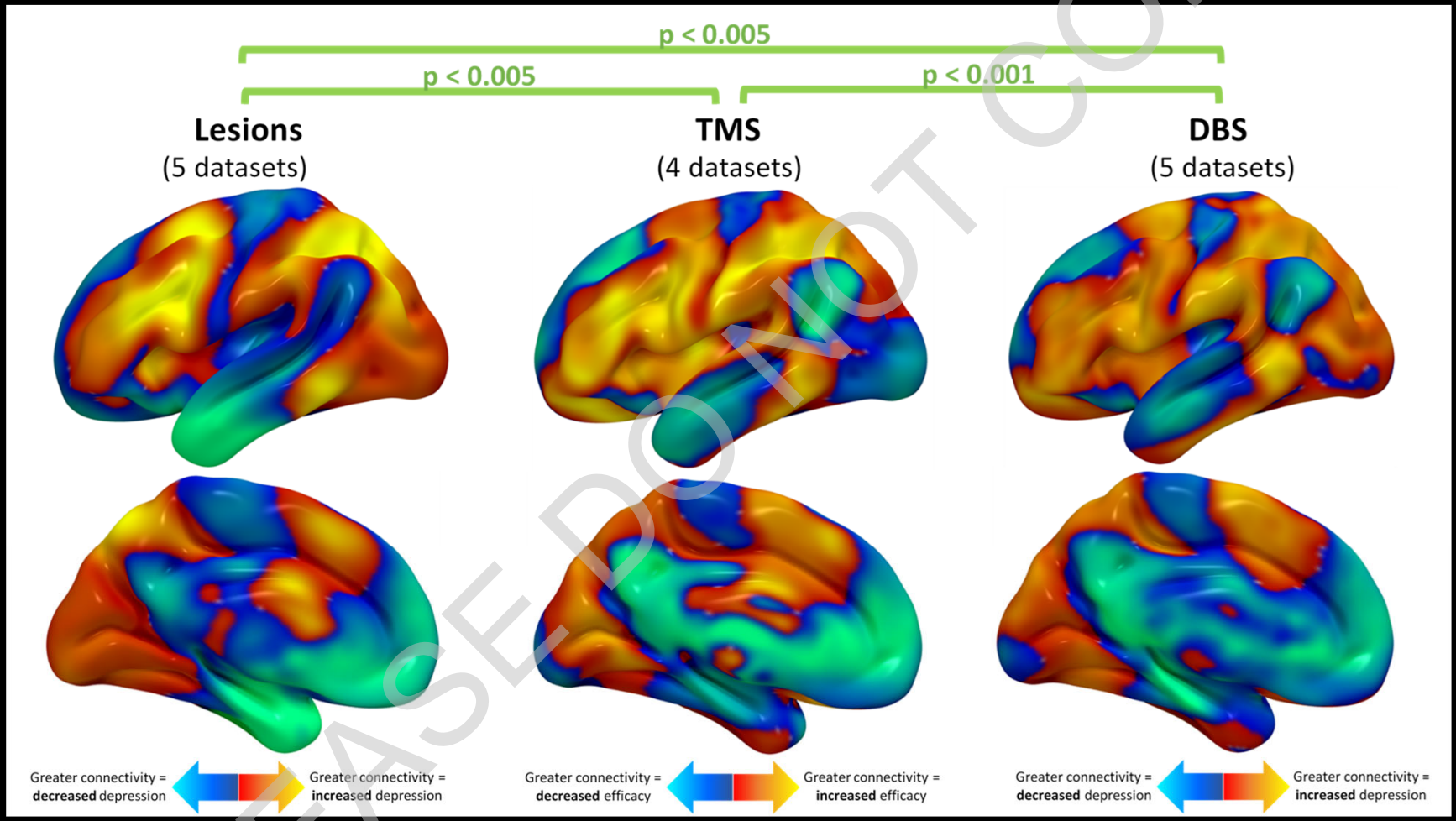

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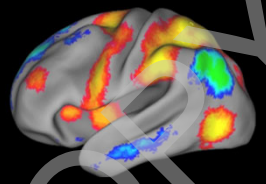
Conclusions



- TMS propagates beyond the stimulation site to modulate brain circuits
- The human connectome can be used to map lesion and stimulation effects to brain circuits
- These brain circuits can be used as therapeutic targets for different forms of neuromodulation

Center for
BRAIN CIRCUIT
THERAPEUTICS

BWH

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Lab / Center

Current
Alex Cohen
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David Lawson
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Grace Burt
Lauren Sanderson
Mae Morton-Dunn
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David Fischer
Andreas Horn
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Juho Joutsa
Tyler Ketchebaw
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Jaya Padmanabhan
Martin Reich
Lois Soussand
Daniel Talmasov
Anne Weigand
Rimona Weil
Molly Schineller
Sandrine Jabbour
Ali Jannati
Jing Jiang
Christopher Lin
William Drew
Max Friedrich

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Adam Stern
Hesheng Liu
Randy Buckner
Verne Caviness
Sashank Prasad
Darin Dougherty
Ellen Bubrick
Lipeng Ning
Tracy Barbour
Joan Camprodan
AND MORE

Non-local
Andrea Kuhn (Charite)
Helen Mayberg (Mt. Sinai)
Ki Sueng Choi (Mt. Sinai)
Jens Volkmann (Wurzburg)
Alfonso Fasano (Toronto Western)
Andreas Lozano (Toronto Western)
Maurizio Corbetta (Wash U)
Jordan Grafman (Northwestern)
Mark George (MUSC)
Linda Carpenter (Butler)
Paul Fitzgerald (Monash)
Stephan Taylor (Michigan)
Goncalo Cotovio (Champalimaud)
Albino J. Oliveira Maia (Champalimaud)
Joel Voss (Northwestern)
Andrew Naidech (Northwestern)
Robin Cash (Monash)
Kevin Johnson (Neuronetics)
Natalia Egorova (Melborne)
Sophia Gozzi (Monash)
Fredrike Irmen (Charite)
Rob Rouhl (Maastricht)

AND SOOO MANY OTHERS

Questions?

Contact: foxmdphd@gmail.com

Twitter: foxmdphd

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