

Advancing Brain-Based Therapeutics to the Forefront of Addiction Care

Victor M. Tang, MD, MSc, FRCPC

BBRF Meet the Scientist Webinar

Feb 10, 2026

camh



Disclosures

Sources of Research Funding:

- Canadian Institutes of Health Research (CIHR)
- Brain & Behavior Research Foundation (BBRF/NARSAD)
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- Academic Scholar Award, Dept of Psychiatry
- PSI Foundation Grant
- CAMH Discovery Fund
- Labatt Family Network
- Research in Addiction Medicine Scholars Program



1

Treatment Gaps in Addiction and Brain-Based Therapeutics

Substance Use Disorders (SUDs)

Globally, approximately 35 million people have SUDs

Global burden due to SUDs is increasing over time (disability adjusted life years)

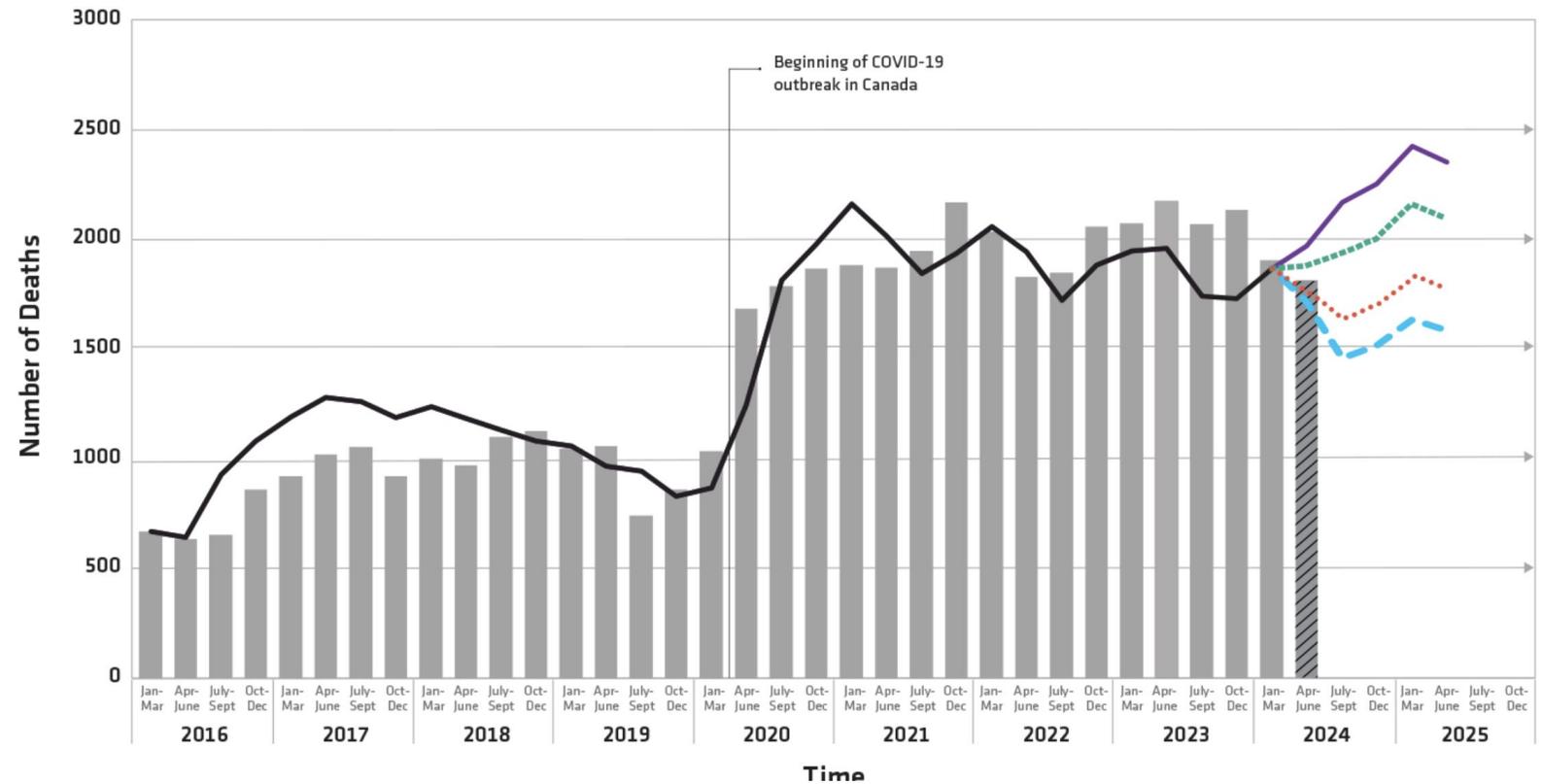
Socioeconomic costs: healthcare, medications, productivity loss, disability, crime

Associated mental and physical comorbidities

Increasing prevalence of harms and a shifting landscape...

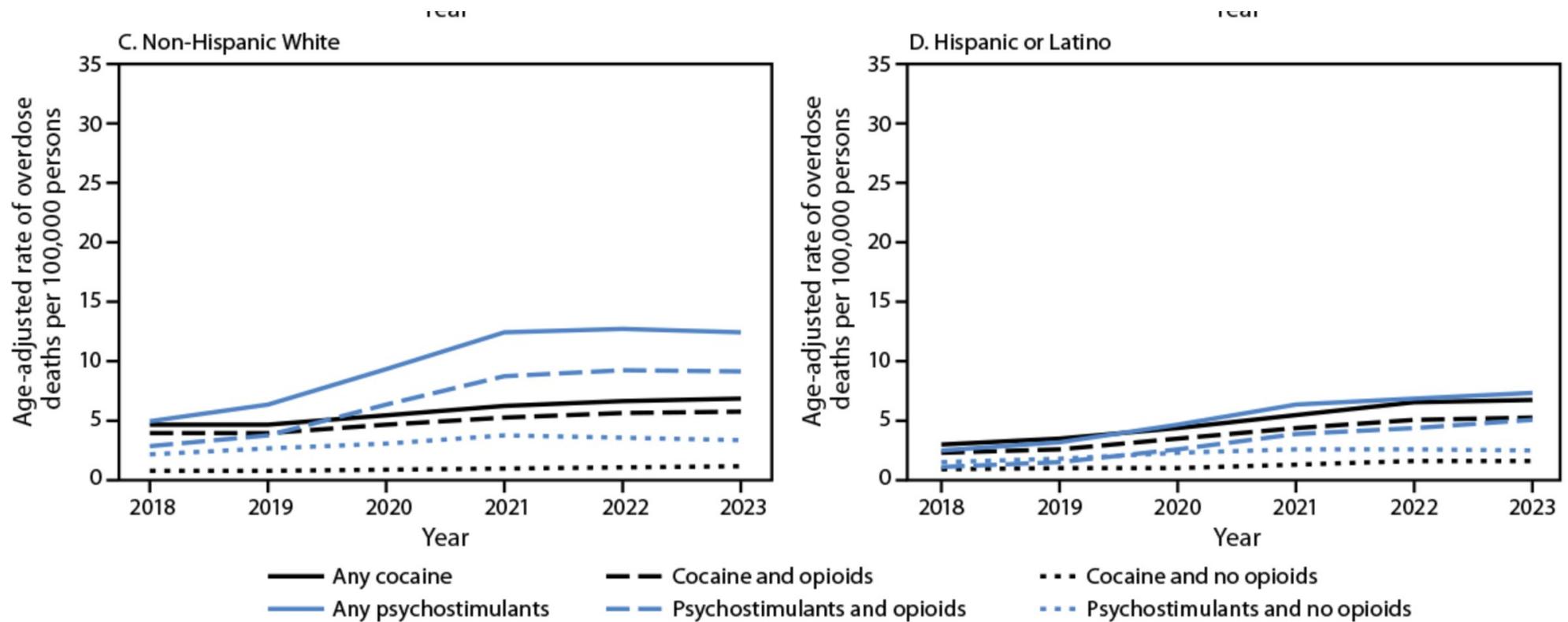
Opioid overdose crisis

Figure 1: Observed and projected apparent opioid toxicity deaths, Canada, January 2016 to June 2025



Increasing prevalence of harms and a shifting landscape...

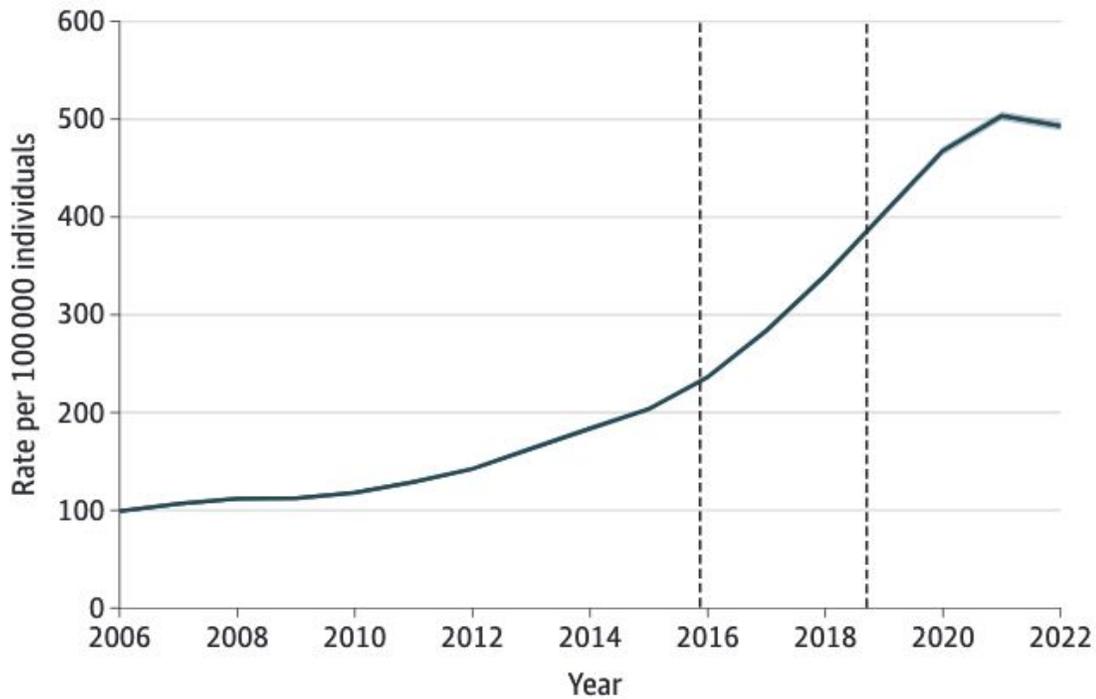
Increasing contribution of stimulant use disorder



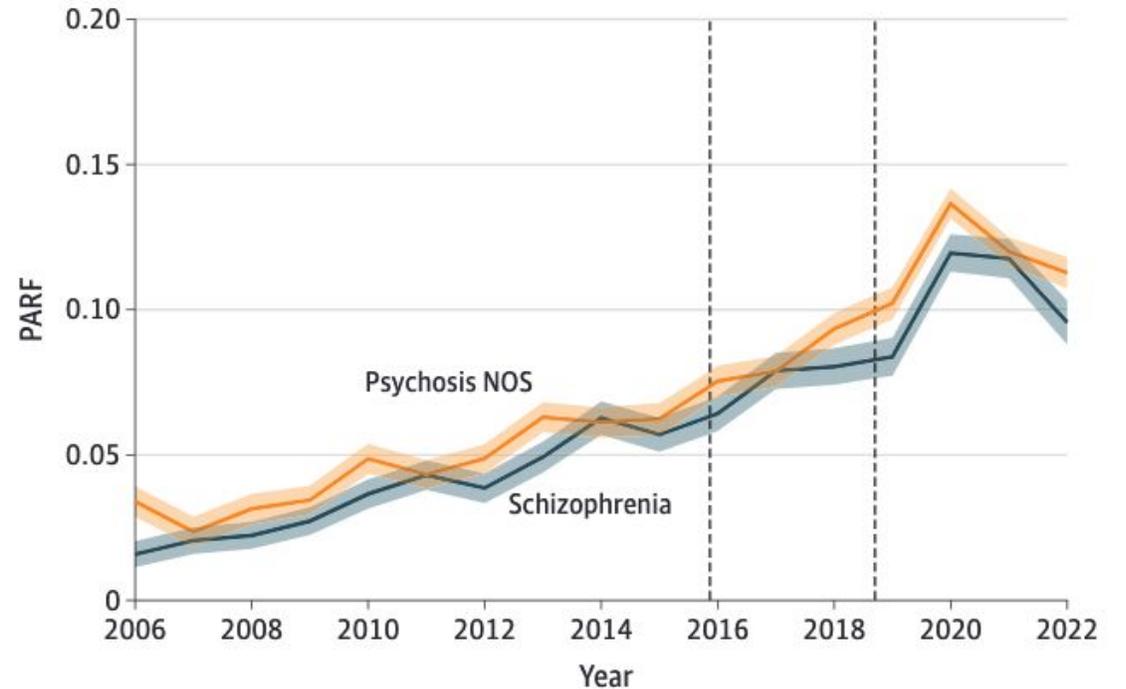
Increasing prevalence of harms and a shifting landscape...

Cannabis legalization, increase in CUD, high potency THC, recreational use, association with severe mental illness, and perceptions changing to cannabis being harmless

A Standardized prevalence of CUD



D Adjusted PARF



Increasing prevalence of harms and a shifting landscape...

Nicotine □ decreasing cigarette use, shifting patterns in youth, shifting to vaping

Smoking tobacco decreasing in prevalence in overall population, but not the same in people with severe mental illness



The Treatment Gap

Nicotine/Tobacco: Currently approved treatments have sustained quit of 10-30% success

Opioids: >50% relapse or discontinue, patients who overdose have had previous treatment

Stimulants/Cannabis: No approved treatments, no evidence-based pharmacotherapy

Psychosocial treatments difficult to access and poorly resourced

Addiction: Concept vs. Disease

- Like many mental health concepts, addiction is subject to misunderstanding
- Similarly, it can describe:
 - A continuum of behaviour
 - A social construct
 - An illness or disease state
 - Normal variation



I'M  ADDICTED TO YOU



The Brain Disease Model of Addiction (BDMA)

- Evidence has advanced in recent decades showing addiction as a disease of the brain
- Brain disease usually refers to:
 - Neurobiological PREDISPOSING factors (e.g. family history, inherent responses to substances)
 - Neurobiological CHANGES as a RESULT of chronic drug use (e.g. transition to compulsive behaviour that is difficult to control)
- Parallels to other chronic diseases defined by the medical model (e.g., diabetes, HTN)

THE LANCET
Psychiatry

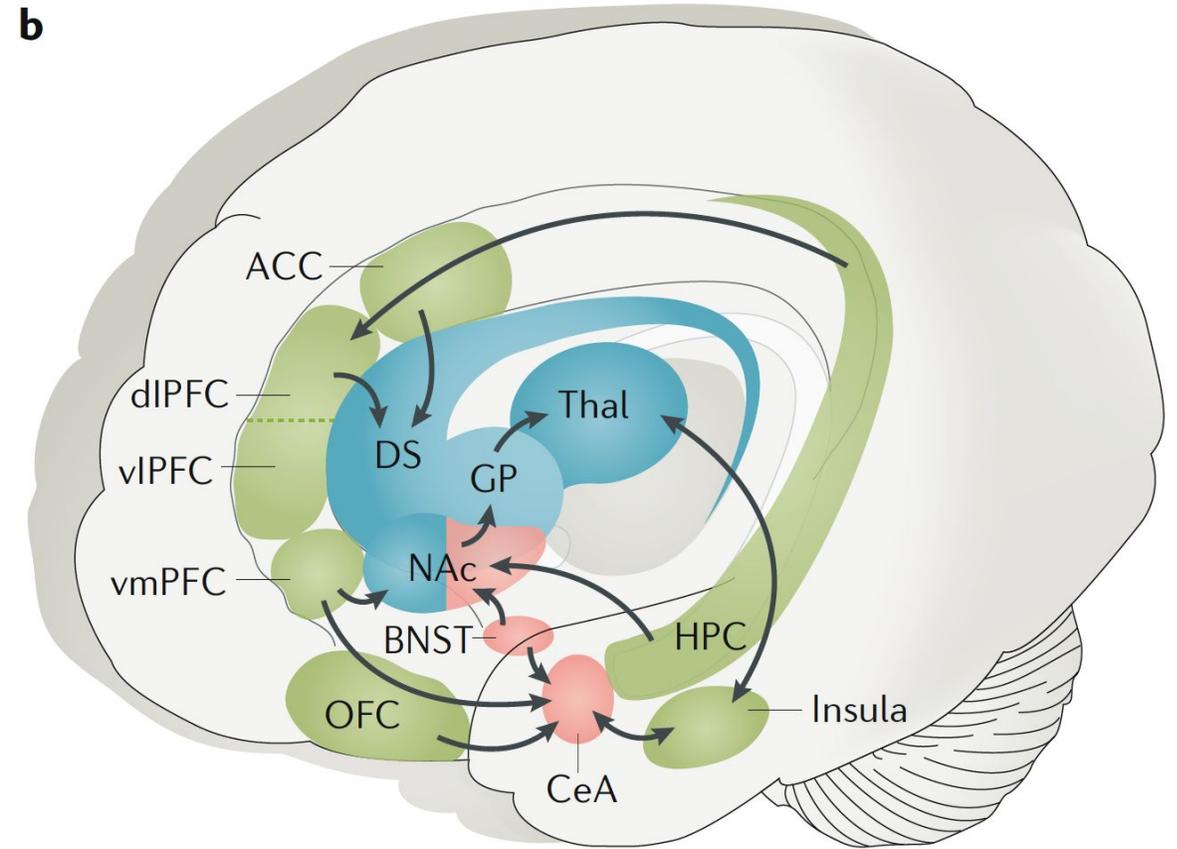
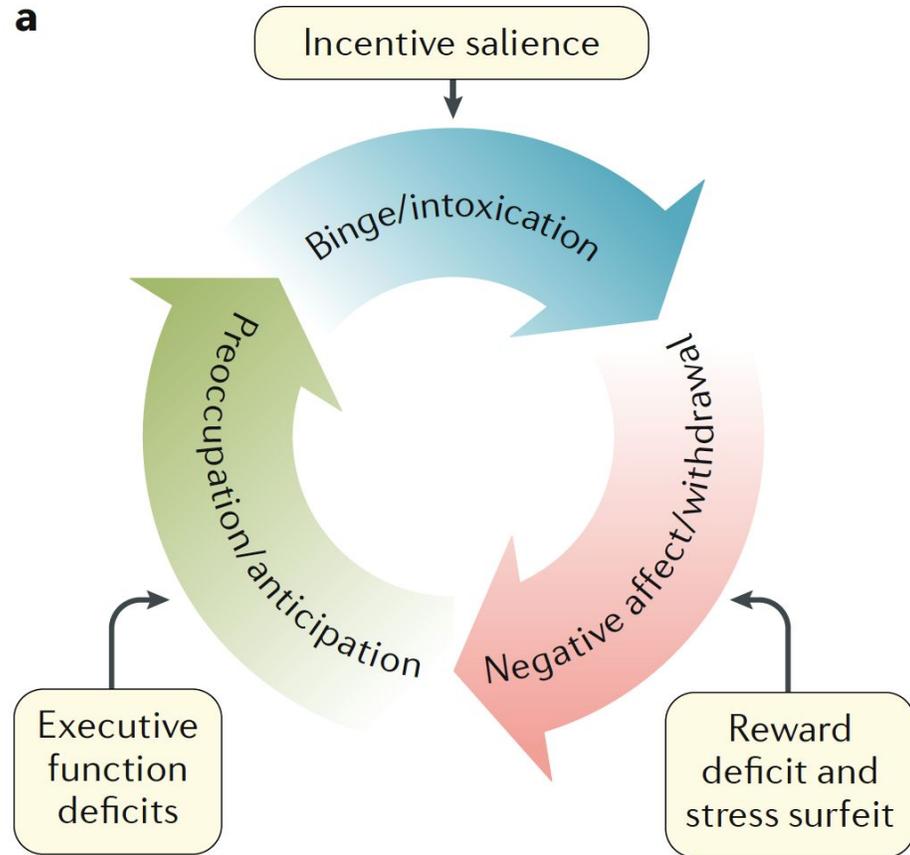
COMMENT | [VOLUME 2, ISSUE 8, P677-679, AUGUST 01, 2015](#)

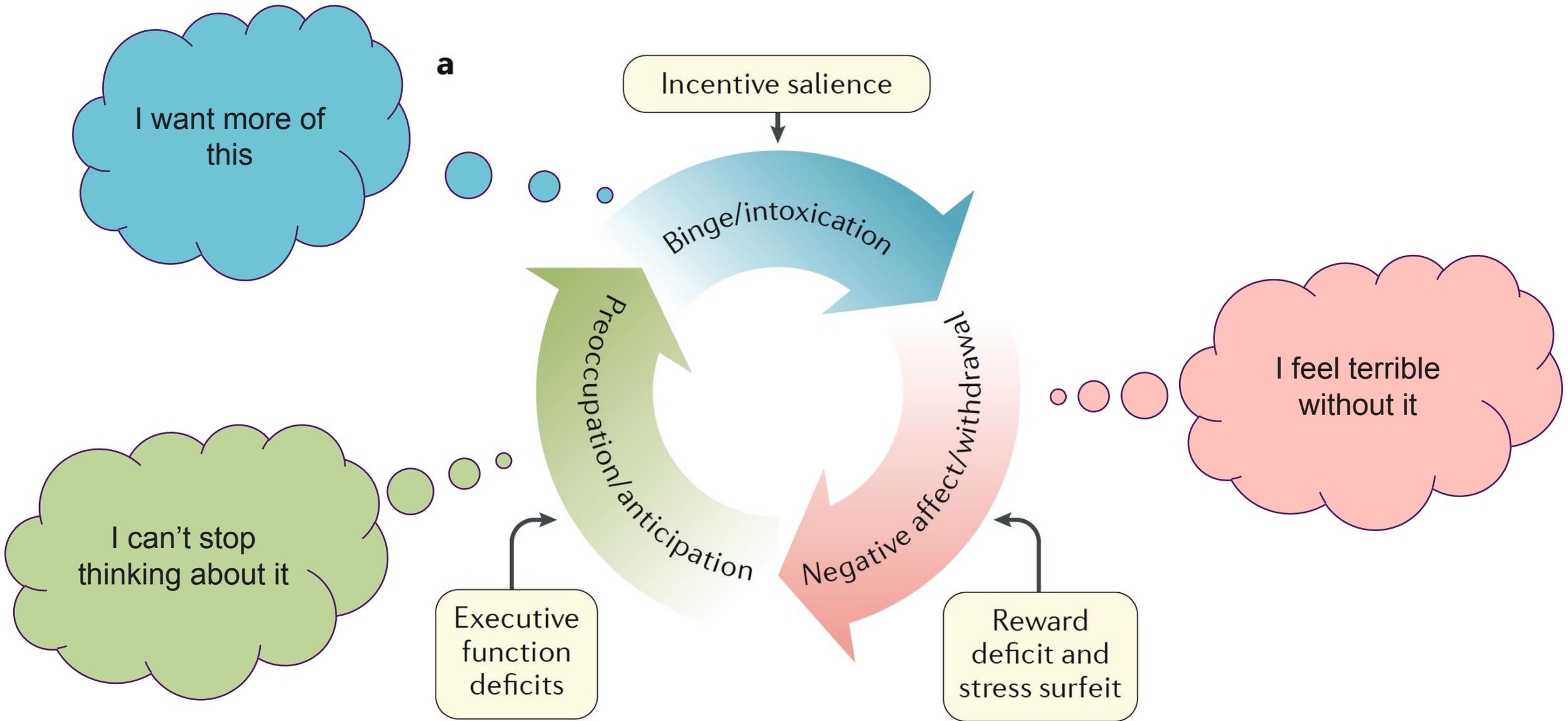
Brain disease model of addiction: why is it so controversial?

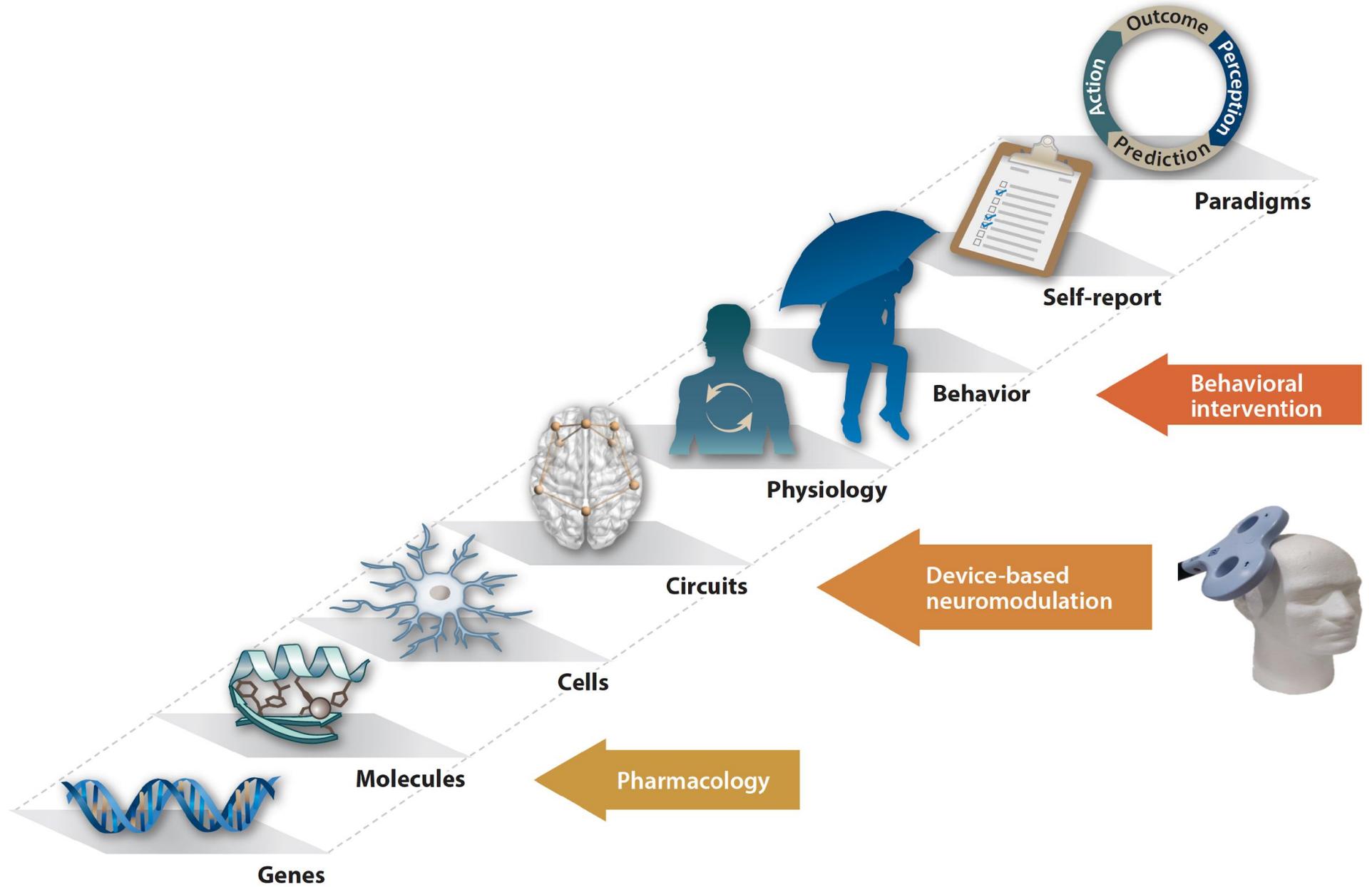
[Nora D Volkow](#) ✉ • [George Koob](#)

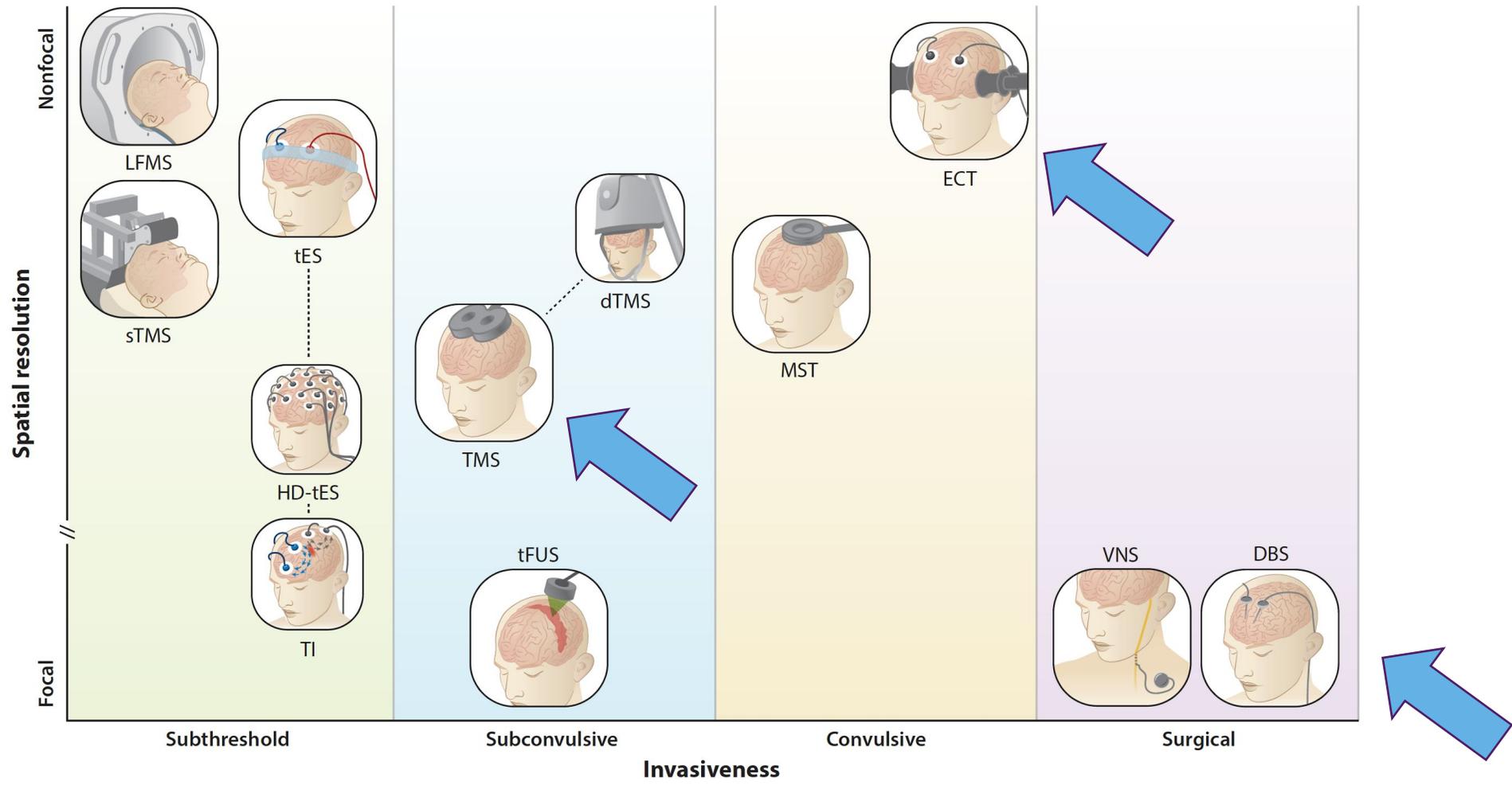
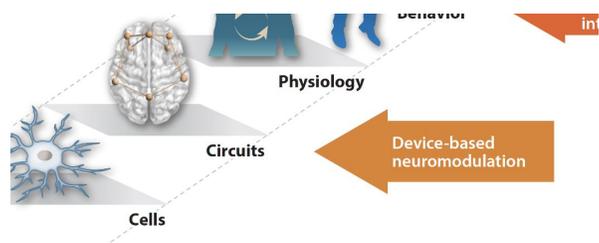
Published: August, 2015 • DOI: [https://doi.org/10.1016/S2215-0366\(15\)00236-9](https://doi.org/10.1016/S2215-0366(15)00236-9)

Neurobiological Framework for Addiction



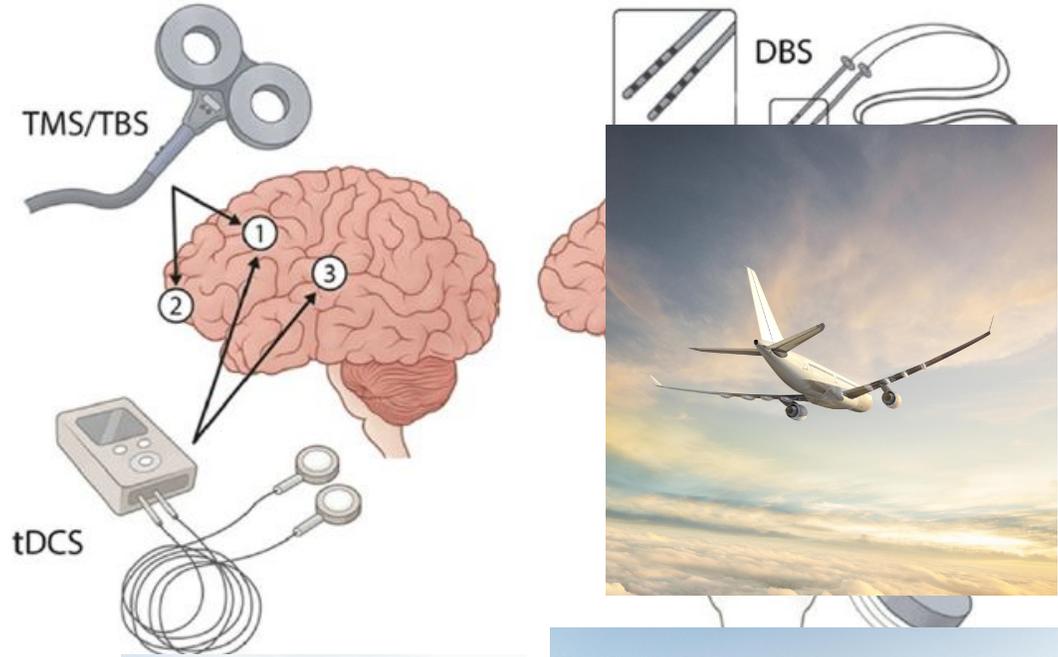
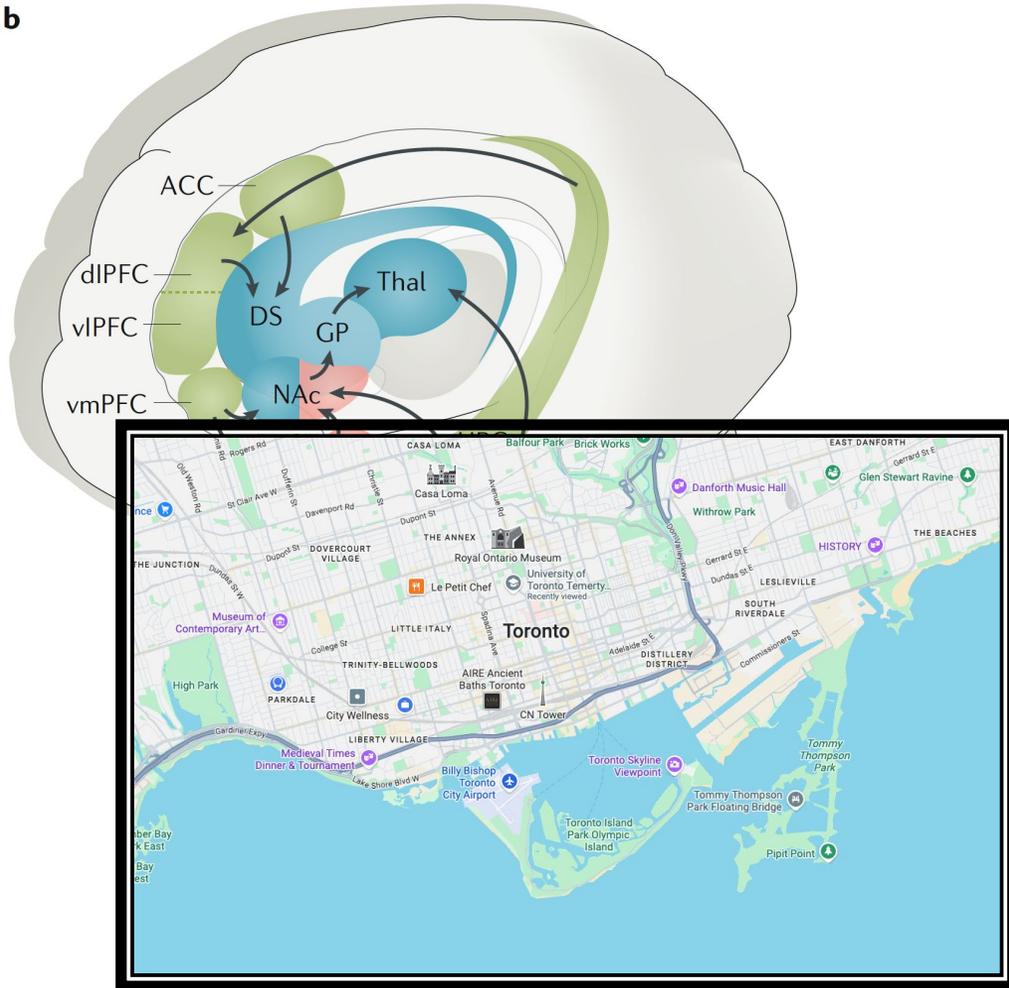






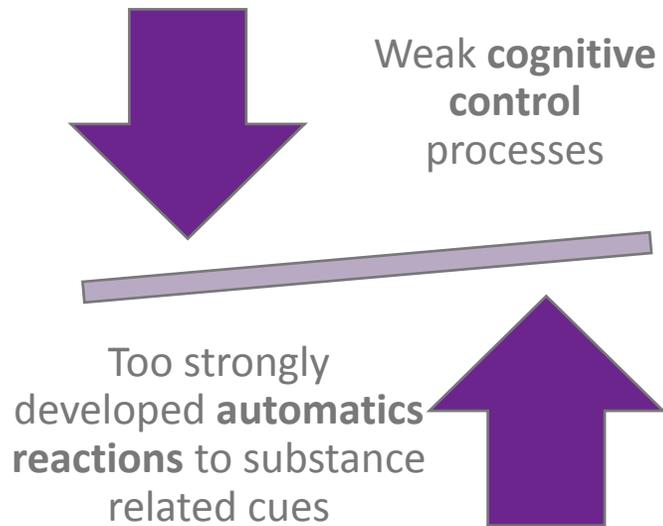
Matching the Tool to the Target

b



rTMS and Addiction

Dual Process Model of Addiction

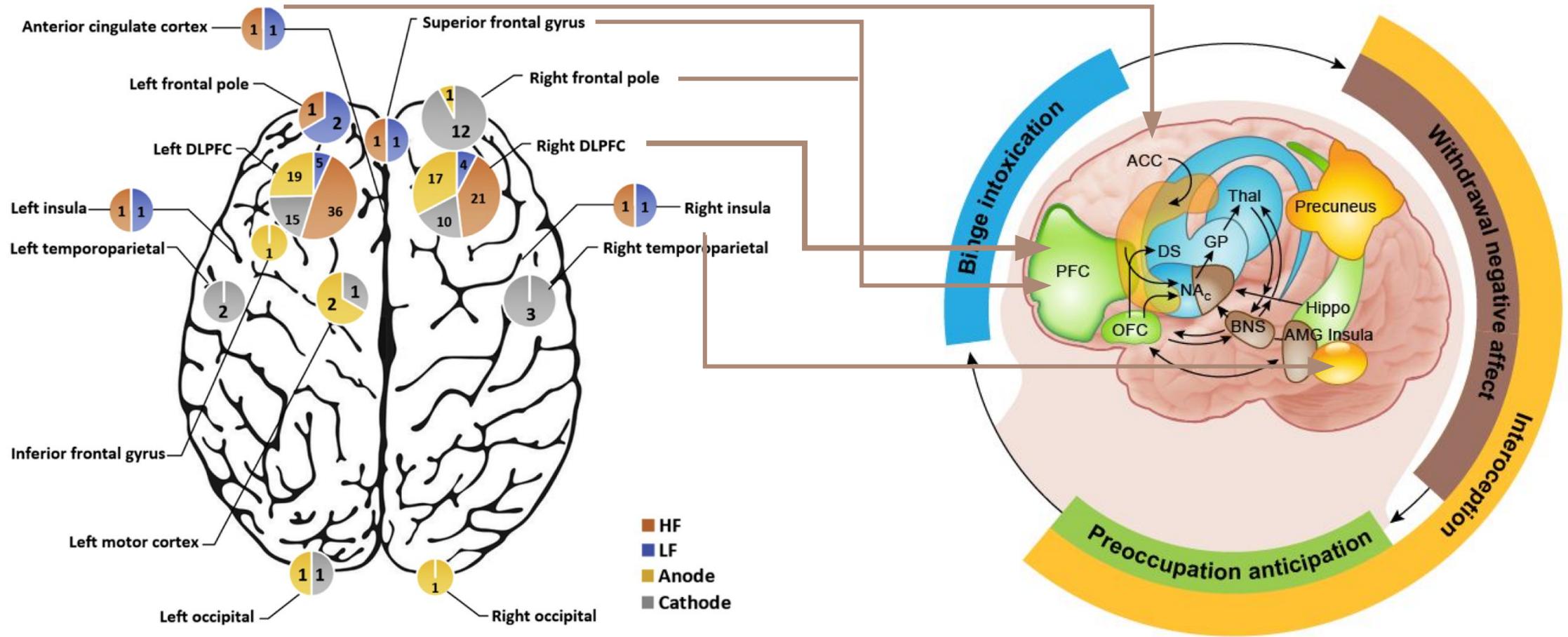


Frontal-striatal loops that govern executive and limbic behaviors

Potential circuit based TMS strategies for addiction

Approach		Example	
↑	Executive Control Loop	LTP-like stimulation	10-20 Hz iTBS
↓	Limbic Arousal Loop	LTD-like stimulation	1-5Hz cTBS

Targets for Brain Stimulation Trials in Addictions



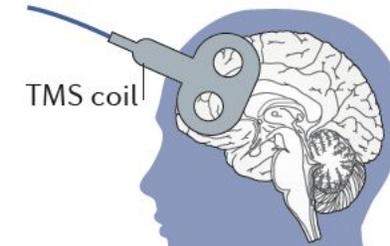
Repetitive Transcranial Magnetic Stimulation (rTMS)

- Non-invasive stimulation with electromagnetic coil to induce electric field in brain



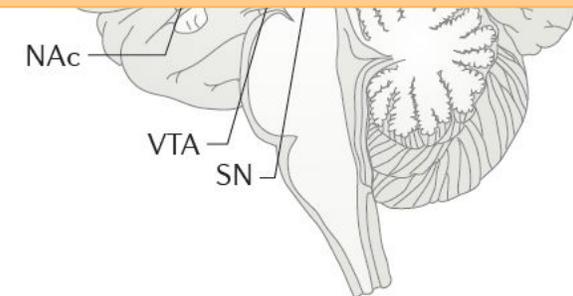
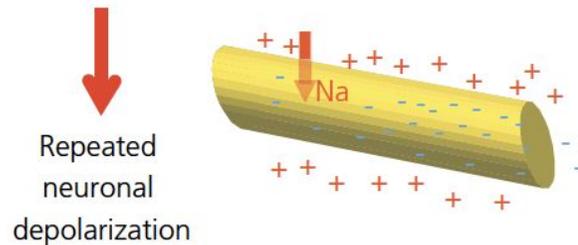
- Target, modulate, change at neurocircuit level

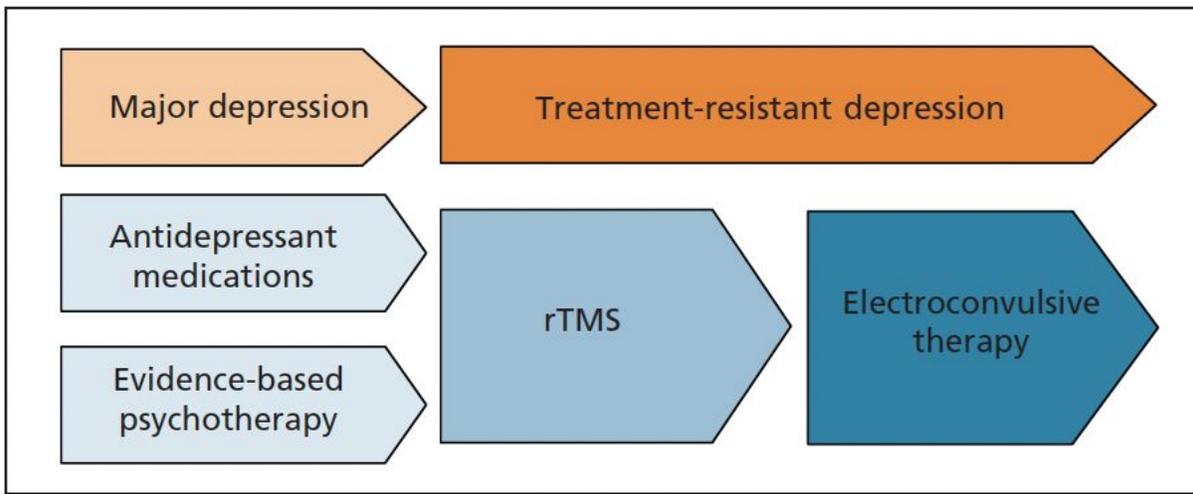
b TMS modulation



Current Clinical Use of rTMS in Psychiatry

- Most common and widespread use: MDD
- Regulatory approvals for MDD, MDD with anxiety, OCD, and smoking cessation
- Evidence for possible efficacy: schizophrenia (negative symptoms), PTSD, and bipolar depression





Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder

Introduction and Methods	506
<i>Raymond W. Lam, Sidney H. Kennedy, Sagar V. Parikh, Glenda M. MacQueen, Roumen V. Milev, Arun V. Ravindran, and the CANMAT Depression Work Group</i>	
Section 1. Disease Burden and Principles of Care	510
<i>Raymond W. Lam, Diane McIntosh, JianLi Wang, Murray W. Enns, Theo Kolivakis, Erin E. Michalak, Jitender Sareen, Wei-Yi Song, Sidney H. Kennedy, Glenda M. MacQueen, Roumen V. Milev, Sagar V. Parikh, Arun V. Ravindran, and the CANMAT Depression Work Group</i>	
Section 2. Psychological Treatments	524
<i>Sagar V. Parikh, Lena C. Quilty, Paula Ravitz, Michael Rosenbluth, Barbara Pavlova, Sophie Grigoriadis, Vytas Velyvis, Sidney H. Kennedy, Raymond W. Lam, Glenda M. MacQueen, Roumen V. Milev, Arun V. Ravindran, Rudolf Uher, and the CANMAT Depression Work Group</i>	
Section 3. Pharmacological Treatments	540
<i>Sidney H. Kennedy, Raymond W. Lam, Roger S. McIntyre, S. Valérie Tourjman, Venkat Bhat, Pierre Blier, Mehrul Hasnain, Fabrice Jollant, Anthony J. Levitt, Glenda M. MacQueen, Shane J. McInerney, Diane McIntosh, Roumen V. Milev, Daniel J. Müller, Sagar V. Parikh, Norma L. Pearson, Arun V. Ravindran, Rudolf Uher, and the CANMAT Depression Work Group</i>	
Section 4. Neurostimulation Treatments	561
<i>Roumen V. Milev, Peter Giacobbe, Sidney H. Kennedy, Daniel M. Blumberger, Zafiris J. Daskalakis, Jonathan Downar, Mandana Modirrousta, Simon Patry, Fidel Vila-Rodriguez, Raymond W. Lam, Glenda M. MacQueen, Sagar V. Parikh, Arun V. Ravindran, and the CANMAT Depression Work Group</i>	

rTMS for Addiction

Neuromodulation for Substance Use Disorders (SUDs)

2023 review and meta-analysis: 94 RCTs across rTMS, tDCS, and DBS

51 rTMS RCTs across, alcohol, tobacco, stimulants, cannabis, opioid use disorders

Most studies were in tobacco or alcohol – meta-analysis

ALCOHOL: Sig. reductions in craving and consumption used for multiple Tx, but not single Tx

TOBACCO: Sig. reductions in consumption for multiple Tx, but not effect on craving. No effect with single Tx.



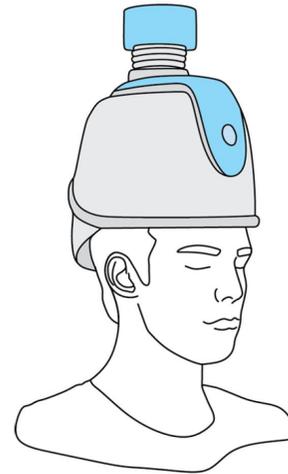
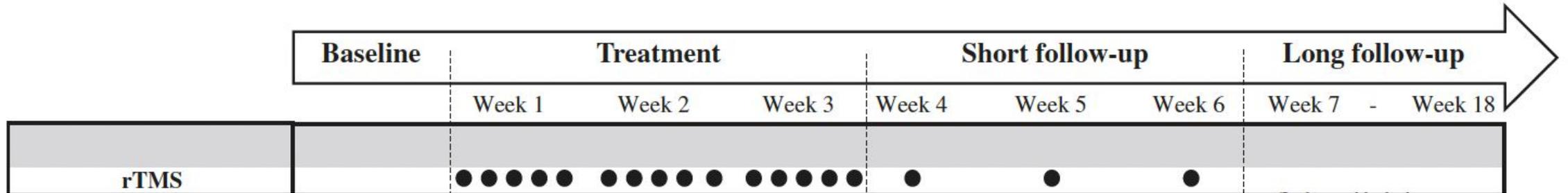
American College of
Neuropsychopharmacology

A systematic review and meta-analysis of neuromodulation therapies for substance use disorders

Dhvani D. Mehta^{1,2}, Angela Praecht^{1,2}, Heather B. Ward³, Marcos Sanches¹, Maryam Sorkhou^{1,2}, Victor M. Tang^{1,2},
Vaughn R. Steele⁴, Colleen A. Hanlon⁵ and Tony P. George^{1,2}

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Treatment Components



Deep TMS

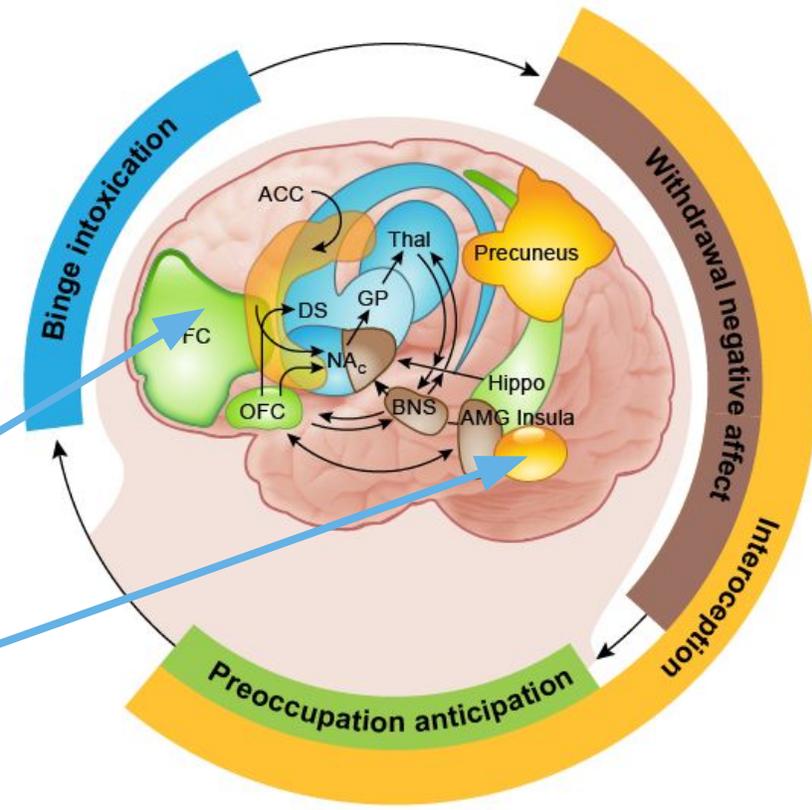
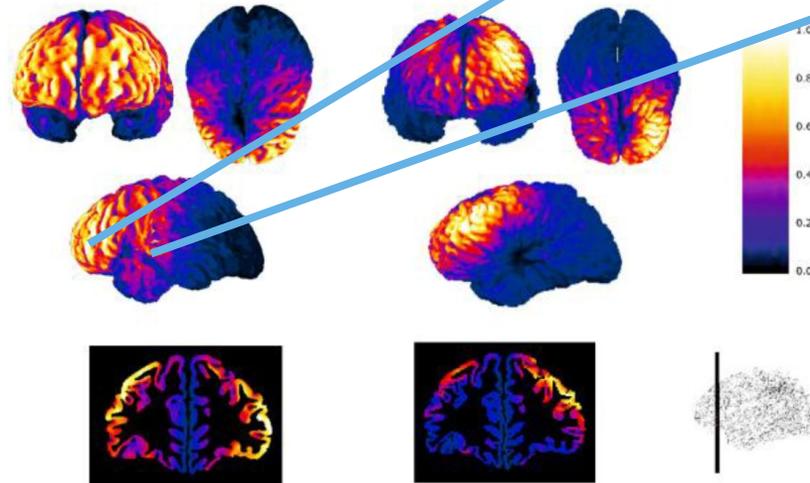
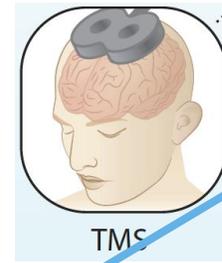
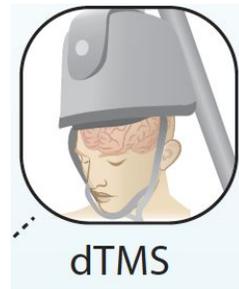
Each treatment includes:

- Smoking provocation
- TMS therapy for 18 minutes
- Brief counselling

Repetitive transcranial magnetic stimulation for smoking cessation

Christine Ibrahim PhD, Victor M. Tang MD MSc, Daniel M. Blumberger MD MSc, Bernard Le Foll MD PhD

Deep TMS (dTMS)



Identifying clinical predictors of response to repetitive transcranial magnetic stimulation for smoking cessation: Secondary analysis of a multicenter RCT

Victor M. Tang   • Laurie Zawertailo • Peter Selby • Abraham Zangen • Dhvani Mehta • Tony P. George • Bernard Le Foll • Kristina M. Gicas • Matthew E. Sloan • Scott Veldhuizen • [Show less](#)

V.M. Tang et al.

Table 1
Results of one-at-a-time interaction testing with logistic regression.

Interaction with treatment arm (active = 1, sham = 0)	OR	SE	z	p	L99 %	U99 %
Age ^a	0.39	0.43	-2.18	0.029	0.13	1.19
Sex (female = 1)	1.68	0.88	0.59	0.55	0.17	16.28
Lifetime quit attempts ^a	0.98	0.42	-0.04	0.97	0.33	2.89
Executive functioning ^{a,b}	1.16	0.42	0.36	0.72	0.39	3.46
Incentive salience ^{a,c}	2.41	0.43	2.06	0.04	0.80	7.24
Negative emotionality ^{a,d}	0.93	0.4	-0.17	0.87	0.34	2.61
FTND ^a	0.72	0.4	-0.82	0.41	0.26	2.01

Although results must be considered non-significant, suggestion that treatment effects were larger among younger people and those with higher levels of abnormal incentive salience for tobacco smoking, as characterized by a higher score on a composite of craving subscales.

COMBINATION WITH MEDICATIONS?



ELSEVIER

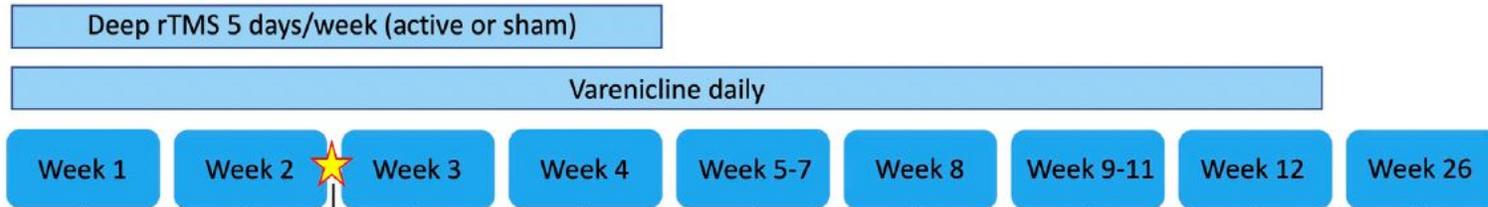
Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Brain Stimulation

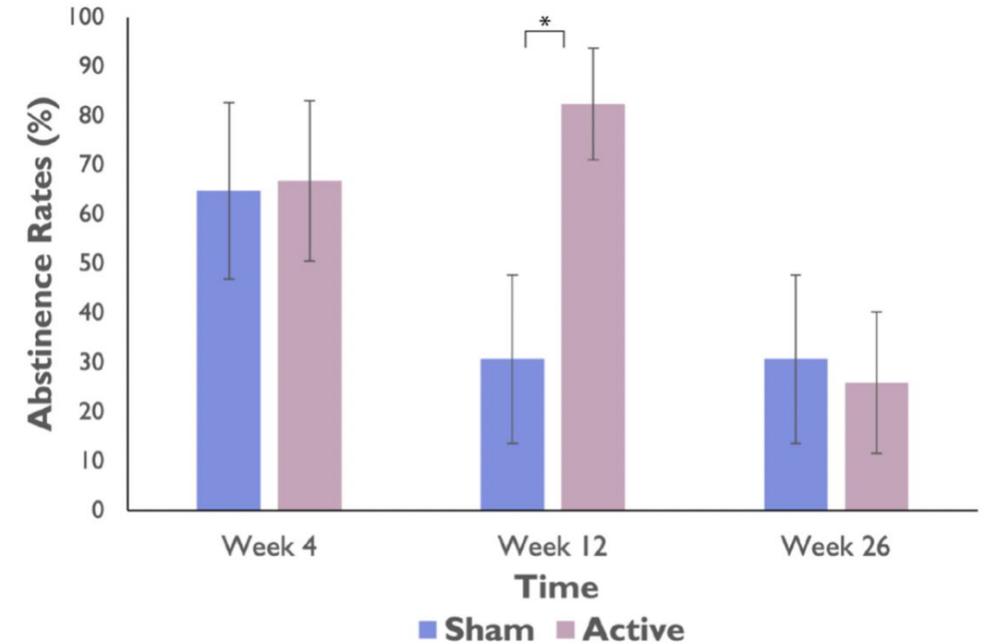
journal homepage: www.journals.elsevier.com/brain-stimulation

Efficacy of insula deep repetitive transcranial magnetic stimulation combined with varenicline for smoking cessation: A randomized, double-blind, sham controlled trial

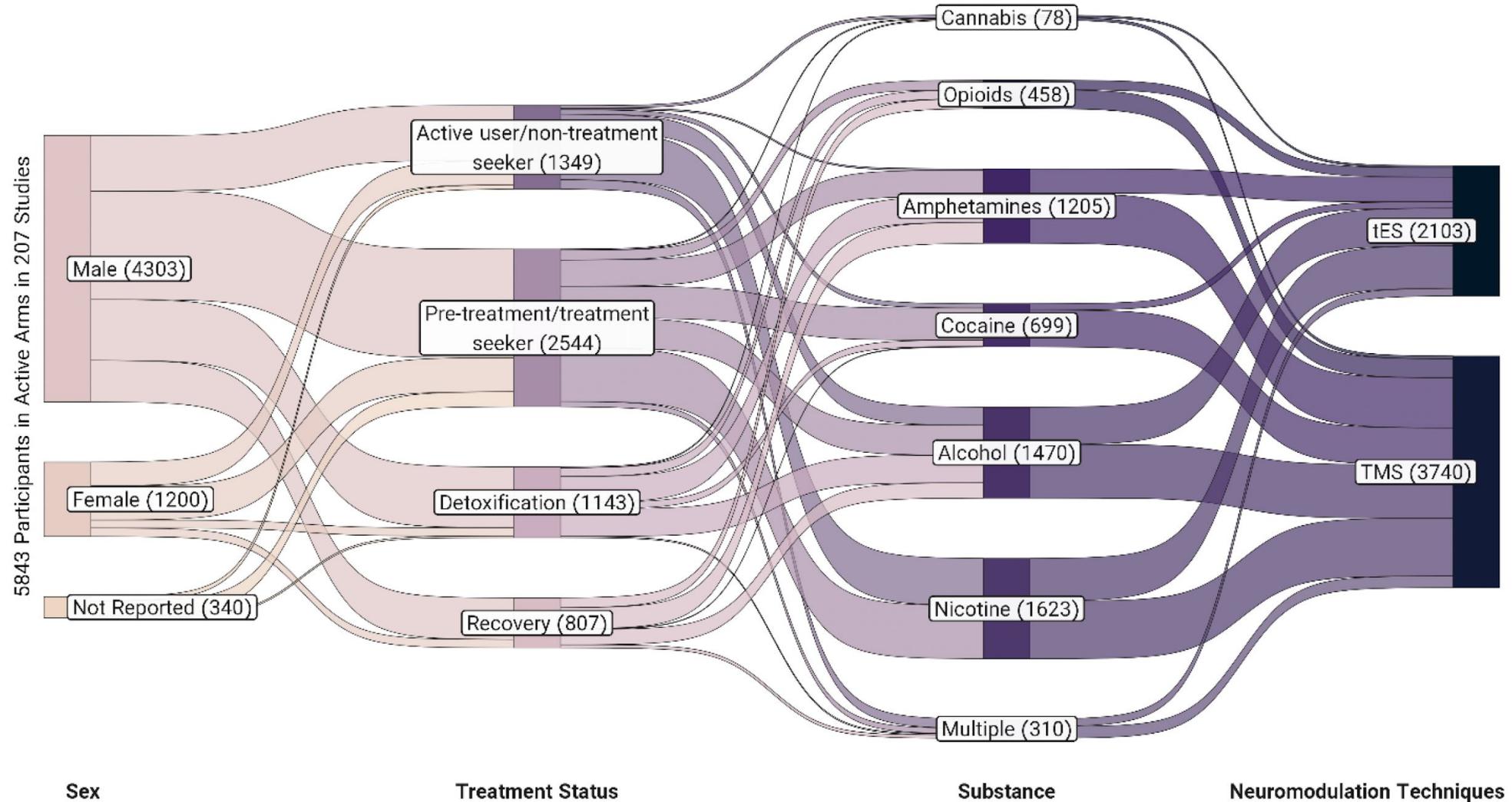
Christine Ibrahim^{a,b}, Victor M. Tang^{c,d,g,j,l}, Daniel M. Blumberger^{d,e}, Saima Malik^f, Rachel F. Tyndale^{b,d,g}, Alisson P. Trevizol^{d,e}, Mera S. Barr^d, Zafiris J. Daskalakis^h, Abraham Zangenⁱ, Bernard Le Foll^{a,b,c,d,g,j,k,l,m,n,*}



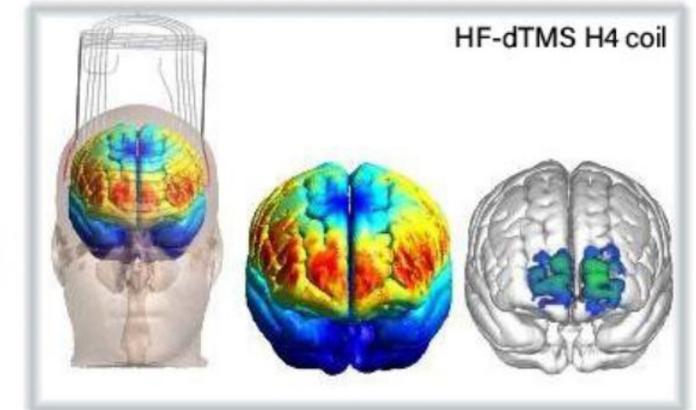
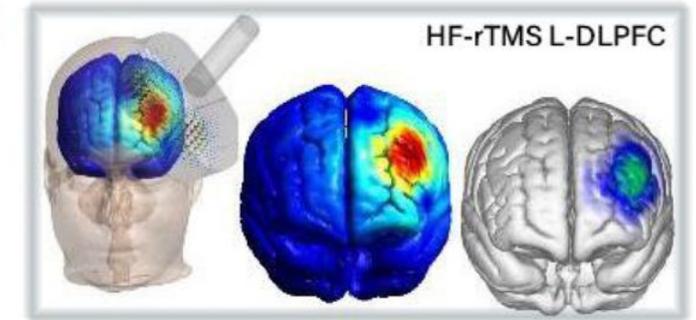
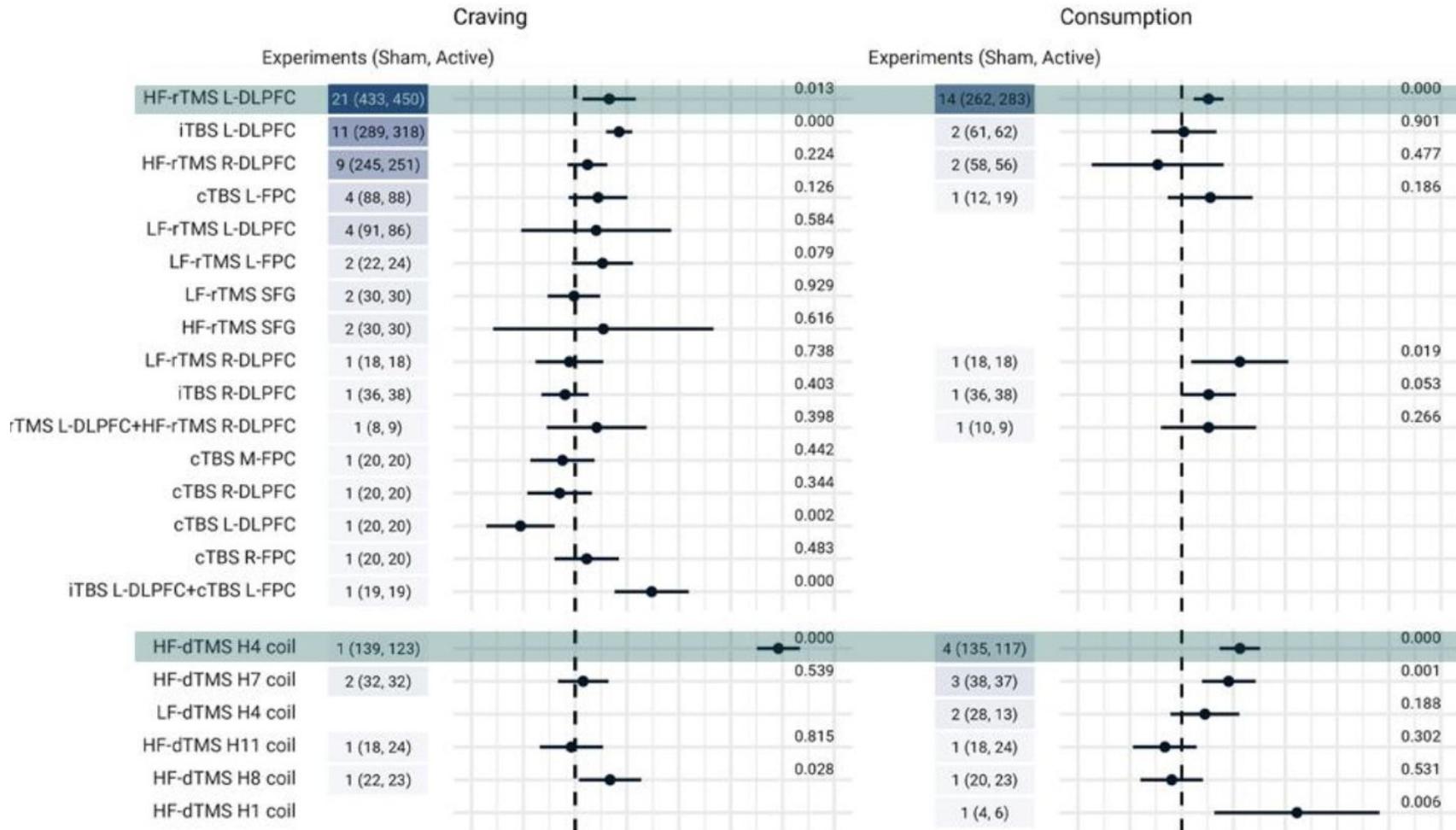
Brain Stimulation 16 (2023) 1501–1509



Types of Substance and Patients in rTMS trials



Types of rTMS – location and electric field



Cannabis Use Disorder

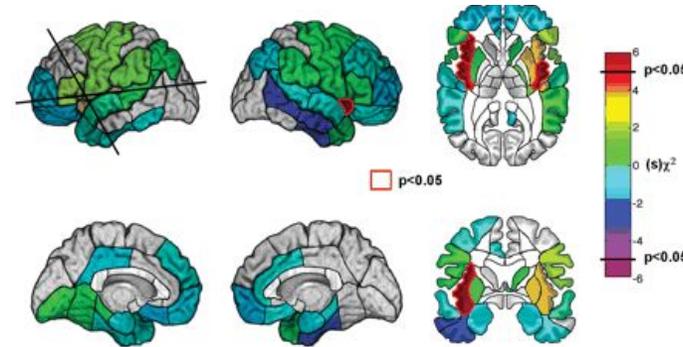


- 200 million cannabis users worldwide
- 33% develop cannabis use disorder
- Substantial health costs and clinical burden
- Negative effects on psychiatric disorders
- ***Despite this, effective treatments are limited***
- ***Least tested SUD with rTMS***

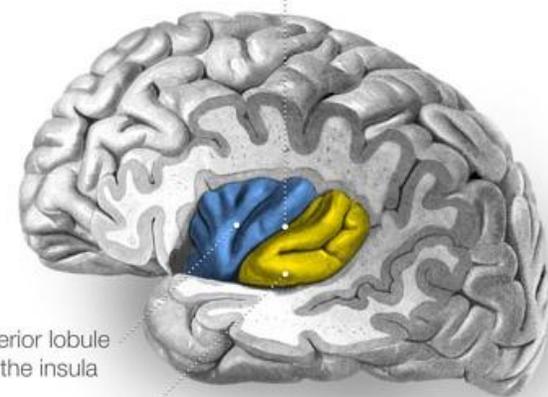
Developing an rTMS treatment for Cannabis Use Disorder: Targeting the Insula and Prefrontal Cortex

Damage to the Insula Disrupts Addiction to Cigarette Smoking

Nasir H. Naqvi,¹ David Rudrauf,^{1,2} Hanna Damasio,^{3,4} Antoine Bechara^{1,3,4*}

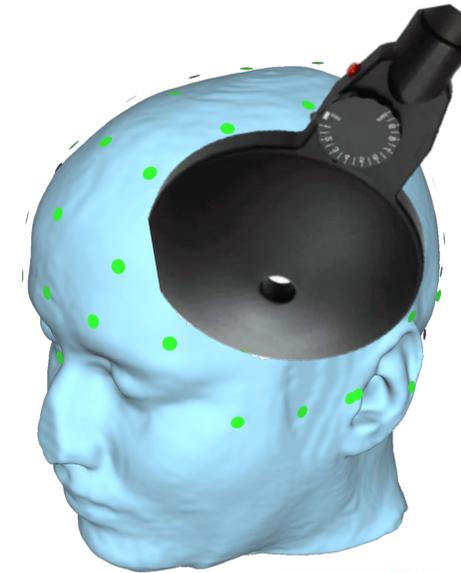
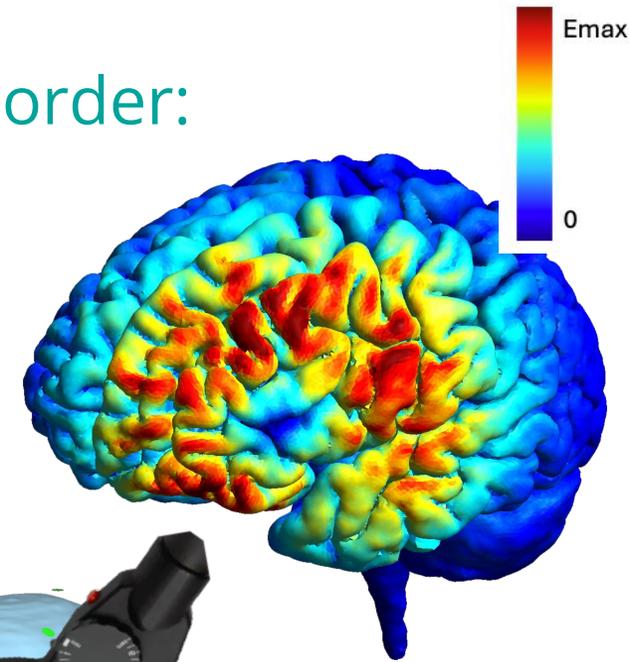


26 JANUARY 2007 VOL 315 SCIENCE www.sciencemag.org

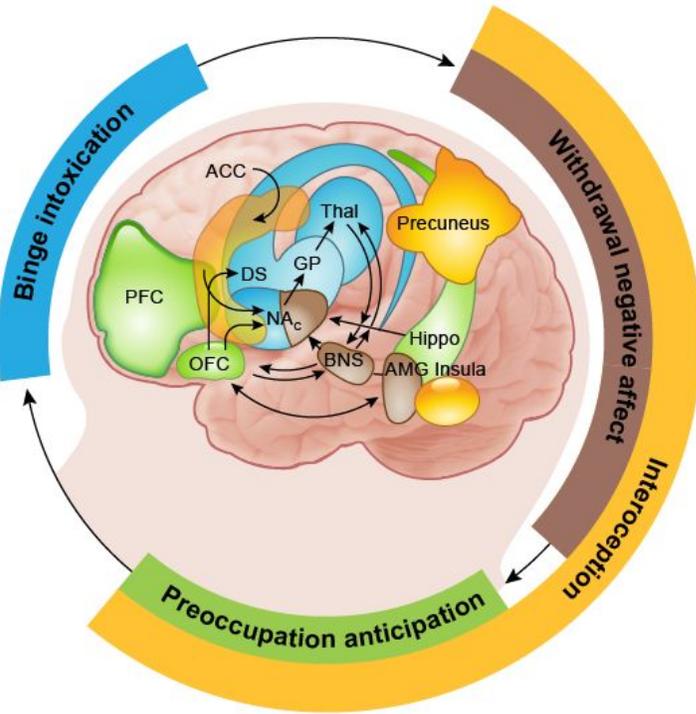


Anterior lobule of the insula

Posterior lobule of the insula



BRAIN & BEHAVIOR
RESEARCH FOUNDATION
Awarding **NARSAD** Grants



Developing an rTMS treatment for Cannabis Use Disorder: Targeting the Insula and Prefrontal Cortex



Pilot RCT:

To test the feasibility of treating CUD with the MMC-140 and comparing High vs. Low frequency stimulation.
20 once-daily treatment course

ClinicalTrials.Gov Registration: NCT05859347

Demonstrated safety, tolerability, and that low frequency may be superior

rTMS and Translation to the Frontline

Feasibility Challenges

- SUDs can be severe and destabilizing conditions. Associated with psychiatric, medical, social, financial, interpersonal instability.
- Infeasible protocols have been reported:
 - Tang (2025) - MDD + OUD difficulty with recruitment, completers 50%
 - Sahlem (2020) - cannabis use disorder difficulty with recruitment, completers 33%

European Psychiatry

www.cambridge.org/epa

Research Article

Cite this article: Tang VM, Le Foll B, Daskalakis ZJ, Wang A-L, Buckley L, Blumberger DM, Voineskos D (2025). Repetitive transcranial magnetic stimulation for the treatment of suicidality in opioid use disorder.

Repetitive transcranial magnetic stimulation for the treatment of suicidality in opioid use disorder: a pilot feasibility randomized controlled trial

Victor M. Tang^{1,2,3,4,5} , Bernard Le Foll^{1,2,3,4,5,6,7,8,9} , Zafiris J. Daskalakis¹⁰, An-Li Wang¹¹, Leslie Buckley^{2,4} , Daniel M. Blumberger^{1,2,5,12}  and Daphne Voineskos^{1,2,5,12,13} 

Can rTMS be practically implemented?

Implementation Challenge

Accessibility

Education and Acceptability

Real-world Clinical Considerations

Issues to resolve

- High operating costs (\$\$\$)
- Infrastructure and staffing
- Travel and distance for patients
- Education and awareness among clinicians
- Patient health literacy and stigma
- Comparative effectiveness
- Where in treatment algorithms?
- Comorbidities



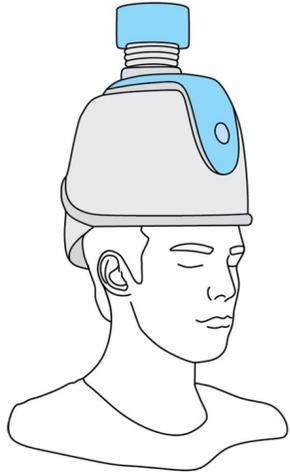
Psychiatry Research
Volume 326, August 2023, 115340



Tang VM, et al. (2023) *Psychiatry Research*

Developing an rTMS treatment for Cannabis Use Disorder: Ensuring scalability and practicality

H. Ekhtiari, et al.



Deep TMS



Awarding **NARSAD** Grants

Current approved
TMS coil –
expensive and
requires operator

MagVenture MMC-140

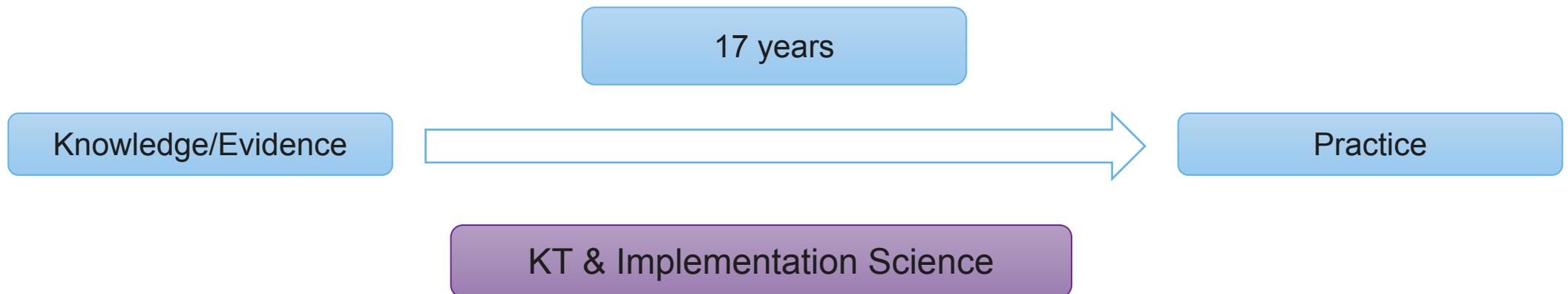
- Lowest cost FDA approved device
- Central opening to visualize and wide field of stimulation = reduced technician demand
- Low freq. stimulation can be used with low cost/portable stimulators

Can rTMS be practically implemented?

rTMS for MDD: Where are we now?

Research since 1980s, FDA approval in 2008

>23 RCTs in the field (Sehatzadeh et al., 2019)



A Mixed-Methods Evaluation of rTMS Implementation barriers and facilitators



Alexandra Sas
(MSc Graduate)

Read an
Infographic

Complete a
Survey

Optional Follow
up Interview

Are you trying to quit smoking? rTMS may help.

rTMS is:

- Repetitive Transcranial Magnetic Stimulation (rTMS).
- A **noninvasive and safe brain stimulation technique** used to treat mental health disorders and nicotine dependence.
- A coil placed above the scalp generates magnetic fields that temporarily modulate areas involved in addiction.

Dorsolateral Prefrontal Cortex
This area plays a role in your decision-making related to smoking. It is involved in controlling your smoking urges.

Insula
This area plays a role in craving cigarettes and in anticipating the rewarding feeling you have when smoking.



An rTMS session overview:

- Patients will be awake and resting in a sitting position during the entire session.
- This procedure does not require any anesthesia or invasive medical methods.
- The treatment is delivered by a trained rTMS technician, and there is doctor oversight in case of any complications.
- The treatment session should take about 20 minutes per day. There is only one session per day.

Who is eligible?

- Eligibility is determined after medical and psychiatric evaluation before starting rTMS treatment.
- Adults ages 18 - 70 years old
- No serious psychiatric disorder, substance use disorder, or seizure disorder that is currently unstable and makes it unsafe to receive rTMS
- No metal implants in the head
- Not pregnant or intending to become pregnant

rTMS Safety

- rTMS is Health Canada and Food and Drug Administration (FDA) Approved for smoking cessation and other conditions such as depression.
- The most possible side effects are headache and pain at the stimulation site, face and neck - which typically resolve once the session is over.
- The most serious adverse event is seizure, which occurs less than 0.01% of the time.

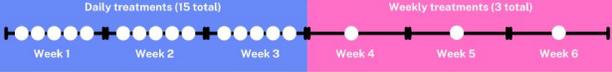
Where is rTMS Delivered?
The treatment does not require admission to a hospital and can be done on an outpatient basis in a clinic.

Click here for more information about rTMS and smoking cessation

At CAMH, rTMS is administered at The Temerty Center on the 2nd Floor of 1025 Queen St W

rTMS treatment regimen for smoking cessation

Daily treatments (15 total) | Weekly treatments (3 total)



Total of 18 sessions in 6 weeks - sessions are 20 minutes

What is the evidence to support rTMS for smoking cessation?

rTMS has been used in 2 clinical trials to treat nicotine dependence.

- Trials included smokers for whom medications were not effective in helping them quit
- Both studies observed decreased cigarette consumption and nicotine dependence at the end of treatment

Contact us:
rtms.smoking@camh.ca
416 - 535 - 8501 ext. 31551

Thank you for your interest in participating in our survey and interview study to help us learn about the feasibility of rTMS as a treatment for short-term smoking cessation.

1. Dioux-Klein L, Dawson P, Haber A, et al. Smoking cessation induced by deep repetitive transcranial magnetic stimulation of the prefrontal and insular cortices: a prospective, randomized controlled trial. *Biol Psychiatry*. 2014;76:743-9.
2. Zangen A, Moolish H, Martinez D, et al. Repetitive transcranial magnetic stimulation for smoking cessation: a pivotal multicenter double-blind randomized controlled trial. *World Psychiatry*. 2021;20:397-404.
3. Christine Ibrahim, Victor M. Tang, Daniel M. Blumberg, Bernard Le Fall. Repetitive transcranial magnetic stimulation for smoking cessation CMAJ Feb 2024; 196 (8): E187-E190. DOI: 10.1503/cmaj.202006

V 2 6/MAY/2024 REB #045/2024

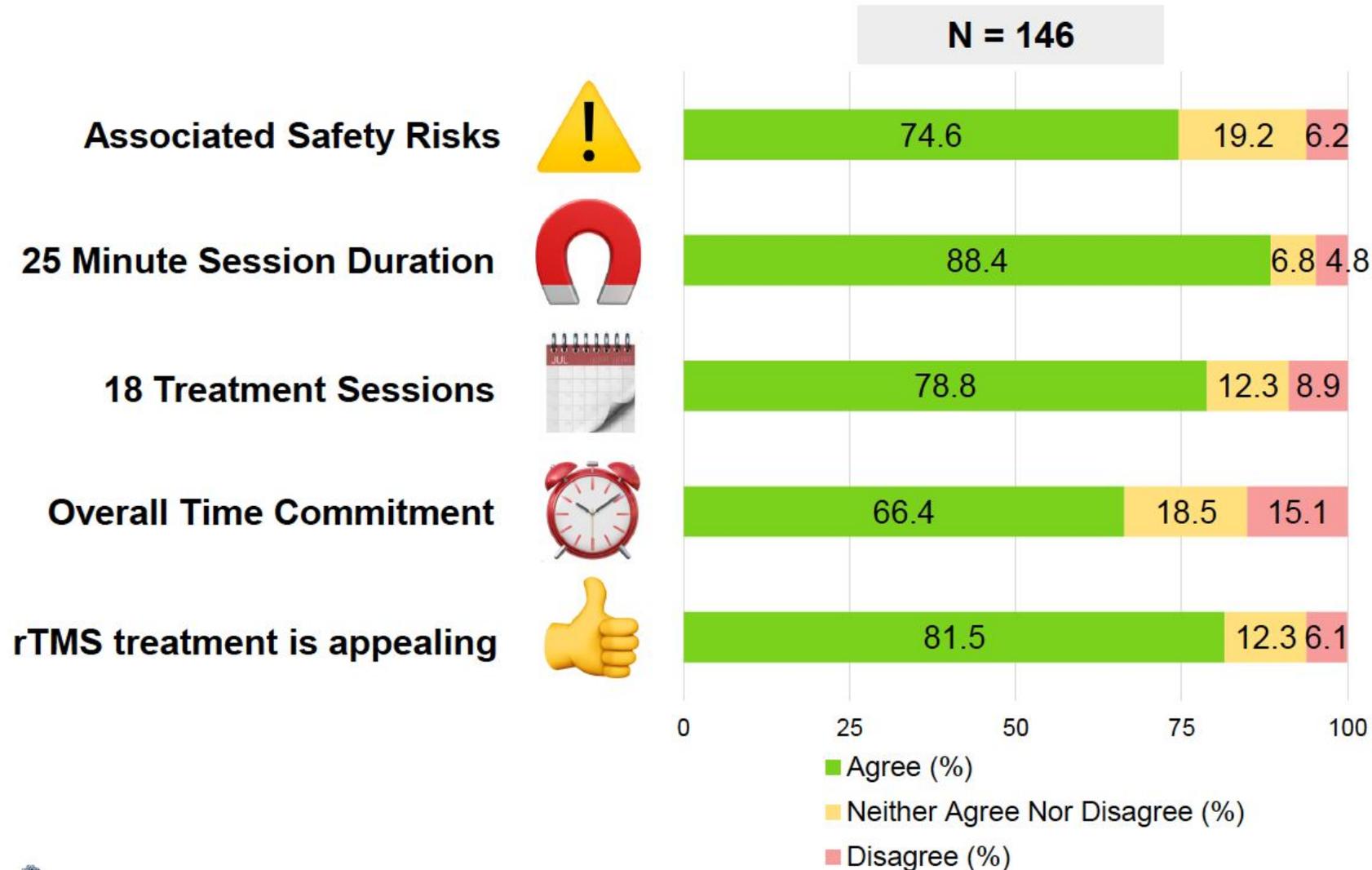
Treatment Seeking Individuals – Prior Knowledge

Survey Participants (n = 146)	
Prior knowledge of rTMS, neuromodulation, or brain stimulation for Smoking Cessation Before Reading the Infographic, n (%)	
Yes	39 (26.9%)
No	106 (73.1%)
Awareness of rTMS, neuromodulation, or brain stimulation for Mental Health Disorders Among Those Unaware of rTMS for Smoking Cessation, n (%)	
Yes	11 (10.7%)
No	92 (89.3%)

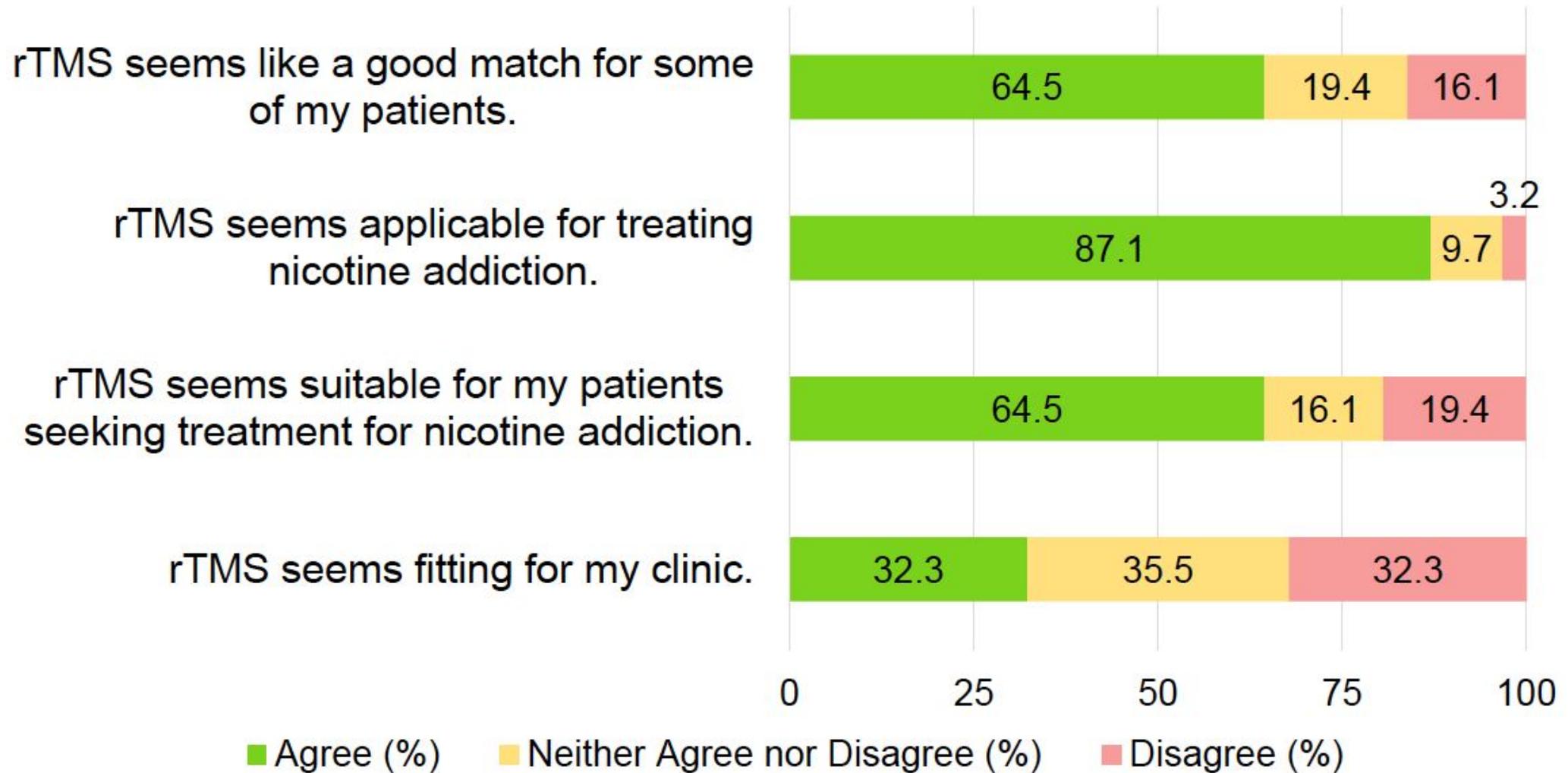
Acceptability of rTMS for Smoking Cessation



Alexandra Sas
(MSc Candidate)



HCP Intervention Appropriateness



Qualitative Themes from 20 Treatment Seeking Individuals

Alexandra Sas
(MSc Candidate)



Motivators for starting rTMS

Dissatisfaction with available treatments



Facilitators for starting rTMS

- Accessibility of rTMS treatment centre
- Flexible schedule



Barriers to starting rTMS

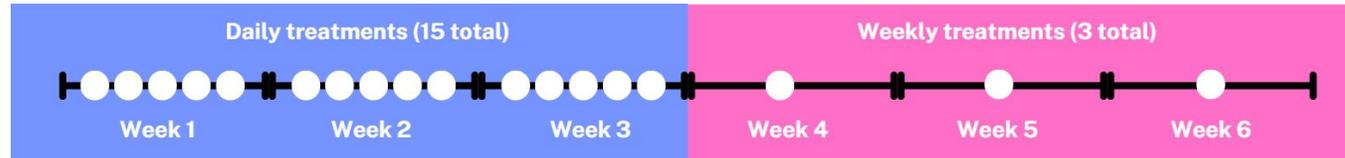
- Time commitment and transportation costs



“I’ve tried the nicotine replacement therapy from the inhaler to the gum, to the patches, to therapy to Champix, to Wellbutrin. ...

So basically, nothing ever worked completely. It would provide some relief, but never to a point – except for Champix, but Champix, you have to be on it for at least six months. And it was like I’m non-functional when I’m on the doses that would get me to quit.”

Scheduling



Standard: once daily acute treatment – spread out maintenance treatment

Day 1	Day 2	Day 3	Day 4	Day 5
iTBS 1800				
50 minute ISI				
iTBS 1800				
50 minute ISI				
iTBS 1800				
50 minute ISI				
iTBS 1800				
50 minute ISI				
iTBS 1800				
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iTBS 1800				
50 minute ISI				
iTBS 1800				
50 minute ISI				

Accelerated: multiple treatments per day, shorter course overall

Flexible: According to patient availability



Treatment Schedule

Feasibility - Setting Matters

- To reduce issues of drop out, safety concerns due to instability, unpredictable substance use status, etc., wrap-around clinical care matters.
- Treatment settings can range from inpatient to outpatient, range in intensity
- Also important to consider detoxification: most protocols or rTMS for SUD involve detoxification protocols before treatment start
- Our recent review found that many AUD studies, and most OUD and StUD rTMS studies were conducted in inpatient settings (Tang et al., 2023).

Treating Depression in Addiction Rehab Centers

Repetitive transcranial magnetic stimulation implementation within residential substance use disorder treatment centers for patients with comorbid depression

Mohammad Ali Shenasa ; Maryam Soltani; Victor Tang; Cory R. Weissman; Lawrence Gregory Appelbaum; Zafiris J. Daskalakis; Dhakshin Ramanathan

Summary of recommendations and conclusions

We suggest treating individuals with TRD admitted to residential SUD treatment centers.

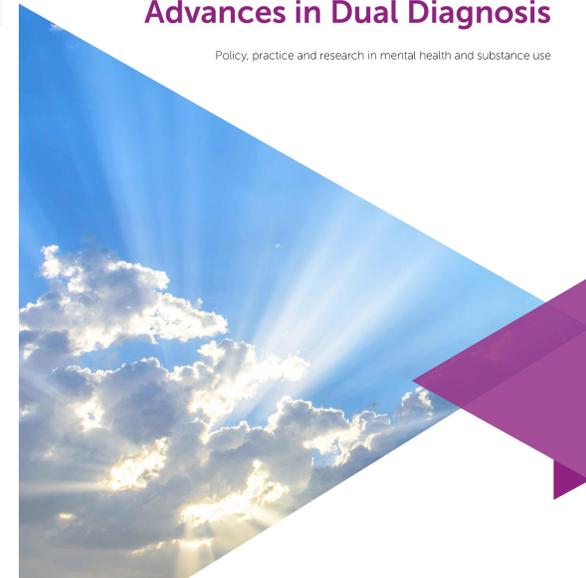
Implementing rTMS into residential substance use treatment centers for patients with comorbid TRD is a feasible and safe avenue to provide therapeutic benefit by improving depression while circumventing aspects of initiating rTMS that are burdensome to patients, thereby increasing access to care.



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Advances in Dual Diagnosis

Policy, practice and research in mental health and substance use



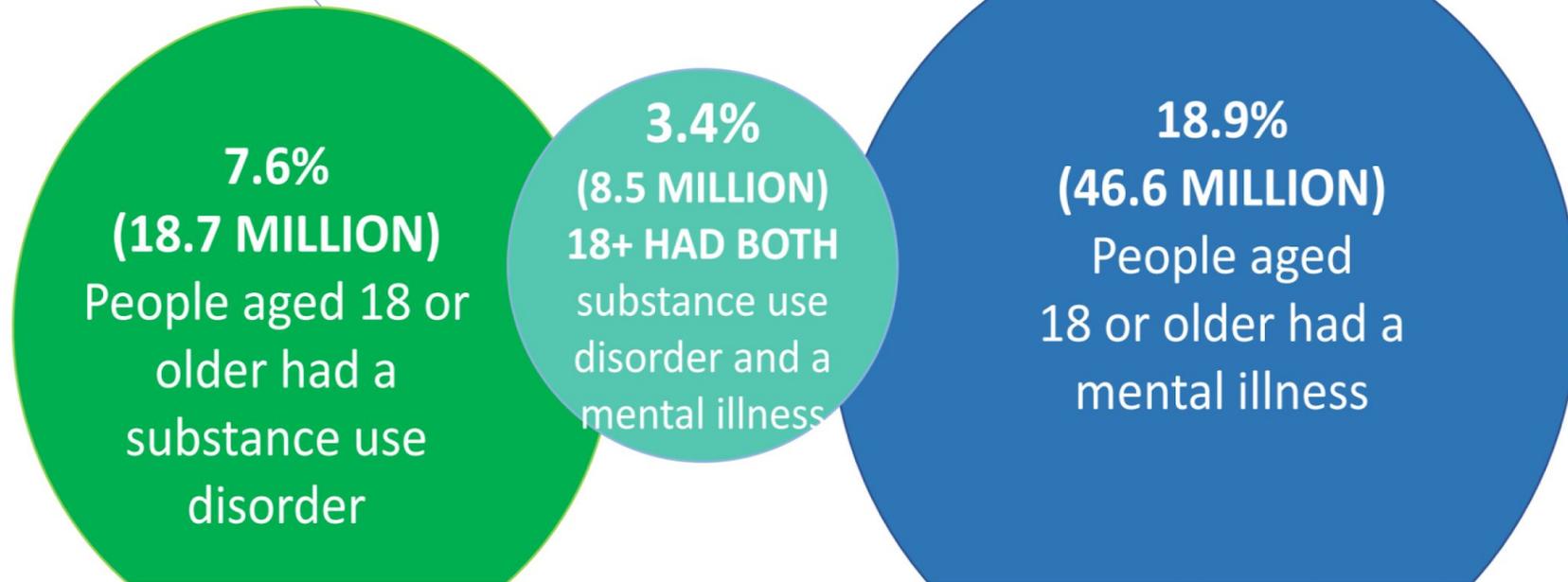
Comorbidity is the rule

Among those with a substance use disorder:

- **3 IN 8 (36.4%)** struggled with illicit drugs
- **3 IN 4 (75.2%)** struggled with alcohol use
- **1 IN 9 (11.5%)** struggled with illicit drugs and alcohol

Among those with a mental illness:

- **1 IN 4 (24.0%)** had a serious mental illness



Case Vignette 1: Mr. J.D. (part 1 of 3)

Mr. J.D. is a 45-year-old male with major depressive disorder (MDD), treated with multiple antidepressants, psychotherapies, but remains unwell.

Approximately 8 years ago, Mr. J.D. began consuming alcohol daily. He reports difficulty quitting due to cravings and insomnia.

He has been able to reduce his drinking behavior to 2-3 drinks per day while binge drinking every 2-3 months and reports total abstinence is a goal for him, but he has not been able to achieve it yet.

Mr. J.D. expresses interest in TMS for his depression



Substance Use is Common in Psychiatric Populations

- Currently, rTMS is used to target major depressive disorder, not most substance use disorders
- However, patients seeking psychiatric treatment will commonly present using substances
 - 40% with mental illness reporting past year illicit drug use; 29% past month binge alcohol (NSDUH 2021)
 - Can range from recreational, occasional, daily, or with addiction
- Substance use during rTMS can:
 - Increase risk of adverse events (e.g., seizures)
 - Interfere with mechanism of action (e.g., alter cortical excitability)
 - Obscure assessment of efficacy



rTMS Efficacy and Safety Questions

- Efficacy: Does rTMS work for depression when there is ongoing substance use?
- Mechanism: Does a psychoactive substance interfere with brain stimulation?
- Safety: headaches, dizziness..
- SEIZURES are rare but serious complication
- Substance use can increase seizure risk and affect seizure threshold

- Current rTMS guidelines too vague:
 - “Substances may be a risk factor...document substances used... and evaluate risks and benefits”¹
 - Substances be documented and “provide education on the effects of alcohol/substance use on rTMS”²

FULL ACCESS | Reviews and Overviews | Published Date: 19 March 2025

Assessment and Management of Concurrent Substance Use in Patients Receiving Repetitive Transcranial Magnetic Stimulation for Depressive, Obsessive-Compulsive, Psychotic, and Trauma-Related Disorders: A Delphi Consensus Study and Guideline

Victor M. Tang, M.D., M.Sc., Scott Aaronson, M.D., Mohamed Abdelghani, M.B.Ch.B., M.Sc., Chris Baeken, M.D., Ph.D., Tracy Barbour, M.D., André R. Brunoni, M.D., Ph.D., Samuel Bulteau, M.D., Ph.D., Linda L. Carpenter, M.D., Paul E. Croarkin, D.O., M.S. , Zafiris J. Daskalakis, M.D., Ph.D., Paul B. Fitzgerald, M.B.B.S., Ph.D., F. Andrew Kozel, M.D., M.S.C.R., Bernard Le Foll, M.D., Ph.D., Urvakhsh Meherwan Mehta, M.D., Ph.D., Yoshihiro Noda, M.D., Ph.D., Frank Padberg, M.D., Christian Plewnia, M.D., Hang Su, M.D., Ph.D., Philip van Eijndhoven, M.D., Ph.D., Eric van Exel, M.D., Ph.D., Iris van Oostrom, Ph.D., Fidel Vila-Rodriguez, M.D., Ph.D. , Daphne Voineskos, M.D., Ph.D., Saydra Wilson, M.D., and Daniel M. Blumberger, M.D., M.Sc.  [SHOW FEWER](#) | [AUTHORS](#)

Topics Covered Prospective Guideline for Clinical & Research

Assessment

- Substance related inclusion/exclusion
- Monitoring tools/tests
- Timeline/type of use

Management

- How to modify protocols
- When to withhold treatment
- Abstinence, reduction, intoxication, withdrawal

Substance Specific

- Focus: Alcohol, Cannabis, Stimulant, Opioid
- Medical/Legal Cannabis
- Prescribed Opioids

Organization

Recommendation “Boxes” for general recommendations, recommendations specific to alcohol, cannabis, stimulants, opioids (31 recommendation statements total)

BOX 1. Clinical practice recommendations for the general assessment and management of substance use during repetitive transcranial magnetic stimulation (rTMS) for depressive, obsessive-compulsive, psychotic, and trauma-related disorders

Efficacy Considerations

- 1.1. At the initial baseline screening visit, assessment of alcohol and substance use should include a clinical evaluation by a qualified member of the clinical team. An evidence-based screening tool for drug or alcohol use (e.g., AUDIT, NIDA screening tool) may be used to aid this evaluation.
- 1.2. Prior to each rTMS treatment, screening should be done for recent substance use, with a focus on specific substances of concern identified on the initial baseline evaluation.
- 1.3. Substance-related medical conditions should be considered exclusionary if they are persistent and the medical condition is neurological in nature.
- 1.4. The application of rTMS to treat substance-induced depressive, obsessive-compulsive, psychotic, or trauma-related disorders should prompt a risk-benefit discussion, as the evidence for efficacy of rTMS therapy is limited to situations where these disorders are independent and primary.

Safety Considerations

- 1.5. If a patient is identified as being intoxicated or in withdrawal from substance use, rTMS is contraindicated.
- 1.6. A history of substance-related seizures is a relative contraindication, but may be acceptable if the number of seizures is low, assuming any seizures are currently in full remission.

Efficacy and Safety Considerations

- 1.7. Recommending a reduction in substance use before the start of rTMS is not recommended. Patients should consider that sudden changes in substance use patterns can influence the efficacy of rTMS. The patient should be advised to avoid substance use, decrease, or discontinue substance use before receiving rTMS, and to report any substance use to the clinician. Patients should be placed on medication withdrawal monitoring during rTMS.

See the online supplement for research recommendations. AUDIT=Alcohol Use Disorders Identification Test; NIDA,

Research recommendations in the supplementary materials

Research Recommendations Supplement

BOX S1. Research recommendations for the general assessment and management of substance use during repetitive transcranial magnetic stimulation (rTMS) for depressive, obsessive-compulsive, psychotic, and trauma related disorders.

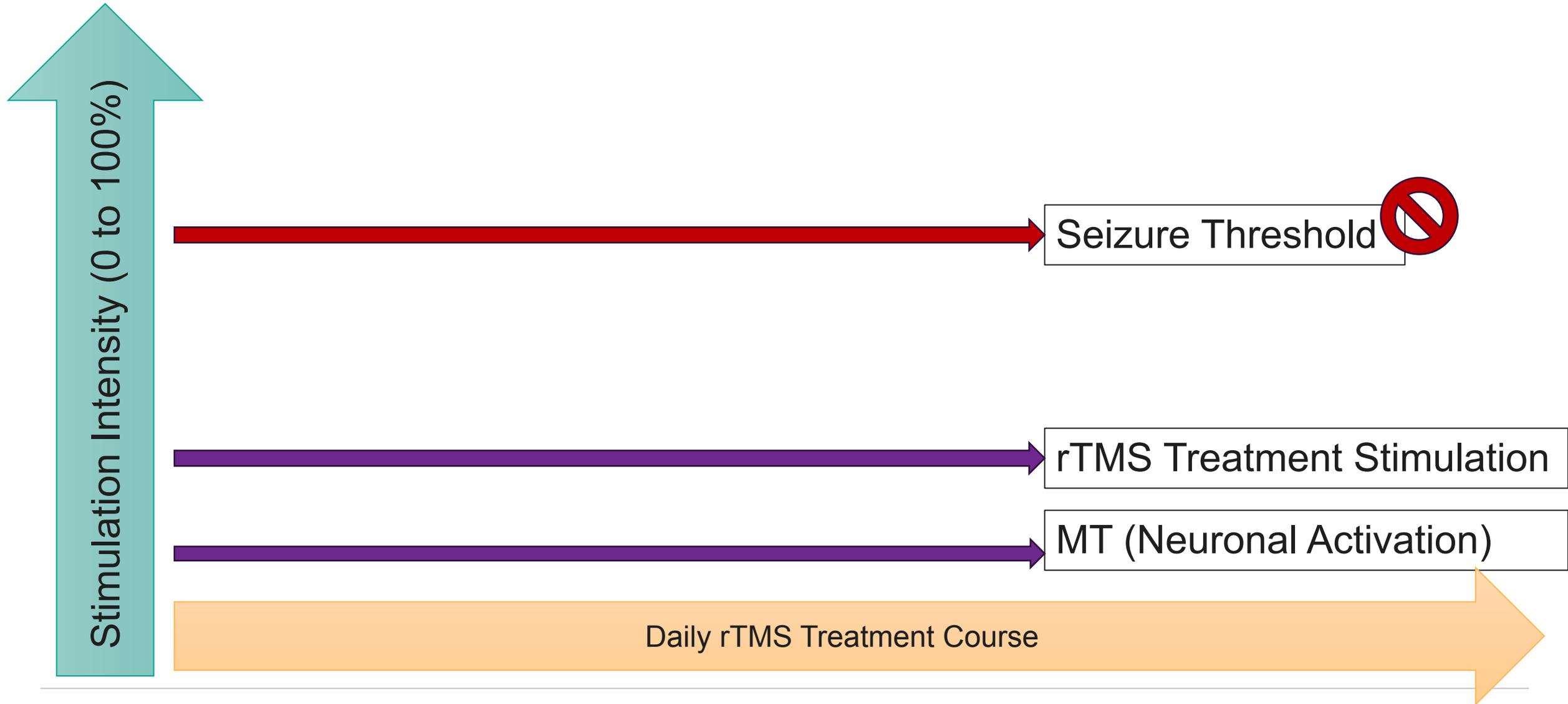
In a research context, follow the same clinical recommendations described in 1.2, 1.5, 1.6, 1.7 as per Box 1.
Efficacy Considerations
S1.1 At the initial baseline screening visit, assessment of alcohol and substance use should include a clinical evaluation by a qualified member of the clinical team. Adding one or more validated substance use screening tools (e.g., AUDIT, SCID, MINI, or other NIDA screening tool) or lab tests of substance use (e.g., urine drug screen) to the clinical assessment is also recommended.
S1.2 A primary diagnosis of substance-induced psychiatric disorder should be ruled out when a participant is being considered for recruitment to a rTMS treatment trial for a primary depressive, obsessive-compulsive, psychotic, or trauma-related disorder.
Safety Considerations
S1.3 Presence of alcohol- or substance-related medical conditions should be considered contraindications, and such cases should be excluded from participation in rTMS studies.

AUDIT, Alcohol Use Disorders Identification Test; MINI, Mini International Neuropsychiatric Interview; NIDA, National Institutes on Drug Abuse; rTMS, repetitive Transcranial Magnetic Stimulation; SCID, Structured Clinical Interview for DSM.

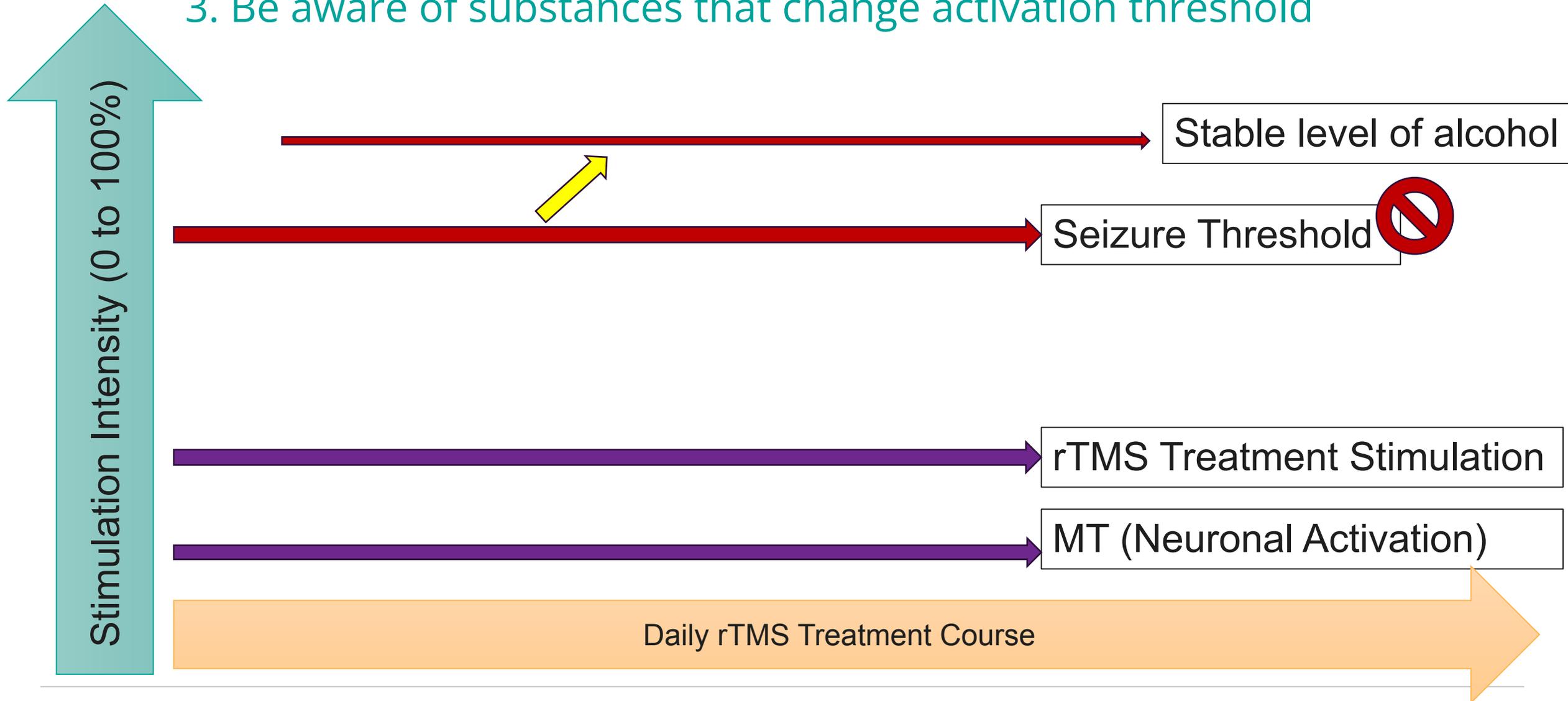
General Themes with Substance Use Assessment/Management

- Recommend the use of a standardized clinical tool (no consensus on the best one) and lab/drug tests only when clinically indicated.
- Abstinence or reduction of recreational substance use may a good overall recommendation or health, but abrupt or big changes to the baseline pattern of substance use are risky.
- Do not categorically exclude all substance users: No specific cut-off number for frequency or amount. Decide based on risk of clinical instability, severity, and safety/seizure risk.
- Less certainty with unregulated drugs, or non-oral routes (e.g., injection)
- Comorbid ADDICTION (substance use disorders): Lack of evidence, outside the scope of this guideline, encourage emerging research efforts, risk/benefit analysis, and certain (i.e., mild-moderate) conditions may favor proceeding with treatment

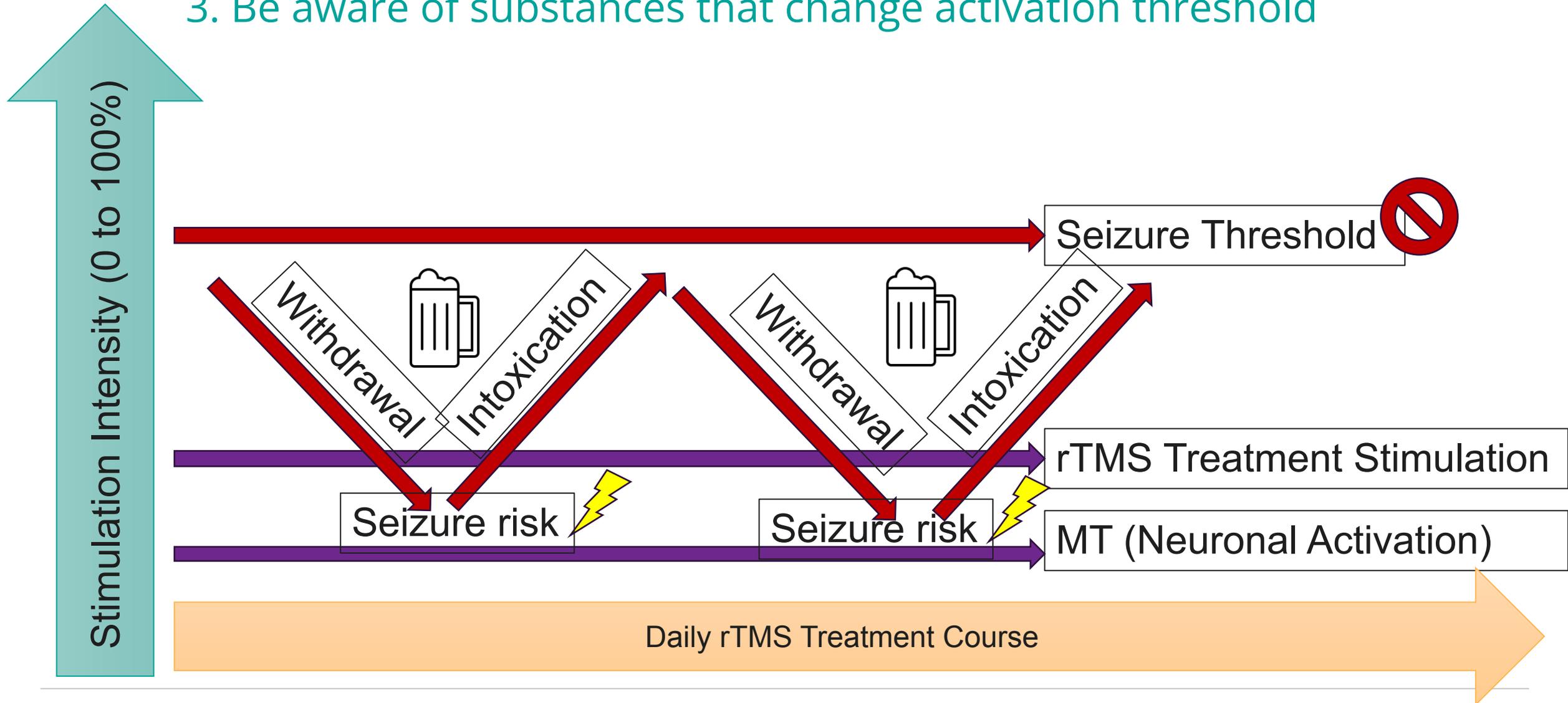
Conceptualizing Efficacy and Risk with rTMS



1. Highest risk is in unstable and unpredictable use patterns
2. Risk state is in intoxication and withdrawal syndromes
3. Be aware of substances that change activation threshold



1. Highest risk is in unstable and unpredictable use patterns
2. Risk state is in intoxication and withdrawal syndromes
3. Be aware of substances that change activation threshold



rTMS for comorbid MDD + SUD Trials

- In general, the literature is limited, and study designs are limited
- Only a handful of trials pertaining to depression + alcohol, nicotine + alcohol

Neuroscience and Biobehavioral Reviews 155 (2023) 105477



Contents lists available at [ScienceDirect](#)

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev



Review article

Managing substance use in patients receiving therapeutic repetitive transcranial magnetic stimulation: A scoping review

Victor M. Tang^{a,b,c,d,e,*}, Christine Ibrahim^{a,b}, Terri Rodak^f, Rachel Goud^a, Daniel M. Blumberger^{b,c,d,g}, Daphne Voineskos^{b,c,d,g,h}, Bernard Le Foll^{a,b,c,d,e}

Current Addiction Reports (2024) 11:342–351

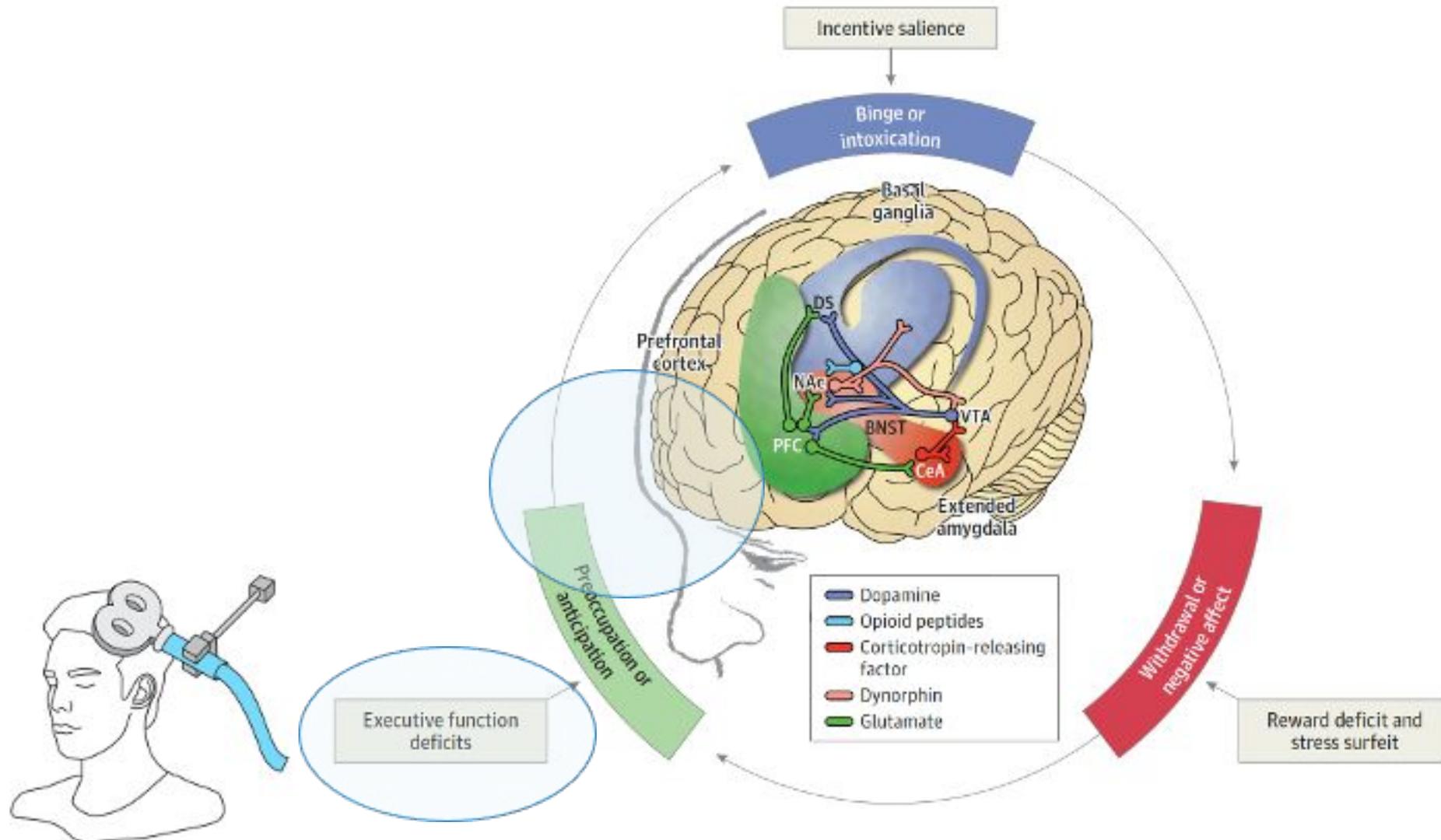
<https://doi.org/10.1007/s40429-024-00542-6>



rTMS for Co-occurring Psychiatric and Substance Use Disorders: Narrative Review and Future Directions

Sophia H. Blyth¹ · Nicole L. Zabik² · Amanda Krosche¹ · James J. Prisciandaro³ · Heather Burrell Ward¹

Can rTMS target overlapping symptom construct/brain circuit in comorbidity?



MDD and Alcohol Use Disorder



Review

Repetitive Transcranial Magnetic Stimulation for Comorbid Major Depressive Disorder and Alcohol Use Disorder

Victor M. Tang ^{1,2,3,*}, Bernard Le Foll ^{2,3,4,5,6,7}, Daniel M. Blumberger ^{1,3,4,5} and Daphne Voineskos ^{1,3,4,5}

Table 2. Selected literature of converging directions for repetitive transcranial magnetic stimulation (rTMS) in major depressive disorder (MDD) and alcohol use disorder (AUD).

	MDD	AUD
rTMS Site/Frequency	HF Left DLPFC [15,30,40] LF Right DLPFC [15,30,40] HF Bilateral PFC ¹ [15,30,40]	HF Right DLPFC [51,56,57] HF Bilateral PFC [62–65,70]
rTMS Coil	Figure-of-8 [15,30,40] Deep TMS [15,30,40]	Figure-of-8 [51,56,57,61] Deep TMS [62–65,70]
Adequate No. of Sessions	20–30 [15,30,40]	≥15 [56,63,64]
Transdiagnostic Symptom Construct	Executive function [77,78]	Executive function [53,60] Craving [74]
Optimization Protocols	Neuroimaging-guided targeting: anatomical (DLPFC) [79] and functional DLPFC to ACC [80,81] Accelerated rTMS [48]	Individualized effects on neuroimaging: ACC and reward circuit [57,66,67] Accelerated rTMS [56,57,82]

HF, high frequency; LF, low frequency; DLPFC, dorsolateral prefrontal cortex; PFC, prefrontal cortex; ACC, anterior cingulate cortex. ¹ Using deep TMS coils, targets DLPFC but extends broadly across the PFC, including deeper structures below the PFC.

rTMS for Psychiatric SYMPTOMS and SUD

See comprehensive review on changes in all different types of psychiatric symptoms in Tang et al. (2023) Neuroscience and Biobehavioral Reviews

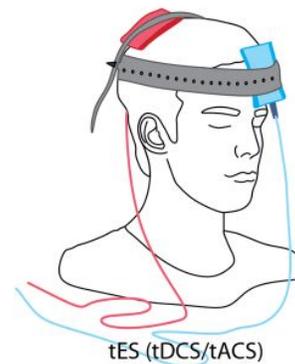
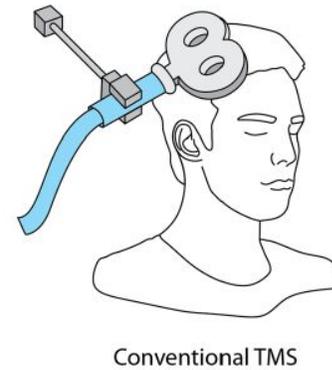
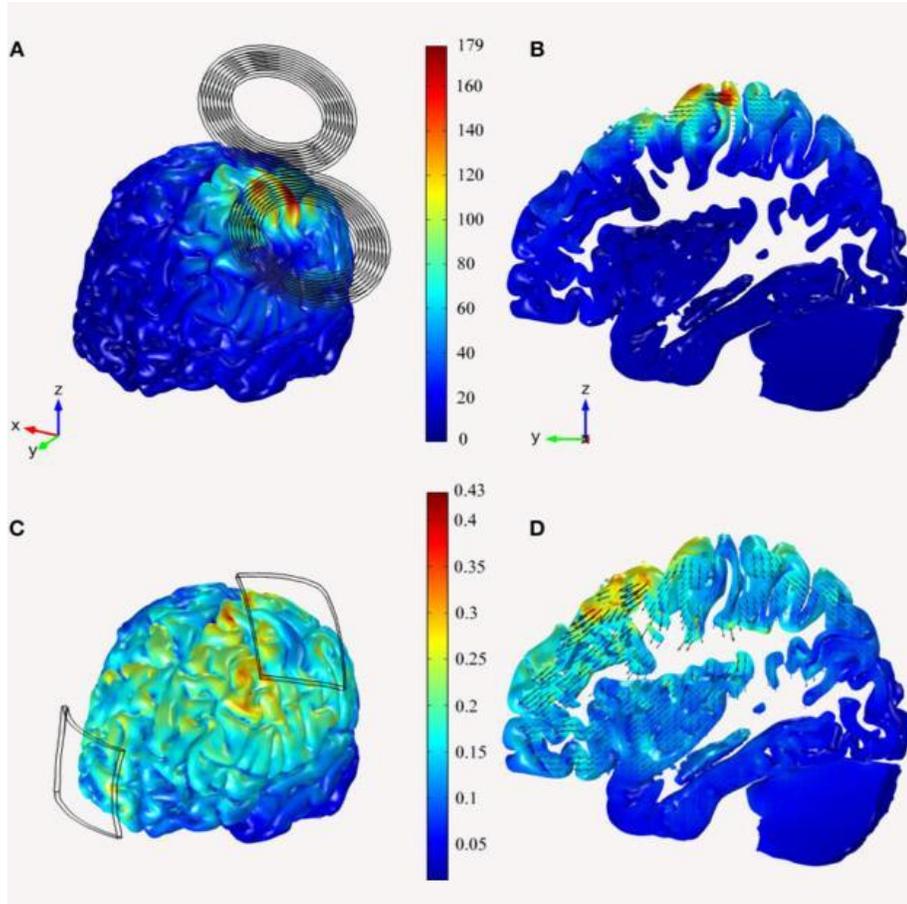
- Most studies show improvement in mood and anxiety symptoms even in the absence of a diagnosis of primary MDD
- Ambiguous whether they are substance induced symptoms or not
- Shows that morbidity and symptomatology improvements can be noticed in patients regardless of what the comorbidities are

Real-world naturalistic studies

Recreational Cannabis use during rTMS for depression

Other Neuromodulation Modalities

Transcranial Direct Current Stimulation



Applying a low-intensity electrical current through electrodes on the scalp.

Modulates cortical excitability by shifting threshold of membrane potential.

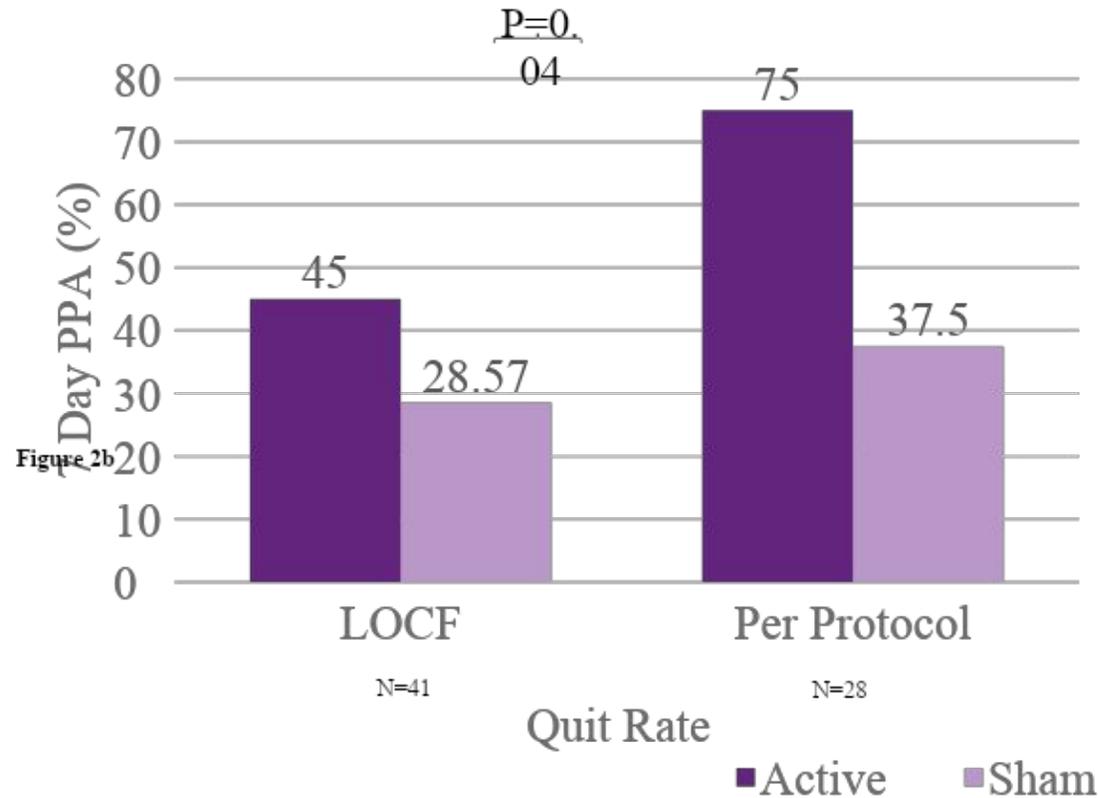
Anodal electrode increases excitability and cathode decreases.

Mild stimulation and minimal side effects.

tDCS vs. sham as an adjunct to varenicline for smoking cessation

Active tDCS was associated with higher continuous abstinence (69%), compared to sham (38%), but this was ultimately not significant ($p=0.12$).

For 7 Day PPA, tDCS was associated with significantly higher quit rates than sham ($p=0.04$).



LOCF= last observation carried forward, **Per protocol** = included all those that completed treatment

Currently Ongoing: A follow up larger RCT using an at-home tDCS protocol

- Unlike other brain stimulation modalities, tDCS is more portable
- Can increase accessibility and reach underserved communities
- Efficacy has been demonstrated in a number of studies in other conditions – including recent FDA approval of an at-home tDCS device for depression!
- We are now conducting a clinical trial of remotely delivered at-home tDCS for the treatment of smoking cessation
- **ClinicalTrials.gov ID** NCT06798324



Dr. Laurie Zawertailo

Deep Brain Stimulation for Refractory OUD

Deep Brain Stimulation: A Neurosurgical Procedure

- Place electrodes in brain circuit
- Standard of care in Parkinson's, essential tremor dystonia
- Can reach deeper targets in the reward circuit –
 - > Nucleus Accumbens and Anterior Limb of the Internal Capsule

The Canadian Journal of Neurological Sciences (2025), 1–4
doi:10.1017/cjn.2025.12



Letter to the Editor: New Observation

Deep Brain Stimulation for Substance Use Disorder: Case Report of Fentanyl Use Disorder and Review of the Literature

Andrew Z. Yang^{1,2,3}, James MacKillop^{3,4,5}, Alexandre Boutet^{6,7} , Anton Fomenko¹, Artur Vetkas¹, Matthew E. Sloan^{2,8,9,10,11,12,13}, Can Sarica¹ , Brendan Santyr¹ , Dana Abdel Hafeez¹⁴, Sharmane Villafuerte¹, Jürgen Germann^{1,7,15}, Ivan Skelin¹⁵, Luka Milosevic^{7,15,16,17,18} , Benjamin Davidson^{1,19,20}, Suneil K. Kalia^{1,7,15,18}, Taufik A. Valiante^{1,7,12,15,16,18,21} , Andres M. Lozano^{1,7,12,15,18} and Victor M. Tang^{2,8,10,12,13} 

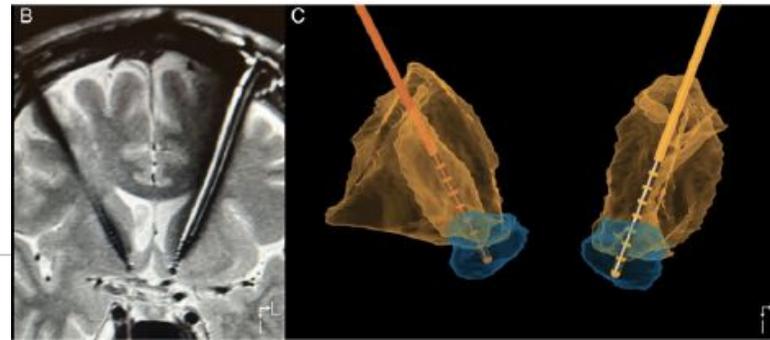


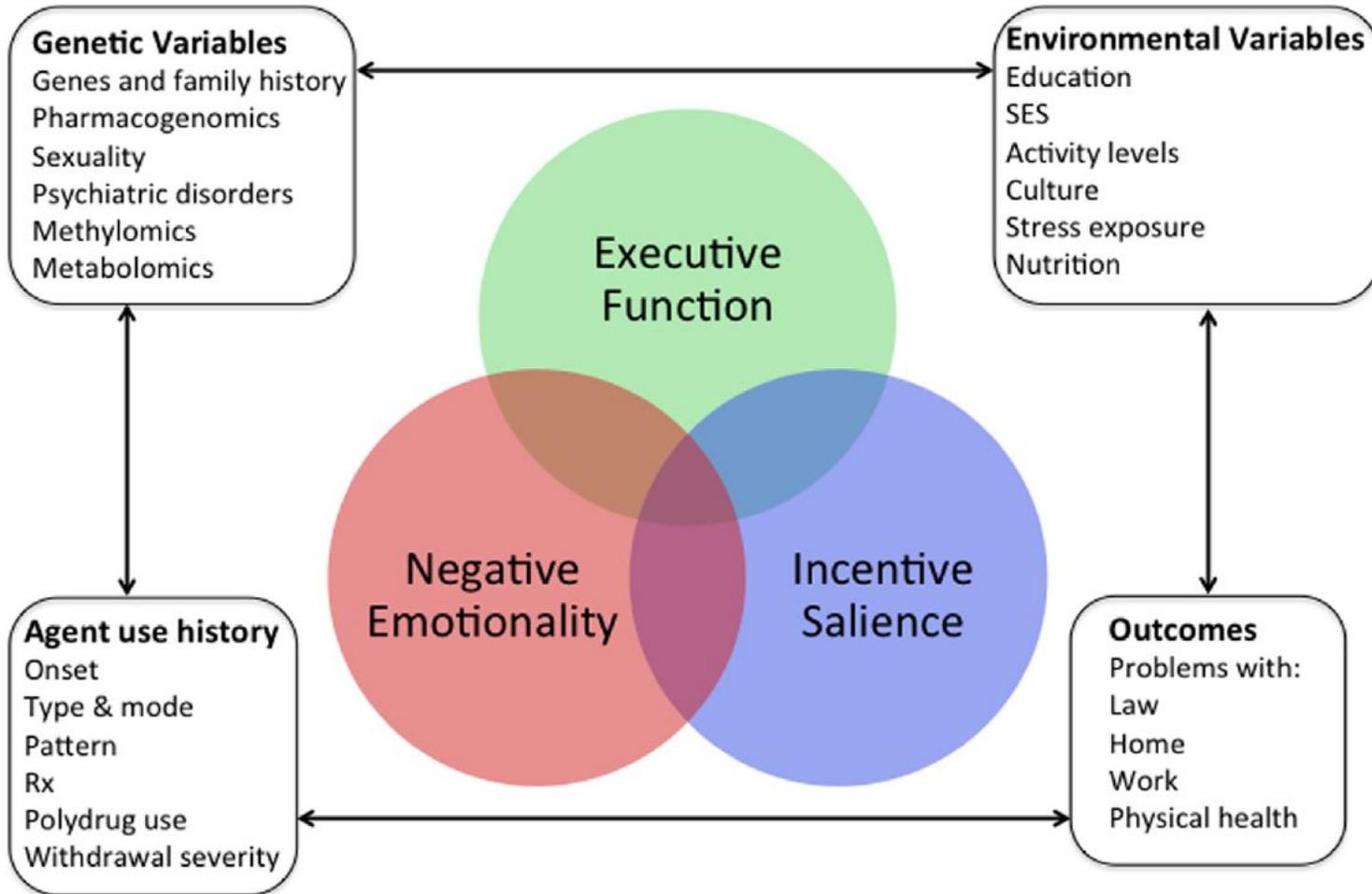
Table 1. Summary of literature review of deep brain stimulation for substance use disorder

OVERVIEW	Studies	<i>k</i> = 29
	Participants	<i>n</i> = 101
DEMOGRAPHICS	Sex	93 male and 8 female
	Mean Age	41.5 ± 8.2 years
INDICATION	Opioids	<i>k</i> = 12
	Alcohol	<i>k</i> = 10
	Stimulants	<i>k</i> = 3
	Nicotine	<i>k</i> = 3
	Dopaminergic medication	<i>k</i> = 1
TARGET	NAc	<i>k</i> = 18
	NAc/ALIC	<i>k</i> = 6
	VC/VS	<i>k</i> = 4
	STN	<i>k</i> = 2
OUTCOME	Unique participants	<i>n</i> = 65
	Mean follow-up	26.1±16.1 months
	Abstinence at longest follow-up	<i>n</i> = 20/58 (34.5%)
	> 50% substance reduction	<i>n</i> = 35/59 (59.3%)
	> 50% craving reduction	<i>n</i> = 34/46 (73.9%)
ADVERSE	No complications	<i>k</i> = 15/29 (51.7%)
EVENTS	Hypomania	<i>n</i> = 7
	Headache	<i>n</i> = 5
	Insomnia	<i>n</i> = 3
	Electrode dislocation	<i>n</i> = 3

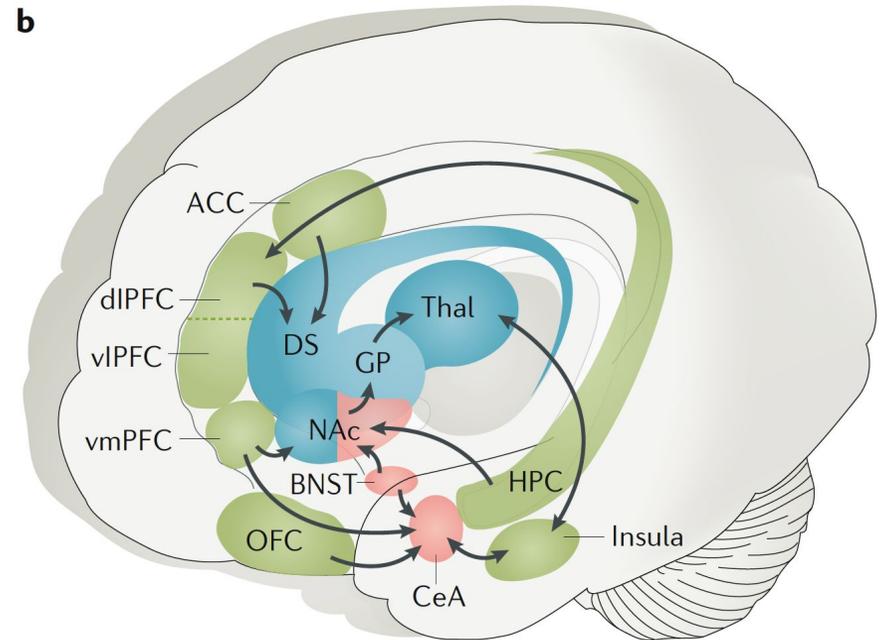
ALIC = anterior limb of the internal capsule; *k* = studies; *n* = participants; NAc = nucleus accumbens; STN = subthalamic nucleus; VC = ventral capsule; VS = ventral striatum.

Advancing Brain & Behavior Assessments in Addiction

The Addictions Neuroclinical Assessment (ANA)



b



The Addictions Neuroclinical Assessment (ANA)

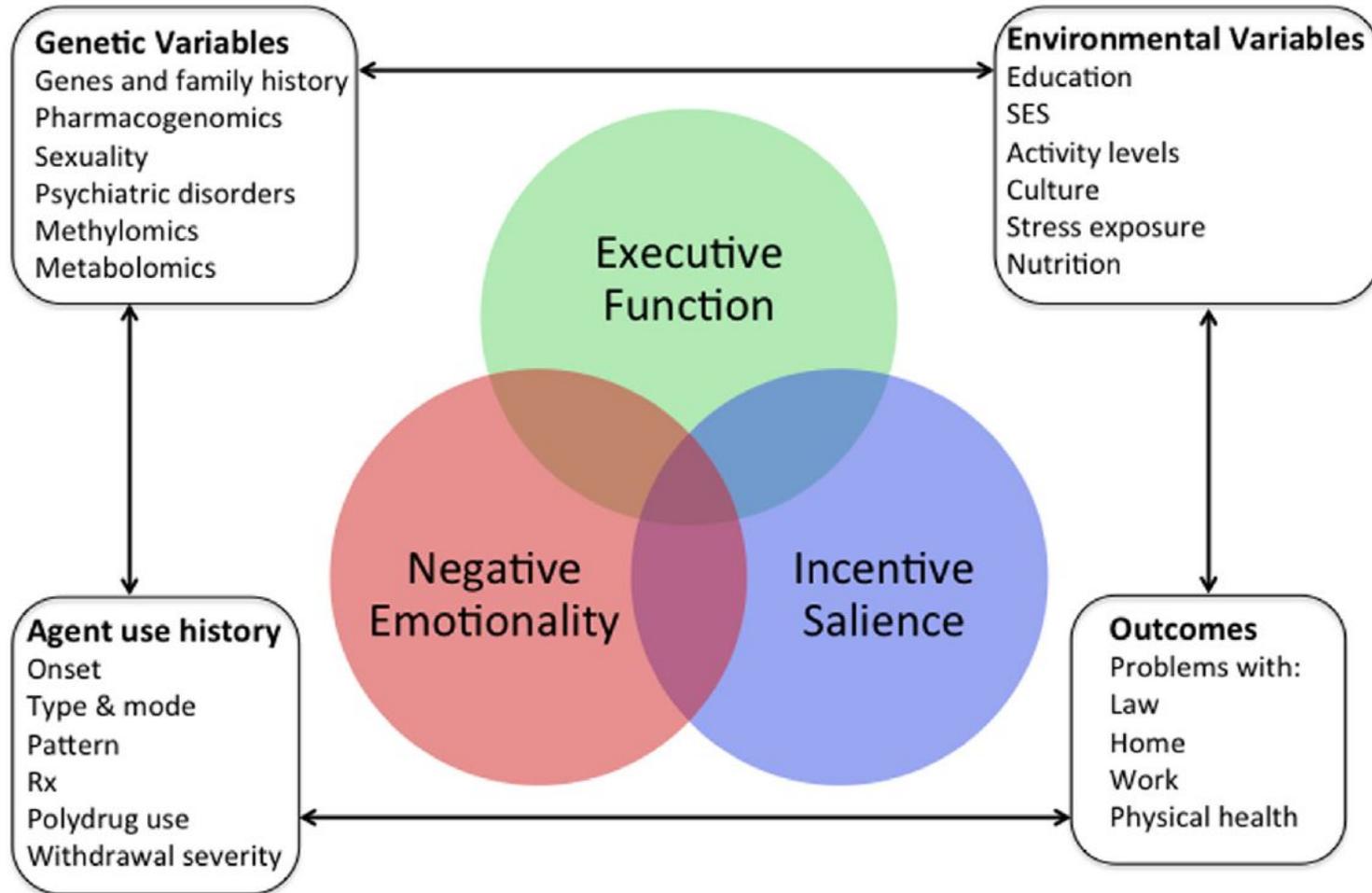


Table 2. Proposed Measures for ANA

Measure
Executive Function
Stop Signal Reaction Task (123)
Appetitive Go-NoGo (124)
Continuous Performance Test (125)
Tower of London (126)
Wisconsin Card Sorting Test (127)
Delay Discounting (128)
N-Back (129)
Beads in a Jar Task (130)
Barratt Impulsiveness Scale (131)
Negative Emotionality
Approach Avoidance Task (132)
Cyberball (133)
Trier Social Stress Test (134)
Cold Pressor Task (135)
Digit Span (136)
Two-Step Task (Model-Free Model-Based) (137)
Beck Depression Inventory (138)
Beck Anxiety Inventory (139)
Fawcett-Clark Pleasure Scale (140)
Toronto Alexithymia Scale (141)
Childhood Trauma Questionnaire (142)
Facial Emotion Matching Task (143)
Incentive Salience
Choice Task (Explicit Version) (144)
Dot-Probe Attentional Bias Task (Cues) (145)
Obsessive-Compulsive Drinking Scale (146)
Cue Reactivity Task (80)
Monetary Incentive Delay Task (147)

ANA, Addictions Neuroclinical Assessment.

Phenotyping Patients With Alcohol and Cannabis Use Disorders Using the Addictions Neuroclinical Assessment



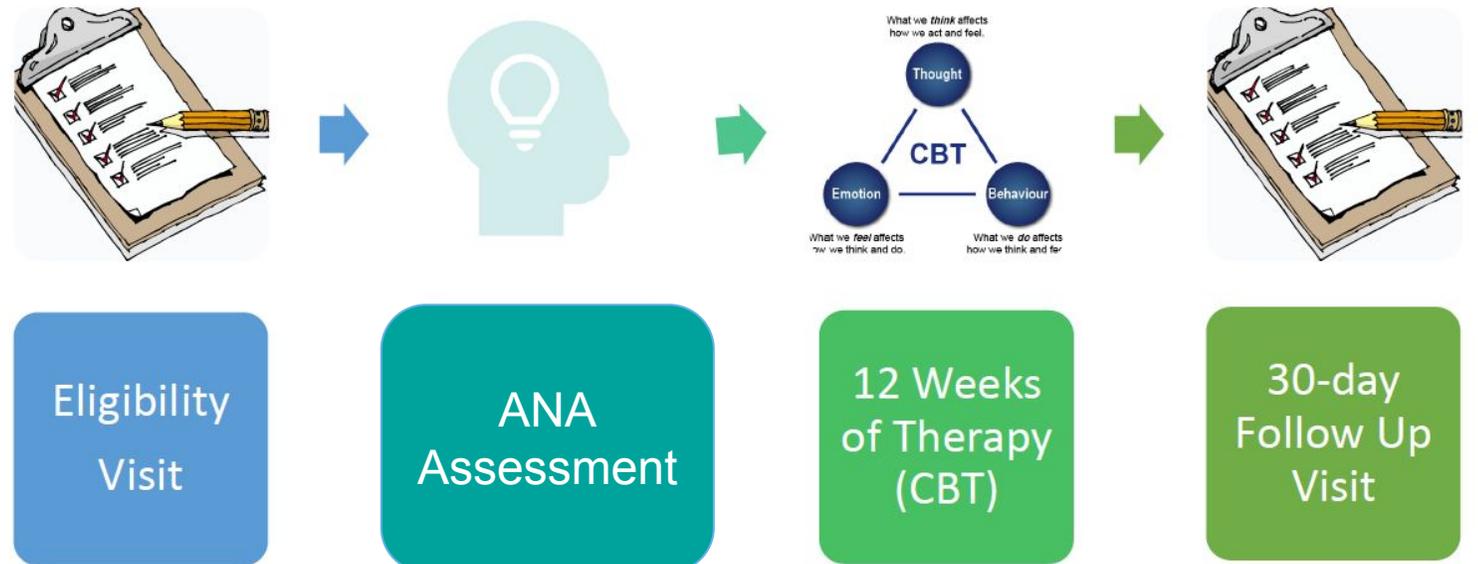
Dr. Matthew Sloan

ClinicalTrials.gov ID NCT05855668

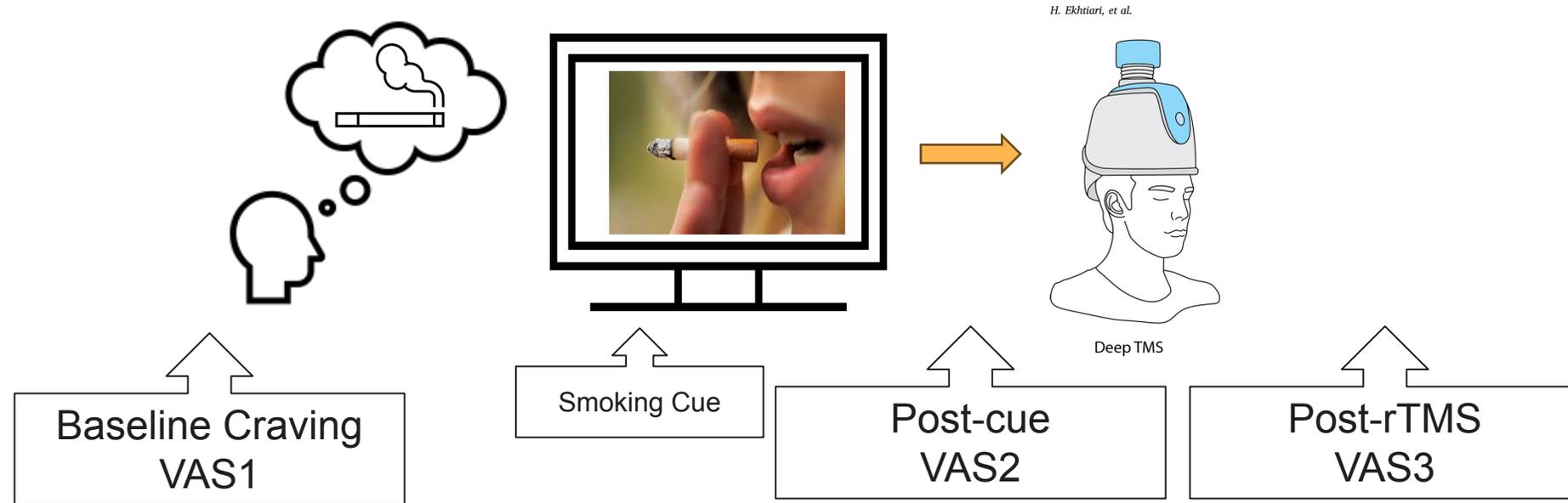
Are there associations between specific ANA domains and treatment response?

- Personalized treatment responses for AUD
- Based on the association for the three ANA domains
 - Executive function
 - Negative emotionality
 - Incentive salience

Study Design



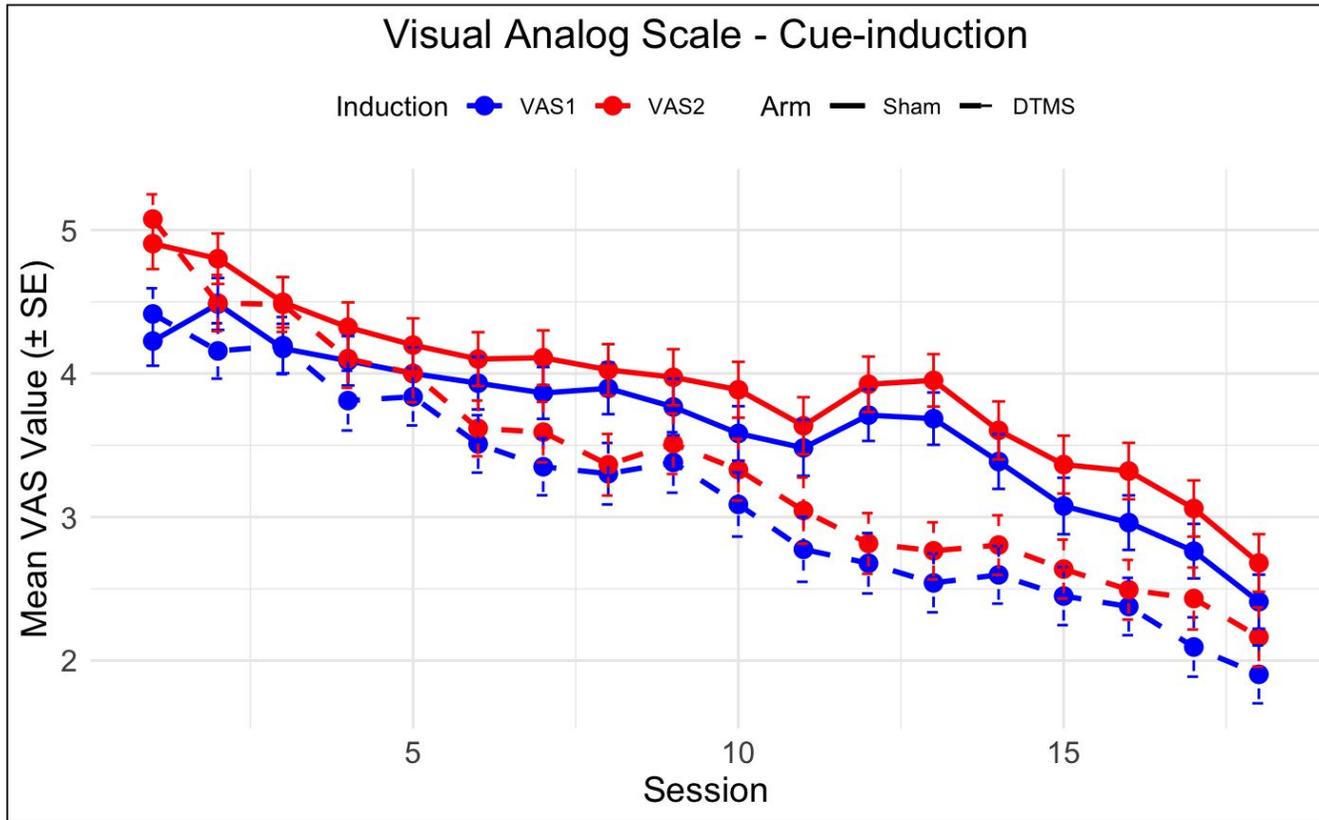
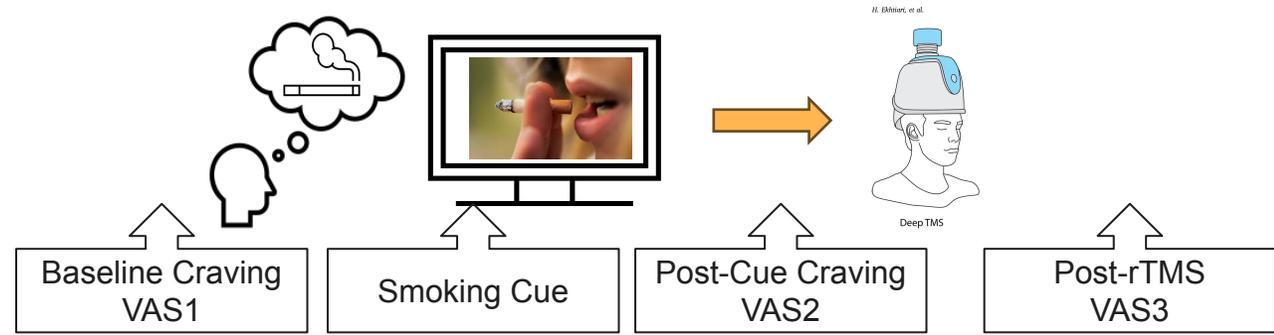
Cue-Induced Craving



- Zangen et al., 2021 Pivotal Trial FDA
- Imagination of personal cigarette cue
 - Viewing images of smoking
 - Handling and lighting real cigarette

- Dinur-Klein et al., 2014 Pilot Study
- Someone lighting up a cigarette and taking one puff 1 meter away from subject

Cue-Induced Craving



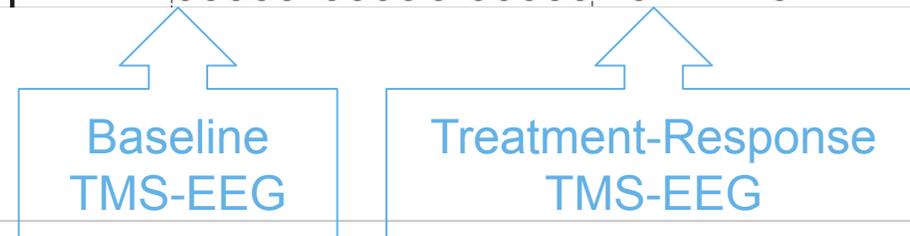
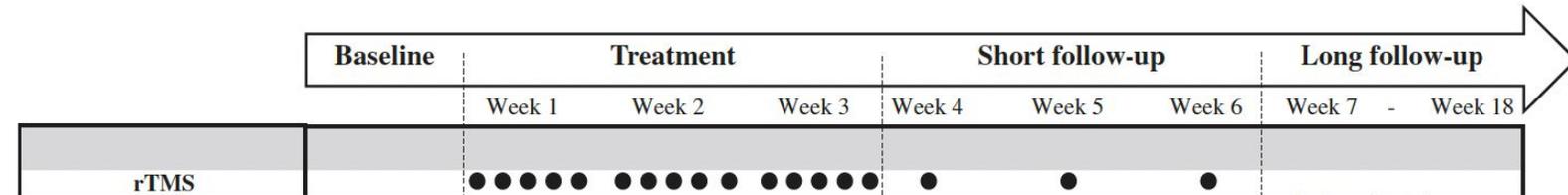
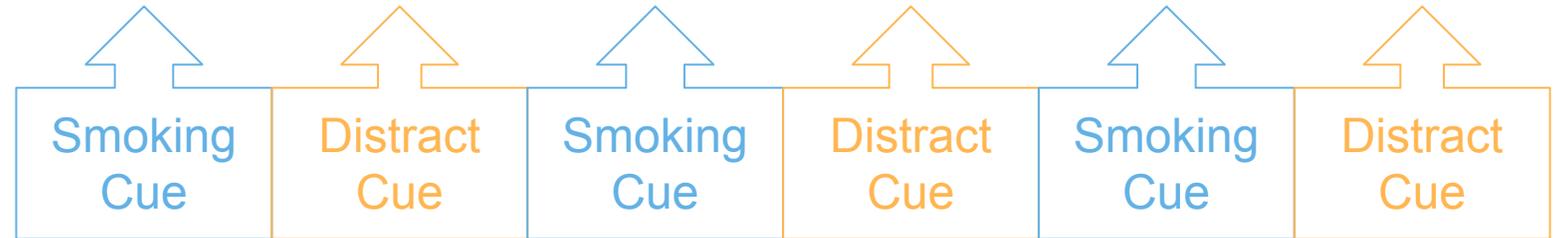
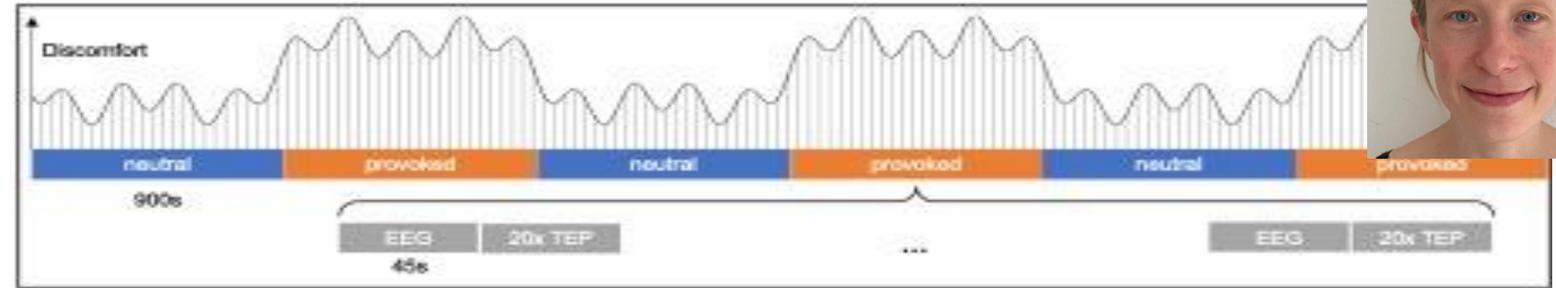
No association between the magnitude of craving induced and quit rate.

Higher craving before rTMS worse outcomes





A Neurophysiological Craving Biomarker? TMS-EEG



Conclusions

rTMS for smoking cessation is an evidence-based, efficacious, and safe approach. Emerging evidence points to its efficacy in other SUDs such as stimulant and alcohol use disorders

Current work is focusing on factors related to enhancing efficacy, determining real-world effectiveness, implementing approaches, and extending to other SUDs.

rTMS for depression has now been implemented into mainstream mental health services and clinicians should become familiar with an approach for those with co-occurring substance use

Neuromodulation represents a novel therapeutic strategy that differs from standard treatment approaches, has the potential to be transdiagnostic (targeting comorbidities), can leverage advances in neuroscientific research, and offers versatility across modalities, parameters, and targets.

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Bernard Le Foll, Daniel Blumberger, Leslie
Buckley, Matthew Sloan, Lena Quilty,
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