Temporal Interference Neurostimulation as a Novel Non-Invasive Approach for Addiction Treatment

Targeting the Nucleus Accumbens

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BACKGROUND

Neurostimulation has emerged as a promising treatment for substance use disorders.[1,2] **Current methods** are limited in terms of scalability and scope, and may not be able to specifically target deep brain regions. Stimulating the **nucleus accumbens (NAcc)**, a key reward processing structure, could be effective for treating addiction.[3]

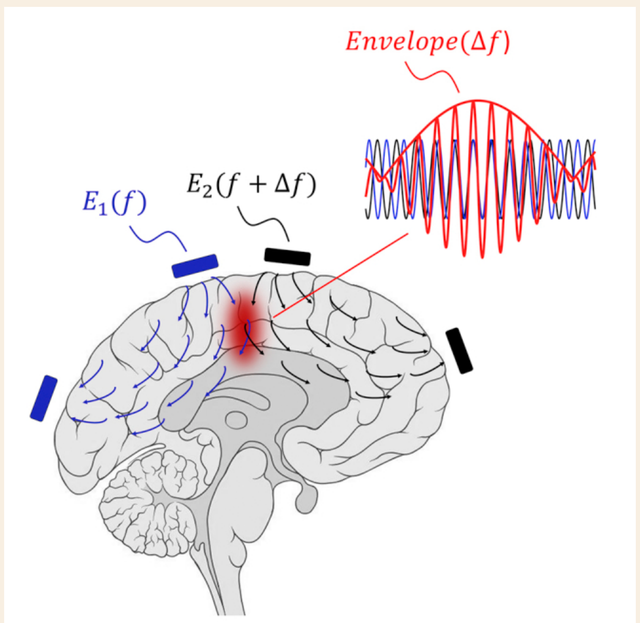


Image sourced from Grossman, et al., 2017

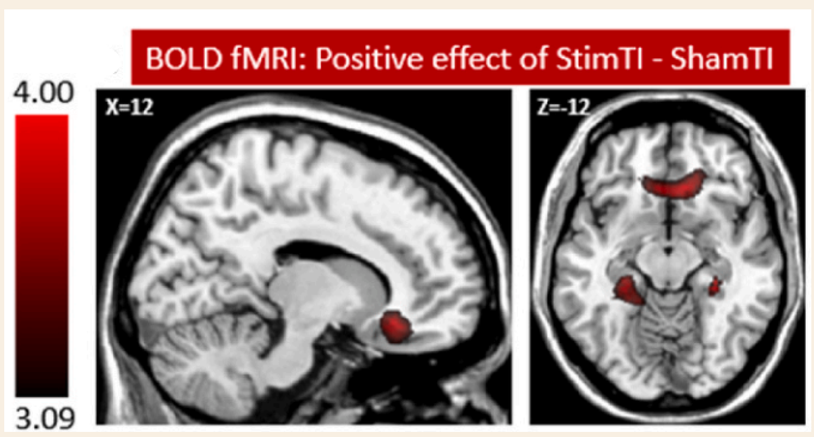
Temporal Interference (TI) neurostimulation is a novel, non-invasive technique that allows for targeting of deep brain regions (e.g., the NAcc) without affecting the overlying cortex using **intersecting electrical fields.**[4,5]

PILOT STUDY

How does TI affect deep brain structures?

Method: N=16 healthy subjects received TI stimulation of the left orbitofrontal cortex (OFC) at **20Hz beat frequency** while in fMRI scanner. We assessed effects of TI vs. sham stimulation.

Result: Active TI stimulation of the left orbitofrontal cortex (OFC) did increase **BOLD activation** in the targeted region compared to sham stimulation (p=0.021).



Positive effect of contrast StimTI-ShamTI in OFC (z-score, across subjects). 'Positive effect' - Positive z-score of any voxel across the subjects for the StimTI - ShamTI contrast. Sourced from Modak et al., 2024.

ONGOING WORK: CLINICAL TRIAL

How does TI impact real-time craving and substance use?

We're using new multi-TI (4 electrode pairs) in our **randomized controlled trial.** 120 subjects will undergo 60 minutes of (a) active TI of the NAcc or (b) sham TI, during which they will have access to our custom **nicotine vaporizer** measuring inhaled vapor volume over time.[6] **Craving** will be reported every 10 minutes. Post-TI, subjects will complete 7 days of **ecological momentary assessment (EMA)** tracking daily nicotine usage and craving. Self-report measures of **comorbid substance use** will be completed at baseline and at 7-day follow up.

Soterix Interferential Neuromodulation System

POTENTIAL IMPACT & FUTURE DIRECTIONS

Pilot findings support TI's ability to modulate **reward-related circuits,** demonstrating potential as a **targeted intervention** for addiction. If validated, TI could offer an affordable, scalable alternative to invasive neuromodulation, expanding access to innovative **addiction treatment** worldwide. Our ongoing research aims to optimize TI parameters and investigate its **long-term effects** on addiction-related behaviors.

REFERENCES

[1] Wang TR, Moosa S, Dallapiazza RF, Elias WJ, Lynch WJ. (2018). Deep brain stimulation for the treatment of drug addiction. *Neurosurg Focus.* 45(2):E11.
[2] Harmelech T, Hanlon CA, Tendler A. (2023). Transcranial magnetic stimulation as a tool to promote smoking cessation and decrease drug and alcohol use. *Brain Sci.* 13(7):1072.
[3] Brown JW. (2023). Transcranial Electrical Neurostimulation as a Potential Addiction Treatment. *Inquiry*. 60:469580231221286.
[4] Grossman N, Bono D, Dedic N, Kodandaramaiah SB, Rudenko A, Suk HJ, ... & Boyden ES. (2017). Noninvasive deep brain stimulation via temporally interfering electric fields. *Cell*. 169(6), 1029-1041.
[5] Modak P, Fine J, Colon B., ... & Brown JW. (2024). Temporal interference electrical neurostimulation at 20 Hz beat frequency leads to increased fMRI BOLD activation in orbitofrontal cortex in humans. *Brain Stimulat.* 17(4):867-875.

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