EVALUATING THE EFFICACY OF A COGNITIVE-EMOTIONAL TRAINING INTERVENTION FOR DEPRESSION

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BACKGROUND

- Cognitive-emotional control training is a promising novel approach to treating Major Depressive Disorder (MDD)[1].
- We report a replication of efficacy in a randomized, controlled, double-blind trial of a cognitive-emotional control training exercise designed to enhance cognitive control for emotional information-processing and target components of the neural networks implicated in MDD[2].
- The intervention was designed to target abnormal activation patterns between dorsolateral prefrontal cortex (DLPEF) and amygdala, which subserve the impairments in cognitive control and emotion regulation observed in MDD (see Figure 1).
- The cognitive-emotional training exercise is a combination of emotion identification and working memory tasks: the Emotional Faces Memory Task (EFMT; Figure 2). The training regimen involves completing 18 sessions over 6 weeks. The sessions are progressively challenging and adapt to the participants' performance.
- In a single, non-progressive session in healthy volunteers, this task simultaneously activated DLPFC and amygdala[3].
- The control group involved an active comparator task, a working memory training that used an identical paradiam to EFMT except the stimuli were neutral shapes.

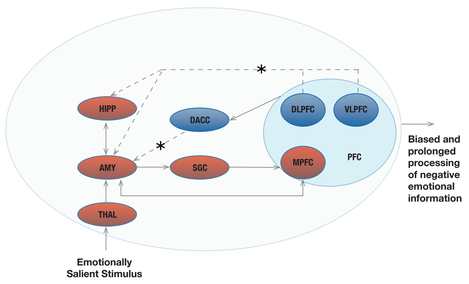


FIGURE 1.
In MDD, hyperactivation (shown in red) of the thalamus (THAL), amygdala (AMY) and hippocampus (HIPP) upon stimulus perception is associated with increased subgenual cingulate (SGC) activity, which integrates limbic feedback and relays to the prefrontal cortex (PFC) via the medial PFC (MPFC). Activity is decreased (shown in blue) in PFC regions (DLPFC, VLPFC) and the dorsal anterior cingulate cortex (DACC), associated with cognitive control. The net result of the hyperactive emotion processing and impaired cognitive control is biased and prolonged processing of negatively-valenced information. Solid arrows (showing intact associations) and dashed arrows (showing attenuated associations) represent functional connections. Asterisks represent targets for cognitive training interventions."

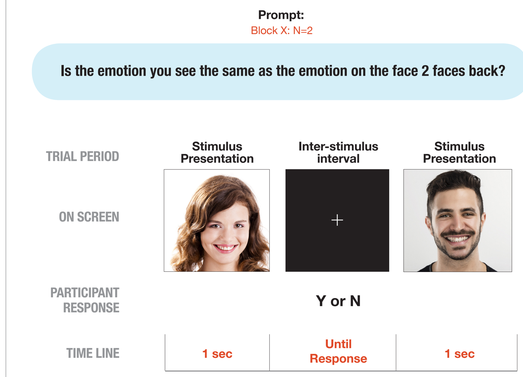


FIGURE 2.
Example event sequence for the EFMT paradigm with N=2

METHODS

PARTICIPANTS

All participants were between the ages of 18-55 and not currently taking an anti-depressant medication

Potential participants were screened with the SCID-IV to confirm MDD diagnosis for inclusion, and HAM-D-17 was administerd to confirm score between 16-27

38 participants signed consent and enrolled in a trial of EFMT versus an active control group

26 participants completed at least 4 weeks of training and were included in the modified intention-to-treat analysis

TABLE 1. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

	EFMT	CONTROL GROUP
N	14	12
AGE(YEARS)	33.64 (10.67)	30.42 (9.00)
GENDER	9 FEMALE, 5 MALE	6 FEMALE, 6 MALE
ETHNICITY	2 AFRICAN-AMERICAN 8 CAUCASIAN 1 ASIAN 1 HAWAIIAN / PACIFIC ISLANDER 2 MULTIRACIAL	4 AFRICAN-AMERICAN 4 CAUCASIAN 1 ASIAN 1 HAWAIIAN / PACIFIC ISLANDER 1 MULTIRACIAL 1 UNKNOWN
BASELINE DEPRESSION SEVERITY (HAM-D-17)	19.21 (2.86)	19.17 (2.55)
DURATION OF CURRENT MDD EPISODE (MONTHS)	19.79 (22.70)	11.5 (13.22)
NUMBER OF PREVIOUS MDD EPISODES	3.14 (4.24)	2.13* (2.95)
AXIS I COMORBIDITIES (CURRENT)	7% SOCIAL PHOBIA 7% SPECIFIC PHOBIA 7% SOMATIZATION DISORDER 7% BODY DYSMORPHIC DISORDER	25% SOCIAL PHOBIA 8% DYSTHYMIC DISORDER

*Note : Standard deviation in parenthesis. * based on sample of n = 8; this value was not collected for 4 participants.*

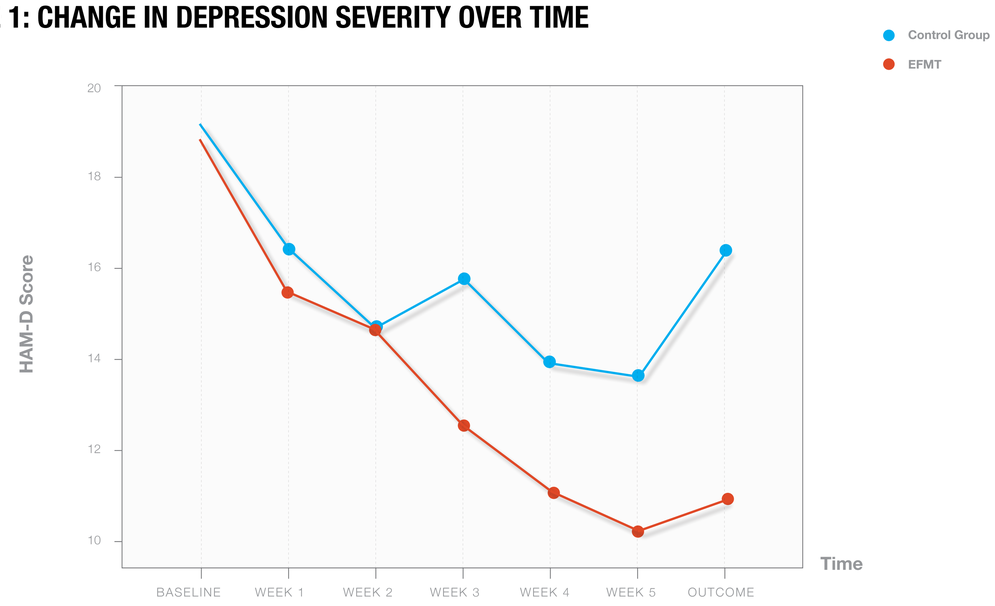
PROCEDURES

- Participants were randomly assigned to the EFMT or an active control group, and completed up to 18 sessions over 6 weeks.
- MDD symptoms (Ham-D-17) were assessed at baseline and weekly through outcome (week 6).

RESULTS

CHANGE IN DEPRESSION SYMPTOM SEVERITY DURING A RANDOMIZED SHAM-CONTROLLED TRIAL OF EMOTIONAL FACES MEMORY TASK IN PATIENTS WITH MDD

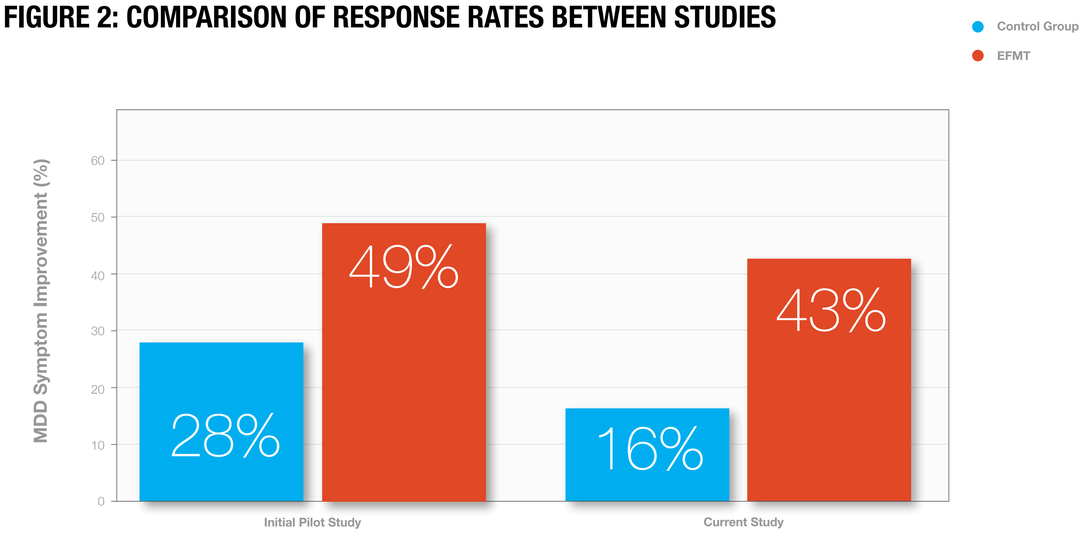
FIGURE 1: CHANGE IN DEPRESSION SEVERITY OVER TIME



Repeated measures ANOVA of HAM-D score across all time-points revealed a significant group x time effect: $F(6,144)= 4.620$, $p< .001$. Follow-up analysis revealed that the groups showed significantly different HAM-D scores at study endpoint (week 6) ($t(24)=3.023$, $p=.006$) and a trend toward a significant difference at week 5 ($t(24)=1.869$, $p= .074$).

COMPARISON OF MDD SYMPTOM IMPROVEMENT BETWEEN STUDIES

FIGURE 2: COMPARISON OF RESPONSE RATES BETWEEN STUDIES



The magnitude of MDD symptom response in both treatment groups was similar to that observed in the previously published study (49% reduction in HAM-D-17 score in study one versus 43% in study two in the EFMT groups; 28% response versus 16% response in the control groups).

CONCLUSION

- Cognitive-emotional training exercises hold promise as a novel paradigm for MDD treatment.
- The present study replicated pilot results demonstrating superior MDD symptom improvement associated with EFMT compared to an active control condition.
- We hypothesize that effective connectivity changes between DLPFC and limbic system result from the training and are associated with symptom response; fMRI studies investigating this hypothesis are underway.

REFERENCES

1 *Iacoviello, B.M., & Charney, D.S. (2015). Developing Cognitive-Emotional Training Exercises as Interventions for Mood and Anxiety Disorders. European Psychiatry 30(1): 75-81.*

2 *Iacoviello, B. M., Wu, G., Alvarez, E., Huryk, K., Collins, K. A., Murrough, J. W., ... & Charney, D. S. (2014). Cognitive-emotional training as an intervention for major depressive disorder. Depression & Anxiety 31(8):699-706.*

3 *Neta M, Whalen PJ (2011): Individual differences in neural activity during a facial expression vs. identity working memory task. NeuroImage 56: 1685-1692.*

DISCLOSURES

- This research was funded by the National Institute of Mental Health grant #5K23MH099223 and Brain and Behavior Research Foundation (issuing NARSAD Grants) Young Investigator Grants #19080 and #24100 awarded to Brian M. Iacoviello, PhD.
- Icahn School of Medicine at Mount Sinai holds, and Drs. Iacoviello and Charney are named inventors on, a patent application for EFMT as an intervention for MDD. Click Therapeutics, Inc. has licensed this technology and intellectual property for development.

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