Accelerated TMS FOR REFRACTORY DEPRESSION

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CONFLICTS OF INTEREST

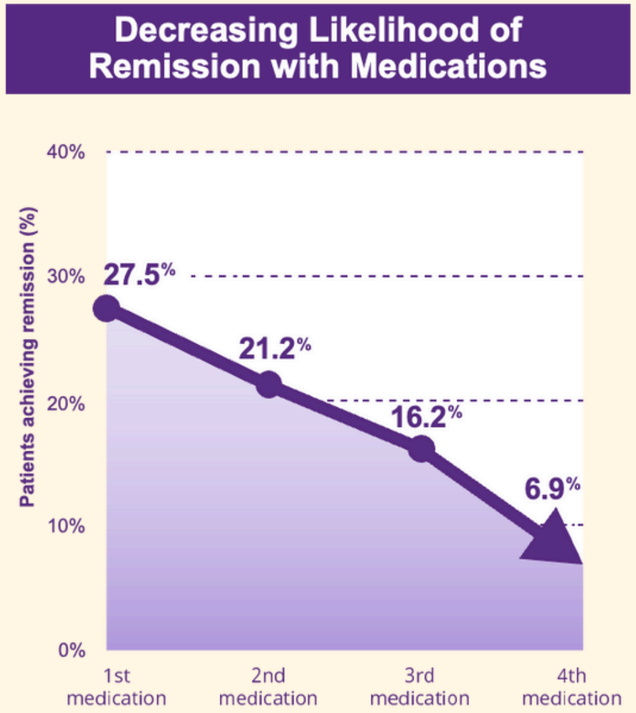
CURRENTLY EMPLOYED BY
NEURONETICS INC.

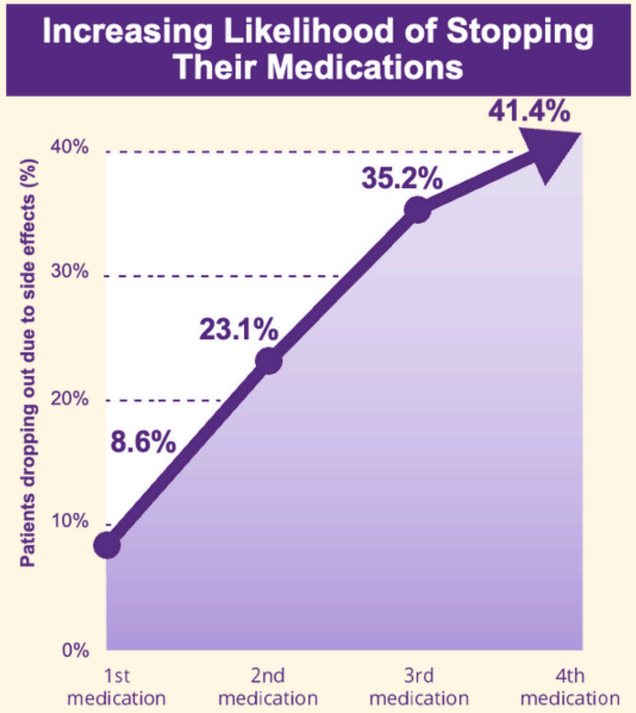
Refractory DEPRESSION

~280 million people have depression

30+% of depressed patients meet criteria for TRD

ANTIDEPRESSANTS





STAR*D trial

4,041 patients

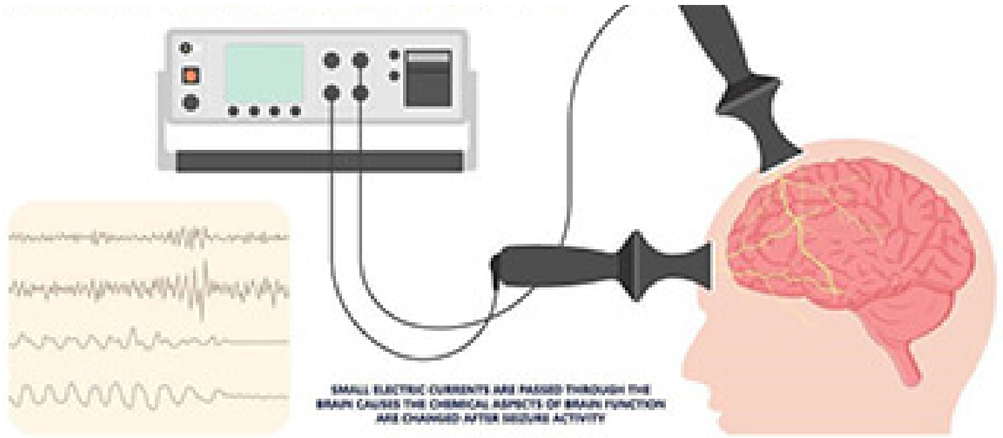
Chances of remission reduce with every antidepressant trial.

4,767

Bed shortage in California

“I slept on a stretcher for the seven nights that we were there... actually started to have some visual hallucinations because of sleep deprivation ...You are pretty much sitting there staring at the wall for the whole entire time.”

ELECTROCONVULSIVE *Therapy*



Still the most effective treatment we have for TRD

~1% of eligible patients receive ECT

ES/KETAMINE

Short-term efficacy but limitations

01 **Side-effects**

Dissociation, hypertension, confusion, nausea, vertigo

02 **Limited durability**

Weeks

03 **Abuse potential**

Drug of abuse
Opoid mechanism

WE NEED A NEW FAST-ACTING TREATMENT

CAN WE TURN

TMS

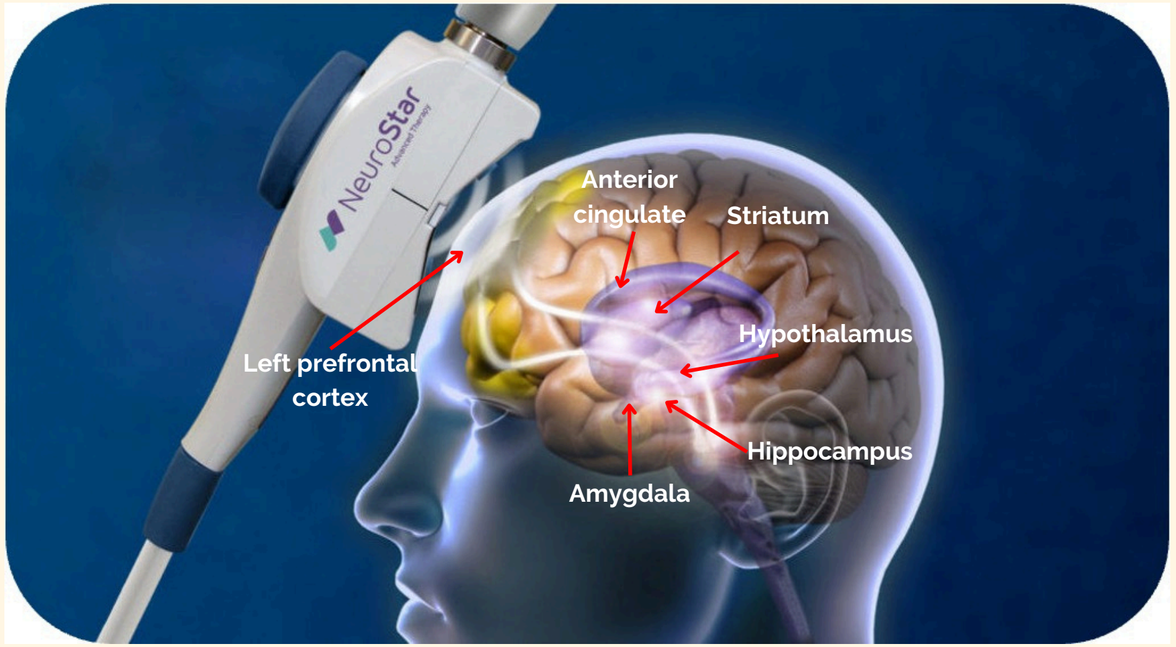
INTO THE TREATMENT WE NEED?

TRANSCRANIAL MAGNETIC STIMULATION

TMS

Non-invasive, targeted

FDA-approved since 2008

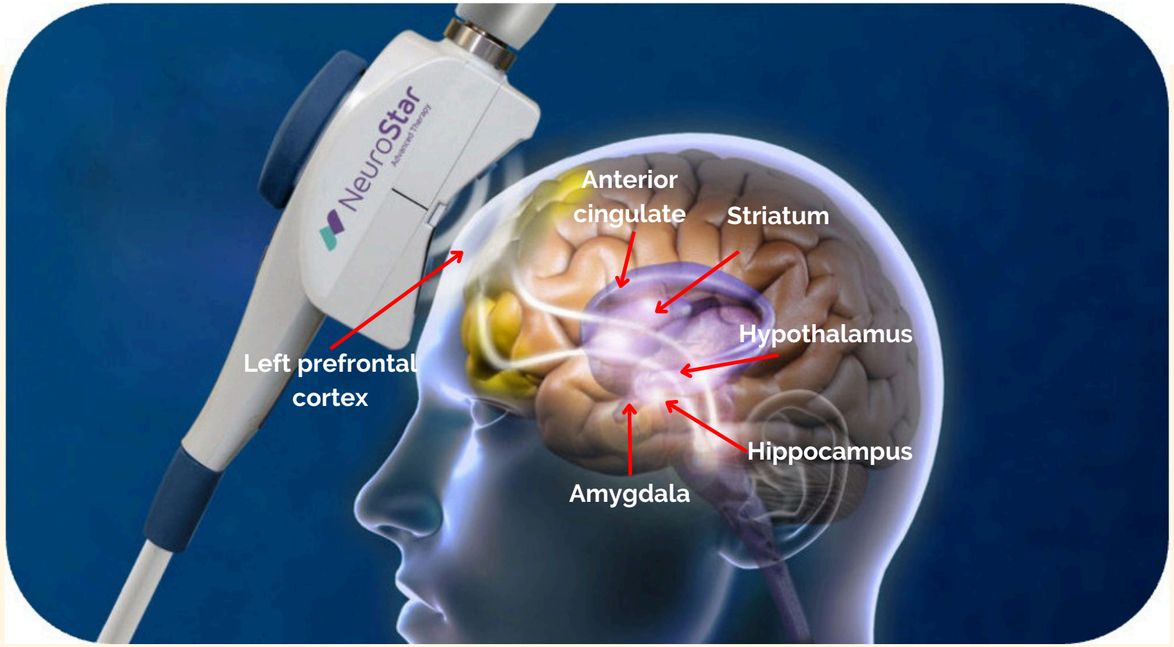


TRANSCRANIAL MAGNETIC STIMULATION: LIMITATIONS

Takes 6-10 weeks

25.7% dropout

60.6% response, 31.2% remission



Sackeïm et al (2020). Journal of Affective Disorders, 277, 65-74. https://doi.org/10.1016/j.jad.2020.08.005

TMS PROTOCOL

LDLPFC

Estimated using scalp measurements

~40 minutes

per session

120% MT

Intensity

Once daily, 6-weeks+

30-36 sessions

ELEMENTS OF TMS PROTOCOL

STIMULATION TARGET

TARGETING METHOD

FREQUENCY OF STIMULATION

TRAIN DURATION

INTER-TRAIN INTERVAL

PULSE DOSE PER SESSION

STIMULATION INTENSITY

SESSIONS PER DAY

INTER-SESSION INTERVAL DURATION

TOTAL PULSE DOSE

SESSIONS PER WEEK

How do we make

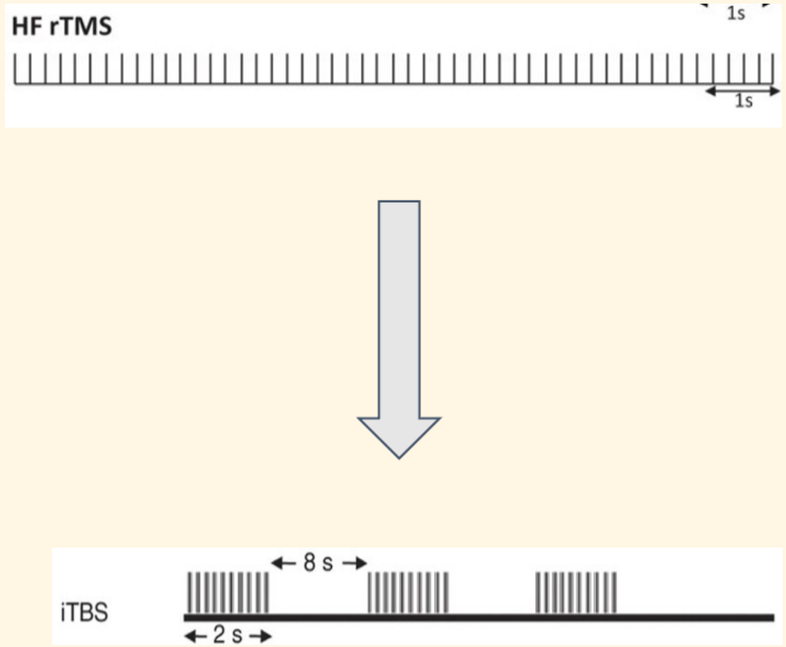
TMS EFFECTIVE FASTER?

How do we make

TMS EFFECTIVE FASTER?

01 Theta-burst

3 mins instead of ~40 minutes



Huang et al. (2005). Neuron, 45(2), 201-206. https://doi.org/10.1016/j.neuron.2004.12.033

How do we make

TMS EFFECTIVE FASTER?

02 Accelerated schedule

More than one session per day

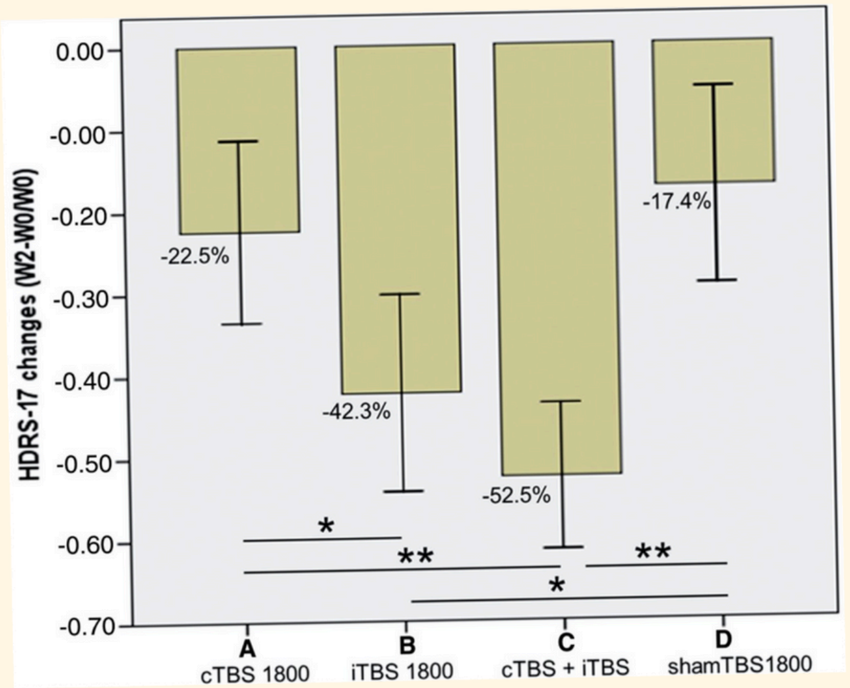
Day 1	Day 2	Day 3	Day 4
iTBS	iTBS	iTBS	iTBS
15 minute interval	15 minute interval	15 minute interval	15 minute interval
iTBS	iTBS	iTBS	iTBS
15 minute interval	15 minute interval	15 minute interval	15 minute interval
iTBS	iTBS	iTBS	iTBS
15 minute interval	15 minute interval	15 minute interval	15 minute interval
iTBS	iTBS	iTBS	iTBS

Duprat et al. (2016). Journal of Affective Disorders, 200, 6-14. https://doi.org/10.1016/j.jad.2016.04.015

How do we make

TMS EFFECTIVE FASTER?

03 More pulses per session



Li et al.,(2014). BRAIN. 137(7):2088–2098. PMID: 24817188

How do we make

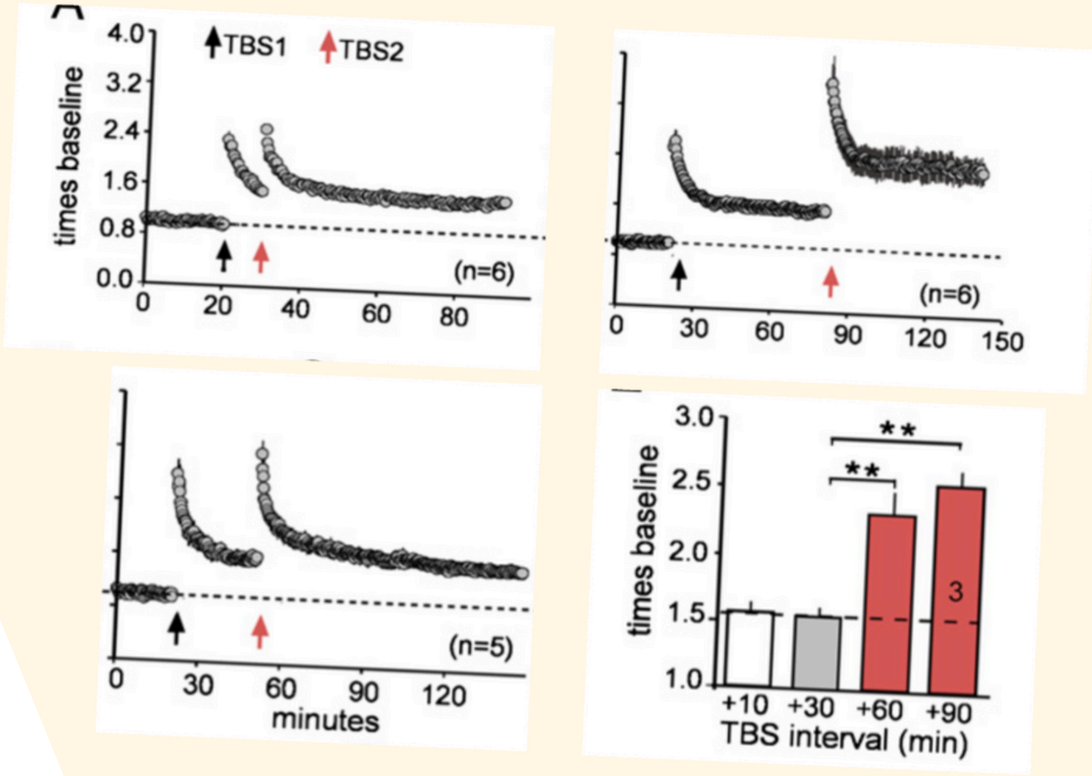
TMS MORE EFFECTIVE?

How do we make

TMS MORE EFFECTIVE?

01 Optimal spacing

60-90 minutes



Kramár et al., (2012). Proceedings of the National Academy of Sciences. 27;109(13):5121–5126. PMCID: PMC3323981

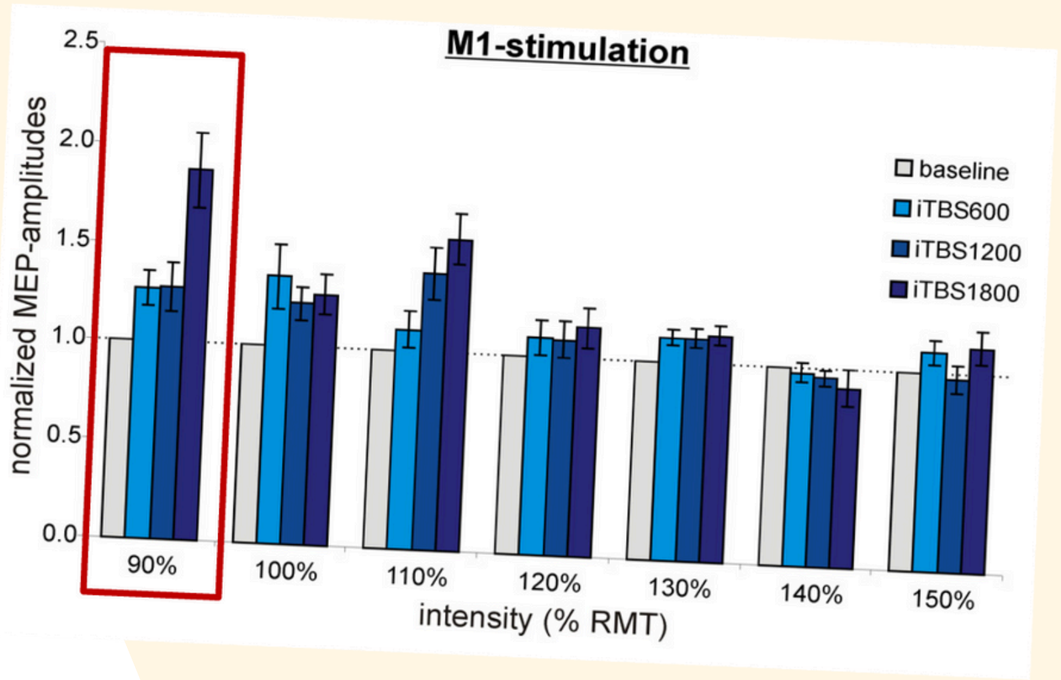
How do we make

TMS MORE EFFECTIVE?

02 Lower intensity

More comfortable

Potentially more effective

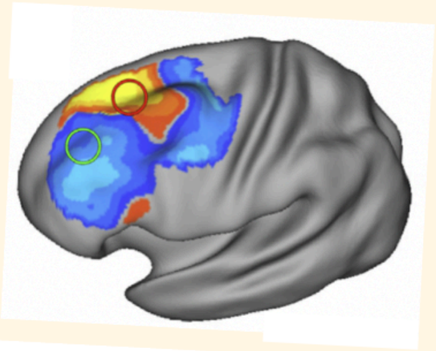


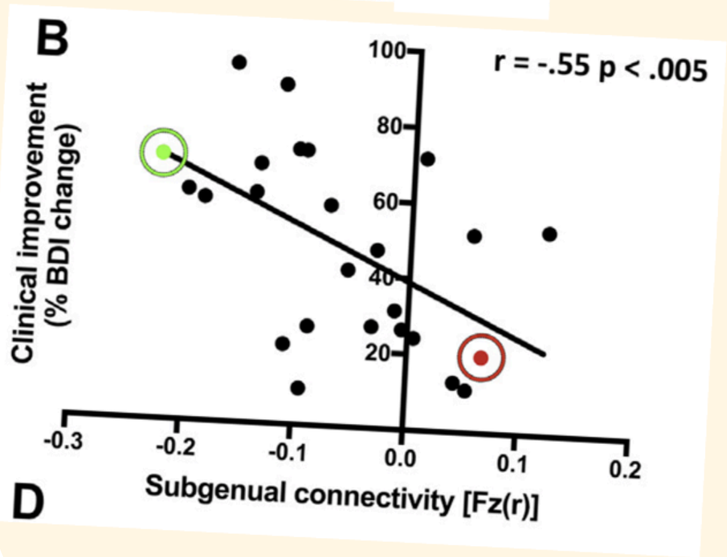
Nettekoven et al., (2014). Journal of Neuroscience. 34(20):6849–6859.
PMCID: PMC4019799

How do we make

TMS MORE EFFECTIVE?

03 fMRI-guided
Personalized



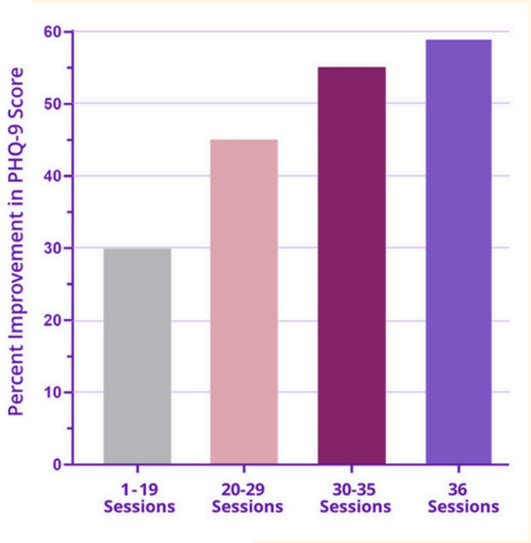


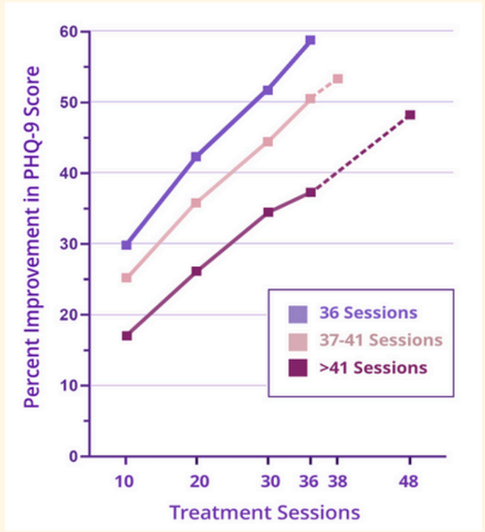
Weigand et al., (2018). Biological Psychiatry. 84(1):28-37. doi: 10.1016/j.biopsych.2017.10.028. PMID: 29274805

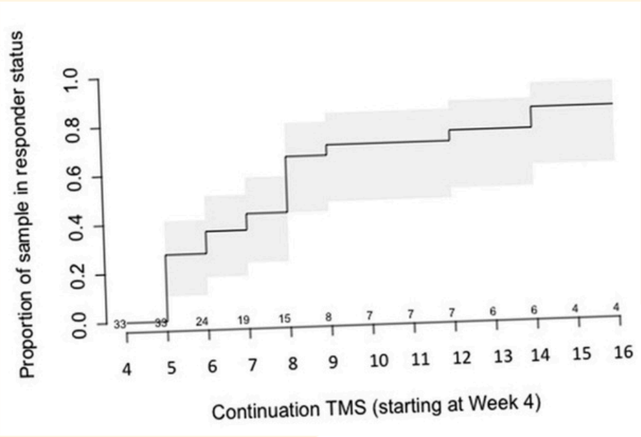
How do we make

TMS MORE EFFECTIVE?

04 More sessions







Yip et al., (2017). Brain Stimulation. 10(4):847–849. PMID: 28330592

SAINT *Protocol*

FMRI TARGET

LDLPFC-sgACC

90%

rMT

10 daily sessions

delivered hourly

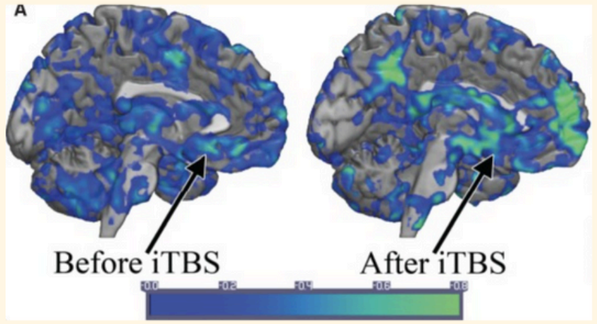
5 days

50 sessions

Initial CLINICAL TRIALS

Open-label SAINT data

ECT non-responders n=6

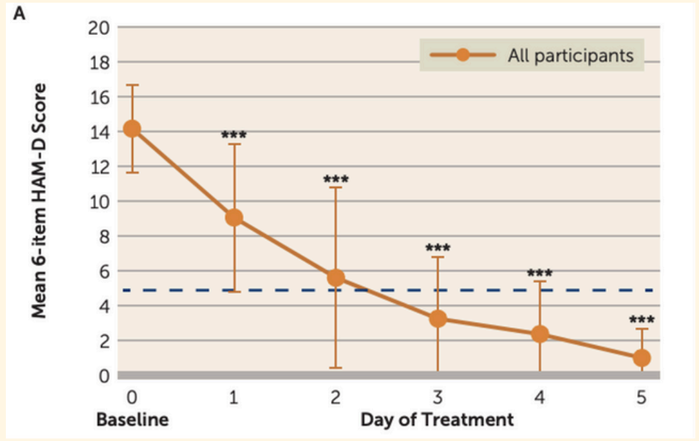


Williams et al., (2018). BRAIN. 141(3):e18

83%

responders after 5 days

Highly treatment-resistant (n=21)



Cole et al., (2020). American Journal of Psychiatry. 177(8): 716-726.

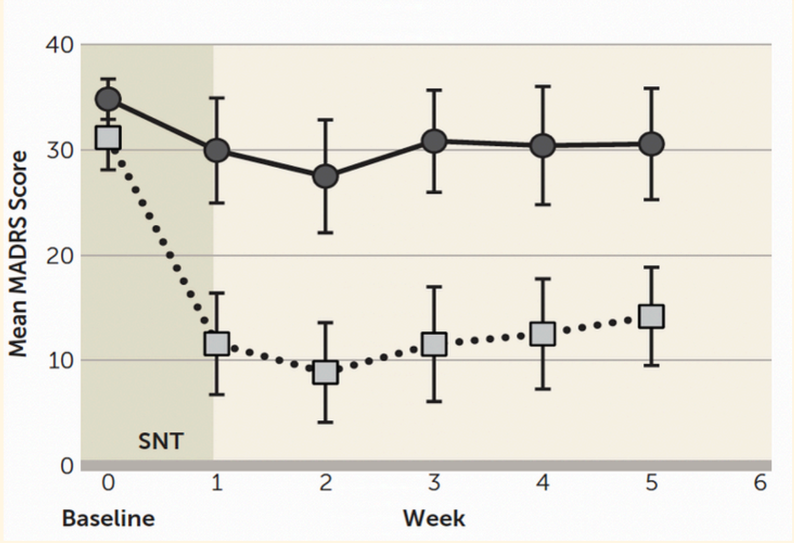
90%

remission after 5 days

Randomized CONTROLLED TRIAL

Highly treatment-resistant (n=29)

Significant antidepressant effect in the active SAINT group for one month post-SAINT



Active: 78.6% remission

Sham: 13.3% remission

Cole et al., (2022). American Journal of Psychiatry. 179(2): 132-141.

Safety PROFILE

Side-effect	Active (n=14)	Sham (n=15)
Fatigue	57% (8)	53% (8)
Neck/Back discomfort	50% (7)	33% (5)
Discomfort at treatment site	36% (5)	27% (2)
Post-SNT headache	57% (8)	13% (2)
Nausea	0% (0)	0% (0)
Anxiety	29% (4)	20% (3)
Dental issues	7% (1)	0% (0)
Jaw discomfort	14% (2)	0% (0)
Other	7% (1)	0% (0)

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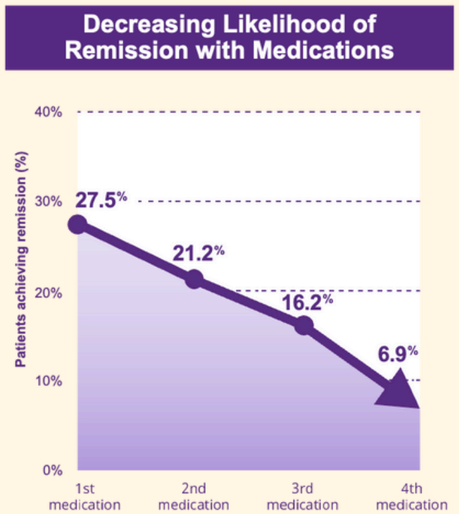
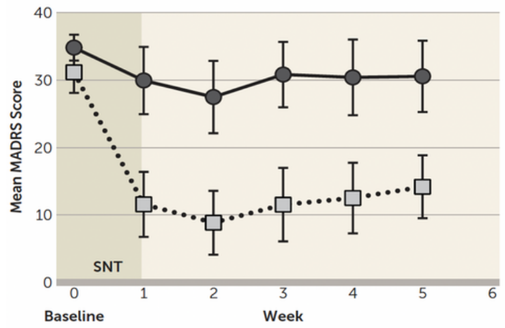
ANTIDEPRESSANTS

<7% remission



SAINT

79-90% remission



Active: 78.6% remission
Sham: 13.3% remission

FDA Saint CLEARED

September 2022

REMAINING QUESTIONS...

Remaining QUESTIONS

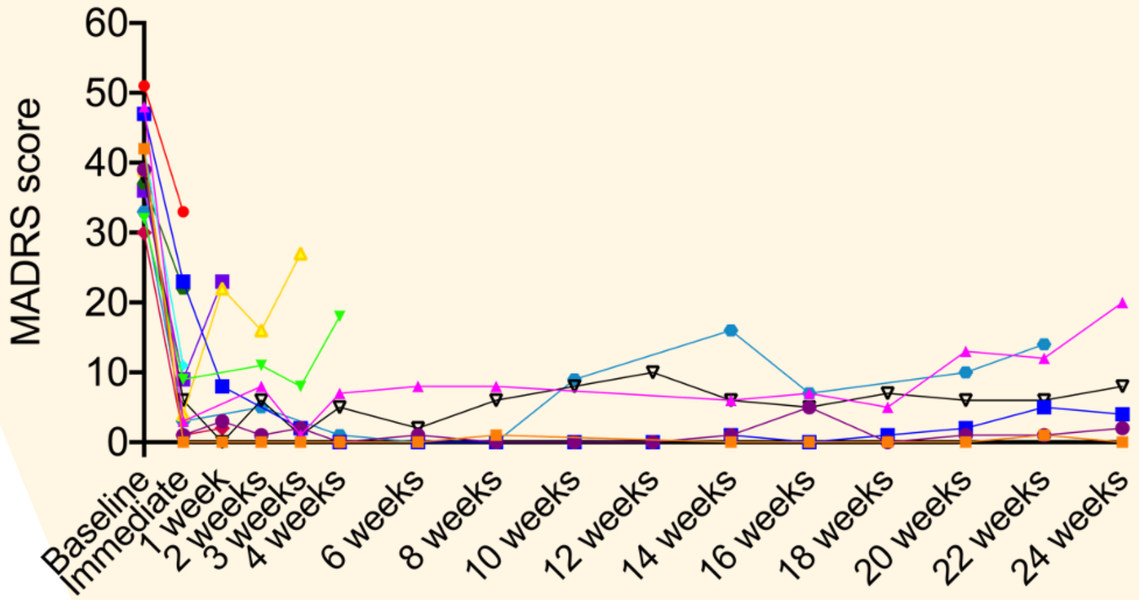
about accelerated TMS

14 Inpatients

86% response, 71% remission

Different patient population to the SAINT trials

01 Is neuromaging needed?



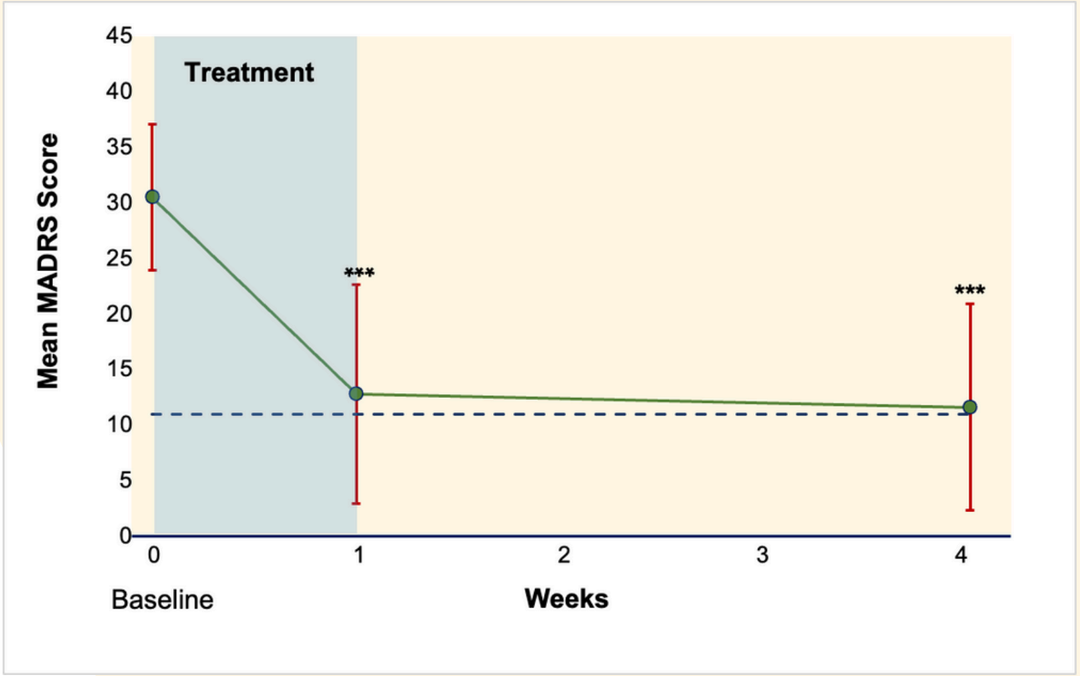
Cole et al., (2020). Clinical Neurophysiology 131 (4), e21

Remaining QUESTIONS

about accelerated TMS

n=20 TRD patients
36 sessions over 5 days
70% response, 55% remission

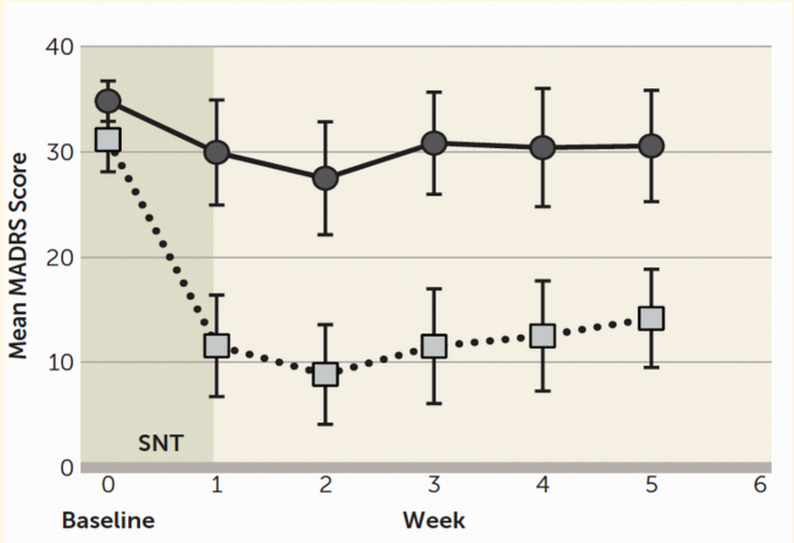
01 Is neuromaging needed?



Remaining QUESTIONS

about accelerated TMS

02 Is it durable?



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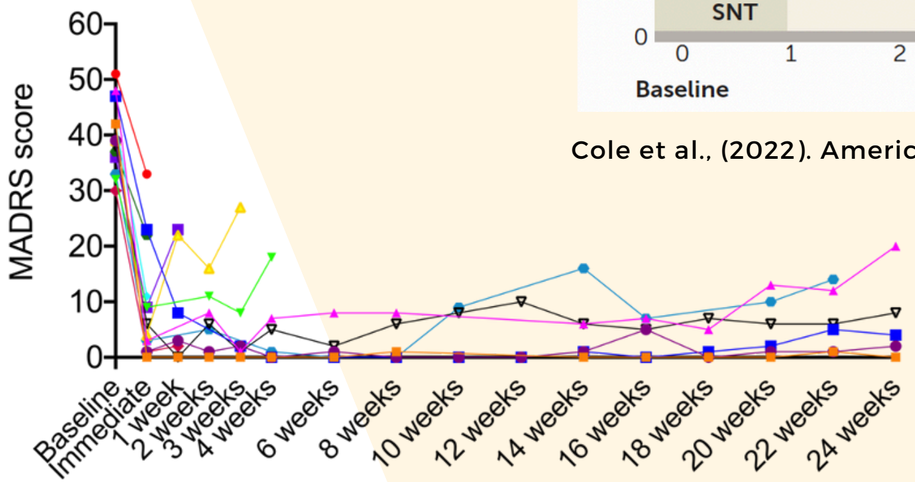
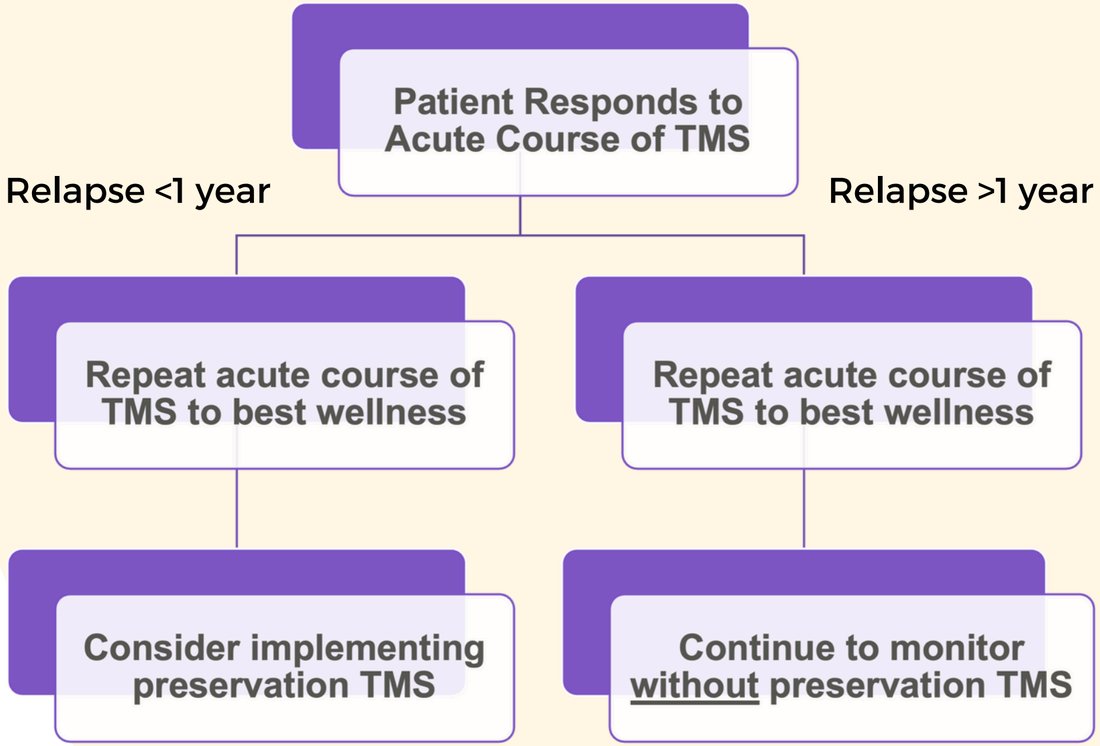


Cole et al., (2020). Clinical Neurophysiology 131 (4), e21

Remaining QUESTIONS

about accelerated TMS

03 Maintenance

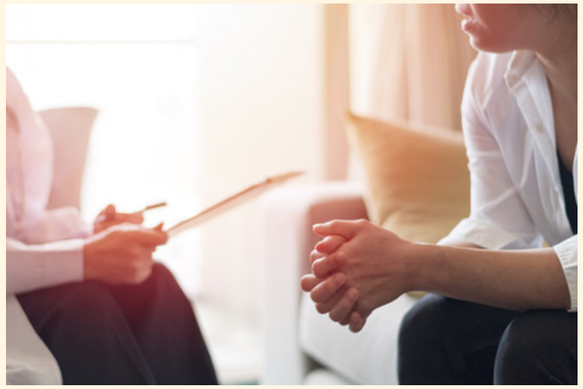


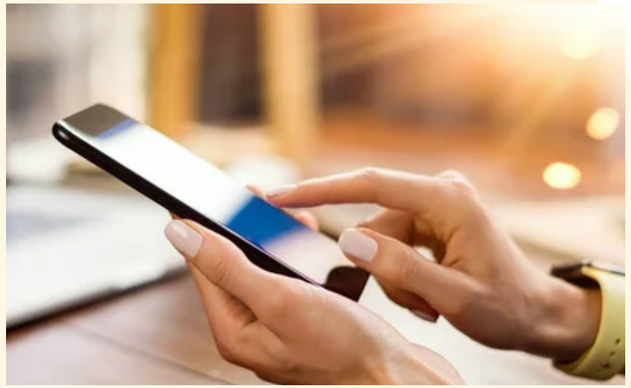
Wilson et al (2022) Journal of Affective Disorders. 296: 79-88.

Remaining QUESTIONS

about accelerated TMS

04 Other interventions





Remaining QUESTIONS

about accelerated TMS

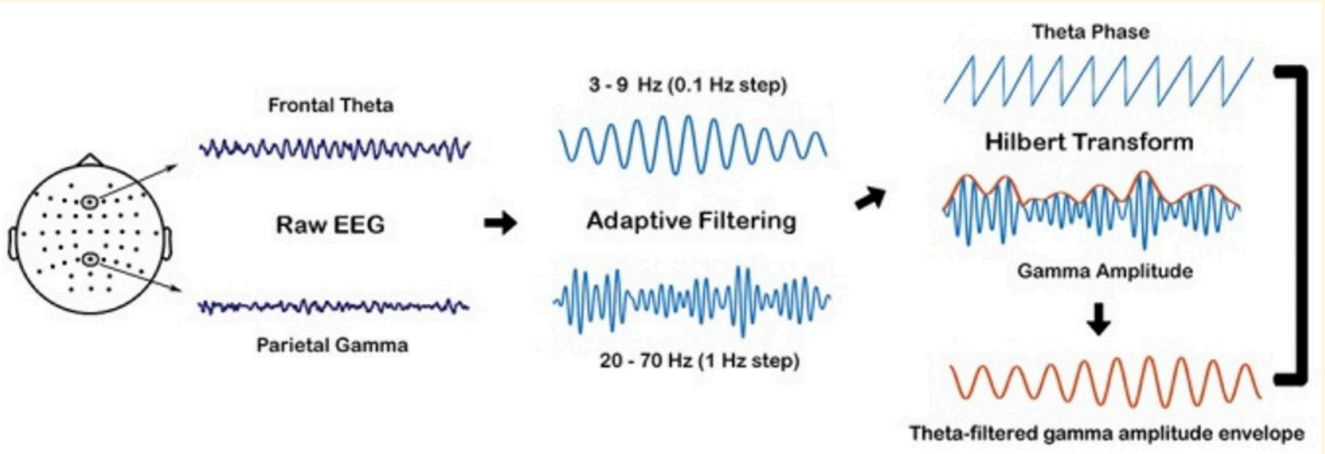
05 Does concurrent medication matter?

Remaining QUESTIONS

about accelerated TMS

Frequency, location, dose

06 Further personalization needed?



Chung et al., (2019). Human Brain Mapping. 40(2): 608–627. PMCID: PMC6865598.

Remaining QUESTIONS

about accelerated TMS

07 Does brain state matter?

Remaining

QUESTIONS

about accelerated TMS

08 Other internal states e.g. hormones

SUMMARY

The potential of accelerated TMS

Rates of depression are increasing
large numbers not receiving effective treatment

New fast antidepressant treatments needed without side-effects & abuse potential

Accelerated TMS

Rapid antidepressant responses
without side-effects or abuse potential

Lots of answered questions
optimizing treatment

THANK YOU

for listening

Contact: Eleanor.cole@neurostar.com