Does sex matter? Effects of Neuromodulation on Self-Reported Depression Scores in Alcohol Use Disorder

McKinney K[1], Verdoorn H, Martinez A, Camchong J[1],
[1]University of Minnesota Department of Psychiatry and Behavioral Sciences

Background

- Transcranial direct current stimulation (tDCS) is a noninvasive brain stimulation method that has been used as an intervention in clinical trials for psychiatric disorders including depression, schizophrenia, and substance use disorder (Mondino et al., 2014). Recent research suggests the effectiveness of tDCS can be enhanced when administered alongside cognitive training exercises that engage higher-order cognitive processes such as reasoning, planning, and decision making (Das et al., 2019).
- We conducted a longitudinal randomized-controlled clinical trial using a neuromodulation intervention that combines transcranial direct current stimulation and cognitive training in individuals with alcohol use disorder (AUD). We found that the intervention has an effect on addiction resting state networks and relapse rates in AUD (Camchong et al. 2022).
- Previous clinical trials have indicated that tDCS at the same stimulation site location (DLPFC; F3 anode/F4 cathode) reduces depressive symptoms (Brunoni et al., 2011)
- Here, we investigate whether the intervention was associated with improvement in self-reported depression, anxiety, and impulsivity symptoms. We also explored gender-related differences.
- **Hypothesis:** We expected to find that those who receive active tDCS would have greater improvements in self-reported depression, anxiety, and impulsivity scores than those who receive the sham treatment.

Methods

56 short term abstinent participants with AUD were recruited. All participants were randomly assigned to undergo 10 sessions of either active transcranial direct current stimulation (tDCS; F3 anode/F4 cathode), or sham. To assess depression severity, participants completed the Beck Depression Inventory (BDI) at baseline and post-intervention. To assess anxiety severity, participants completed the Stait-Trait Anxiety Inventory (STAI) and baseline and post- intervention. To assess impulsivity, participants completed the Barratt Impulsiveness Scale (BIS) at baseline and post-intervention.

Because the literature and our data (Camchong et al. 2022) suggest sex differences on rate of relapse, we investigated whether there are sex differences on change in depression, anxiety, and impulsivity symptoms.

Figure 1. Intervention Design: Transcranial direct current stimulation (2mA, anode of F3, cathode on F4) combined with cognitive training for 5 consecutive days twice a day (two sets of 13 minute stimulation). **Random assignment to either active tDCS or sham.**

Results

Table 1. Depression, Anxiety, and Impulsivity Outcomes in Participants with Complete fMRI Data

		Intervention Group		
	All AUD (n=56)	Active tDCS (n=29)	Sham (n=27)	Active tDCS vs. Sham
Characteristic	**Mean (SD) *or n (%)***	**Mean (SD) *or n (%)***	**Mean (SD) *or n (%)***	**T-test or X^2 *(italics)***
BDI Pre-Intervention	22.13 (11.28)	20.89 (10.25)	24.30 (12.61)	p = 0.27
BDI Post-Intervention	9.43 (7.93)	10.15 (7.25)	9.52 (8.87)	p = 0.78
STAI Pre-Intervention	19.35 (10.19)	20.11 (12.35)	18.96 (5.46)	p = 0.67
STAI Post-Intervention	17.52 (7.10)	19.27 (7.86)	16.38 (5.46)	p = 0.73
BIS Pre-Intervention	71.07 (14.15)	70.96 (11.01)	72.46 (14.09)	p = 0.66
BIS Post-Intervention m	67.73 (15.05)	69.16 (13.31)	69.28 (12.67)	p = 0.97

Table 1. Depression, Anxiety, and Impulsivity Outcomes Beck Depression Inventory, State-Trait Anxiety Inventory, and Barratt Impulsiveness scores at baseline and post-intervention for participants who received active tDCS and sham.

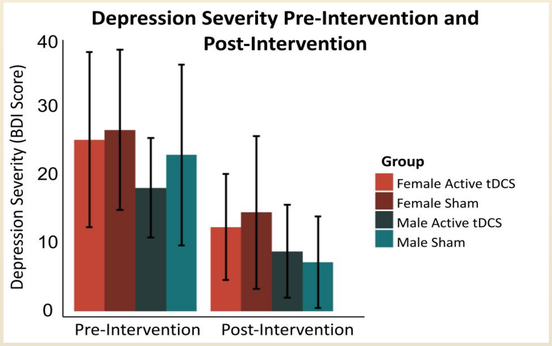

Figure 2. Depression Severity Pre-Intervention and Post-Intervention Participants who received the intervention did not have a greater reduction in depression severity than participants who received sham $t(48) = -1.70$, $p = .10$. When the sample was split by gender, men who received the intervention did not have a greater reduction in depression severity than men who received sham $t(29) = -1.99$, $p = .055$ and women who received the intervention did not have a greater reduction in depression severity than women who received sham $t(17) = -0.49$, $p = .63$.

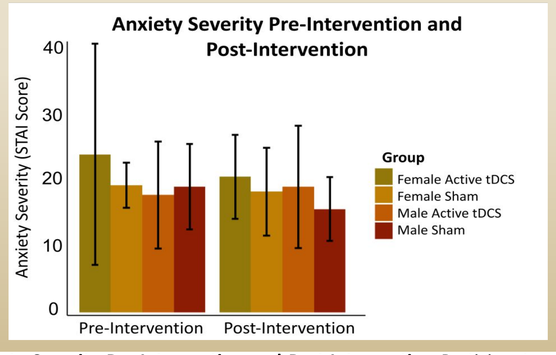

Figure 3. Anxiety Severity Pre-Intervention and Post-Intervention Participants who received the intervention did not have a greater reduction in anxiety severity than participants who received sham $t(45) = -0.4$, $p = .66$. When the sample was split by gender, men who received the intervention did not have a greater reduction in anxiety severity than men who received sham $t(27) = -1.3$, $p = .21$ and women who received the intervention did not have a greater reduction in anxiety severity than women who received sham $t(16) = 0.6$, $p = .59$

Results

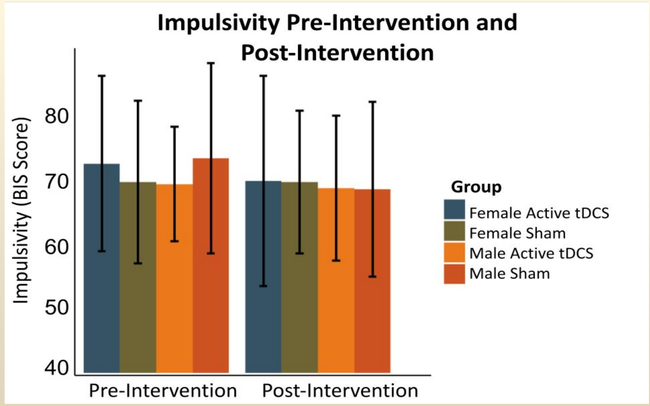

Figure 4. Impulsivity Severity Pre-Intervention and Post-Intervention Participants who received the intervention did not have greater changes in impulsivity than participants who received sham $t(46) = -0.78$, $p = .44$. When the sample was split by gender, men who received the intervention did not have a greater change in impulsivity than men who received sham $t(28) = -1.52$, $p = .13$ and women who received the intervention did not have a greater change in impulsivity than women who received sham $t(16) = 1.57$, $p = .14$

Discussion

- In our clinical trial, tDCS and cognitive training did not have an effect on self-reported depression, anxiety, and impulsivity symptoms on individuals with alcohol use disorder enrolled in an inpatient treatment program.
- One explanation for our results is that the participants in our sample were not severely depressed (moderate levels of depression at baseline) and did not have as much room for improvement as participants with more severe depression.
- Small sample size may also have influenced our results. It is possible significant results would be found with a larger sample size.
- Depression severity decreased for all participants between baseline and post-intervention regardless of gender or intervention group, $t(59) = 9.21$, $p < 0.0001$. Due to the lack of differences between intervention groups, it is likely that depression severity decreased because participants were in a safe, controlled environment and not because of the intervention.
- Anxiety severity and impulsivity did not change significantly between baseline and post-intervention.

Acknowledgements

This project was supported by the University of Minnesota's Office of Undergraduate Research, K01AA026349 (NIH-NIAAA); Westlake Wells Foundation; and the National Institutes of Health's National Center for Advancing Translational Sciences, grant UL1TR002494. The content is solely the responsibility of the authors and does not necessarily represent the official views of supporters.

References

Brunoni AR, Ferrucci R, Bortolomasi M, et al. Transcranial direct current stimulation (tDCS) in unipolar vs. bipolar depressive disorder. *Progress in neuropsychopharmacology & biological psychiatry.* 2011;35(1):96–101.

Das, N., Spence, J. S., Aslan, S., Vanneste, S., Mudar, R., Rackley, A., Quiceno, M., & Chapman, S. B. (2019). Cognitive Training and Transcranial Direct Current Stimulation in Mild Cognitive Impairment: A Randomized Pilot Trial. Frontiers in neuroscience, 13, 307. https://doi.org/10.3389/fnins.2019.00307

Mondino, M., Bennabi, D., Poulet, E., Galvao, F., Brunelin, J., & Haffen, E. (2014). Can transcranial direct current stimulation (tDCS) alleviate symptoms and improve cognition in psychiatric disorders? The World Journal of Biological Psychiatry, 15(4), 261–275. https://doi.org/10.3109/15622975.2013.876514