

# Transcranial magnetic stimulation as an interventional tool for hedonic hunger and food cravings in metabolic and bariatric surgery patients: Theory and application

Vaughn R. Steele, Ph.D.

Assistant Professor  
Department of Psychiatry  
School of Medicine  
Yale University

[vaughn.steele@yale.edu](mailto:vaughn.steele@yale.edu)



# Disclosures:

## Funding:



NIDA – K12 DA000167



NIMH – R01 MH132044

Yale SCHOOL OF MEDICINE  
Department of Psychiatry

Hartford  
Hospital

A Hartford HealthCare Partner



BRAIN &  
BEHAVIOR  
RESEARCH FOUNDATION

Awarding **NARSAD** Grants



YCCI Yale Center for  
Clinical Investigation

## Yale Psychiatry

Godfrey D. Pearlson, M.D.  
Marc N. Potenza, M.D., Ph.D.  
Stephanie O'Malley, Ph. D.  
Hedy Kober, Ph.D.  
Sarah Yip, Ph.D.

## Olin Neuropsychiatry Research Center

Godfrey D. Pearlson, M.D.  
Michal Assaf, M.D.  
Michael Stevens, Ph.D.

## Project Team

Dale Bond, Ph.D.  
Pavlos Papasavas, M.D.  
Godfrey Pearlson, M.D.  
Hollie Raynor, Ph.D.  
Tara McLaughlin, Ph.D.  
Yin Wu, Ph.D.  
Darren Tishler, M.D.  
Devika Umashanker, M.D.  
Patrick Fang, B.A.  
Kira Gresser, B.A.  
Dongyu Kang, M.D.

## The Steele Lab:



Patrick Fang



Kira Gresser



Dongyu Kang



Alyssa Michel





# Come Work at Yale



Yale SCHOOL OF MEDICINE



Olin Neuropsychiatry  
Research Center

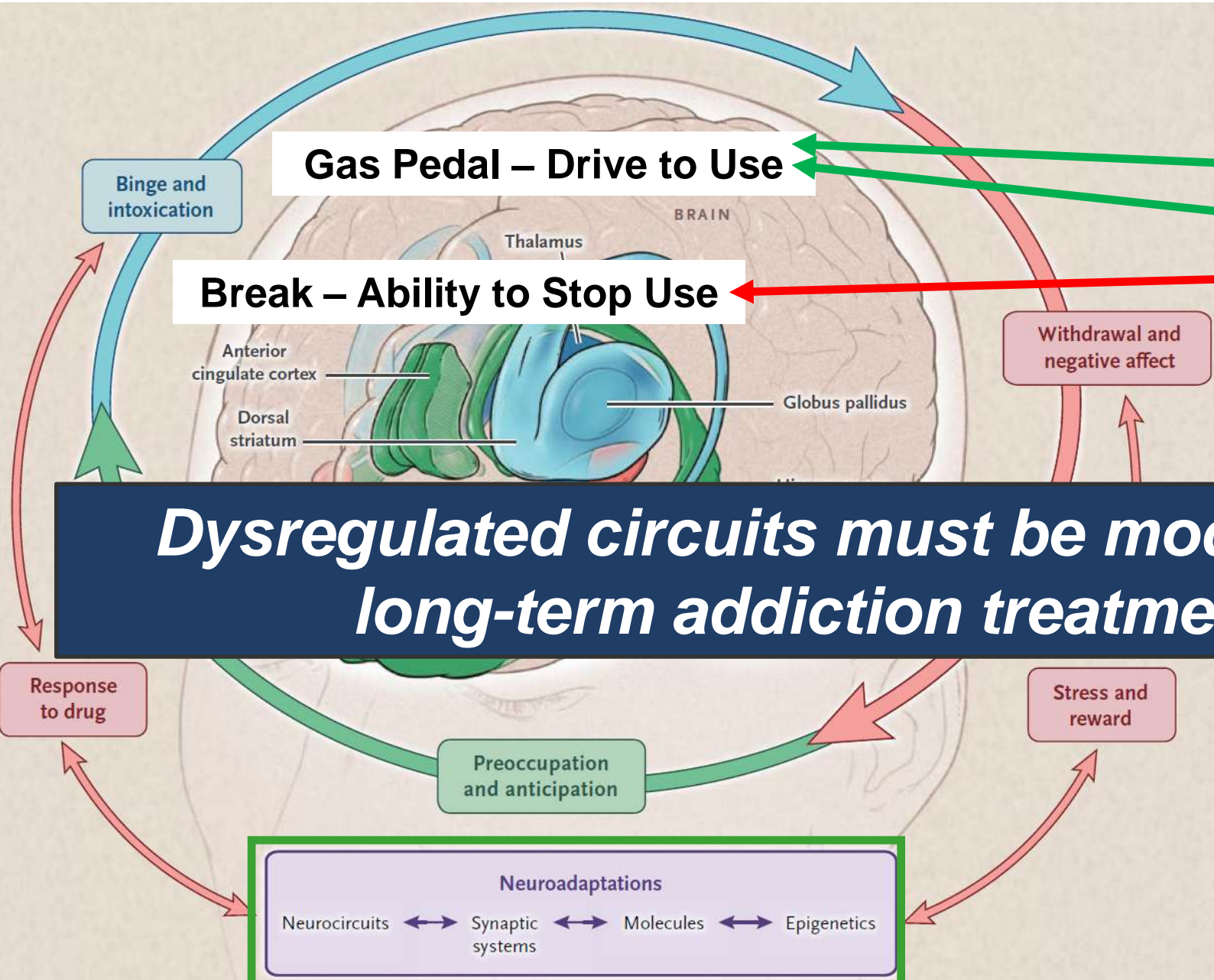
Contact me:  
[vaughn.steele@yale.edu](mailto:vaughn.steele@yale.edu)



# Balanced vs Imbalanced Gas and Break



# Brain Addiction Disease Model



Dysregulation:

- Affect
- Reward
- Cue Reactivity
- Executive Control

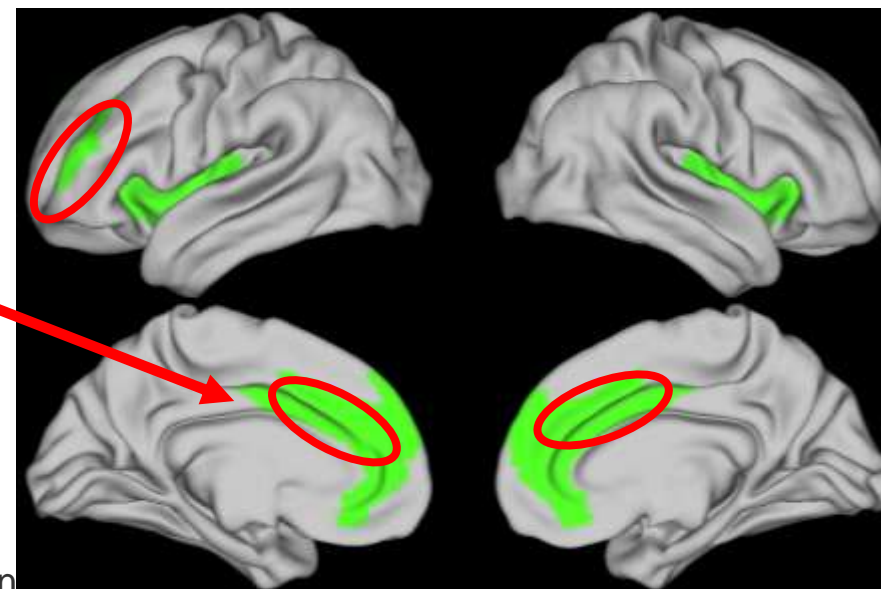
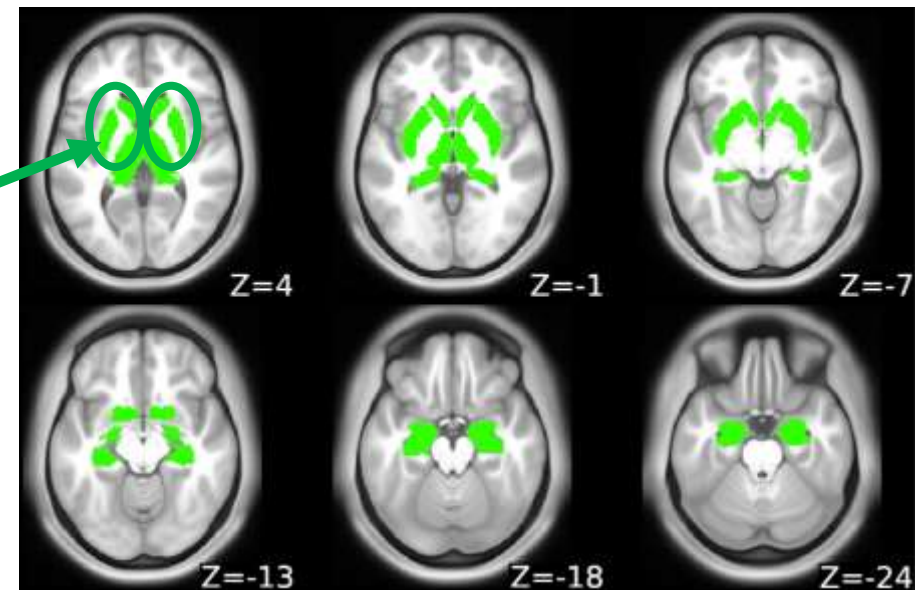
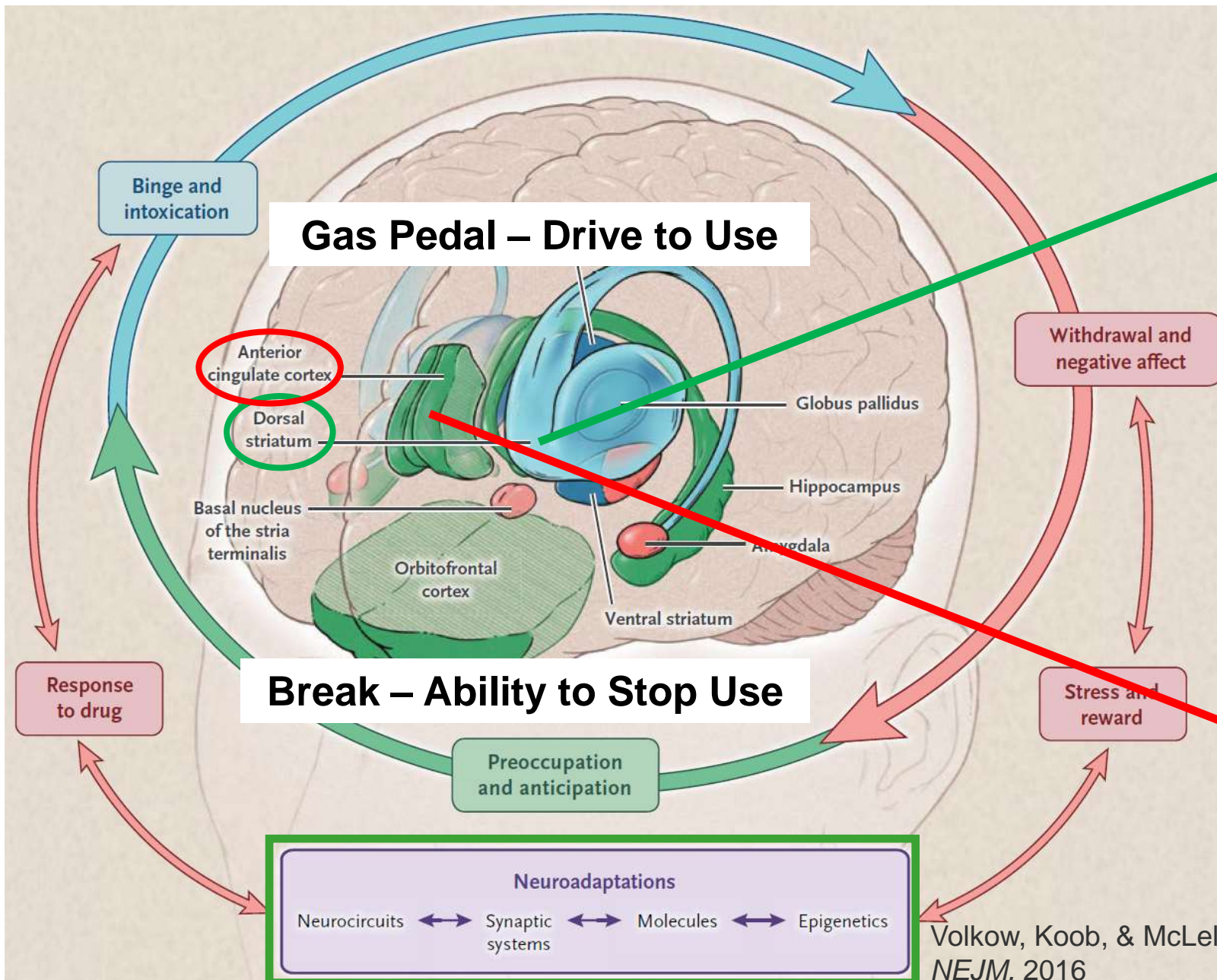
Drug agnostic model

***Dysregulated circuits must be modulated for positive long-term addiction treatment outcomes***

Neuroplasticity



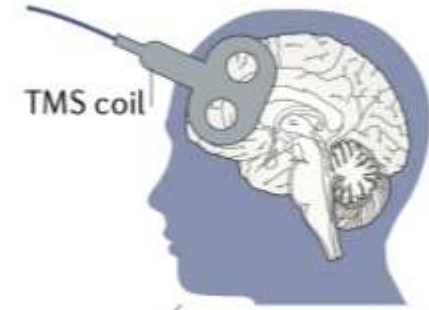
# Brain Addiction Disease Model



# Transcranial Magnetic Stimulation (TMS)



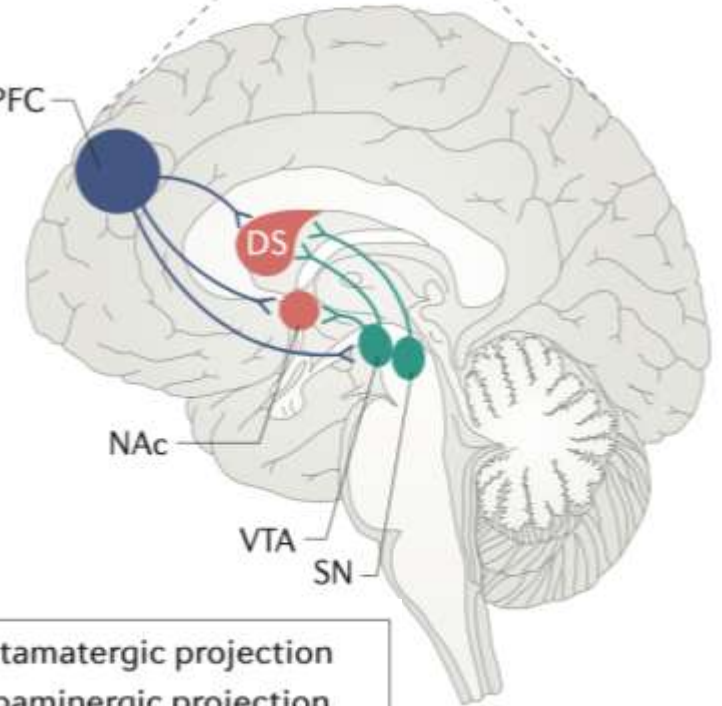
TMS modulation



Primary Activations



DLPFC



Secondary Activations

## Additional Reading/Discussion:

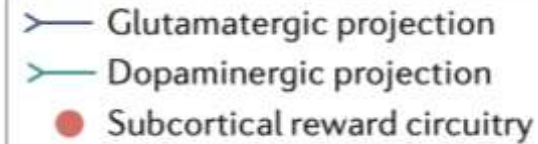
Steele, *Biological Psychiatry*, 2021;

Steele, *EBioMedicine*, 2020;

Steele, *Front Neurosci*, 2020

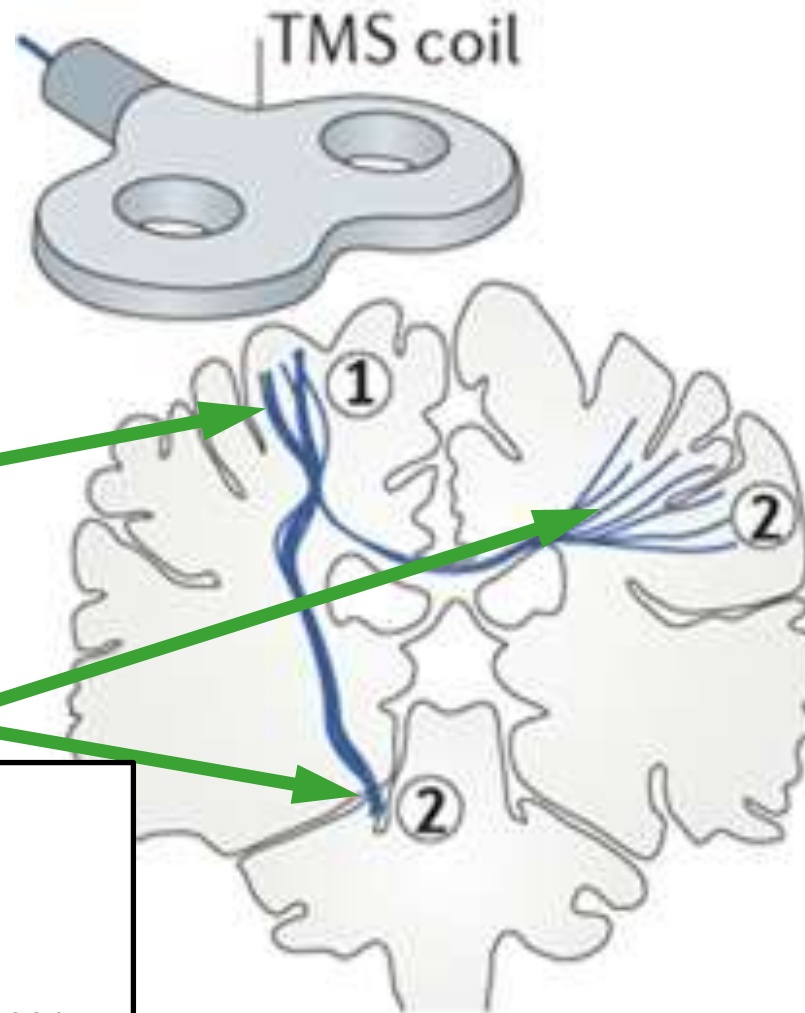
Steele & Maxwell, *Pharm, BioChem, Beh*, 2021;

Diana et al., 2017, *Nature Reviews Neuroscience*





# Transcranial Magnetic Stimulation

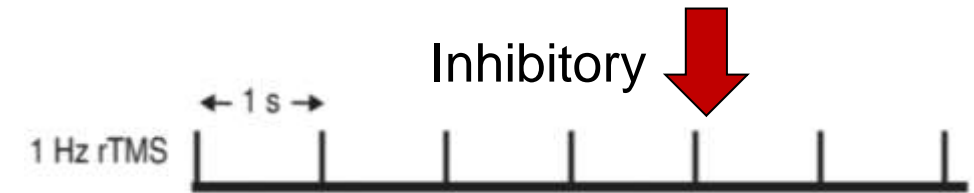


Primary Activations

Secondary Activations

## Repetitive TMS (rTMS)

Continuous Theta-Burst Stimulation (cTBS)



Excitatory



Intermittent Theta-Burst Stimulation (iTBS)

### Additional Reading/Discussion:

Steele, *Biological Psychiatry*, 2021;

Steele, *EBioMedicine*, 2020;

Steele, *Front Neurosci*, 2020

Steele & Maxwell, *Pharm, BioChem, Beh*, 2021;

Diana et al., 2017, *Nature Reviews Neuroscience*



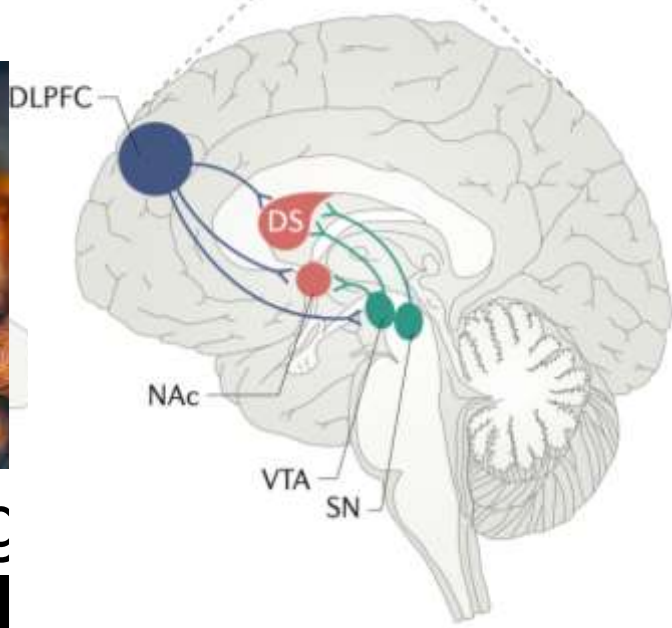


# Cue Reactivity



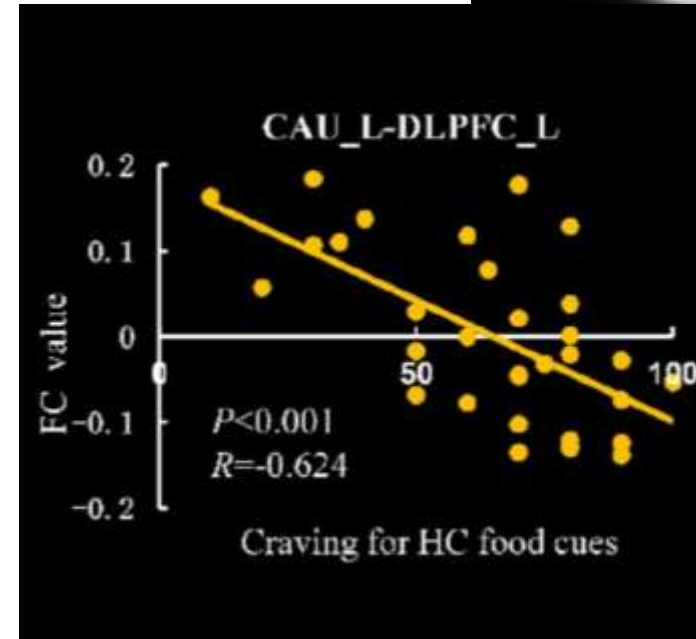
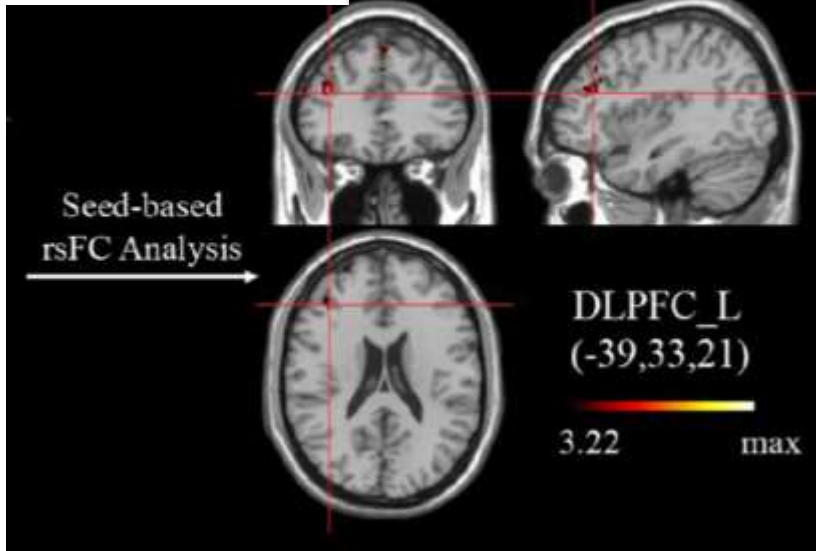
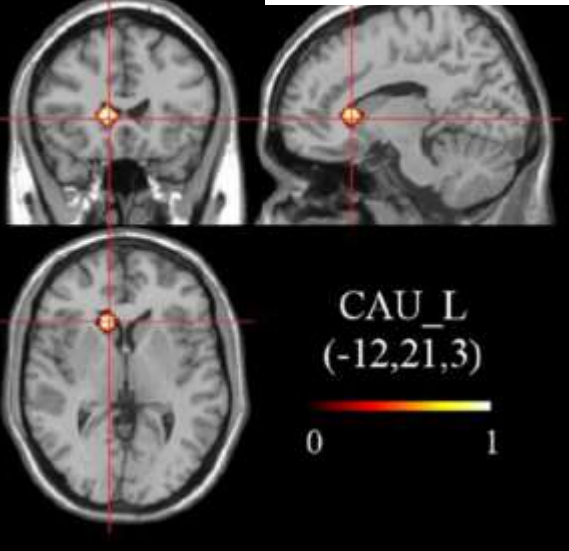
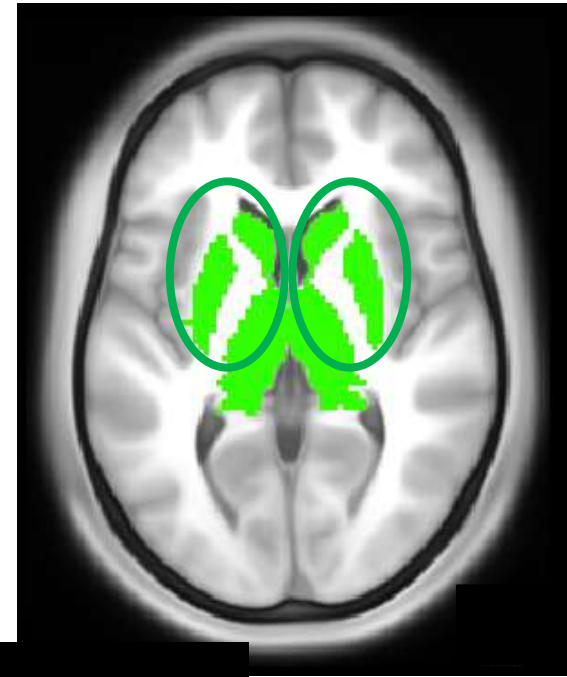
Resting

View



Diana et al., 2017, *Nature Reviews Neuroscience*

Measure:



Tan et al, *Brain Topography*, 2022



# Current Study

EEG



## Stage 1



Obese – pre-bariatric surgery

- Treatment-Seeking
- Active vs sham acute iTBS
  - Within participant manipulation

***How do neural changes relate to behavioral changes?***

**Arrive to study days fasted**

Assessing changes related to:

- Relative-reinforcing value of food (RRV)
- Monetary reward task

***Which circuits are malleable?***

Proposed N = 10

To date: N = 5

1 male/ 4 females

Mean age: 44.33

Mean BMI: 48.58

Power of Food mean: 4.25

Disinhibition of food mean: 4.33

Screened N = 36

Enrolled: N = 12

Completed: N = 5

In processes: N = 3

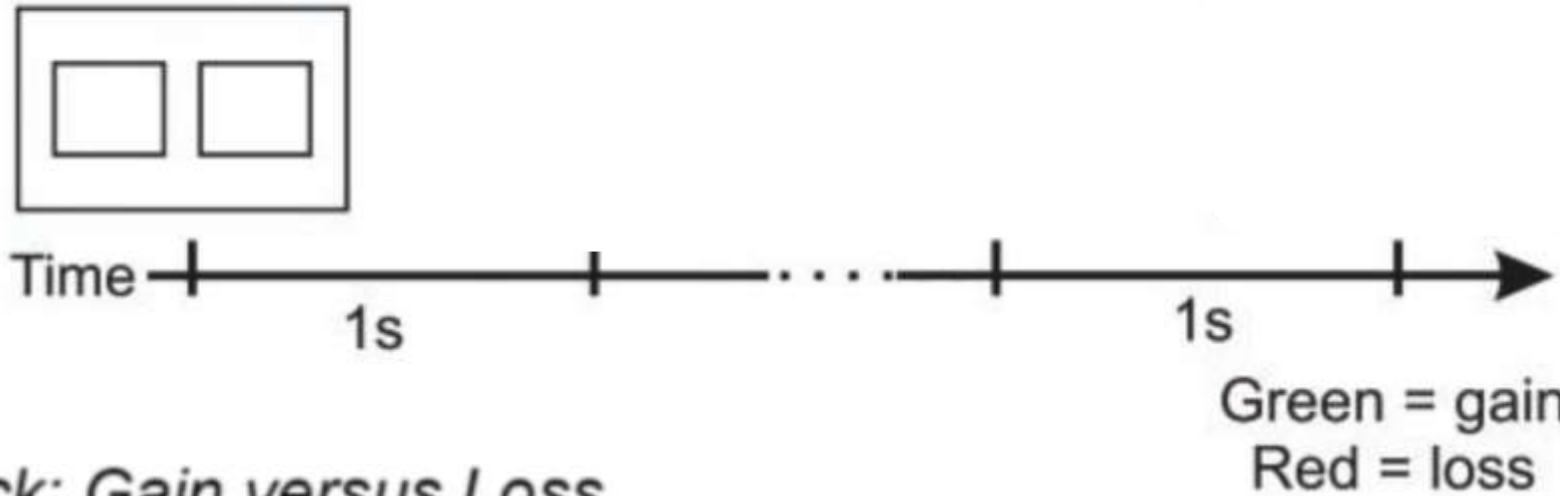
Withdrew: N = 3

Excluded: N = 1



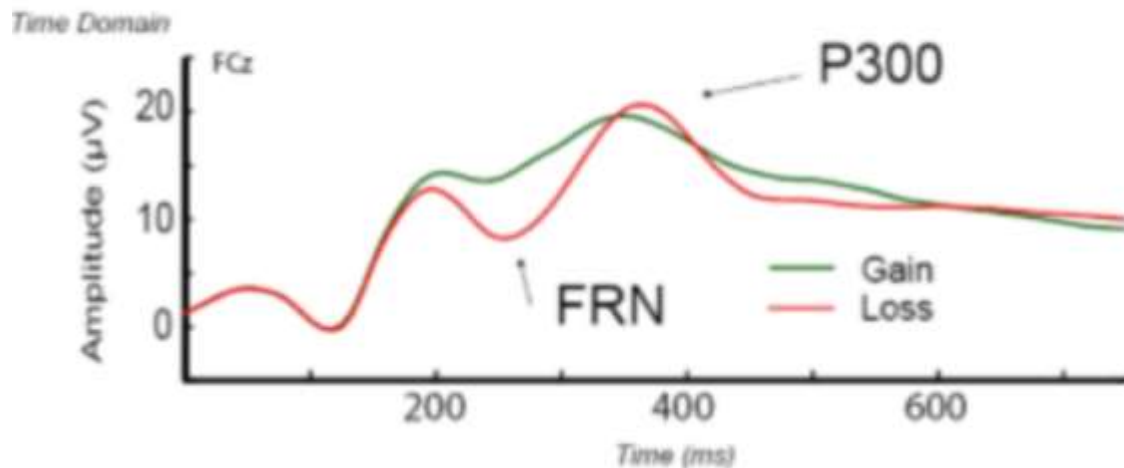


# Current Study: Monetary Reward Task



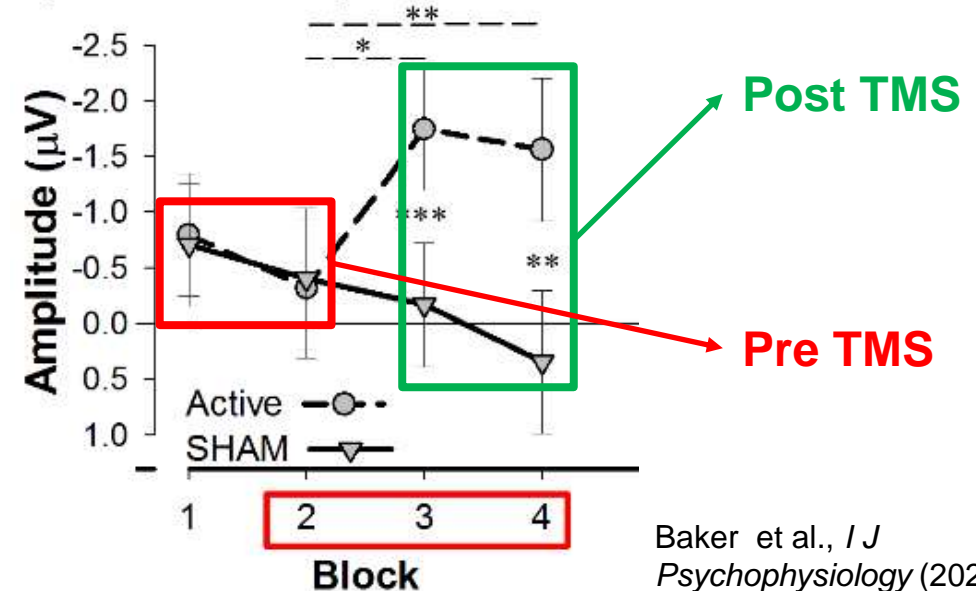
Gehring & Willoughby, *Science*, (2002)

## Feedback: Gain versus Loss



Bernat, Nelson, Steele, et al., *J Abnormal Psychology*, (2011)

## C) Block x Group Interaction



Baker et al., *I J Psychophysiology* (2020)

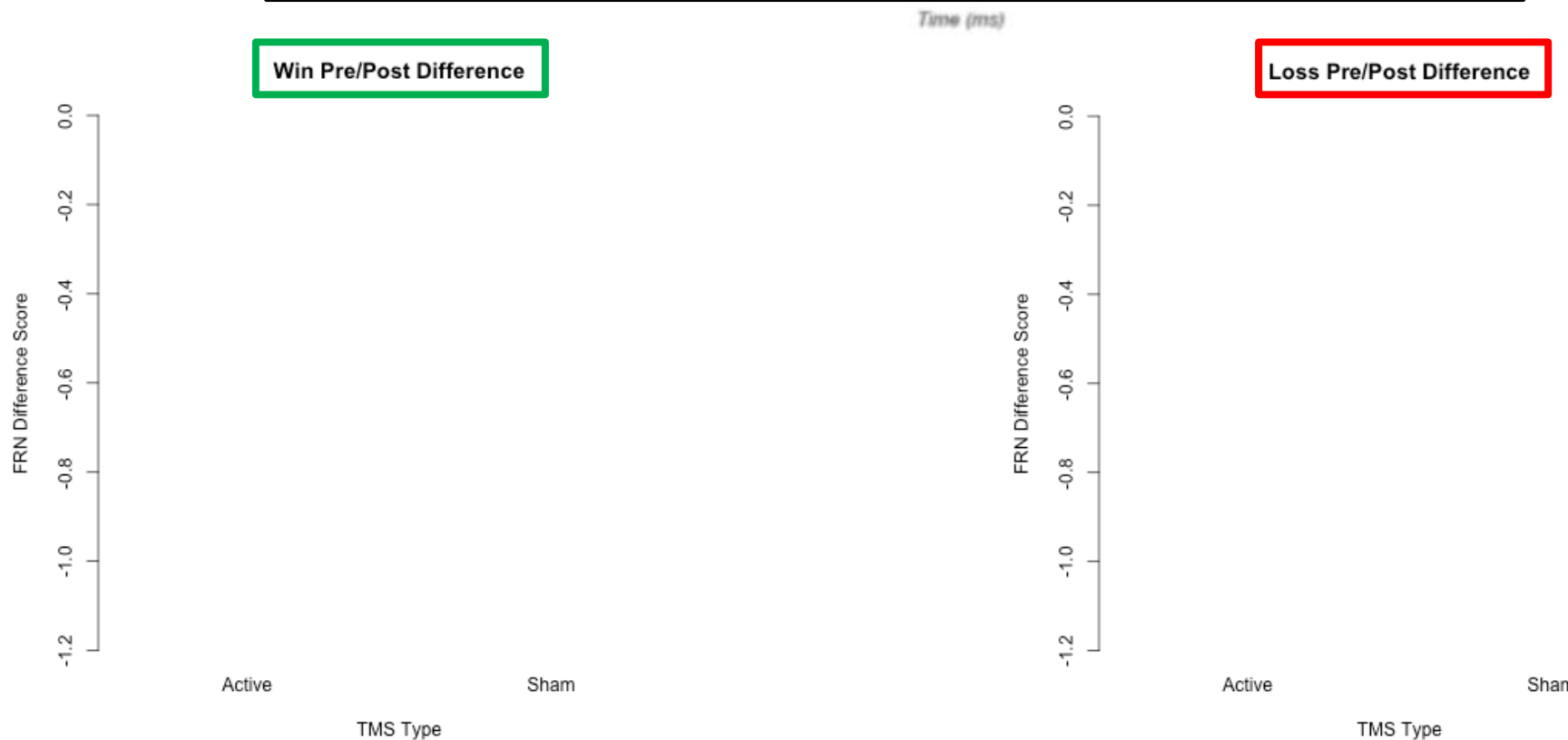


# Current Study: Monetary Reward Task

Feedback: Gain versus Loss

**Acute rTMS:  
Increased reward processing  
brain signals**

et al., Nelson, Steele, et al., *J  
ournal of Experimental Psychology*, (2011)





# Current Study: RRV



Choice #	Food	Button Presses	Money	Button Presses
1	Food (100 kcals)	20	Money (\$0.25)	20



# Current Study: RRV



Choice #	Food	Button Presses	Money	Button Presses
1	Food (100 kcals)	20	Money (\$0.25)	20
2	Food (100 kcals)	40	Money (\$0.25)	20
3	Food (100 kcals) <b>Post TMS</b>	60	Money (\$0.25)	20
4	Food (100 kcals)	80	Money (\$0.25)	20
5	Food (100 kcals)	100	Money (\$0.25)	20

**Pre TMS**

15	Food (100 kcals)	300	Money (\$0.25)	20
16	Food (100 kcals)	320	Money (\$0.25)	20



**Break Point**

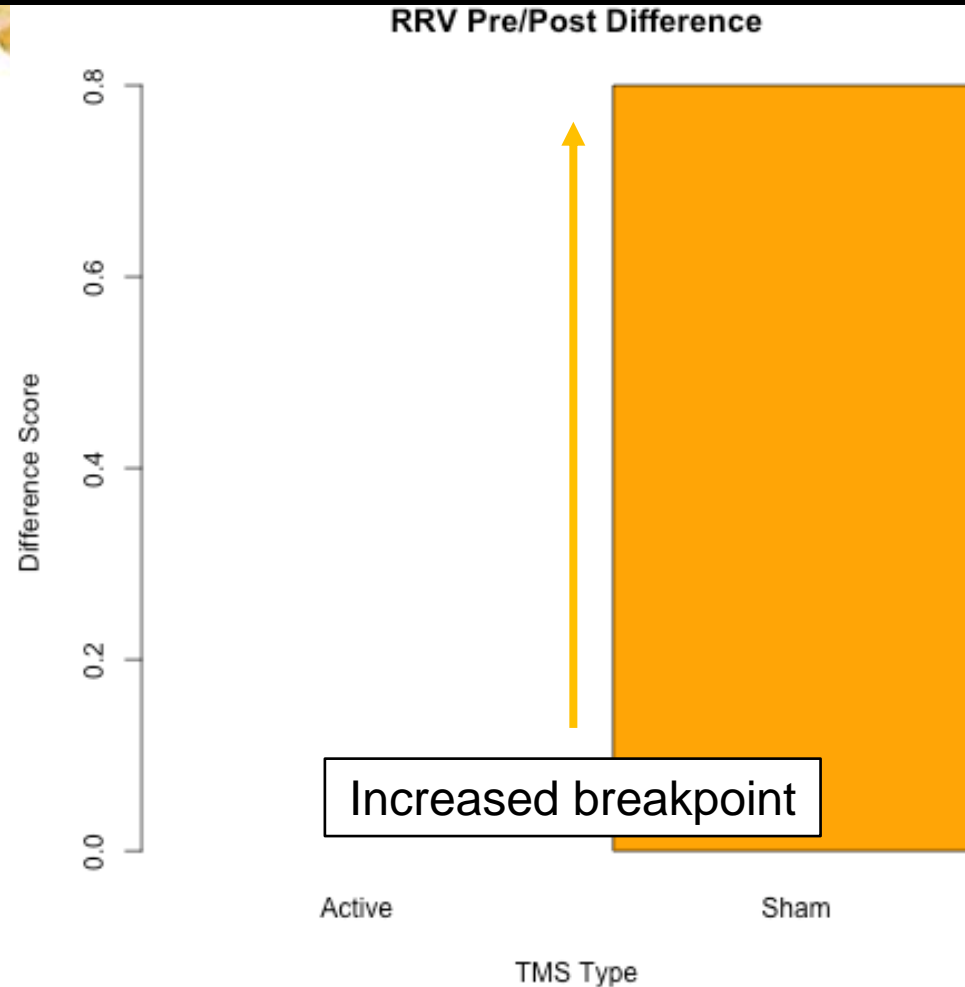




# Current Study: RRV



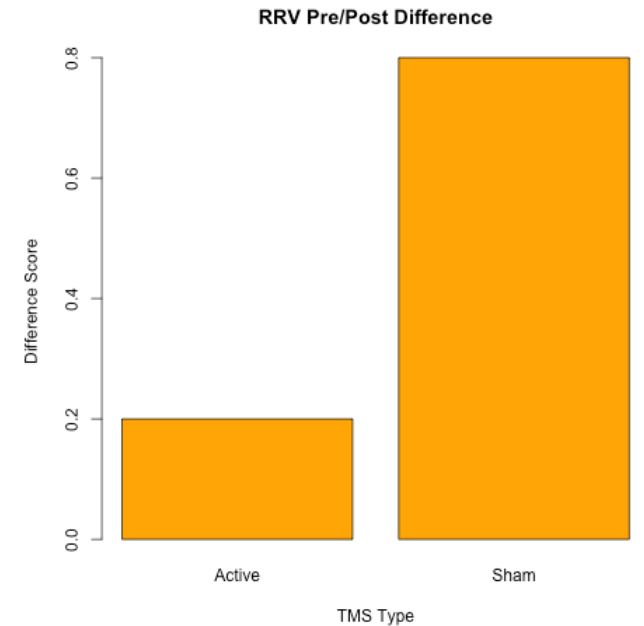
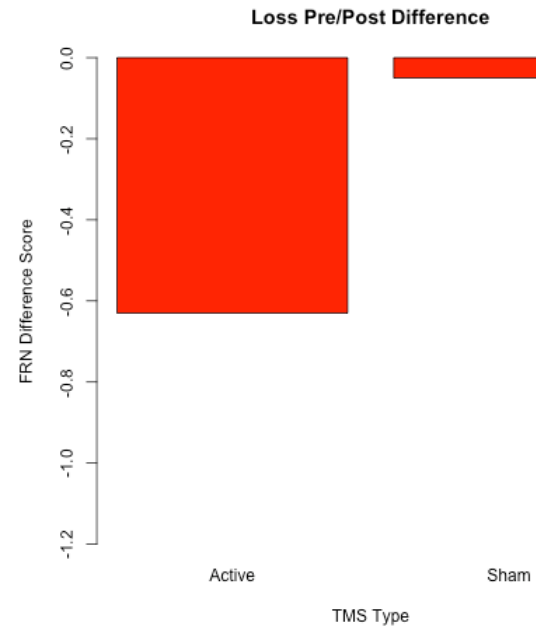
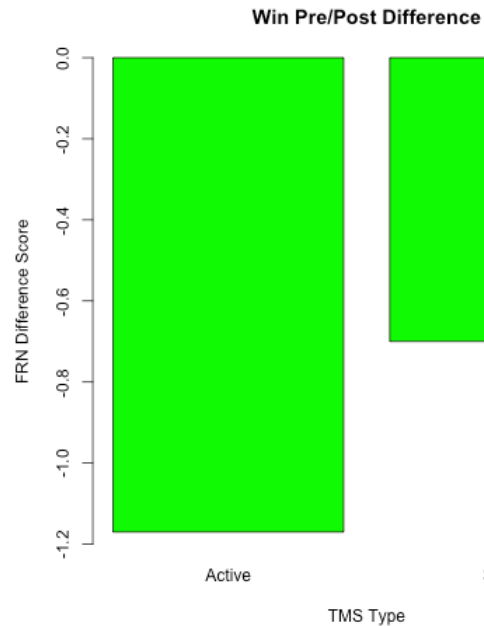
***Acute rTMS:  
Decreased food wanting***



# Summary & Next Steps

- Preliminary evidence in a pilot study that
  - rTMS may be an effective way to...
    - Increase reward processing
    - decrease food wanting

A very promising beginning...





# Summary & Next Steps

- Many potential next steps
  - More rTMS pulses
  - More rTMS sessions
  - Longitudinal behavioral measures
  - etc.
- This opens the door to applying rTMS in other clinical populations
  - This is not a silver bullet
  - rTMS could modulate a targeted circuit to affect brain and behavioral changes in many situations

**Additional Reading/Discussion:**

Steele, *Biological Psychiatry*, 2021;

Steele, *EBioMedicine*, 2020;

Steele, *Front Neurosci*, 2020

Steele & Maxwell, *Pharm, BioChem, Beh*, 2021;



# Thank you!

---

vaughn.steele@yale.edu

## **Join the Steele Lab**

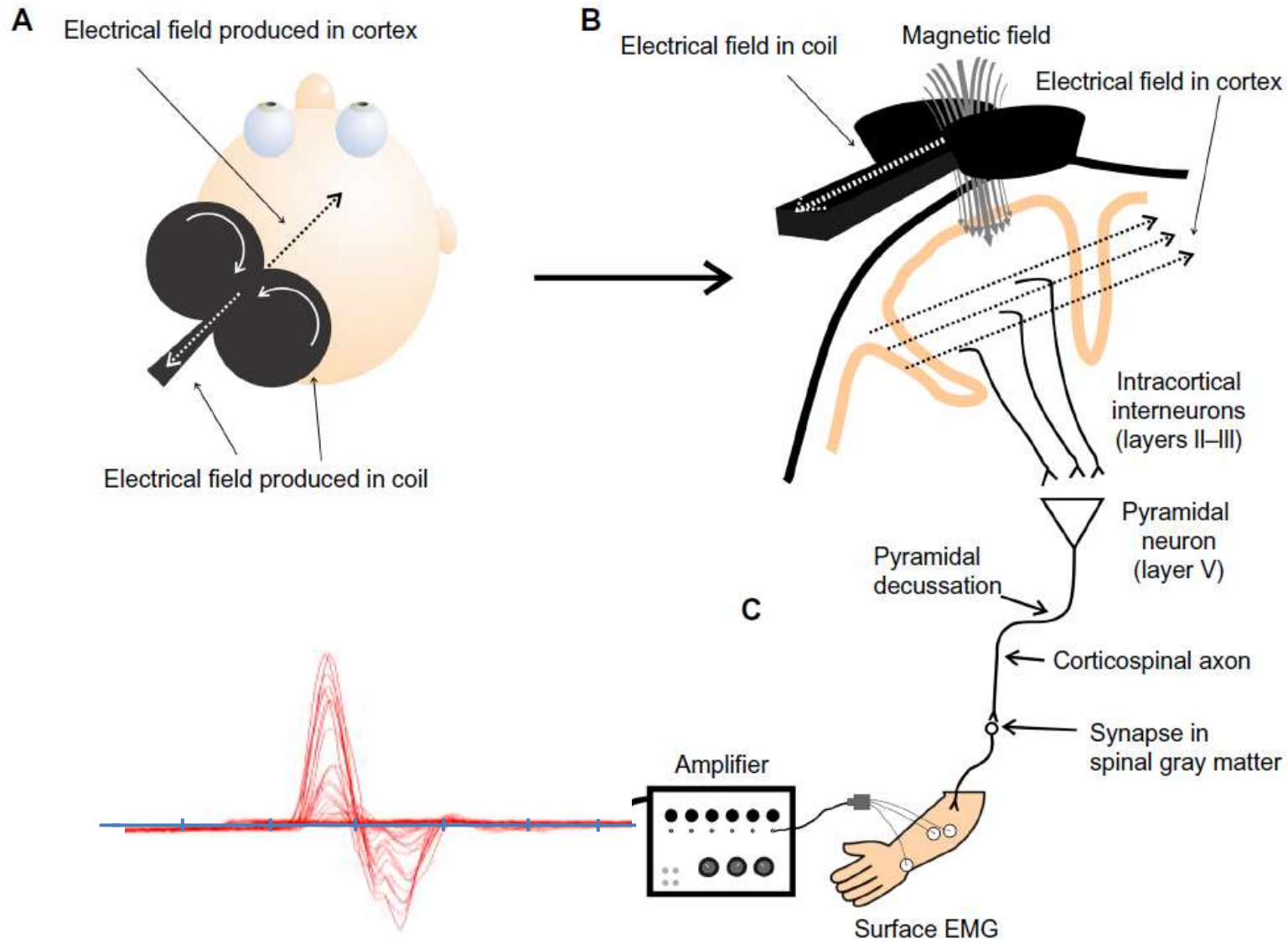
- Post-Doctoral Fellow**
- Research Assistant**







# Dosing TMS



Brown et al, 2014



# Current Study

EEG



## Stage 1



- Obese – pre-bariatric surgery
- Treatment-Seeking
  - Active vs sham acute iTBS

***How do neural changes relate to behavioral changes?***

**Arrive to study days fasted**  
Assessing changes related to:  
Relative-reinforcing value of food (RRV)  
Monetary reward task

***Which circuits are malleable?***

RRV + reward task during EEG

Active rTMS

RRV + reward task during EEG

RRV + reward task during EEG

Sham rTMS

RRV + reward task during EEG





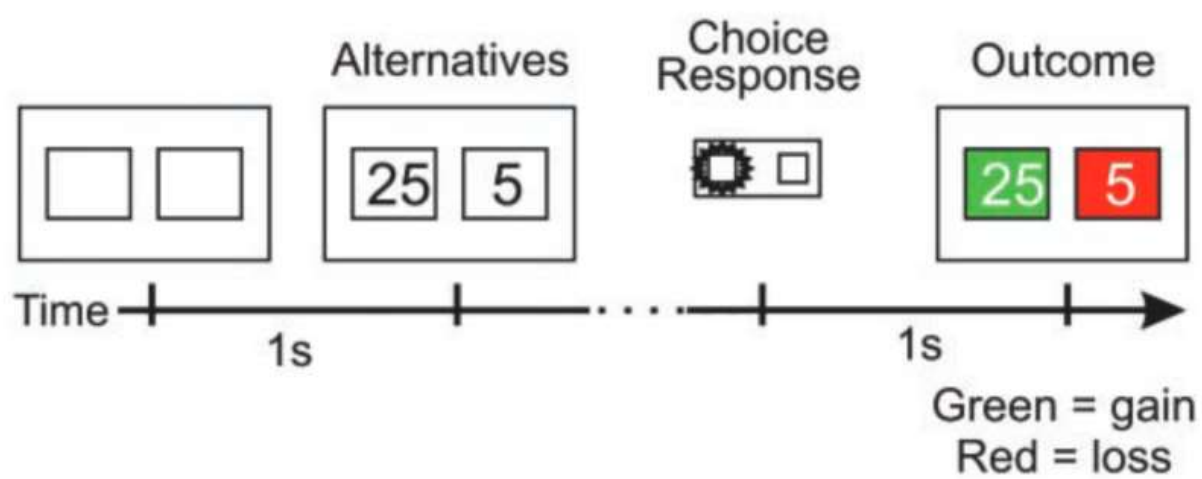
# Current Study: Monetary Reward Task

Feedback Stimulus		Outcome Valence	Relative Outcome	Feedback Stimulus		Outcome Valence	Outcome Magnitude
5	25	Gain	Correct	5	5	Gain	Small
5	25	Gain	Error	25	25	Gain	Large
5	25	Loss	Correct	5	5	Loss	Small
5	25	Loss	Error	25	25	Loss	Large

○ = Selected Outcome

Bernat et al., *Psychophysiology*, (2015)





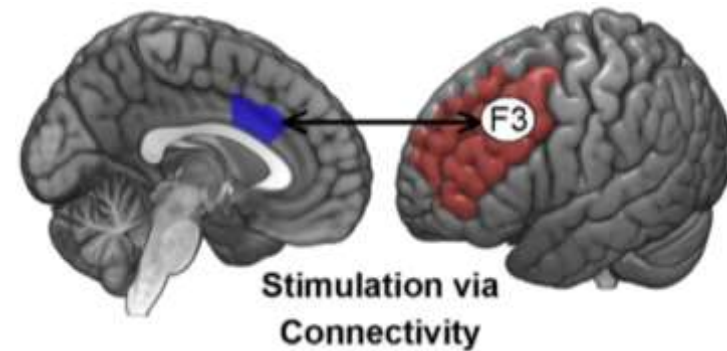
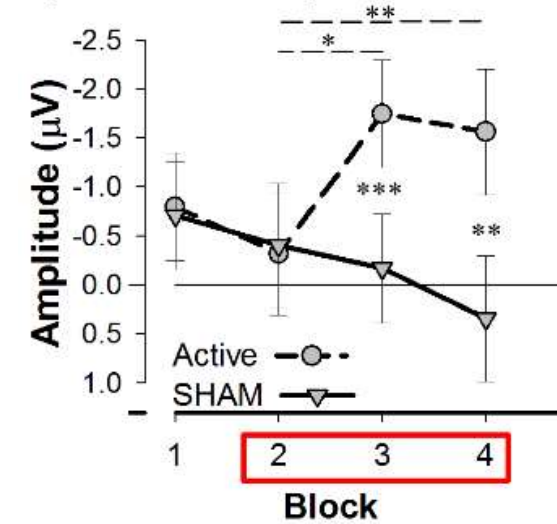
Gehring & Willoughby, *Science*, (2002)

Feedback Stimulus	Outcome Valence	Relative Outcome	Feedback Stimulus	Outcome Valence	Outcome Magnitude
<span style="background-color: green; color: white; padding: 2px;">5</span> <span style="border: 1px solid black; border-radius: 50%; background-color: green; color: white; padding: 2px;">25</span>	Gain	Correct	<span style="background-color: green; color: white; padding: 2px;">5</span> <span style="background-color: green; color: white; padding: 2px;">5</span>	Gain	Small
<span style="border: 1px solid black; border-radius: 50%; background-color: green; color: white; padding: 2px;">5</span> <span style="background-color: green; color: white; padding: 2px;">25</span>	Gain	Error	<span style="background-color: green; color: white; padding: 2px;">25</span> <span style="background-color: green; color: white; padding: 2px;">25</span>	Gain	Large
<span style="border: 1px solid black; border-radius: 50%; background-color: red; color: white; padding: 2px;">5</span> <span style="background-color: red; color: white; padding: 2px;">25</span>	Loss	Correct	<span style="background-color: red; color: white; padding: 2px;">5</span> <span style="background-color: red; color: white; padding: 2px;">5</span>	Loss	Small
<span style="background-color: red; color: white; padding: 2px;">5</span> <span style="border: 1px solid black; border-radius: 50%; background-color: red; color: white; padding: 2px;">25</span>	Loss	Error	<span style="background-color: red; color: white; padding: 2px;">25</span> <span style="background-color: red; color: white; padding: 2px;">25</span>	Loss	Large

○ = Selected Outcome

Bernat et al., *Psychophysiology*, (2015)

C) Block x Group Interaction



Baker et al., *I J Psychophysiology* (2020)



# FDA Phase 0: Feasibility Study

	Week 1	Week 2	Week 3	Weeks 4	Week 7
Visits	1-2	3-7	8-12	13	14
	iTBS			Follow-Up	

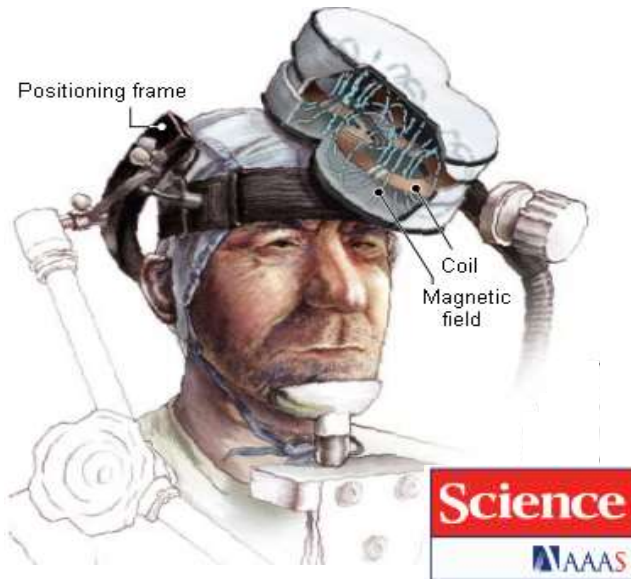
Does chronic rTMS decrease cocaine use?

Are other behaviors affected?

**10 Participants**  
with Cocaine Use Disorder  
Open-label

Steele et al., *Brain Stimulation*, 2018; Steele et al., *Frontiers in Neuroscience*, 2019

L-DIPFC targeted for iTBS

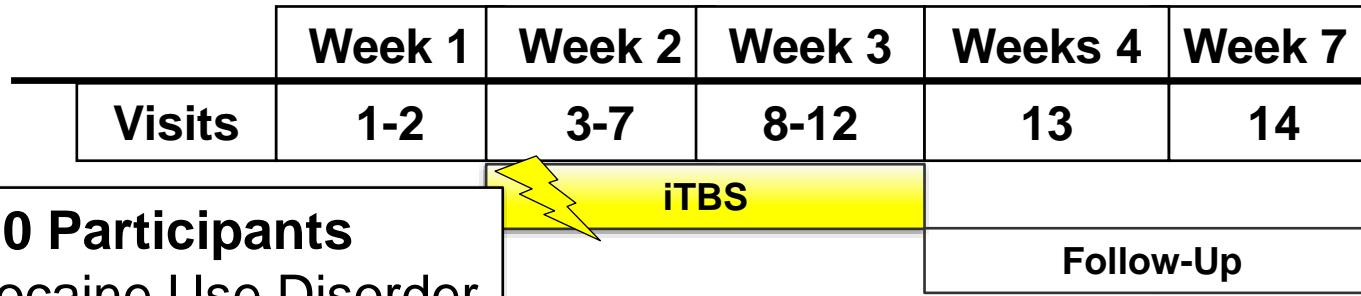


Down regulation of craving  
during iTBS





# FDA Phase 0: Feasibility Study



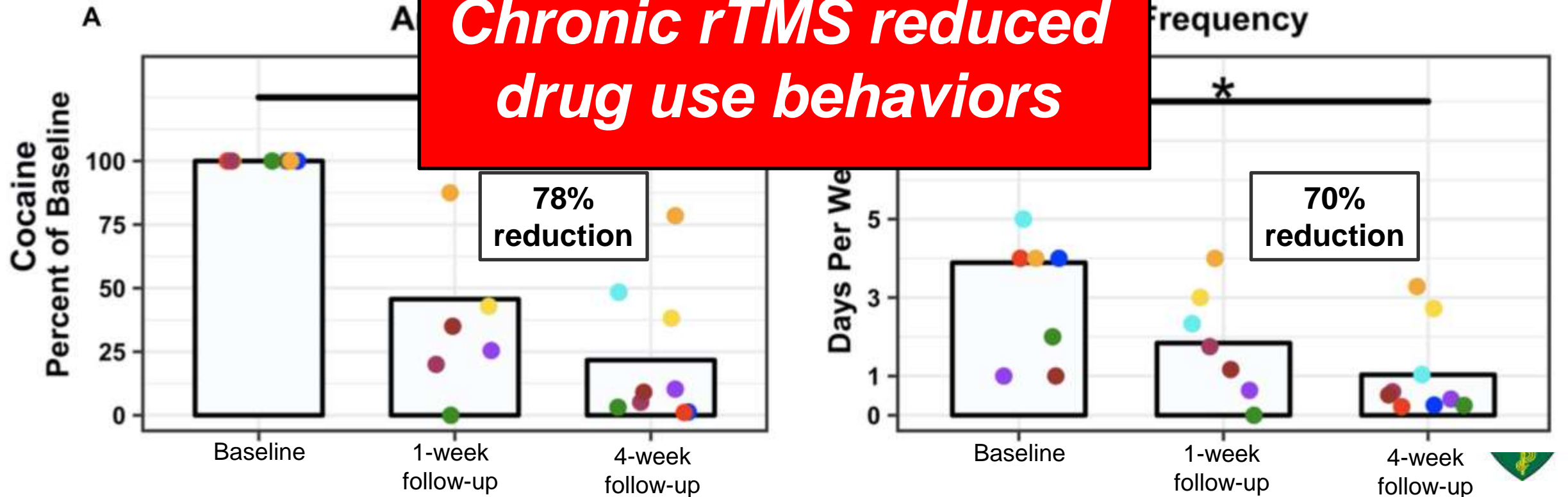
Does chronic rTMS decrease cocaine use?

Are other behaviors affected?

10 Participants  
with Cocaine Use Disorder  
Open-label

Steele et al., *Brain Stimulation*, 2018; Steele et al., *Frontiers in Neuroscience*, 2019

**Chronic rTMS reduced drug use behaviors**



# Current and Future Studies

## Stage 1

EEG fMRI



Methadone maintained

- Treatment-Seeking
- Active vs sham acute iTBS/cTBS

***How do neural changes relate to behavioral changes?***

Assessing neural changes related to:  
Cue reactivity  
Inhibitory control

***Which circuits are malleable?***

## Stage 2

EEG fMRI



Intervention Trial

Methadone maintained

- Treatment-Seeking
- Active vs sham, chronic iTBS/cTBS

Assessing behavioral changes related to chronic rTMS:  
Opioid use; other substance use  
Off-target changes (mood, etc.)

***Is behavior malleable?***

