

NEUROMODULATION IN EATING DISORDERS

PROFESSOR ULRIKE SCHMIDT

LUCY GALLOP

MICHAELA FLYNN

PRESENTATION OVERVIEW

1) An Introduction to Neuromodulation in Psychiatry

2) Repetitive transcranial magnetic stimulation (rTMS)

- Including an overview of our RCT using TMS in Anorexia Nervosa (The TIARA Trial)

3) Transcranial Direct Current Stimulation (tDCS)

- Focusing on studies in binge eating disorder and the use of tDCS alongside other treatments

3) Discussion and Future Directions

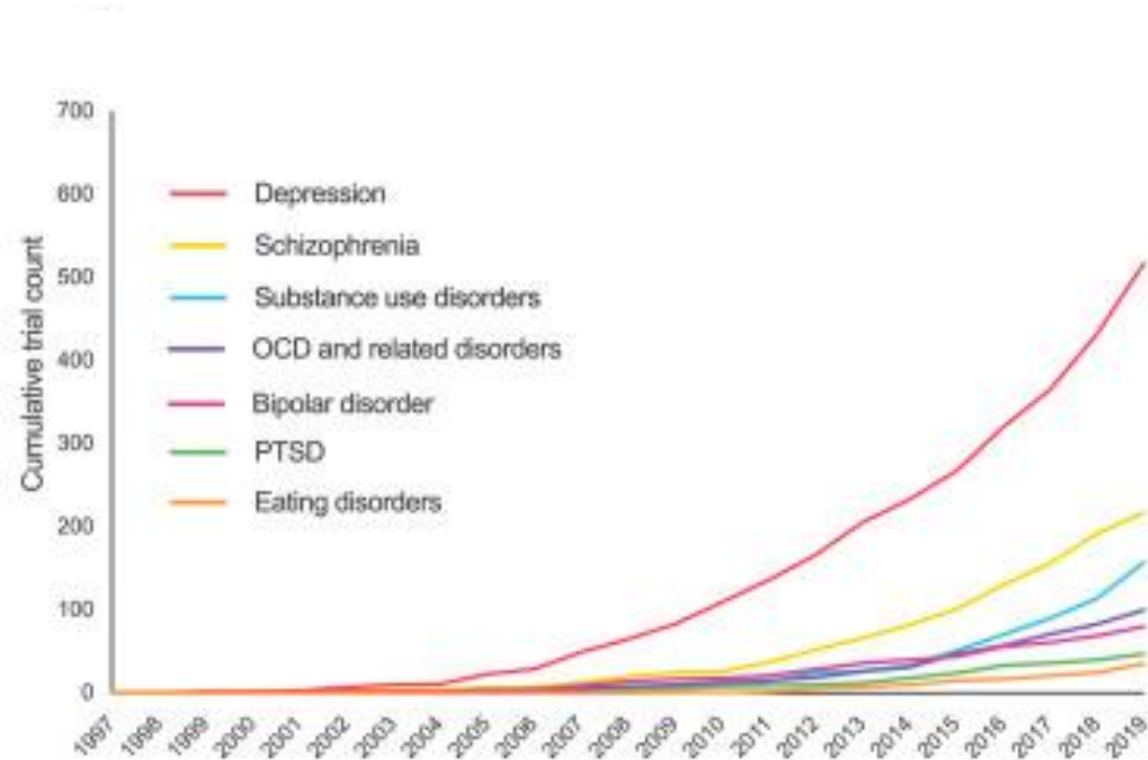
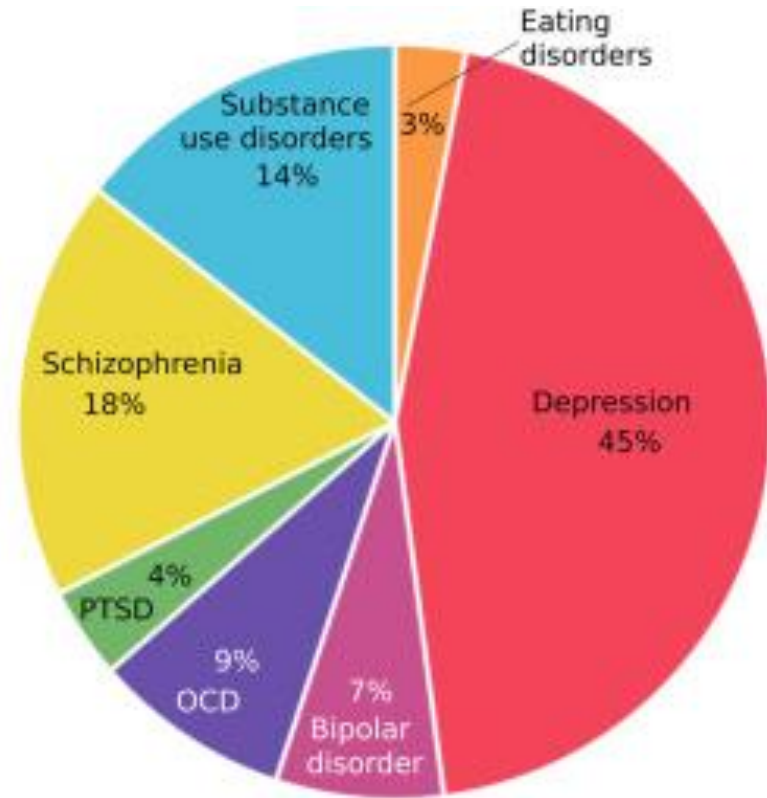
What is Neuromodulation?

“The alteration of nerve activity through targeted delivery of a stimulus, such as electrical stimulation or chemical agents, to specific neurological sites in the body”

NON-INVASIVE	INVASIVE
Repetitive Transcranial Magnetic Stimulation (rTMS)	Deep Brain Stimulation (DBS)
Theta Burst Stimulation (TBS)	Vagus Nerve Stimulation (VNS)
Electroconvulsive therapy (ECT)	
Transcranial Direct Current Stimulation (tDCS)	

Gallop et al., (2022)

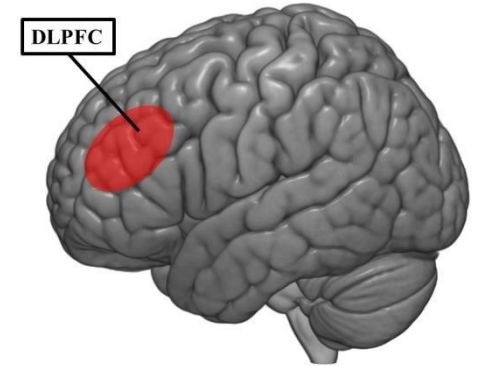
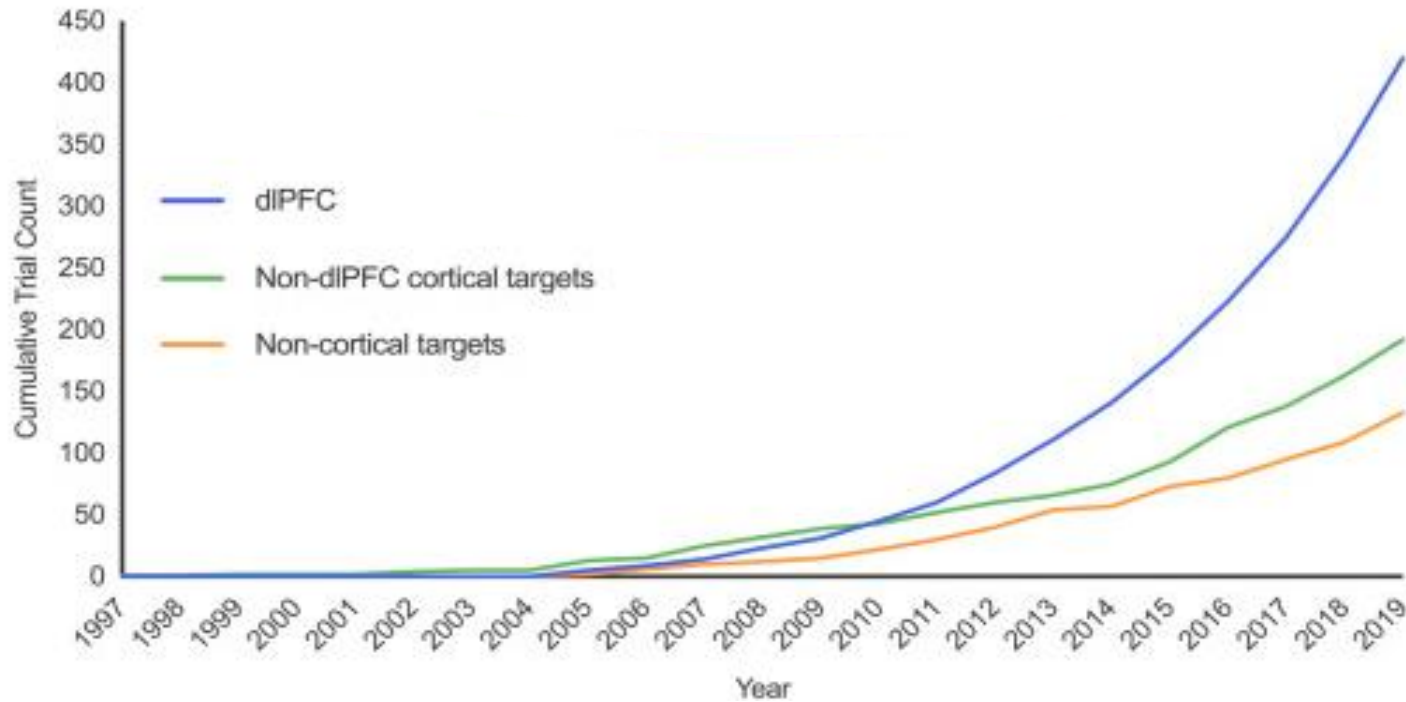
Neuromodulation use in psychiatric disorders



NB – A significant proportion of these studies has been done in Australia!

Elias et al., (2021)

Neuromodulation use in psychiatric disorders: What areas of the brain are being targeted?



dIPFC = dorso-lateral prefrontal cortex

Elias et al., (2021)

Why do we deliver neuromodulation to the DLPFC in EDs?

Reward models

- Imbalance between bottom-up and top-down regions of the brain

Emotion dysregulation

- Increased activity in regions involved in emotion processing and regulation

Habit model

- Behaviour moves away from being rewarding to more habitual

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (rTMS)



Pulses of electrical current



Magnetic field



Current in the brain



Depolarised neurones



Synaptic plasticity

Pros and Cons of rTMS

Non-invasive

- Well tolerated with few side-effects
- Common side effects are transient headaches and neck pain

Time demands

- Requires daily sessions for 4-6 weeks
- Research is looking at ways to reduce this

rTMS in Bulimia Nervosa (BN)

- Case studies/series report reductions in bingeing and/or purging
- Small RCTS report no significant differences between real or sham rTMS in binge-purge symptoms

rTMS in Binge Eating Disorder (BED)

- Evidence is lacking
- Results are pending from an RCT conducted in Brazil

rTMS in Anorexia Nervosa (AN)

- Proof-of-concept trials & case series report reductions in ED and affective symptoms
- The first RCT (TIARA trial) was conducted by our research group

tiana



TMS and imaging in anorexia

Randomised double blind trial:

- 20 sessions (5/week) real high-frequency rTMS (to the DLPFC) vs 20 sessions sham treatment

Participants

- Adults with diagnosis of AN; BMI: 18.5 - 14.0 kg/m², medically stable
- ≥ 3 years illness duration and \geq one unsuccessful previous treatment

Assessments:

- Baseline; 1 month (end of treatment) & 4 months (follow-up)
- Clinical, neurocognitive & neuroimaging assessments & qualitative interviews

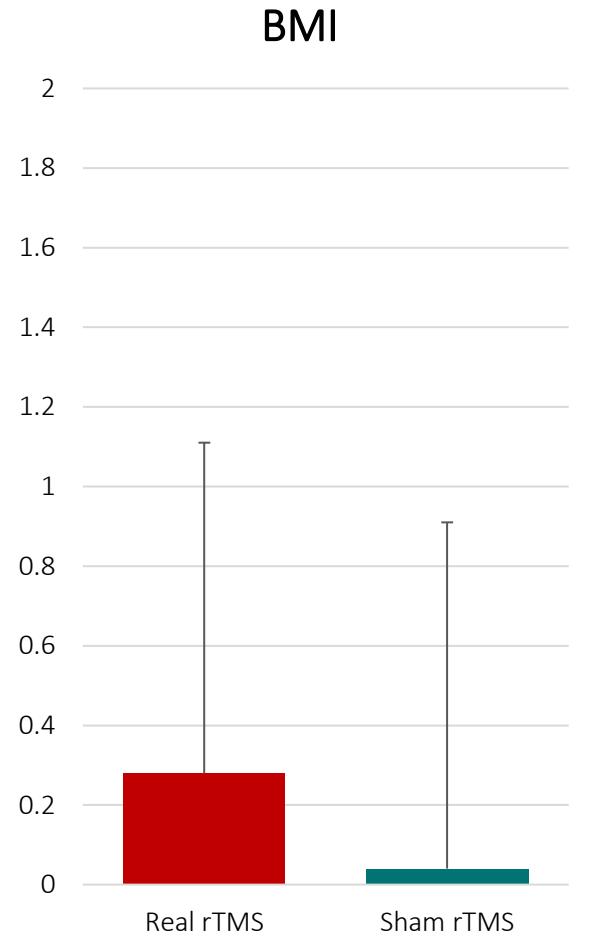
After the Trial:

- Sham completers were offered real rTMS after 4/12
- All trial participants completed an open 18/12 follow-up.

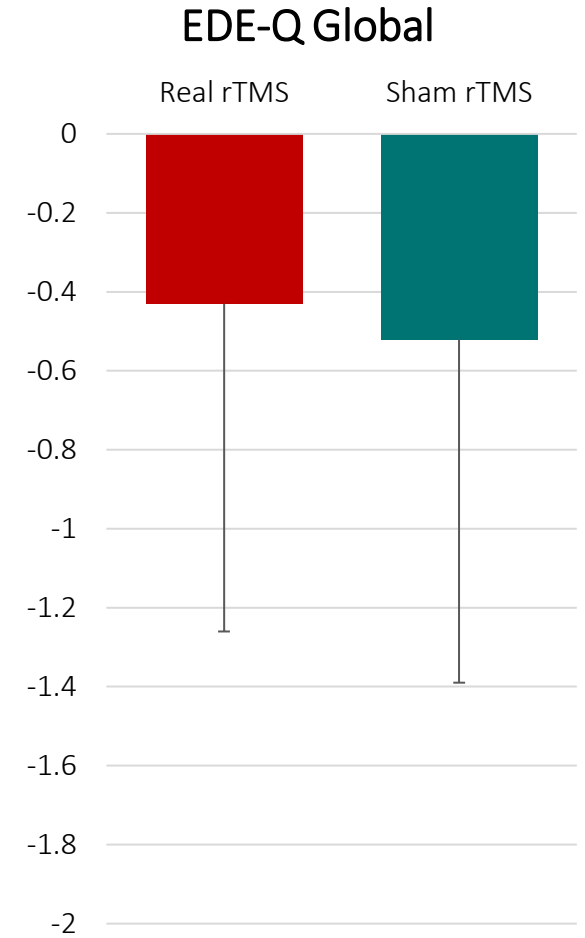
Baseline Characteristics TIARA Study

	Real rTMS	Sham rTMS
Age (Years)	28.5 (9.5)	31.0 (11.3)
Illness Duration (Years)	13.8 (10.7)	14.4 (11.1)
BMI	15.8 (1.6)	16.3 (1.2)
EDE-Global Score	4.1 (1.3)	4.3 (0.9)
Restricting vs BP- AN	10 / 6	10 / 6
Months previously spent in hospital	12.4 (2.5)	8.5 (10.8)
Taking an antidepressant	65%	59%

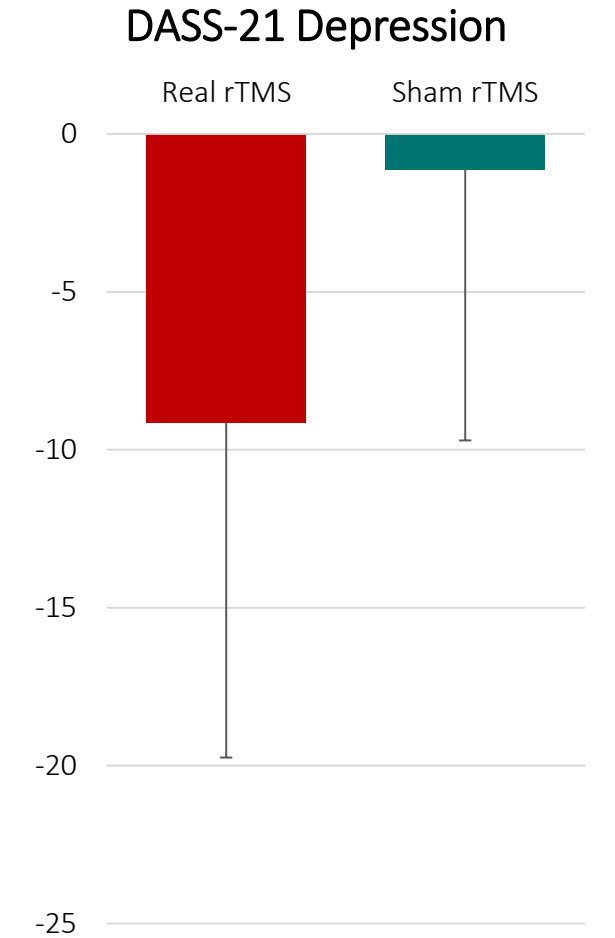
Clinical Trial Outcomes: 4-Months



$d=0.20$ (95% CI -0.49 to 0.90)



$d=0.10$ (95% CI -0.60 to 0.79)



$d=-0.83$ (95% CI -1.55 to -0.10)

Effects on Mood & Quality of Life

Something began to feel clearer some weeks after the study finished...My mood seemed lighter and clearer.

I'm being able to put people before the eating disorder. That's been the biggest change since having the treatment



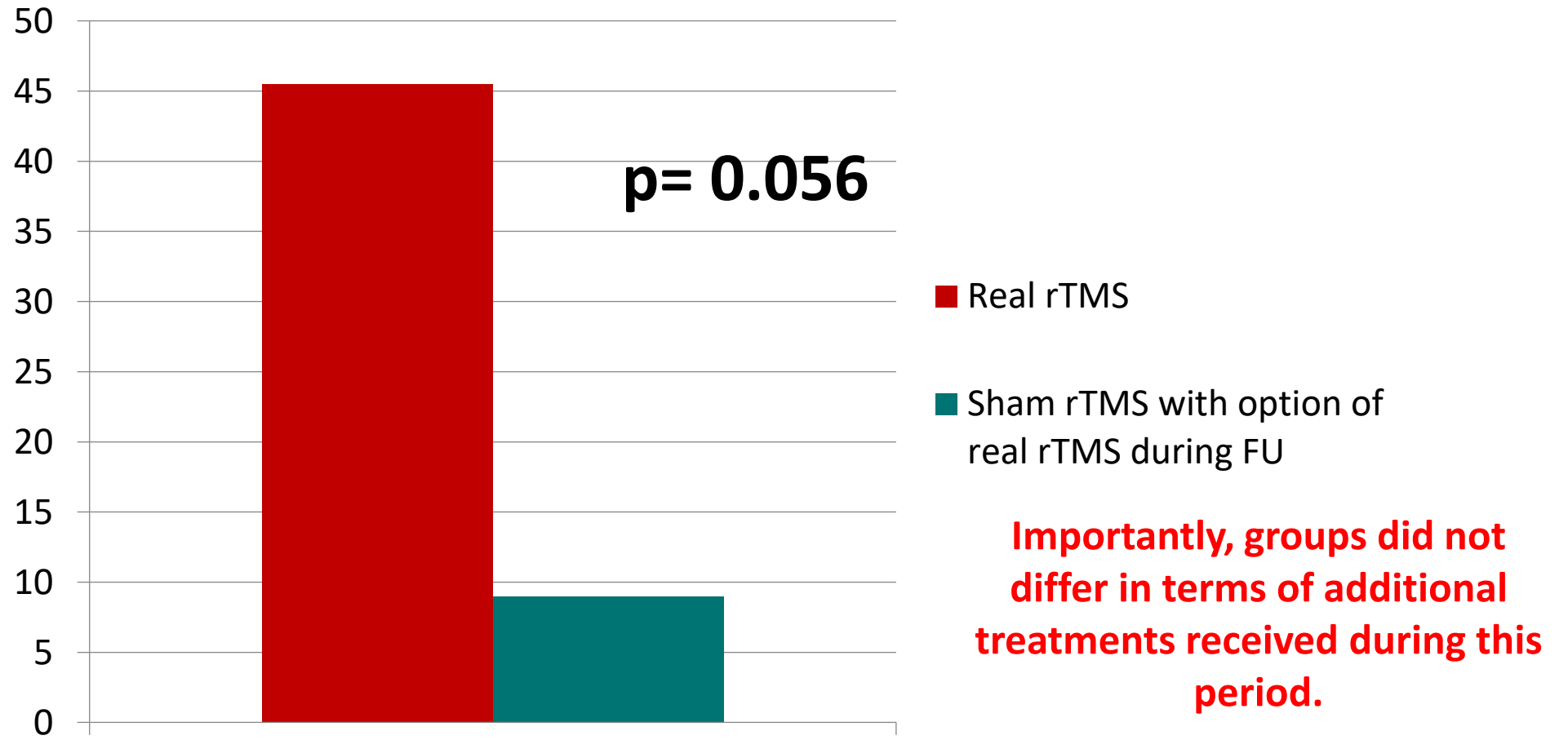
Patient Experience of Food & Eating after rTMS

And recently in the last few weeks, I eat normally and eat whatever I want to.

My eating pattern has changed ... I'm finding I'm eating more different foods

I think I am a lot more open to .. eating out and stuff than I have ever been before

Open Follow-Up: 18-Months - Weight Recovery (%)



Neurocognitive mechanisms of rTMS

Food Choice Task → food-related decision making and self-control

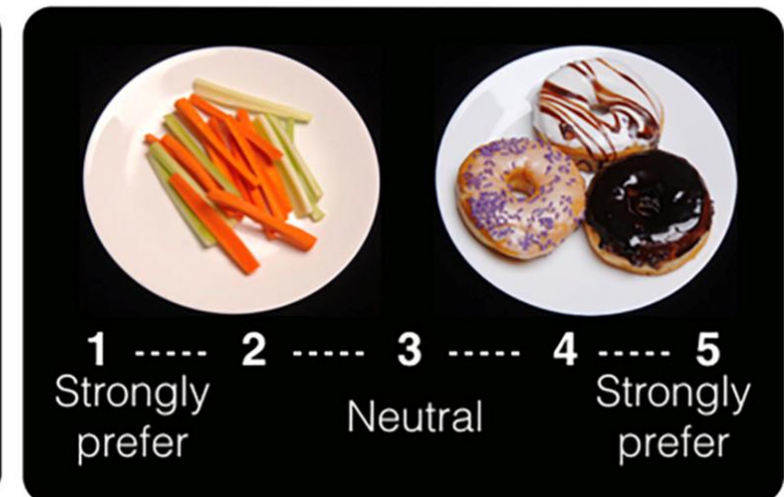
Health rating



Taste rating



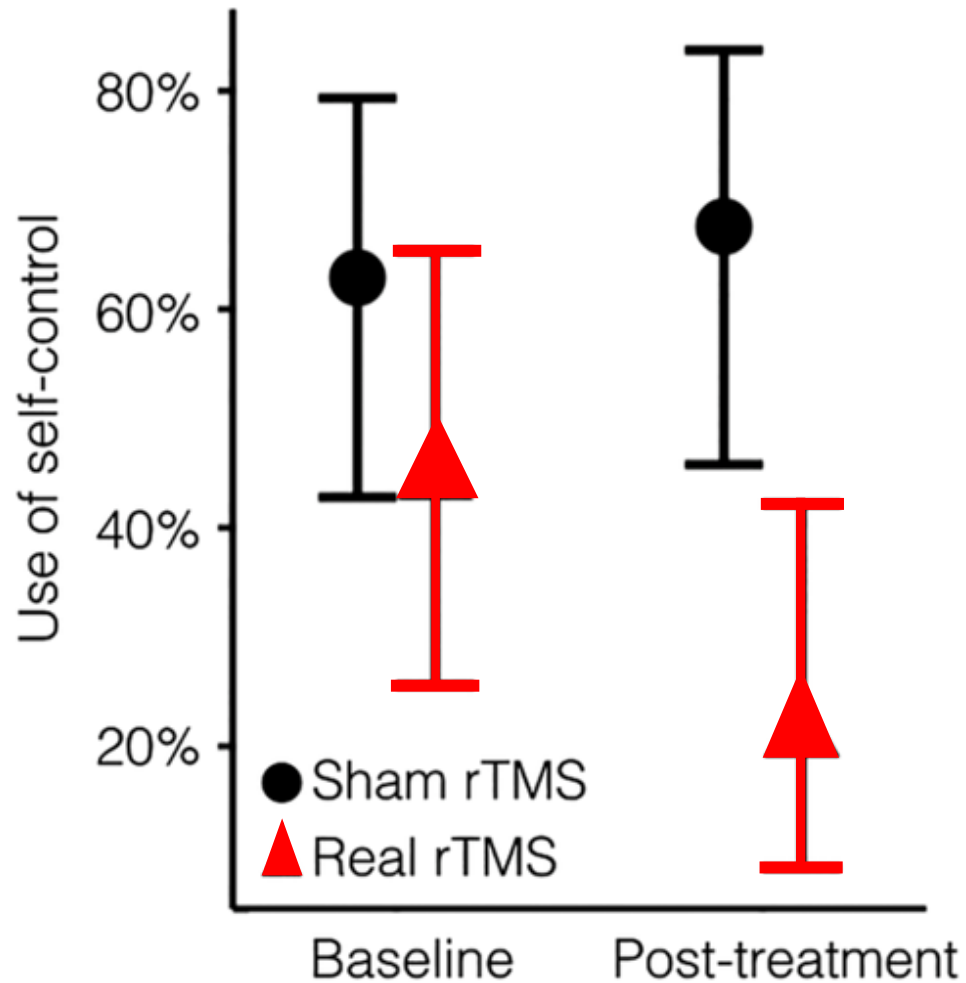
Food choice



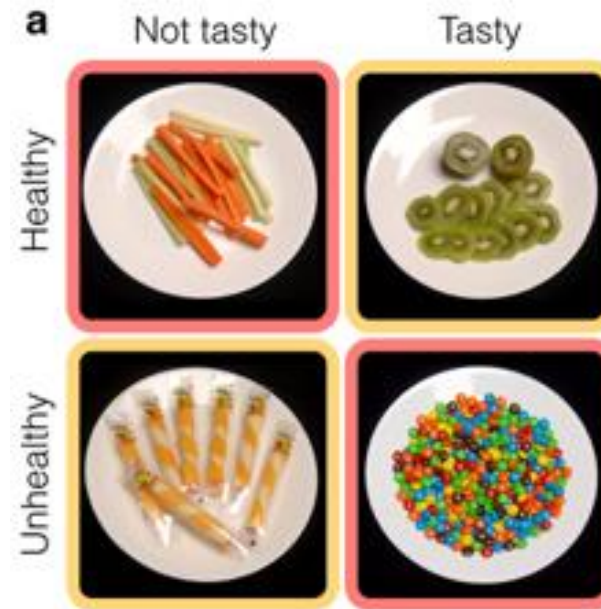
Examples of the three blocks of the Food Choice Task

Dalton et al., 2020
Steinglass & Walsh (2016)

Food Choice Task - Relaxed self-control with real TMS

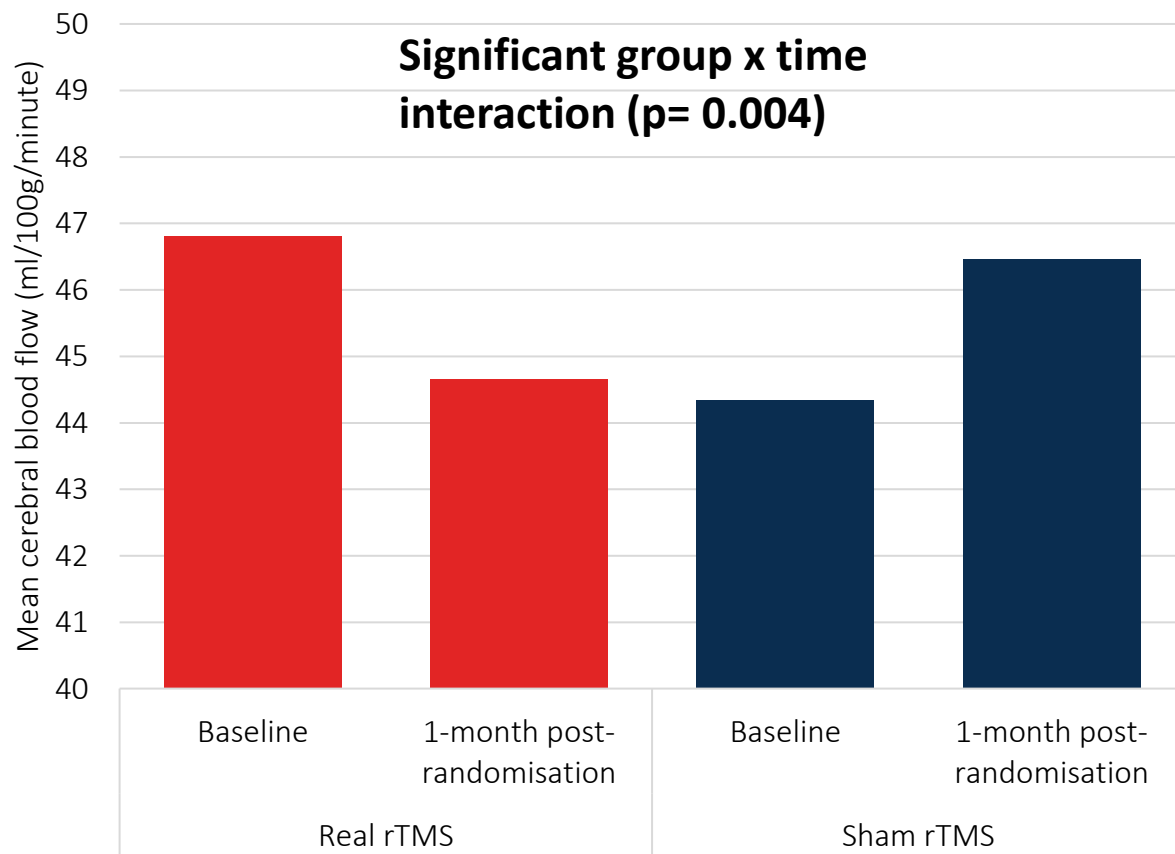


Self control = when a more healthy, less tasty food item *is* selected or a less healthy, tastier food item *is not* selected.



Change in amygdala cerebral blood flow (CBF) following TMS

Amygdala rCBF changes

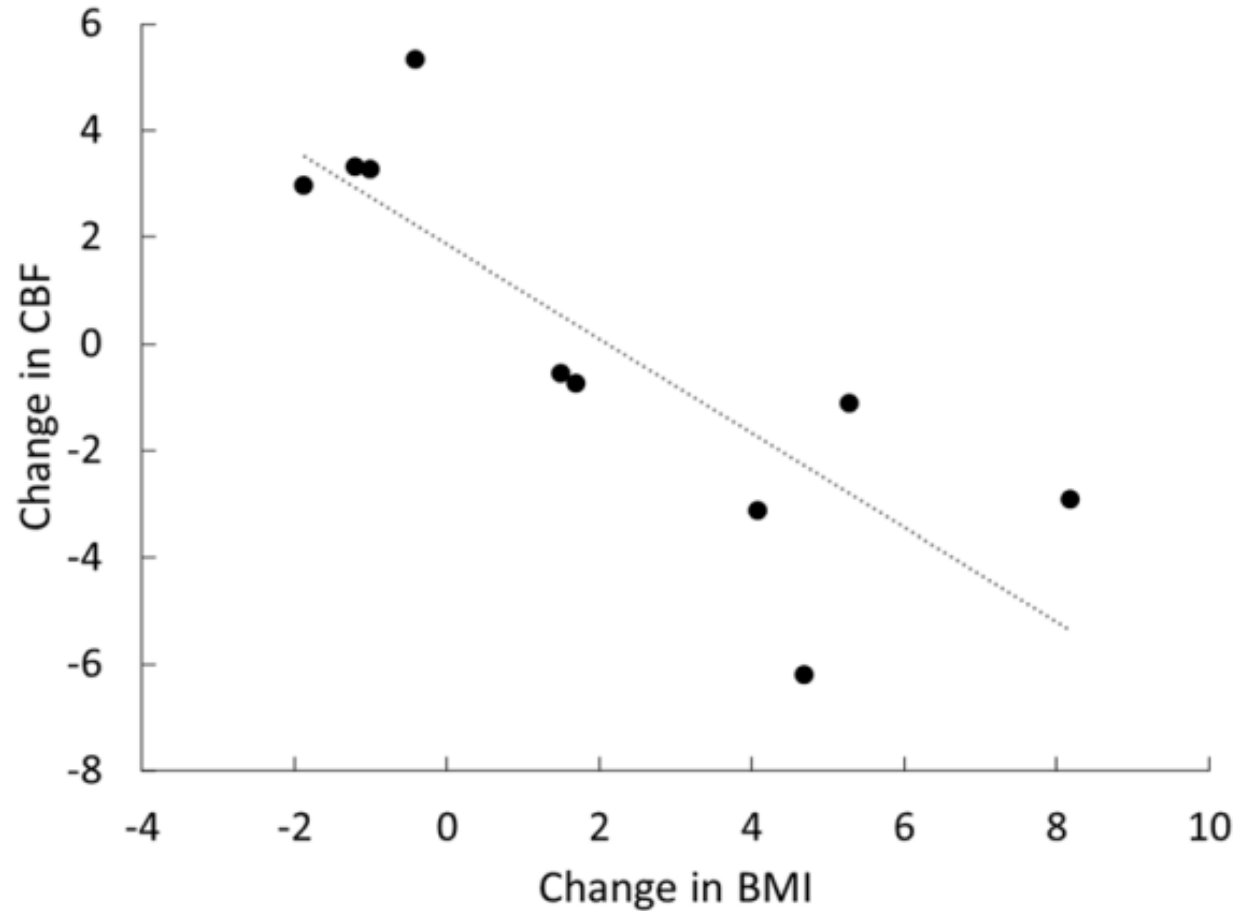


At end of treatment (1/12):

- Compared to sham, after real rTMS there was:
 - A reduction in regional cerebral blood flow in the amygdala (Dalton et al., 2021).
 - Changed attention to food, i.e. participants no longer avoided looking at food stimuli (Werthmann et al., submitted)
 - Shifted food choices in the direction of more liked and more calorific foods (Dalton et al., 2020b)

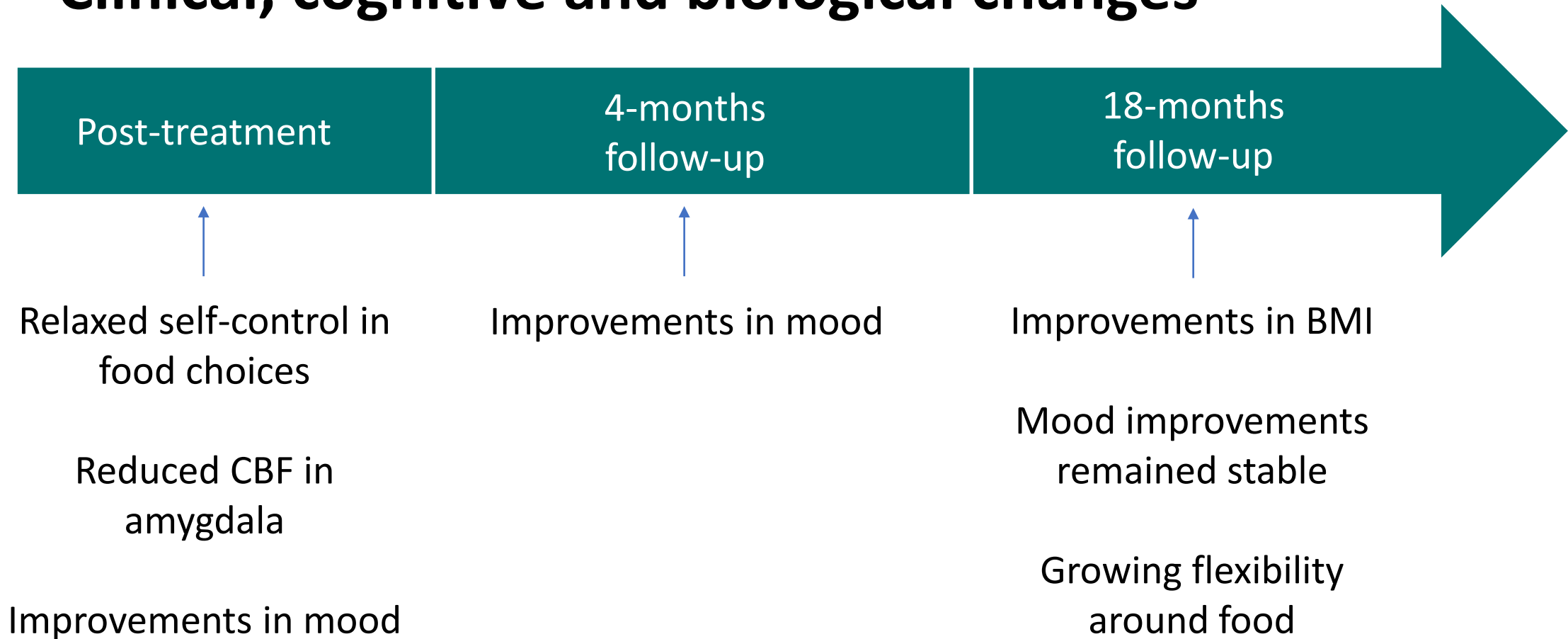
Reduction in rCBF in real rTMS predicted increase in BMI at 18/12

Reduced amygdala CBF → weight gain at 18-months

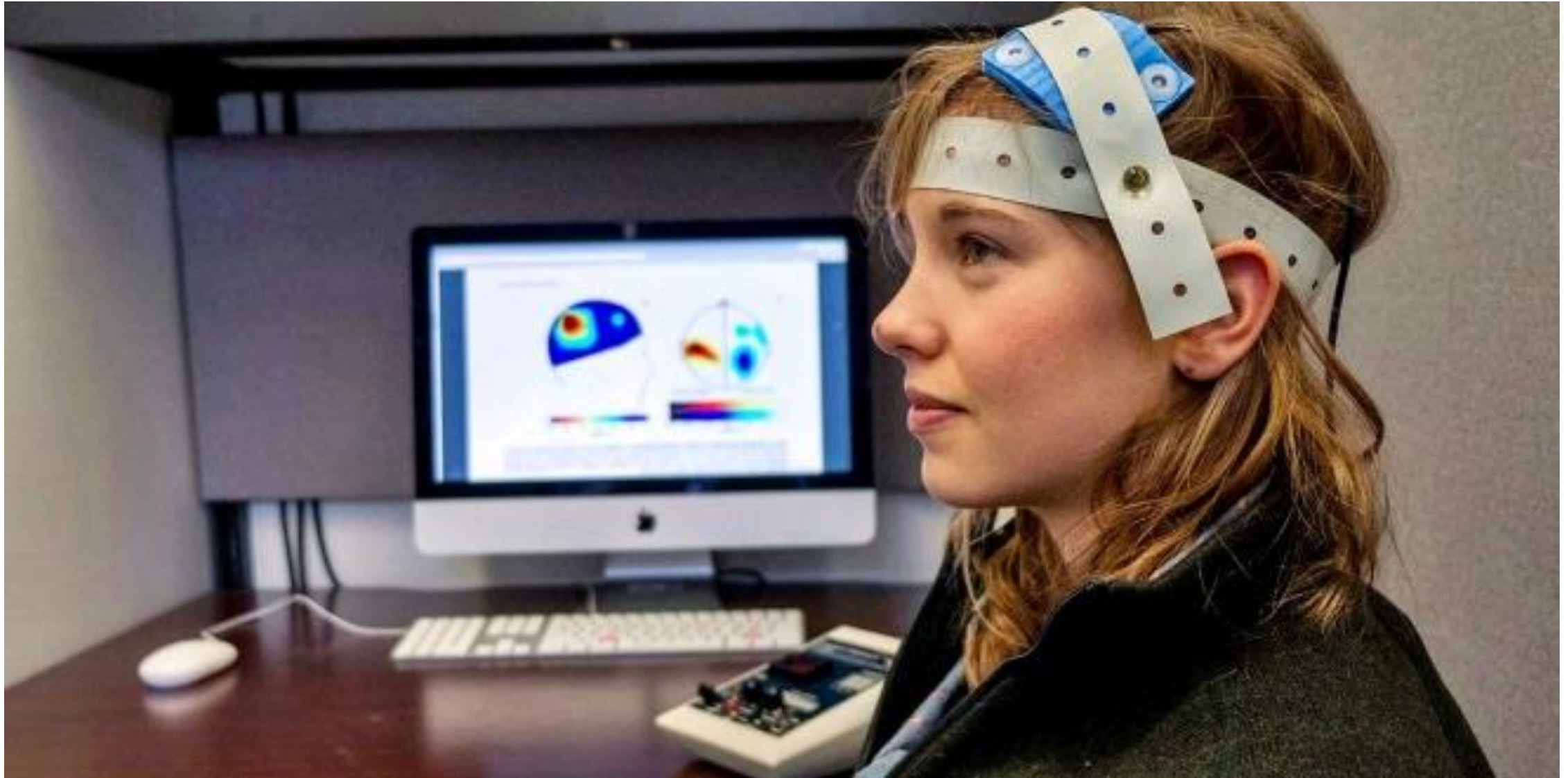


Change in amygdala CBF predicts change in BMI from baseline to 18-month follow-up

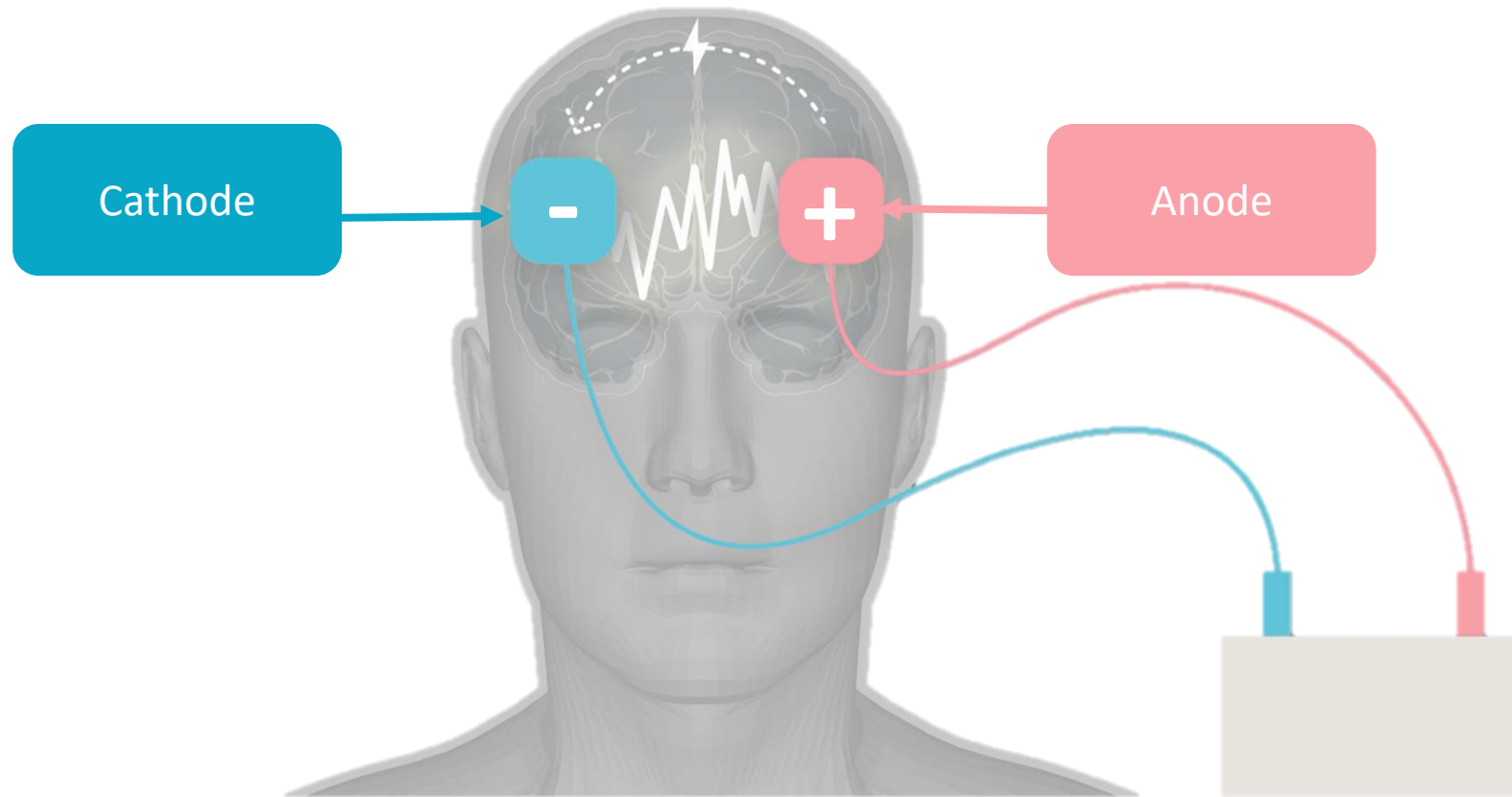
Clinical, cognitive and biological changes



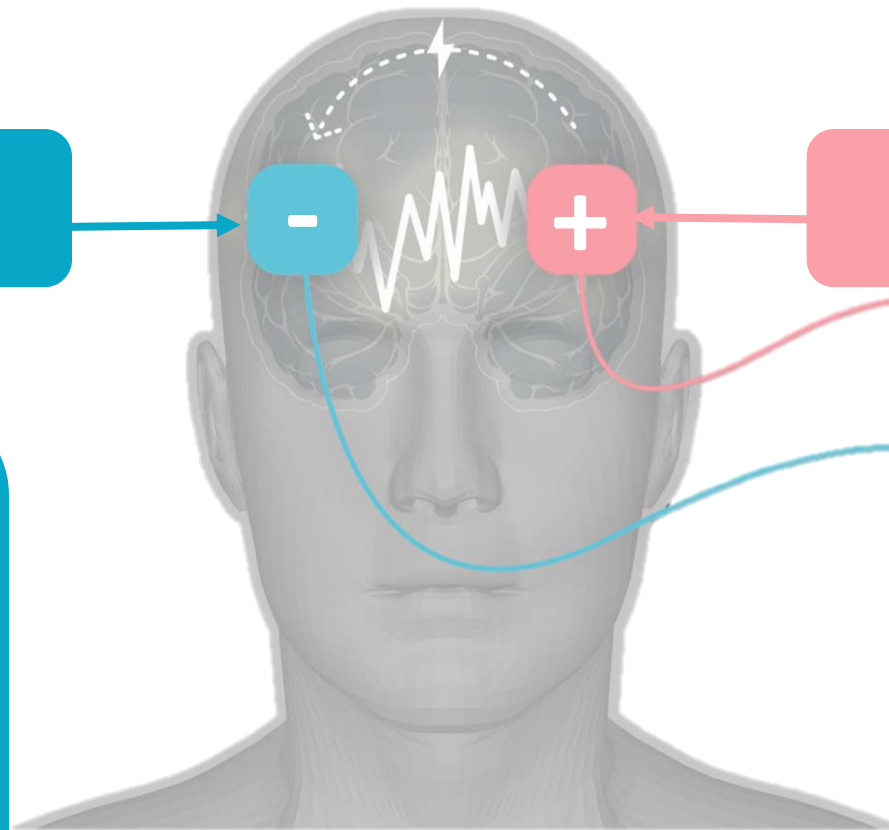
Transcranial Direct Current Stimulation



What is tDCS?



What is tDCS?



Cathode

Anode

Cathodal Stimulation
Hyperpolarises resting membrane potential making the neuron less likely to fire.

Anodal Stimulation
Depolarises resting membrane potential making the neuron more likely to fire.



Studies in Anorexia

- One randomised controlled trial which included 43 inpatients (Baumann et al., 2021):
 - **No significant effect of tDCS** on ED pathology or weight
 - Real tDCS associated with greater reduction in dietary rigidity and greater improvement in body image than sham ($p < 0.05$)
- One single-blind study which included 23 adolescents receiving outpatient treatment (Costanzo et al., 2018)
 - **Positive effect of tDCS** on ED psychopathology
 - Greater increase in BMI was observed in the cohort who received tDCS alongside treatment as usual (Costanzo et al., 2018)
- One open label study involving 10 inpatients (Strumila et al., 2019)
 - 20 sessions of anodal DLPFC tDCS over 2 weeks
 - **Positive effect of tDCS** on ED psychopathology and symptoms of comorbid depression in 9/10 inpatients

Studies in Bulimia Nervosa and Binge Eating Disorder

- In bulimia nervosa, only single-session studies are available and these report mixed findings.
- More multi-session trials looking at tDCS in binge eating disorder. These collectively suggest that, anodal tDCS to the right dorsolateral prefrontal cortex (DLPFC) may:
 - Reduce binge frequency
 - Help with weight loss
 - Reduce craving for food
 - Improve mood

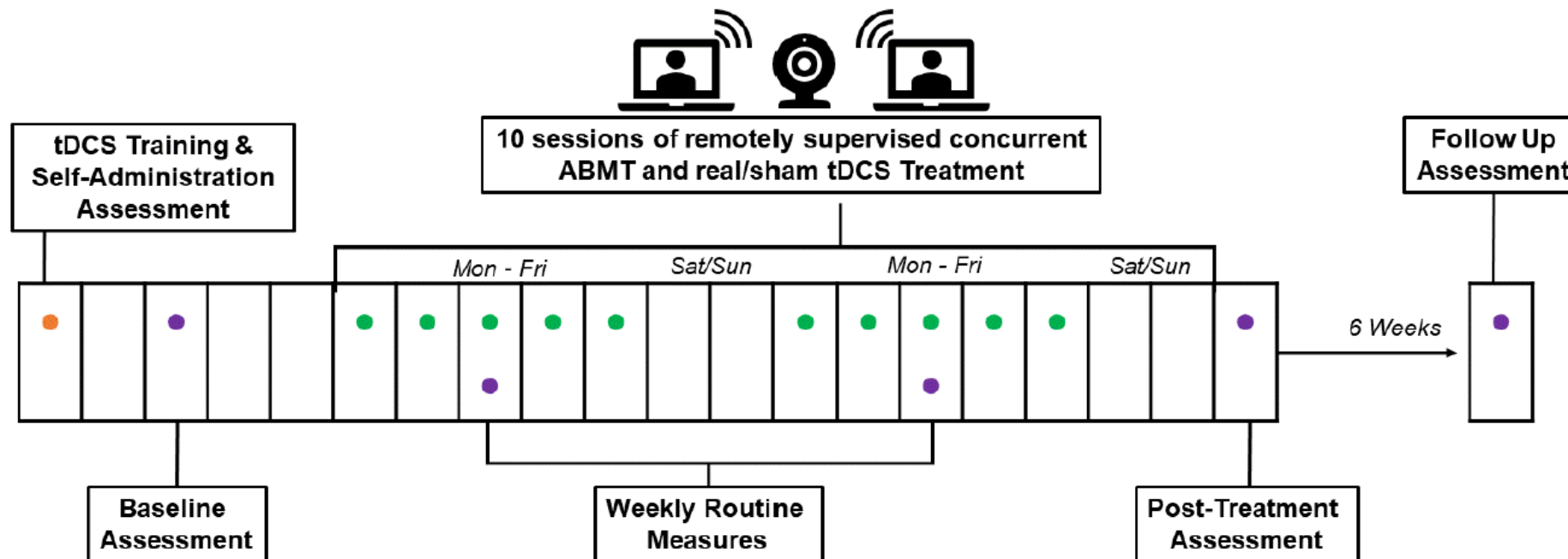
tDCS as an Adjunct to Treatment

- Good scientific rationale for combining tDCS with other interventions
- Cognitive Bias Modification Training (CBM) is one possible add on intervention which aims to retrain or change cognitive processes triggered by food cues.
- tDCS and CBM may affect the brain in similar ways, so it is possible that when we combine these two treatments we may achieve superior outcomes from treatment.



TANDEM: At home tDCS + Attention Training in BED

- Randomised sham-controlled trial
- 10 sessions of at-home self-administered tDCS cognitive bias modification training over 2 weeks
- CBM focused on changing food related biases in attention
- 80 participants across 4 Groups



The TANDEM Look



TANDEM: Baseline Characteristics

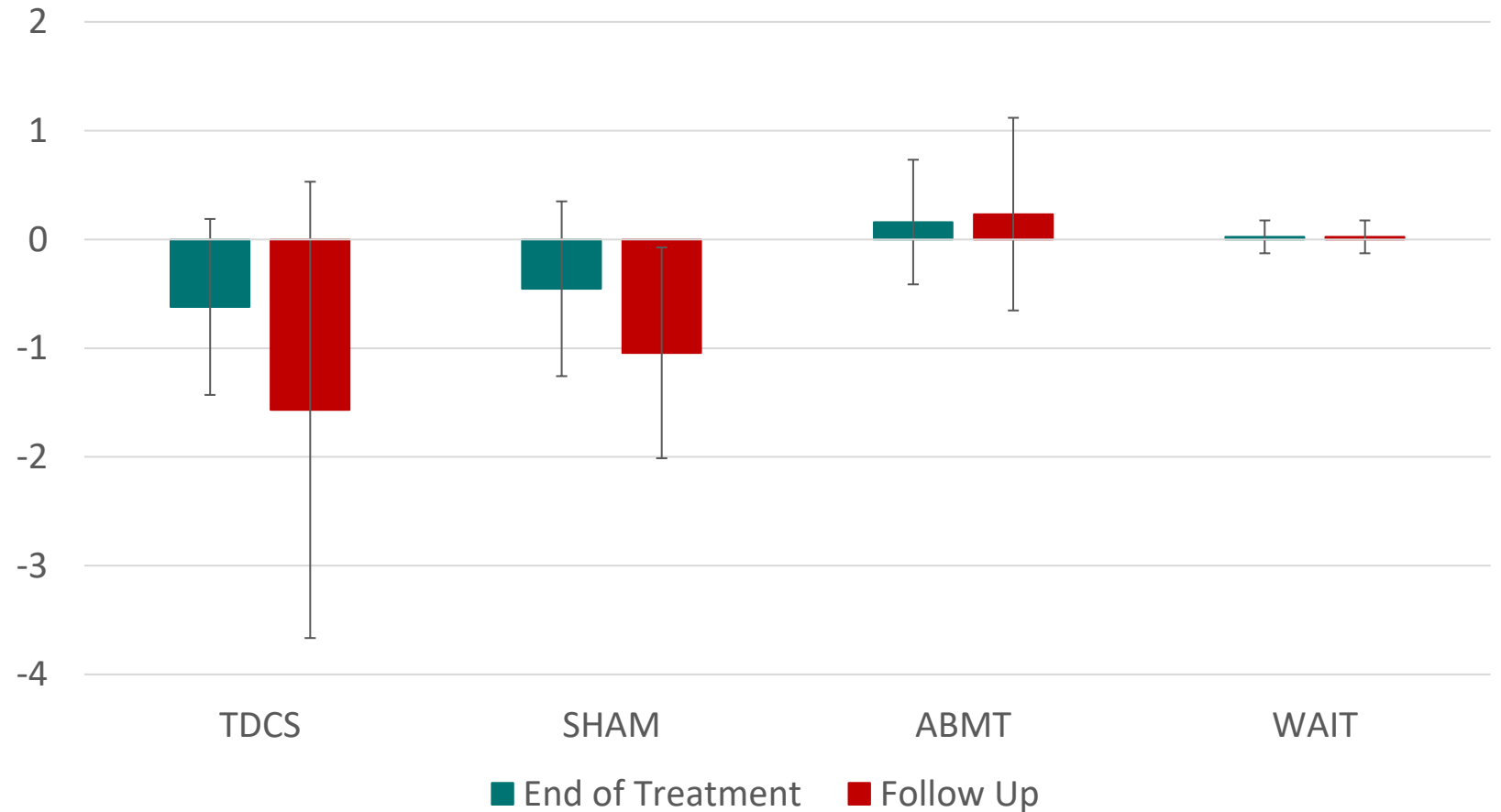
	Real tDCS + ABMT (n=20)	Sham tDCS + ABMT (n=20)	ABMT Only (n=20)	Wait (n=20)
Age (years)	39.80 (10.09)	40.45 (7.88)	43.70 (10.60)	43.53 (9.85)
BMI	39.12 (6.70)	39.26 (8.70)	42.46 (8.82)	40.32 (6.53)
EDE-Global Score	4.01 (0.80)	3.98 (0.79)	4.20 (0.80)	3.98 (1.11)
Monthly Binges	34.10 (9.28)	27.70 (12.22)	21.05 (8.81)	23.32 (21.91)
Depression	9.05 (5.77)	7.15 (5.01)	8.90 (5.83)	7.95 (6.03)
Anxiety	3.70 (3.35)	4.10 (4.13)	4.5 (3.36)	3.63 (2.52)
Stress	9.35 (5.31)	8.30 (3.69)	9.25 (3.57)	8.32 (3.73)

* Values reflect the mean and standard deviations

** Depression, anxiety and stress scores obtained using the DASS-21

TANDEM: At home tDCS + Attention Training in BED

Change in BMI at Post-Treatment and 6-Week Follow



Post Treatment:

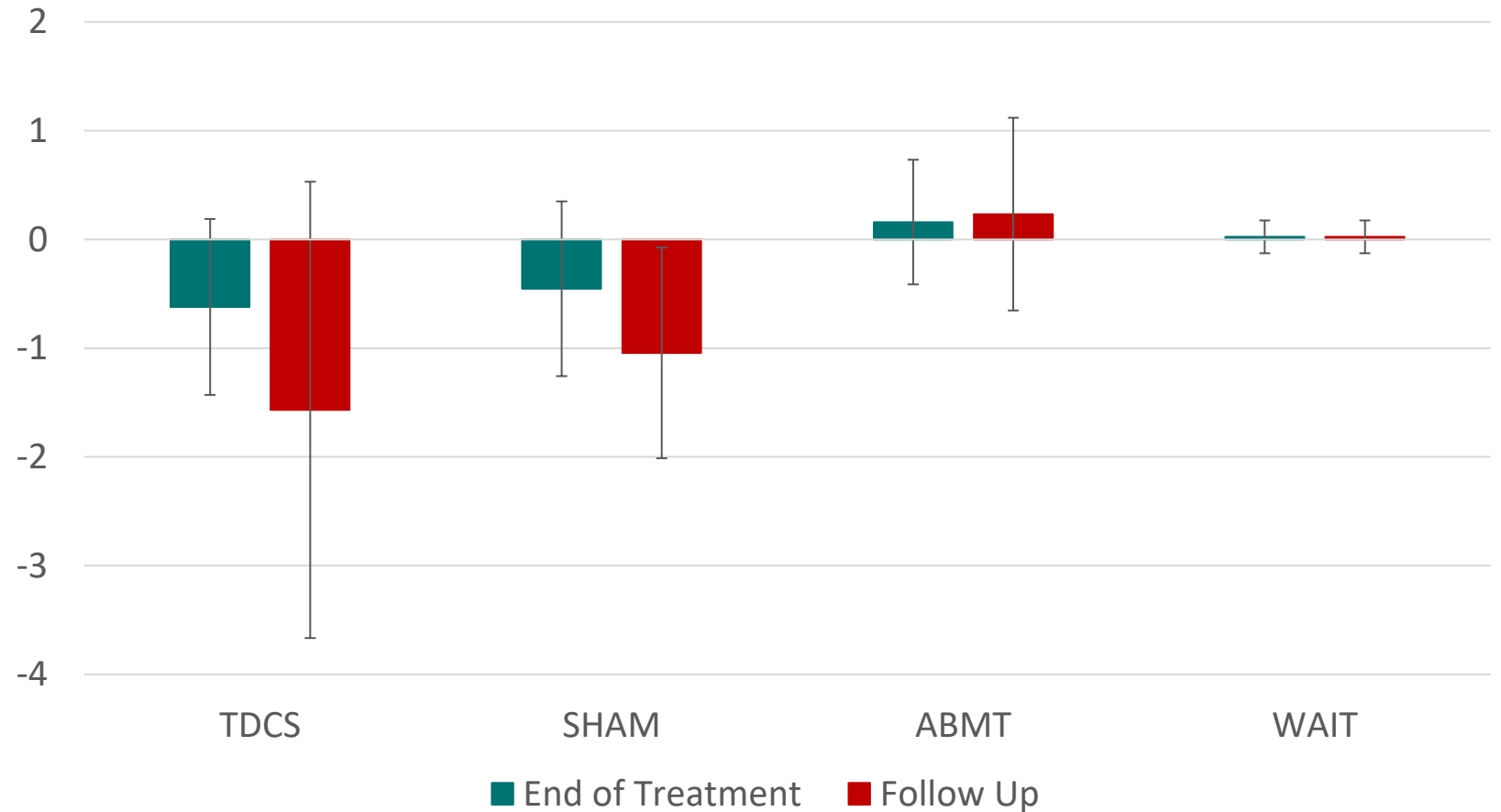
Change in BMI was greater for real tDCS+ABMT than for ABMT only and for waiting control.

Change in BMI greater for sham+ABMT than ABMT only.

No significant difference between real and sham tDCS groups.

TANDEM: At home tDCS + Attention Training in BED

Change in BMI at Post-Treatment and 6-Week Follow



6-Weeks Post-Treatment:

Greater change in BMI for SHAM+ABMT than for ABMT only and for waiting.

No other differences are statistically significant.

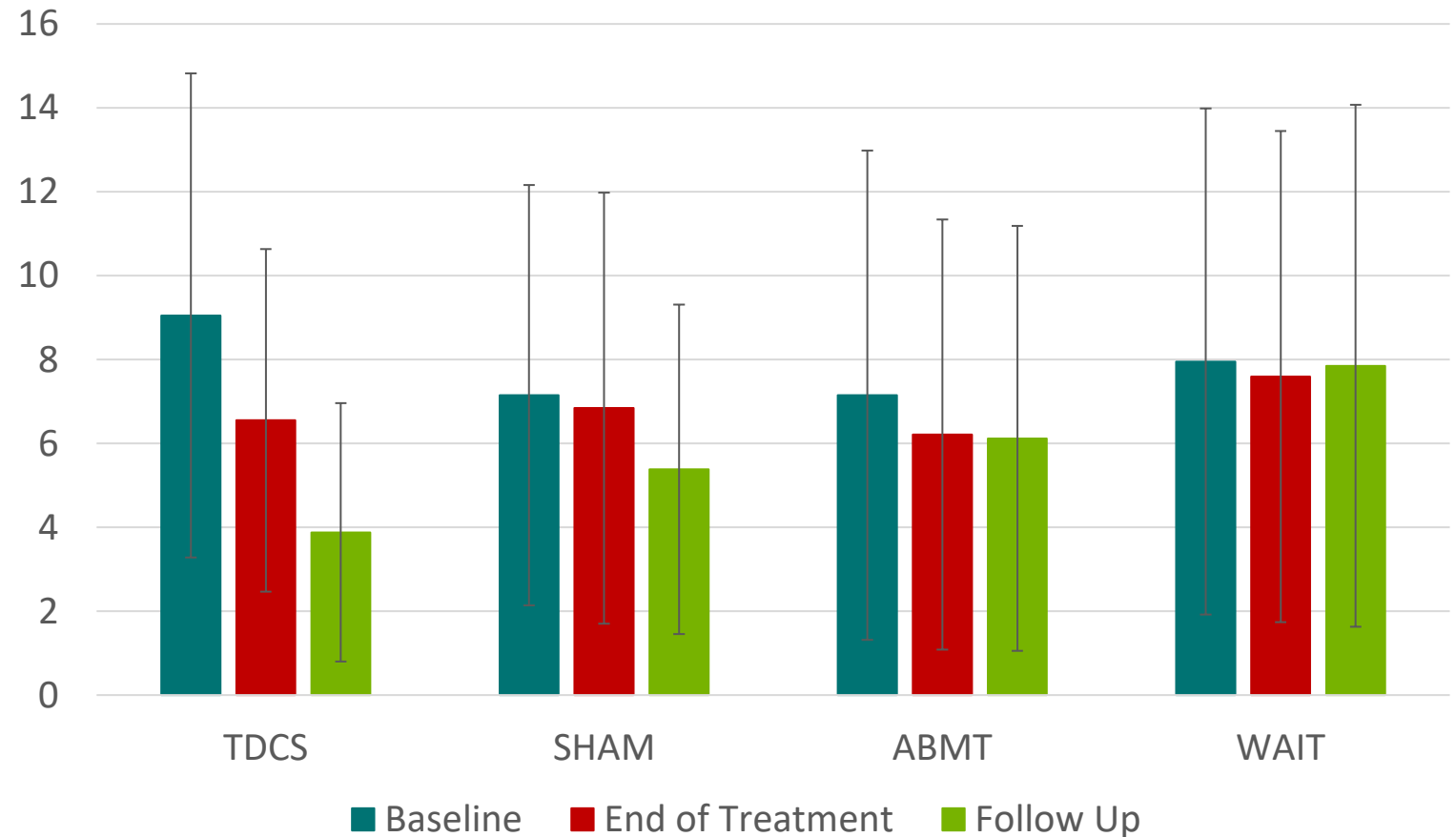
TANDEM: At home tDCS + Attention Training in BED

Follow Up:

By follow-up mood scores differ between groups.

By follow up, TDCS+ABMT had a superior effect on mood than both SHAM+ABMT and waiting.

Change in Mood from Baseline to Follow Up



Patient Perspective

Since TANDEM, I have felt more able to think about other things. Food doesn't overwhelm me like it used to.

My mood has improved so much. My daughter even said that I am much brighter to be around.

I was able to do this for myself because I could do it at home at a time that worked for me. I haven't been able to make time to get help like this before.

Status of tDCS as a treatment for EDs?

- tDCS may improve some symptoms associated with EDs
- May be benefits for those with comorbid depression
- tDCS pairs well with complementary interventions and doing so may drive superior outcomes from treatment
- Affordable, easy to use, safe, and well liked by people who use it.

HOWEVER

- Findings are mixed with limited data available from gold-standard trials, particularly for AN and BN
- Our understanding of HOW it works is limited
- We do not know the optimal parameters for treatment



Summary, Conclusion & Next Steps

We have shown you a small glimpse of the work that we are doing

Neuromodulation is an emerging area of research

- We still know very little & lots of questions remain
- We need more & larger studies exploring...
 - Different types of neuromodulation
 - Different brain targets & stimulation parameters
 - Different clinical groups

Next steps for us:

- Treating adolescents with persistent AN with a newer variant of rTMS
- Combining tDCS with different forms of cognitive training (e.g. mindfulness)

Thank you!

PROFESSOR ULRIKE SCHMIDT

(ULRIKE.SCHMIDT@KCL.AC.UK)

LUCY GALLOP (LUCY.GALLOP@KCL.AC.UK)

MICHAELA FLYNN (MICHAELA.FLYNN@KCL.AC.UK)