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Efficacy of a Food Response and Attention Training Treatment for Obesity: A Randomized Placebo Controlled Trial

Eric Stice[a1]

Stanford University

Sonja Yokum[b]

Jeff Gau[b]

Oregon Research Institute

Harm Veling[c]

Radboud University Nijmegen

Natalia Lawrence[d2]

University of Exeter

Eva Kemps[e2]

Flinders University

1: corresponding author.
2: joint last authors.
a. Department of Psychiatry and Behavioral Sciences, Stanford University, 401 Quarry Road, Stanford CA 94305 USA; estice@stanford.edu
b. Oregon Research Institute, 1776 Millrace Drive, Eugene OR 97403 USA
c. Behavioural Science Institute, Radboud University Nijmegen, PO Box 9104 6500 HE Nijmegen, The Netherlands
d. School of Psychology, University of Exeter, Exeter EX4 4QG, UK
e. School of Psychology, Flinders University, GPO Box 2100, Adelaide, SA 5001, Australia

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Abstract

Elevated brain reward and attention region response, and weaker inhibitory region response to high-calorie foods has predicted future weight gain, suggesting that an intervention that reduces reward and attention region response and increases inhibitory region response to such foods might reduce overeating. We conducted a randomized controlled trial to test whether a multi-faceted food response and attention training protocol with personalized high- and low-calorie food images would reduce body fat and valuation and reward region response to high-calorie foods compared to a placebo control training protocol with non-food images in an effort to replicate findings from two past trials. Participants were community-recruited adults with overweight/obesity (N=179; *M* age=27.7 ±7.0) who completed assessments at pretest, posttest, 3-month, 6-month, and 12-month follow-ups. Participants randomized to the food response inhibition and attention training showed significantly greater increases in palatability ratings of low-calorie foods than controls (*d*=.27) at posttest, but did not show body fat loss, reductions in palatability ratings and monetary valuation, or reward region response, to high-calorie foods. The lack of expected effects appears to be related to weaker learning compared to the learning in past trials, potentially because we used more heterogenous high-calorie and low-calorie food images in the present training.

KEYWORDS: reward; attention; response training; attention training, obesity treatment; fat loss

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Obesity accounts for over 2.8 million deaths annually and is ranked the second leading cause of premature mortality (World Health Organization, 2021). Unfortunately, the most common treatment, behavioral weight loss programs, almost never produce lasting weight loss (Turk et al., 2009), suggesting that there is a need to evaluate treatments that use a different approach.

Prospective studies have found that individuals who exhibit elevated responsivity of brain reward regions (striatum, orbitofrontal cortex) to images of high-calorie foods show elevated future weight gain (Demos, Heatherton & Kelley, 2012; Stice, Burger, Yokum, 2015; Yokum, Gearhardt, Harris, Brownell & Stice, 2014; Yokum, Gearhardt, & Stice, 2021). Attentional bias for high-calorie food also predicts greater future *ad lib* intake (Nijs, Muris, Euser, & Franken, 2010; Werthmann, Field, Roefs, Nederkoorn, & Jansen, 2014) and future weight gain (Calitri, Pothos, Tapper, Brunstrom & Rogers, 2010). Moreover, weaker recruitment of an inhibitory region (dorsolateral PFC) in response to high-calorie food images predicted elevated future *ad lib* intake (Cornier, Salzberg, Endly, Bessesen & Tragellas, 2010). Further, lower inhibitory region (inferior, middle, and superior frontal gyri) recruitment during a delay-discounting task predicted elevated future weight gain (Kishinevsky et al., 2012), converging with evidence that lower inhibitory control in response to high-calorie foods predicted elevated future weight gain (Evans, Fuller-Rowell, & Doan, 2012; Francis & Susman, 2009; Schlam, Wilson, Shoda, Mischel, & Ayduk, 2013; Seeyave et al., 2009). These prospective relations are consistent with the theory that obesity results from increased reward and attention region response to high-calorie foods that is coupled with weaker inhibitory control (Boswell & Kober, 2016; Nederkoorn, Houben, Hofmann, Roefs, & Jansen, 2010; Stice & Yokum, 2016).

These findings suggest that an intervention that reduces reward and attention region response to high-calorie foods and increases inhibitory region response may reduce overeating that occurs in response to exposure to high-calorie food images and cues, and produce weight loss. Experiments show that relative to control training, go/no-go and stop-signal computer training in which participants are signaled to repeatedly respond with a button press to low-calorie food or non-food images, and repeatedly inhibit behavioral responses to high-calorie food images, which we refer to as response training, was associated with decreased palatability ratings for the high-calorie foods paired with response inhibition signals and less *ad lib* intake of those foods (Chen et al., 2016; Houben & Jansen, 2011; Lawrence et al., 2015; Veling et al., 2013) and weight loss among overweight participants (Allom & Mullan, 2015 Study 1; Lawrence et al., 2015; Veling, van Koningsbruggen, Aarts & Stroebe, 2014). However, other trials did not find that food response training produced weight loss among overweight participants (Allom & Mullan, 2015 Study 2; Forman et al., 2019; Memarian, Moradi, Hasani, & Mullan, 2021).

There is also evidence that attention training can reduce attentional bias for high-calorie food cues, which should decrease the potential for these cues to induce overeating. Randomized experiments have found that participants who complete dot-probe training in which attentional bias for high-calorie food is reduced and attentional bias for low-calorie foods is increased results in reductions in attentional bias for and intake of high-calorie foods (Kakoschke, Kemps, & Tiggemann, 2014; Kemps, Tiggemann, & Hollitt, 2014; Kemps, Tiggemann, Orr, & Grear, 2014). However, a training paradigm lacking a behavioral response element (Werthmann, Field, Roefs, Nederkoorn, & Jansen, 2014) did not reduce attentional bias that emerged in the dot-probe training that included behavioral responses, implying that the motor response element of attention training may be essential.

We conducted a randomized pilot trial to test the hypothesis that a multifaceted training protocol including both food response and attention training would be associated with greater reductions in body fat than a parallel generic response and attention training with non-food images (Stice, Yokum, Veling, Kemps, & Lawrence, 2017). We used high-calorie and low-calorie foods that were tailored to the preferences of participants. Overweight or obese adults who completed the multifaceted response inhibition training with high-calorie foods and attend-away training from high-calorie foods, and response training with low-calorie foods and attend-to training with low-calorie foods showed greater body fat loss from pretest to posttest, and reduced fMRI-assessed reward region (putamen; mid insula) and attention region (inferior parietal lobe) response to, and palatability ratings and monetary valuation of, high-calorie foods than placebo controls who completed the training with nonfood images. Another trial similarly found that food response inhibition training reduced valuation of high-calorie foods and reward region (mid-insula) response to high-calorie foods, though it did not observe reductions in weight (Yang, Morys, Wu, Li, & Chen, 2021). A third trial found that adding this food response and attention training to a dissonance-based obesity prevention program resulted in significantly greater body fat loss from pretest to posttest compared to completing the obesity prevention program and placebo response and attention training with non-food images (Stice et al., 2021). However, we did not observe significant reductions in palatability or monetary valuation of the high-calorie food images or attentional bias for those images.

Given the evidence that this multifaceted food response and attention training reduced body fat in two trials, we initiated a large randomized trial that tested the hypothesis that food response and attention training would produce significantly greater reductions in body fat (our primary outcome) than placebo response and attention training involving non-food images. We also

tested the hypothesis that the food response and attention training would reduce fMRI-assessed reward and attention region response to high-calorie food images and that this would mediate the effects of the intervention on body fat loss effects. Finally, we tested the hypothesis that food response and attention training would produce significantly larger body fat loss effects for participants whose weight control problems stem from factors that the food response and attention training has shown to target (i.e., a strong pre-potent approach tendency to high-calorie foods). We hypothesized that a) greater innate reward responsivity as measured by a genetic propensity for greater dopamine signaling in reward circuitry (Yokum, Marti, Smolen, & Stice, 2015), b) greater pretest reward and attention region response to high-calorie food images (Stice, Burger, & Yokum, 2015), and c) weaker pretest inhibitory control region response and weaker behavioral inhibitory control to high-calorie food images (Evans et al., 2012; Kishinevsky et al., 2012) would amplify the effects of the food response and attention training on body fat loss.

Methods

Participants and procedures.

We recruited 179 adults with overweight/obesity (76% female; *M* age = 27.7 ± 7.0; 66% White, 17% Hispanic ethnicity, 10% multi-racial, 4% Asian, 2% Black, and 1% American Indian; *M* % body fat = 40.0 ± 8.1; *M* BMI = 31.9 ± 4.8) for a weight loss trial (see Figure S1 for participant flow diagram). Participants were recruited in a US city (Eugene, Oregon) between 2017-2020. Maximum parental education was high school graduation or less (17%), some college (24%), college graduate (36%), and advanced degree (23%). Recruitment material (mass email messages and advertisements) invited individuals with weight concerns to participate in a weight control trial. This trial was approved by the Oregon Research Institute Institutional Review Board (Protocol title: Translational Neuroscience: Response Training for Obesity

Treatment). We randomly assigned participants to a food response and attention training condition (*n* =104) or a parallel placebo response and attention training comparison condition involving non-food images (*n* =75). We randomized more participants to the intervention condition because we decided to omit a few images of foods that were originally classified as low-calorie, but depicted high-calorie food (e.g., a picture of a cheese plate); however, there were no significant differences in change in our primary outcome when we compared participants who completed the original training (n=39) versus the one with refined food images (n=65) so we combined the data for analyses. A brief phone screen interview verified inclusion and exclusion criteria. Weight concerns and a BMI of 25 or greater were required for inclusion. Exclusion criteria were current DSM-IV eating disorders. A research assistant used a random number table to randomize participants to condition. Assessors were not informed of the allocation of participants to condition.

During the first visit to the lab, all participants rated the palatability (1 = least appetizing to 9 = most appetizing) of 112 color images of high-calorie foods/beverages and 100 images of low-calorie foods/beverages; they also completed surveys, and height, weight, and body composition measurements before randomization. Within 1.5 weeks after their first visit (*M* days = 8.2 ± 3.6), participants were scanned and completed the first of their four weekly training sessions. Participants returned to the lab for their second and third training sessions. Immediately after their 4th training session, participants rated the palatability of the high-calorie and low-calorie food images again, completed their second scan, and completed surveys, height, weight, and body composition measurements; the latter three outcomes were also assessed at 6- and 12-month follow-ups. Participants received $35/hour for completing assessments.

Response training intervention.

Participants completed 4 50-min weekly training visits in the lab wherein they completed stop-signal training, go/no-go training, dot-probe attention training, and visual search training (10 mins each). We used different tasks because we thought it would increase acceptability and produce stronger learning. Participants first completed brief written activities to create dissonance about unhealthy lifestyle behaviors (3 prompts from a bank of questions on benefits of healthy lifestyle/costs of unhealthy lifestyle, health/fitness goal generation, and reframing/circumnavigating barriers). The stop-signal and go/no-go tasks involve being cued repeatedly to respond behaviorally with a button press to low-calorie food images and repeatedly inhibit a behavioral response to high-calorie food images. The dot-probe paradigm reinforces people for looking at low-calorie foods because that is where the probe appears on 90% of the trials, thereby training attention to low-calorie foods and away from high-calorie foods. The visual-search task trains people to rapidly allocate their attention to the 1 low-calorie food within an array of high-calorie foods, training them to ignore the latter foods. We included dot-probe training because it targets the orienting attention network and visual-search training because it targets the executive attention network (Posner, Sheese, Odludas, & Tang, 2006).

The project coordinator selected images of commonly consumed high-calorie foods and low-calorie foods to maximize generalizability. We retained 112 images of high-calorie foods and 100 images of low-calorie foods, which four research participants from other projects were able to correctly classify as either high-calorie or low-calorie foods. We used the 80 images from the 112 high-calorie food images and 80 images of the 100 low-calorie food images that each participant rated the most palatable to ensure that the images were tailored to participants' tastes (palatability rating scales ranged from 1 to 10). All training tasks involved explore to this set of 160 images. We originally started with slightly more food images, but eliminated some to create

a sharper distinction between the high-calorie and low-calorie food images. Participants also rated how much they would be willing to pay (<$1 to $10+) for a serving of each of the foods. Participants were asked to complete 5-min booster sessions weekly via the internet during the 12-month follow-up. They could select which of the 4 trainings they preferred. They received a $50 gift card for completing all booster sessions.

Stop-signal training. In this training task, which was based on Veling et al. (2014), participants saw images with either a dark blue or light gray border. They were told to press the space bar as quickly as possible when the border was blue (go trials) and to withhold a response when the border was gray (no-go trials). Images were presented for 1250 ms or until the participant responded followed by a 500 ms inter-trial interval (Fig 1A). The blue or gray border appeared around the image 100 ms after image onset. Because of this fixed delay this training is a blend between a stop signal task and a go/no-go task: The task resembles a stop signal task at the start, but becomes more like a go/no-go task once participants learn the contingencies. After an erroneous response or omission a red cross appeared for 500 ms, which occurred in all training tasks. The 80 high-calorie food images were always framed with a gray border and the 80 low-calorie food images by a blue border. The task was divided into 2 5-minute blocks of ~178 trials (blocks contained 50% low-calorie foods and 50% high-calorie foods; ~355 trials total). After each block participants were presented with their % correct responses and mean reaction time, and encouraged to improve their scores from block to block, to maintain motivation. Similar feedback was presented in each training paradigm.

Go/no-go training. In this task, which was based on Lawrence et al. (2014), participants were told that pictures would appear in the left or right-hand side of a rectangle for 1250 ms. They were told to press a button (‘c’ for left and ‘m’ for right) as quickly as possible to indicate

the side of presentation (go-trials). On half of the trials, the rectangular frame surrounding the picture was dashed instead of a solid line, which was a signal for them to withhold their response (no-go trials, Fig 1B). Each of the 80 high-calorie food images, 80 low-calorie food images, and 40 water glass filler images were randomly selected with replacement (~450 trials total). We included filler images so that we could measure learning during this task (response time should decrease more for go images versus filler images and commission errors should decrease more for no-go images versus filler images). The task was divided into 2 5-minute blocks of ~225 trials each (blocks contained 40% low-calorie foods, 40% high-calorie foods, and 20% water glasses). High-calorie food images were always paired with inhibition signals whereas low-calorie foods were never paired with inhibition signals. Filler images of glasses of water were associated with go and no-go signals on a 50:50 basis, except in a subset of participants who, due to a technical error, saw filler images associated with go signals only (Table 2).

Dot-probe training. In this task, which was based on Kemps et al. (2014), participants were trained to direct their attention away from high-calorie food images and toward low-calorie food images (Fig 1C). Each of the 80 high-calorie food images was randomly paired with one of the 80 low-calorie food images. Each food picture pair was presented for 500 ms side by side, preceded by a fixation cross for 500 ms. Immediately after the images disappeared, a small dot probe appeared in the location of one of the images. Participants had to indicate as quickly as possible whether the probe appeared in the location previously occupied by the left or the right image by pressing response keys. The probe appeared in the location previously occupied by a high-calorie food image 10% of the time and in the location previously occupied by a low-calorie food image 90% of the time. The probe remained until a response was made. We added a stop signal tone that indicated that participants should not respond to probes that appeared behind

high-calorie foods half the time they were presented with a probe (5% of trials) to provide more direct inhibitory training. Each of the 80 picture pairs was presented 4 times, with each picture presented twice on each side of the screen. The training was divided into 2 5-minute blocks of ~153 trials (~306 trials in total).

Visual-search training. In this task, which was based on Stice et al. (2017), participants searched for one low-calorie food image in a 4 x 4 array of high-calorie food images, by touching the low-calorie food as quickly as possible (Fig 1D). As such, this task trained attention toward low-calorie foods while training attention away from high-calorie foods. Images were randomly selected for presentation on a touch-screen laptop. Participants completed 2 5-minute training blocks containing 77 arrays each (~155 trials total), with each array presented until the participant responded or for 3000 ms if they did not respond. When participants touched the low-calorie food image, it was framed in green and zoomed toward them, while the high-calorie food images zoomed away (1000 ms). For incorrect responses, all images zoomed away and a red x appeared over the images (1000 ms).

Placebo response training control condition. Following Stice et al. (Stice et al., 2017), controls completed parallel response and attention training with non-food images, based on evidence that this does not lead to any changes in caloric intake or weight (Lawrence et al., 2015; Veling, van Koningsbruggen, Aarts, & Stroebe, 2014). This allowed us to tell participants that both interventions were designed to improve response inhibition, which should produce weight loss given that impulsivity increases risk for overeating, ensuring credibility of the control intervention. Although it might be argued that mere exposure to high-calorie food images could produce weight loss, two trials confirmed that repeated exposure to high-calorie food images without response training did not produce weight change (Allom & Mullan, 2015). Further,

controlled laboratory studies have shown that response training decreases responses to food compared to control conditions in which people respond to food in some way (Houben & Jansen, 2011; van Koningsbruggen, Veling, Stroebe, & Aarts, 2014). We used 80 images of birds and 80 images of flowers for the control response and attention training; we included images of mammals as filler images. We selected these categories to control for the visual complexity and intensity of food images used in the response and attention training. This represents a rigorous control, as it parallels the duration of the food response intervention, with the exception that the training is generic, rather than food-specific.

Measures

Body fat. We used air displacement plethysmography (ADP) via the Bod Pod S/T to assess percent body fat because this is a more sensitive measure of adiposity than BMI (Stice et al., 2021; Stice, Yokum, et al., 2015; Stice et al., 2017). Further, the goal was to reduce excess body fat, rather than lean muscle mass or bone mass and BMI does not distinguish fat mass from muscle or bone mass. Body density is calculated as body mass divided by body volume; body density is used to calculate percent body fat. ADP percent body fat shows high test-retest reliability (r = .92-.99) and correlates with DEXA and hydrostatic weighing estimates (r = .98-.99), with ADP estimated percent body fat falling an average of only 1.7% different than DEXA estimates (Weyers et al., 2002). Participants were asked not to consume any food or beverages (other than water) for at least 3 hours, refrain from using nicotine for at least 3 hours, and refrain from vigorous exercise for at least 24 hours prior to Bod Pod measurements. We also report the effects on BMI to facilitate comparisons with other trials that used that outcome.

Eating disorder symptoms and binge eating. We used the semi-structured Eating Disorder Diagnostic Interview (EDDI; Stice, Rohde, Shaw, & Gau, 2018) to assess eating disorder

symptoms, including the frequency of binge eating, over the past 3 months at baseline and since previous interview at follow-ups on a month-by-month basis using time-line follow-back. The symptom composite has shown internal consistency (α=.92), inter-rater agreement (ICC *r*=.93), 1-week test-retest reliability (ICC *r*=.95), and sensitivity to detecting prevention and treatment interventions (Stice et al., 2018).

Behavioral inhibitory control. We used a food-specific Stop Signal Task (Houben, Nederkoorn, & Jansen, 2014), adapted from the Stop Signal Task (Logan, Schachar, & Tannock 1997) to assess behavioral inhibitory control at baseline. Response-inhibition training produced larger reductions in high-calorie food intake for individuals with greater impulsivity on this task (Houben, 2011). Impulsivity is indexed by the difference between the reaction time to go signals and stop signal delay, which varies in an adaptive fashion to make inhibitory responses more difficult. This widely used behavioral measure of impulsivity has shown test-retest reliability and convergent validity (Weafer, Baggott, & de Wit, 2013).

fMRI food image exposure paradigm. Participants were asked to refrain from eating or drinking caffeinated beverages for 3-4 hours preceding their scans. Average hours since last eaten was 7.10 ± 5.0. During the food image exposure paradigm, participants were exposed to 20 high-calorie food images each participant rated highest in palatability, 20 low-calorie food images each participant rated highest in palatability, and 20 pictures of glasses of water (all images were used in the training). The food images were presented for 5 secs in a randomized order. Between each picture was a 2-4 sec jitter during which a blank screen with a crosshair was presented. Stimuli were presented in one scanning run.

Genotyping. In total, 151 participants provided saliva, from which epithelial cells were collected, using a commercial product, Oragene® (DNAgenotek, Ottawa, ON, Canada). For each

participant, we calculated a multilocus genetic composite, paralleling the general approach used by previous studies (Stice, Yokum, Burger, Epstein, & Smolen, 2012; Yokum et al., 2015), reflecting the total number of the five genotypes associated with greater dopamine signaling: *TaqIA* (rs1800497)*, COMT* val^{158}met (rs4680), *DRD2*-141C Ins/Del (rs1799732), *DRD4* exon 3 48-bp VNTR*,* and SLC6A3 30 40-bp VNTR (*DAT1*). Further details are available in Supplemental Material.

Imaging and statistical analysis

Data were acquired using a Siemens Skyra 3 Tesla MRI scanner. A 32-channel head coil acquired data from the entire brain. Functional scans used a T2* weighted echo-planar plus sequence (72 slices, TE = 25 ms, TR = 2000 ms, flip angle = 90°, matrix size = 100 x 100, voxel size = 2 mm^3, axial slices = 72, FOV = 200; multiband acceleration factor = 3). Structural scans were collected using a high-resolution anatomical T1-weighted MP-RAGE scan (TE = 3.43 ms, TR = 2500 ms, 256 x 256 matrix, voxel size = 1 mm^3, sagittal slices = 176, FOV = 256).

Neuroimaging data were preprocessed and analyzed using previously published procedures (Stice et al., 2017). In total, 162 participants (92 intervention; 70 control) completed the pre-test fMRI scan and 148 (84 intervention; 64 control) completed both pre- and post-scans. One participant (control condition) failed the movement inclusion criteria (within-run movement exceeding 3 mm in translational movement and 3° in rotational movement) at both pre- and post-scan and was excluded from fMRI analyses.

To identify brain regions activated by high-calorie food images, we contrasted BOLD activation during high-calorie food images versus low-calorie food images and versus glasses of water. To identify brain regions activated by low-calorie food images, we contrasted BOLD activation during low-calorie food images versus high-calorie food images and versus glasses of

water. Individual maps were constructed to compare the activations within each participant for pretest and posttest separately (e.g., pretest high-calorie > low-calorie and pretest low-calorie > high-calorie; posttest high-calorie > low-calorie and posttest low-calorie > high-calorie). Next, we conducted a 2 Group (intervention, control) x 2 Time (pre, post) repeated-measures ANOVA to examine group differences in change in neural response between conditions using these individual maps. Hours since last food intake and time of scan were included as covariates. Whole-brain analyses were conducted. To determine the minimal cluster extent threshold (k) equivalent to $P = 0.05$, family-wise error-corrected (FWE-corrected) for multiple comparison across the whole brain, we calculated the cluster extent thresholds for the analyses at $p < 0.001$ with the SPM cluster size threshold tool (https://github.com/ CyclotronResearchCentre/SPM ClusterSize Threshold). The threshold was $k \geq 35$. Data were inspected to ensure that outliers did not drive significant effects. Effect sizes (r) were derived from the Z-values ($Z/\sqrt{N}$).

To examine if BOLD responses at baseline moderated the intervention effects on body fat loss (see moderation analyses described below), we extracted subject-level parameter estimates from main effects analyses from brain regions previously implicated in food reward (striatum; Demos, Heatherton, & Kelley, 2012; Yokum, Gearhardt, & Stice, 2021), attention (precuneus; Stice et al., 2017), and inhibitory control (inferior frontal gyrus [IFG], dorsolateral prefrontal cortex [dlPFC]; Kober et al., 2010). For the dlPFC, we used a spherical ROI (6 mm diameter sphere) that was built centered at MNI coordinates x = -36, y = -1, z = 55 and x = 36, y = -1, z = 55) (Kober et al., 2010). For all other brain regions, we used anatomically-defined regions-of-interest (ROIs) (Maldjian, Laurienti, Kraft, & Burdette, 2003).

Statistical Analyses of Non-Imaging Data

Preliminary analyses included descriptive analysis of the study sample and study outcomes. We compared participants assigned to the two conditions at baseline to evaluate equivalency of the participants randomized to groups. Attrition analysis compared participants who dropped from the study to those who did not on baseline data. The COVID-19 pandemic contributed to very high missing data over follow-up (63% at 1-year follow-up). Rates of missing data due to dropout and inability to measure participants in the lab were very high compared to studies conducted prior to the pandemic; in the last obesity prevention trial we completed before the pandemic, attrition was 3% by 1-year follow-up (Stice et al., 2018). Due to concerns that implementing missing data techniques with the excessive rates of missing data would result in spurious estimates, we restricted our intent-to-treat analyses to pretest to posttest data only. We then conducted a complier analysis first considering analysis through the 12-month assessment, but the number of available cases became prohibitively low (n= 40). Thus, the complier analyses included pretest to 6-month follow-up for participants with complete data through the 6-month assessment (n= 33 response training and n= 38 generic inhibition control).

Intent-to-treat analyses of condition effects from pretest to posttest were evaluated using fixed effects growth models fit using SAS 9.2 PROC MIXED (SAS/STAT, 2011) and estimated with maximum likelihood because this is a preferred method for handling missing data (Graham, 2009). Individual variability in outcomes from pretest to posttest was predicted with condition (coded 1 for response training and 0 for generic inhibition training), time (coded in months since pretest) and a condition × time interaction term. The condition × time interaction term informed on whether differential pretest to posttest condition effects were realized. Effect sizes, based on the condition × time interaction estimates, are equivalent to Cohen's d (Feingold, 2009). We then tested whether the baseline moderators interacted with condition in the prediction of change in

body fat in the intent-to-treat analyses by adding the hypothesized moderator and higher order interaction terms with condition and time. We expanded the intent-to-treat models for the complier analyses and evaluated pretest to 6-month condition effects after restricting the sample to participants with complete data through the 6-month assessment.

Results

Preliminary analyses. Table 1 shows a descriptive summary for the study outcomes, by condition. Measures of skew and kurtosis and visual inspection of plots showed outcomes approximated a normal distribution with the exceptions of eating disorder symptoms and binge eating which were normalized with a log transformation.

Participants randomized to the 4-week response-training intervention attended on average 3.6 (*SD*=1.0) of the 4 sessions and completed on average 6.0 (*SD*=12.0) booster sessions. Participants randomized to the generic inhibition-training control group attended on average 3.6 (*SD*=1.1) of the 4 sessions and completed on average 6.8 (*SD*=10.6) booster sessions. Groups were compared on demographic characteristics (age, gender, maximum parental education), baseline measures of the outcomes, and amount of training and booster sessions. No significant group differences were found (all *p*-values >.106) indicating randomization produced initially equivalent groups.

Rates of missing data were 2% at baseline, 15% at posttest, 43% at 3-month follow-up, 52% at 6-month follow-up, and 63% at 12-month follow-up. Across all assessments, 13% of participants completed one assessment, 20% two assessments, 16% three assessments, 29% four assessments, and 22% complete all five assessments. Participants with complete data through 6-months (the complier sample [*n*=71]) were compared to participants who did not complete all assessments through 6-months (*n*=108), on demographic characteristics (age, gender, maximum

parental education) and pretest measures of the outcomes. The only significant difference detected (t[173]= 2.00, p=.047) showed that participants who did not provide complete data through the 6-month assessment had lower baseline BMI scores compared to the complier sample (31.08 vs. 32.50, Cohen's d=.30), suggesting that participants with a lower initial BMI were more likely to drop out.

Training Task Performance. Task performance accuracy in all tasks and training sessions (weekly visits) was high (at least 88%) suggesting that all participants were engaged in the training. Table 2 displays mean group errors (expressed as a proportion of all trials of that type) and mean go reaction time (RT) for the first and final (fourth) training session from both the food response training condition and the generic training control condition to illustrate performance over time (see Supplementary Material for more details). Repeated measures ANOVAs showed that the intervention and control groups showed similar performance and improvements over time in most tasks but there were some important differences. In the go/no-go task, controls showed responses consistent with stimulus-response learning (i.e., the expected lower commission errors to the 100%-associated versus 50%-associated [filler] stimuli), but this was not seen in the intervention group. Our sensitivity to detect stimulus-specific inhibition learning was limited because (due to a coding error for filler trials) we had to combine commission errors for no-go and go trials. However, the findings from these combined commission errors failed to support stimulus-response learning in the intervention group. In contrast, both groups showed evidence of learning the stimulus-go associations in the go/no-go task, as demonstrated by faster reaction times to the 100% versus 50% go-associated stimuli. Similarly, both groups showed an increase in attentional bias, which was most pronounced in the intervention group. Intervention participants, relative to the control group, showed slower RT in the visual-search task overall

(suggesting greater motivational salience of food versus non-food images). Overall, results suggest that participants in both conditions were generally matched for task demands and engagement but showed some differences in measures of stimulus-specific learning.

Main Effects. Results of the intent-to-treat models (Table 3) show that participants in the response training group had significantly greater increases in palatability ratings for low-calorie foods relative to placebo controls (d=.27) from pretest to posttest. No other significant condition × time effects were found. Results of the complier models are summarized in Table 4 and no condition × time effects were found.

Intervention effects on neural response to high-calorie versus low-calorie food images. There were no significant group differences in scan time and hours since last food intake (all p-values > .295). Whole brain analyses showed no significant group x time differences in BOLD signal in response to high-calorie food images > low-calorie food images, high-calorie food images > glasses of water, low-calorie food images > high-calorie food images, and low-calorie food images > glasses of water.

Moderation. Neural responsivity in three brain regions at baseline significantly moderated the effects of the intervention on reductions in body fat. Significant moderator of condition × time effects were neural response in IFG to high-calorie foods compared to low-calorie foods (t=2.53, p=.013), neural response in IFG to high-calorie foods compared to water glasses (t=2.00, p=.048), and neural response in precuneus to high-calorie food compared to water glasses (t=2.08, p=.039). Individual differences in neural responsivity in the striatum, a genetic propensity for greater dopamine signaling in reward circuity and deficits in behavioral inhibitory control in response to high-calorie food images did not moderate the effects of the intervention on change in body fat. Decomposition of the significant moderating effects included examination

of the condition × time effects, separately, at values above and below the median split of the moderator. Although non-significant condition × time effects were found above the median for response in IFG to high-calorie foods compared to low-calorie foods (estimate =-0.77, *t*=-1.17, *p*=.248, *d*=-.09) or below the median (estimate =0.75, *t*=1.47, *p*=.145, *d*=.09), the valence of the effect changed direction. Participants with higher IFG response to high-calorie foods compared to low calorie foods showed decreases in body fat from pretest to posttest, whereas participants with lower IFG response to high-calorie foods showed increases in body fat. Similar non-significant decomposition findings were found for neural response in IFG to high-calorie foods compared to water glasses. Participants with higher IFG response to high-calorie foods compared to water glasses showed decreases in body fat from pretest to posttest (estimate =-0.94, *t*=-1.53, *p*=.132, *d*=-.11), whereas participants with lower IFG response to high-calorie foods compared to water glasses showed increases (estimate =0.85, *t*=1.54, *p*=.129, *d*=.11). Significant differences in decomposition of neural response in precuneus to high-calorie food compared to water glasses were found. Participants with higher precuneus response to high-calorie food compared to water glasses showed significant increases in body fat from pretest to posttest (estimate =1.22, *t*=2.59, *p*=.012, *d*=.15). Participants with lower precuneus response to high-calorie food compared to water glasses showed lower, but non-significant decreases in body fat (estimate =-0.91, *t*=-1.45, *p*=.152, *d*=-.12).

Discussion

Contrary to expectations and the results from the pilot trial (Stice et al., 2017), as well as the trial in which we added food response and attention training to an obesity prevention program (Stice et al., 2021), participants who were randomized to the food response inhibition and attention training did not show significantly greater reductions in body fat. Further, although

participants in the food response inhibition and attention training showed significantly greater increases in palatability ratings of low-calorie foods, food response and attention training did not produce significant changes in neural responsivity to high-calorie food images and reductions in monetary valuation and palatability ratings of high-calorie foods. These non-significant findings converge with those from past trials that have evaluated the effects of go/no-go, stop-signal, and dot-probe trainings (Allom & Mullan, 2015 Study 2; Forman et al., 2019; Memarian, Moradi, Hasani, & Mullan, 2021; Werthmann et al., 2014). Although results may suggest that the combined response and attention training does not reliably reduce weight, it is important to consider other possible explanations for the null findings.

It is possible that participants in the present trial did not show body fat loss because they did not show optimal learning during the training. Compared to our earlier pilot (Stice et al., 2017), learning was not as strong on some of the tasks in the current trial. In particular, there was no difference in commission errors between foods (100% predictive of a response) and filler stimuli (50% predictive) in the go/no-go task in the intervention group, suggesting that learning to associate high-calorie foods with inhibition may not have occurred. Further, participants in the current trial made about three times more no-go commission errors to high-calorie foods (2.9%) than in our pilot trial (1%). Given the important role of associative inhibition learning and accuracy in mediating the effects of food go/no-go training (Jones et al., 2016; Porter, Gillison, Wright, Verbruggen, & Lawrence, 2021), the weaker learning may have contributed to the negative results. In addition, the increase in attentional bias from pre to post-test was less pronounced here relative to our earlier pilot, both in the intervention and control groups. Moreover, response times in the SST and visual search task were overall slower here than in the pilot (despite participants making more errors), which could also point to weaker learning of

stimulus-response associations, as these would have made the tasks more predictable and faster/easier.

One explanation for the weaker learning in the present trial versus the past two trials that produced body fat loss effects (Stice et al., 2021; Stice et al., 2017) is that in the trainings for those earlier trials, we only included images of fruits and vegetables in the low calorie (go/attend) category. As noted, we decided to include images of other types of low-calorie foods here taken from ten different categories, including whole grain foods, sushi, eggs, fish and lean meats. The high-calorie foods also encompassed a diverse range of 10 sub-categories, including sweet foods, pizza, meats, fast food, drinks. The diversity of food images included in both the low- and high-calorie food categories may have 'blurred' the boundaries between these, resulting in weaker associative learning at the category-level. Some studies have demonstrated associative learning and devaluation of food at the item-specific level but these have generally included fewer food items (e.g. 20) compared to the current (80) (e.g. Chen, Veling, Dijksterhuis, & Holland, 2016). We recommend that future studies use images from more narrow, distinct and 'meaningful' categories of low-calorie and high-calorie foods to promote stimulus-response learning at the category level (Serfas, 2017). Such learning could also be encouraged by giving participants more explicit instructions about the categories in the task and what to attend to, and by including fewer different food images. Refining the training tasks so that participants focus more on inhibition than on go-responding (i.e., switching their attention away from go stimuli) might also contribute to stronger inhibitory learning. Finally, future research should include sensitive measures of stimulus-response learning within the training tasks, such as inhibition accuracy to foods vs. fillers (Lawrence et al., 2015) or memory for stimulus-response contingencies (Chen et al., 2018) to check that the target mechanisms have been successfully

modified, as recommended for studies using cognitive bias modification (Wiers, Boffo, & Field, 2018).

Another possibility is that the pandemic may have made it more difficult to detect body fat loss effects. Although nearly all participants had provided posttest data before the lockdown from the pandemic prevented in-person contact with research participants, the lockdown contributed to much higher attrition than we observed in past obesity treatment trials, making it impossible to evaluate the longer-term effects of the intervention. Moreover, lockdowns have been related to increases in unhealthy food consumption and reductions in physical activity, especially among overweight individuals (Poelman et al., 2021; Robinson et al., 2021), which may further reduce chances to find long-term effects. Interestingly, the *d* for body fat loss effects from pretest to 12-month follow-up based on the per observed means was .32 (Table 3), implying that we might have been able to detect longer-term effects on body fat if the pandemic did not result in such high attrition. In this context it is important to note that we did not detect any systematic differences in the demographics of the sample used in the present trial and the past two trials that appeared to explain the differences in the findings across the studies.

Controlled laboratory experiments have demonstrated that response training effects on behavior are mediated by decreased valuations of not-responded to stimuli (Johannes, Buijzen, & Veling, 2021; Veling, Aarts, & Stroebe, 2013). Applied trials have found effects of response training or multifaceted training on reductions in palatability of high calorie food and reduced brain reward responses to such food, although such effects do mediate effects on body weight (Lawrence et al., 2015; Stice et al., 2017; Yang et al., 2021). Here, we did not replicate effects on high calorie foods, but we found that food response and attention training produced greater increases in palatability ratings of low-calorie foods compared to control participants. This result

dovetails with the findings of Chen and colleagues (2016) and suggests that the food response and attention training increased valuation of low-calorie foods. However, this finding is the opposite of the results in our pilot trial (Stice et al., 2017) where effects of the intervention on palatability were found for high- but not for low-calorie foods. The relatively stronger effect on low-calorie food valuation seen here is consistent with the evidence of learning to go or attend to these foods in the training tasks (from the go/no-go and attentional bias tasks). However, these (go/attend) learning effects were weaker than those observed in our pilot trial, perhaps due to the previously discussed 'fuzzy categories'. Learning may have occurred at the specific item-level to some of the healthy foods that may have stood out from other (high- and low-calorie) foods based on some unknown feature (e.g., greenness or rawness), even with "fuzzier" categories. Alternatively, because memory representations for Go associated stimuli are stronger than for no-go associated stimuli (Yebra et al., 2019), effects of the training may be stronger for go stimuli, especially in the case of fuzzy categories, as learning in that case relies on item level learning. Although increased palatability of low calorie foods is an encouraging effect, it did not translate into reduced body fat, which would likely require changes in high-calorie food valuation.

Completion of the food response inhibition and attention training versus generic response training did not produce significant pre-post changes in neural responsivity to high-calorie food images (versus low-calorie food images and glasses of water) in regions implicated in reward processing, attention, and inhibitory control. These null findings are in contrast with findings from our pilot trial (Stice et al., 2017), which found that the food response inhibition and attention training resulted in greater pre-post reductions in regions that appear to play a role in attention (inferior parietal lobe) and reward processing (putamen, mid insula). It is possible that

the weaker learning observed in the present trial attenuated the changes in reward, attention, and inhibitory control region response to high-calorie foods.

There was evidence that pretest neural activation in regions implicated in inhibitory control (i.e., IFG) and attention (i.e., precuneus) moderated the condition effects on pretest to posttest change in percent body fat: participants with higher IFG response to high-calorie foods compared to low calorie foods and water glasses and those with lower precuneus response to high-calorie foods compared to water glasses showed greater decreases in percent body fat from pretest to posttest. Exploratory analyses found a significant negative correlation between pretest stop-signal reaction time in the food-specific Stop Signal Task and pretest IFG response to high- versus low-calorie foods (r = -0.21, p = 0.04) but not IFG response to high-calorie foods versus glasses of water (r = -0.13, p = 0.20). These results suggest that the effects of the food response inhibition and attention training were moderated by individual differences in inhibitory control capacity and attentional bias when exposed to palatable high-calorie food cues. These findings converge with evidence that weaker inhibitory control region response to high-calorie food images (Evans et al., 2012; Francis & Susman, 2009; Schlam et al., 2013; Seeyave et al., 2009) and greater attentional bias for high-calorie food words (Calitri, Pothos, Tapper, Brunstrom, & Rogers, 2010) predict future weight gain, but they are not consistent with evidence that food response training produces stronger reductions in *ad lib* intake of high-calorie foods for individuals with less inhibitory control (e.g., Houben, 2011). Unfortunately, decomposition of the effects did not identify any subgroups that showed significant body fat loss in response to food response/attention training.

It is important to consider the limitations of the present study. First, the pandemic resulted in much higher attrition than we have observed in past trials of weight loss interventions, which

made it impossible to reliably assess the longer-term effects of food response inhibition and attention training. Second, we refined the intervention during this trial, which might have reduced sensitivity to detecting intervention effects because it introduced excess noise into the data. Third, the coding error made it difficult to fully assess differences in inhibitory learning in this trial versus previous trials.

In conclusion, the present trial did not generate evidence that the food response and attention training intervention produced significant body fat loss effects. The lack of effects for the primary outcome appear related to the fact that we used a more heterogeneous set of high-calorie and low-calorie food images in the present trial versus the two prior trials that produced body fat loss effects (Stice et al., 2021; Stice et al., 2017), which resulted in weaker learning and appears to have attenuated the reduction in reward region response to high-calorie foods and the reductions in palatability ratings of, and monetary valuation of the high-calorie foods which were observed previously (Stice et al., 2017). This interpretation suggests that future food response and attention trials should use image sets of high-calorie and low-calorie foods that are more homogeneous and distinct. Although it is disappointing that the present trial did not observe the hypothesized effects, we hope these findings contribute to a better understanding of the factors that optimize learning and clinical benefit from food response and attention training.

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References

Allom, V., & Mullan, B. (2015). Two inhibitory control training interventions designed to improve eating behaviour and determine mechanisms of change. *Appetite, 89*, 282-290. doi:10.1016/j.appet.2015.02.022

Calitri, R., Pothos, E. M., Tapper, K., Brunstrom, J. M., & Rogers, P. J. (2010). Cognitive biases to healthy and unhealthy food words predict change in BMI. *Obesity (Silver Spring), 18*(12), 2282-2287. doi:10.1038/oby.2010.78

Chen, Z., Veling, H., de Vries, S. P., Bijvank, B. O., Janssen, I. M. C., Dijksterhuis, A., & Holland, R. W. (2018). Go/no-go training changes food evaluation in both morbidly obese and normal-weight individuals. *J Consult Clin Psychol, 86*(12), 980-990. doi:10.1037/ccp0000320

Chen, Z., Veling, H., Dijksterhuis, A., & Holland, R. W. (2016). How does not responding to appetitive stimuli cause devaluation: Evaluative conditioning or response inhibition? *J Exp Psychol Gen, 145*(12), 1687-1701. doi:10.1037/xge0000236

Demos, K. E., Heatherton, T. F., & Kelley, W. M. (2012). Individual differences in nucleus accumbens activity to food and sexual images predict weight gain and sexual behavior. *J Neurosci, 32*(16), 5549-5552. doi:10.1523/JNEUROSCI.5958-11.2012

Evans, G. W., Fuller-Rowell, T. E., & Doan, S. N. (2012). Childhood cumulative risk and obesity: the mediating role of self-regulatory ability. *Pediatrics, 129*(1), e68-73. doi:10.1542/peds.2010-3647

Feingold, A. (2009). Effect sizes for growth-modeling analysis for controlled clinical trials in the same metric as for classical analysis. *Psychol Methods, 14*(1), 43-53. doi:10.1037/a0014699

Forman, E. M., Manasse, S. M., Dallal, D. H., Crochiere, R. J., Loyka, C. M., Butryn, M. L., . . . Houben, K. (2019). Computerized neurocognitive training for improving dietary health and facilitating weight loss. *J Behav Med, 42*(6), 1029-1040. doi:10.1007/s10865-019-00024-5

Francis, L. A., & Susman, E. J. (2009). Self-regulation and rapid weight gain in children from age 3 to 12 years. *Arch Pediatr Adolesc Med, 163*(4), 297-302. doi:10.1001/archpediatrics.2008.579

Graham, J. W. (2009). Missing data analysis: making it work in the real world. *Annu Rev Psychol, 60*, 549-576. doi:10.1146/annurev.psych.58.110405.085530

Houben, K. (2011). Overcoming the urge to splurge: influencing eating behavior by manipulating inhibitory control. *J Behav Ther Exp Psychiatry, 42*(3), 384-388. doi:10.1016/j.jbtep.2011.02.008

Houben, K., & Jansen, A. (2011). Training inhibitory control. A recipe for resisting sweet temptations. *Appetite, 56*(2), 345-349. doi:10.1016/j.appet.2010.12.017

Houben, K., Nederkoorn, C., & Jansen, A. (2014). Eating on impulse: the relation between overweight and food-specific inhibitory control. *Obesity (Silver Spring), 22*(5), E6-8. doi:10.1002/oby.20670

Johannes, N., Buijzen, M., & Veling, H. (2021). Beyond inhibitory control training: Inactions and actions influence smartphone app use through changes in explicit liking. *J Exp Psychol Gen, 150*(3), 431-445. doi:10.1037/xge0000888

Jones, A., Di Lemma, L. C., Robinson, E., Christiansen, P., Nolan, S., Tudur-Smith, C., & Field, M. (2016). Inhibitory control training for appetitive behaviour change: A meta-analytic investigation of mechanisms of action and moderators of effectiveness. *Appetite, 97*, 16-28. doi:10.1016/j.appet.2015.11.013

Kakoschke, N., Kemps, E., & Tiggemann, M. (2014). Attentional bias modification encourages healthy eating. *Eat Behav, 15*(1), 120-124. doi:10.1016/j.eatbeh.2013.11.001

Kemps, E., Tiggemann, M., & Hollitt, S. (2014). Biased attentional processing of food cues and modification in obese individuals. *Health Psychol, 33*(11), 1391-1401. doi:10.1037/hea0000069

Kemps, E., Tiggemann, M., Orr, J., & Grear, J. (2014). Attentional retraining can reduce chocolate consumption. *J Exp Psychol Appl, 20*(1), 94-102. doi:10.1037/xap0000005

Kishinevsky, F. I., Cox, J. E., Murdaugh, D. L., Stoeckel, L. E., Cook, E. W., 3rd, & Weller, R. E. (2012). fMRI reactivity on a delay discounting task predicts weight gain in obese women. *Appetite, 58*(2), 582-592. doi:10.1016/j.appet.2011.11.029

Kober, H., Mende-Siedlecki, P., Kross, E. F., Weber, J., Mischel, W., Hart, C. L., & Ochsner, K. N. (2010). Prefrontal-striatal pathway underlies cognitive regulation of craving. *Proc Natl Acad Sci U S A, 107*(33), 14811-14816. doi:10.1073/pnas.1007779107

Lawrence, N. S., O'Sullivan, J., Parslow, D., Javaid, M., Adams, R. C., Chambers, C. D., . . . Verbruggen, F. (2015). Training response inhibition to food is associated with weight loss and reduced energy intake. *Appetite, 95*, 17-28. doi:10.1016/j.appet.2015.06.009

Logan, G. D., Schachar, R.J., & Tannock, R. (1997). Impulsivity and inhibitory control. *Psychological Science, 8*(1), 60-64.

Maldjian, J. A., Laurienti, P. J., Kraft, R. A., & Burdette, J. H. (2003). An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *Neuroimage, 19*(3), 1233-1239. doi:10.1016/s1053-8119(03)00169-1

Memarian, S., Moradi, A., Hasani, J., & Mullan, B. (2021). Can sweet food-specific inhibitory control training via a mobile application improve eating behavior in children with obesity? *Br J Health Psychol*. doi:10.1111/bjhp.12566

Poelman, M. P., Gillebaart, M., Schlinkert, C., Dijkstra, S. C., Derksen, E., Mensink, F., . . . de Vet, E. (2021). Eating behavior and food purchases during the COVID-19 lockdown: A cross-sectional study among adults in the Netherlands. *Appetite, 157*, 105002. doi:10.1016/j.appet.2020.105002

Porter, L., Gillison, F. B., Wright, K. A., Verbruggen, F., & Lawrence, N. S. (2021). Exploring Strategies to Optimise the Impact of Food-Specific Inhibition Training on Children's Food Choices. *Front Psychol, 12*, 653610. doi:10.3389/fpsyg.2021.653610

Posner, M. I., Sheese, B. E., Odludas, Y., & Tang, Y. (2006). Analyzing and shaping human attentional networks. *Neural Netw, 19*(9), 1422-1429. doi:10.1016/j.neunet.2006.08.004

Robinson, E., Boyland, E., Chisholm, A., Harrold, J., Maloney, N. G., Marty, L., . . . Hardman, C. A. (2021). Obesity, eating behavior and physical activity during COVID-19 lockdown: A study of UK adults. *Appetite, 156*, 104853. doi:10.1016/j.appet.2020.104853

Schlam, T. R., Wilson, N. L., Shoda, Y., Mischel, W., & Ayduk, O. (2013). Preschoolers' delay of gratification predicts their body mass 30 years later. *J Pediatr, 162*(1), 90-93. doi:10.1016/j.jpeds.2012.06.049

Seeyave, D. M., Coleman, S., Appugliese, D., Corwyn, R. F., Bradley, R. H., Davidson, N. S., . . . Lumeng, J. C. (2009). Ability to delay gratification at age 4 years and risk of overweight at age 11 years. *Arch Pediatr Adolesc Med, 163*(4), 303-308. doi:10.1001/archpediatrics.2009.12

Serfas, B. G., Florack, A., Büttner, O.B., & Voegeding, T. (2017). What does it take for sour grapes to remain sour? Persistent effects of behavioral inhibition in go/no-go tasks on the evaluation of appetitive stimuli. *Motiv Sci, 3*(1), 1-18.

Stice, E., Burger, K. S., & Yokum, S. (2015). Reward Region Responsivity Predicts Future Weight Gain and Moderating Effects of the TaqIA Allele. *J Neurosci, 35*(28), 10316-10324. doi:10.1523/JNEUROSCI.3607-14.2015

Stice, E., Rohde, P., Gau, J. M., Butryn, M. L., Shaw, H., Cloud, K., & D'Adamo, L. (2021). Enhancing efficacy of a dissonance-based obesity and eating disorder prevention program: Experimental therapeutics. *J Consult Clin Psychol, 89*(10), 793-804. doi:10.1037/ccp0000682

Stice, E., Rohde, P., Shaw, H., & Gau, J. M. (2018). An experimental therapeutics test of whether adding dissonance-induction activities improves the effectiveness of a selective obesity and eating disorder prevention program. *Int J Obes (Lond), 42*(3), 462-468. doi:10.1038/ijo.2017.251

Stice, E., Yokum, S., Burger, K., Epstein, L., & Smolen, A. (2012). Multilocus genetic composite reflecting dopamine signaling capacity predicts reward circuitry responsivity. *J Neurosci, 32*(29), 10093-10100. doi:10.1523/JNEUROSCI.1506-12.2012

Stice, E., Yokum, S., Burger, K., Rohde, P., Shaw, H., & Gau, J. M. (2015). A pilot randomized trial of a cognitive reappraisal obesity prevention program. *Physiol Behav, 138*, 124-132. doi:10.1016/j.physbeh.2014.10.022

Stice, E., Yokum, S., Veling, H., Kemps, E., & Lawrence, N. S. (2017). Pilot test of a novel food response and attention training treatment for obesity: Brain imaging data suggest actions shape valuation. *Behav Res Ther, 94*, 60-70. doi:10.1016/j.brat.2017.04.007

van Koningsbruggen, G. M., Veling, H., Stroebe, W., & Aarts, H. (2014). Comparing two psychological interventions in reducing impulsive processes of eating behaviour: effects on self-selected portion size. *Br J Health Psychol, 19*(4), 767-782. doi:10.1111/bjhp.12075

Veling, H., Aarts, H., & Stroebe, W. (2013). Using stop signals to reduce impulsive choices for palatable unhealthy foods. *Br J Health Psychol, 18*(2), 354-368. doi:10.1111/j.2044-8287.2012.02092.x

Veling, H., van Koningsbruggen, G. M., Aarts, H., & Stroebe, W. (2014). Targeting impulsive processes of eating behavior via the internet. Effects on body weight. *Appetite, 78*, 102-109. doi:10.1016/j.appet.2014.03.014

Weafer, J., Baggott, M. J., & de Wit, H. (2013). Test-retest reliability of behavioral measures of impulsive choice, impulsive action, and inattention. *Exp Clin Psychopharmacol, 21*(6), 475-481. doi:10.1037/a0033659

Werthmann, J., Field, M., Roefs, A., Nederkoorn, C., & Jansen, A. (2014). Attention bias for chocolate increases chocolate consumption--an attention bias modification study. *J Behav Ther Exp Psychiatry, 45*(1), 136-143. doi:10.1016/j.jbtep.2013.09.009

Weyers, A. M., Mazzetti, S. A., Love, D. M., Gomez, A. L., Kraemer, W. J., & Volek, J. S. (2002). Comparison of methods for assessing body composition changes during weight loss. *Med Sci Sports Exerc, 34*(3), 497-502. doi:10.1097/00005768-200203000-00017

Wiers, R. W., Boffo, M., & Field, M. (2018). What's in a Trial? On the Importance of Distinguishing Between Experimental Lab Studies and Randomized Controlled Trials: The Case of Cognitive Bias Modification and Alcohol Use Disorders. *J Stud Alcohol Drugs, 79*(3), 333-343.

World Health Organization. (2021). Obesity. Available from: https://www.who.int/news-room/facts-in-pictures/detail/6-facts-on-obesity.

Yang, Y., Morys, F., Wu, Q., Li, J., & Chen, H. (2021). Pilot Study of Food-Specific Go/No-Go Training for Overweight Individuals: Brain Imaging Data Suggest Inhibition Shapes Food Evaluation. *Soc Cogn Affect Neurosci*. doi:10.1093/scan/nsab137

Yokum, S., Gearhardt, A. N., & Stice, E. (2021). In Search of the Most Reproducible Neural Vulnerability Factors that Predict Future Weight Gain: Analyses of Data from Six Prospective Studies. *Soc Cogn Affect Neurosci*. doi:10.1093/scan/nsab013

Yokum, S., Marti, C. N., Smolen, A., & Stice, E. (2015). Relation of the multilocus genetic composite reflecting high dopamine signaling capacity to future increases in BMI. *Appetite, 87*, 38-45. doi:10.1016/j.appet.2014.12.202

Table 1.
Test of Group Differences on Demographic Characteristics and Baseline Measures

	Generic Response		Response Training	
Female *[n, (%)]*	60	(80.0)	76	(73.1)
Age [*M*, (*SD*)]	28.8	(6.4)	26.9	(7.4)
Race *[n, (%)]*				
White	72	71.3	44	59.5
Hispanic	14	13.9	17	23.0
Multiracial	10	9.9	7	9.5
Asian	4	4.0	3	4.1
Black	1	1.0	2	2.7
Native American	0	0.0	1	1.4
Parental education [*n, (%)]*				
Grade school	2	(2.7)	2	(2.0)
Some high school	6	(8.2)	2	(2.0)
High school degree	8	(11.0)	10	(9.9)
Some college	16	(21.9)	25	(24.8)
College degree	30	(41.1)	33	(32.7)
Advanced degree	11	(15.5)	29	(28.7)

Table 2.
Comparison of Performance on the Go/No-Go task, Stop-Signal Task, Dot-Probe Task, Visual-search Task, and Respond Signal Task between the Intervention and Control Group.

Group	Intervention (1; n = 87)		Control (2; n = 59)	
Time-point	Session 1	Session 4	Session 1	Session 4
Go/No-go				
Comm errors (Foods)	.021 (.01)[#]	.018 (.01)[#]	.026 (.04)[#]	.017 (.02)[#]
Comm errors (Fillers)	.009 (.01)[#]	.013 (.02)[#]	.016 (.04)[#]	.015 (.02)[#]
Category effect	**-.013 (.01)**	**-.005 (.02)**	**-.011 (.05)**	**-.002 (.02)**
Go RT ms (LC)	554.41(64.1)[#]	493.14 (52.4)[#]	517.77 (74)[#]	483.17 (59.5)[#]
Go RT ms (Filler)	539.60(50.1)[#]	493.32 (47.4)[#]	520.27 (79.1)[#]	488.17 (65.9)[#]
Category effect	**-14.81 (22.9)**	**0.18 (14.75)**	**2.5 (14.1)**	**5 (16.25)**
Stop-Signal				
Stop errors (HC)	.009 (.02)[2]	.023 (.02)[2]	.013 (.02)[4]	.03 (.03)[4]
SST Go RT ms (LC)	589.1 (80.8)[2]	409.7 (32.4)[2]	556.8 (59.3)[4]	407.2 (44.2)[4]
Dot-Probe				
Target RT ms (LC)	412.5 (73.7)	347.9 (67.6)	405.6 (56.4)	363.3 (61.4)
Target RT ms (HC)	497.9 (88.4)	463.2 (82.5)	441.9 (64.3)	421.5 (69.8)
Attentional bias (ms)	**85.4 (76.1)**	**115.3 (86.9)**	**36.4 (52.9)**	**58.3 (51.4)**
Visual-search				
Target RT ms (LC)	1951.8 (251)[5]	1760.4 (292)[5]	1123.1 (244)[3]	1149.8 (305)[3]

Notes. Standard deviations are given between parentheses. Go RTs are means for correct trials. Errors = proportion of no-go or stop trials with incorrect response. HC = High-calorie foods or their control task equivalents (birds); Filler = Water filler stimuli or their control task equivalents (small mammals); LC = low-calorie food images or their control task equivalents (flowers). [1]Numbers in superscript refer to data missing from this number of participants in this cell, e.g. [1] Data missing from 1 participant in this cell, [2]Data missing from 2 participants etc. # Analysis of data from the Go/No-go task was limited to a subset of 53 intervention and 19 control participants who saw filler stimuli with the correct 50% go and 50% no-go associations (remaining participants saw fillers with 100% go signals). The Category effect shows the difference between 100% and 50% associated stimuli (or for the dot-probe between the HC and LC foods) – with larger positive numbers indicating quicker responding and lower inhibition errors to 100% vs. 50% predictive stimuli.

Table 3.
Descriptive Summary of Study Outcomes by Condition.

	Generic Response		Response Training	
	Mean	*SD*	*Mean*	*SD*
Percent body fat				
Pre	40.2	8.3	39.6	7.9
Post	39.1	8.4	39.0	8.2
3-month	38.7	7.6	38.4	9.4
6-month	39.4	7.1	38.6	8.8
12-month	39.0	9.1	35.8	9.1
BMI				
Pre	32.0	4.6	31.9	4.9
Post	31.7	4.4	31.6	4.6
3-month	31.5	4.3	31.8	4.6
6-month	31.0	4.0	31.1	4.6
12-month	31.1	4.5	30.6	4.2
Eating disorder symptoms				
Pre	12.2	13.1	10.8	11.1
Post	7.8	11.2	6.2	5.1
3-month	5.7	4.6	4.9	3.9
6-month	6.1	5.8	5.6	5.4
12-month	5.4	4.4	4.9	5.0
Binge eating				
Pre	5.2	13.3	4.3	11.5
Post	4.0	11.9	3.2	8.1
3-month	0.2	0.6	0.2	0.9
6-month	0.9	3.1	0.4	1.6
12-month	0.0	0.0	0.4	1.7
Palatability rating high calorie foods				
Pre	6.6	1.3	6.5	1.5
Post	5.9	1.2	5.6	1.8
Palatability rating low calorie foods				
Pre	6.0	1.5	5.8	1.4
Post	5.7	1.7	5.9	1.3
Monetary rating high calorie foods				
Pre	5.4	1.4	5.2	1.5
Post	5.2	1.3	4.9	1.4
Monetary rating low calorie foods				
Pre	5.2	1.5	5.0	1.4
Post	5.1	1.5	5.2	1.4

SD = standard deviation.
Eating disorder symptoms and binge eating reported in original metric.

Table 4.
Intent-to-Treat Pretest to Posttest Condition × Time Effects from Growth Models

	Estimate	*SE*	*t*-value	*p*-value	*d*
Percent Body Fat	0.033	0.415	0.08	.936	.004
BMI	-0.153	0.153	-1.00	.318	-.032
Eating disorder symptoms	0.062	0.053	1.17	.245	.065
Binge eating	0.023	0.020	1.11	.267	.073
Palatability rating high calorie foods	-0.334	0.180	-1.86	.065	-0.24
Palatability rating low calorie foods	0.384	0.149	2.57	.011	0.27
Monetary rating high calorie foods	-0.115	0.231	-0.50	.618	-0.08
Monetary rating low calorie foods	0.357	0.252	1.42	.159	0.25

SE = standard error, *d* = Cohen's d-statistic.

Table 5.
Complier Pretest to 6-Month Condition × Time Effects from Growth Models

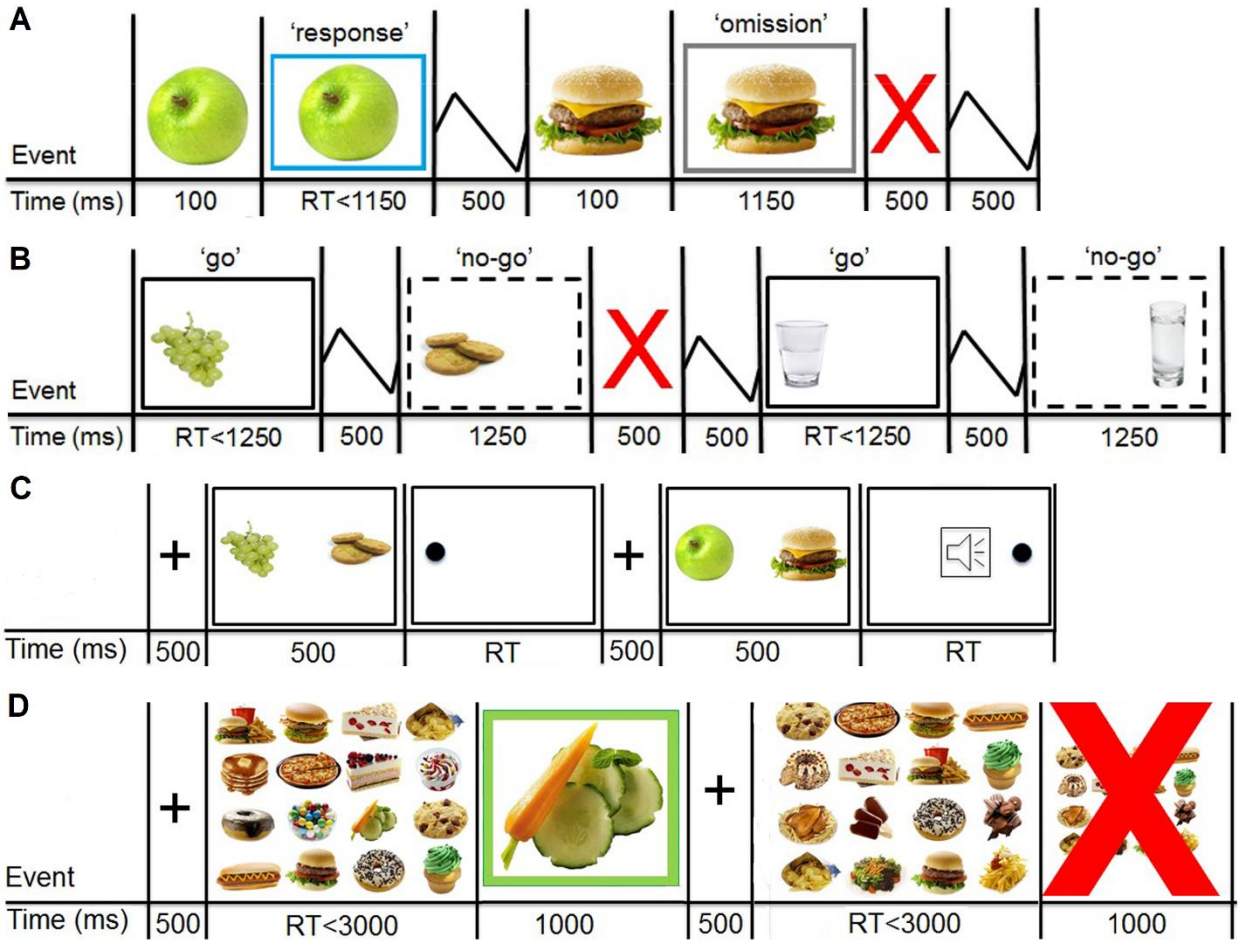
	Estimate	*SE*	*t*-value	*p*-value	*d*
Percent Body Fat	-0.005	0.114	-0.05	0.964	-0.004
BMI	-0.007	0.063	-0.11	0.911	-0.010
Eating disorder symptoms	-0.012	0.021	-0.56	0.576	-0.088
Binge eating	-0.017	0.018	-0.97	0.331	-0.394

SE = standard error, *d* = Cohen's d-statistic.

Figure legends

Figure 1. Example of timing and ordering of presentation of events during A) the stop-signal task, B) the go/no-go task, C) the dot-probe task, and D) the visual-search training task.

Figure 1.


A
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'omission'
Event
Time (ms)
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RT<1150
500
100
1150
500
500
B
'go'
'no-go'
'go'
'no-go'
Event
Time (ms)
RT<1250
500
1250
500
500
RT<1250
500
1250
C
Time (ms)
500
500
RT
500
500
RT
D
Event
Time (ms)
500
RT<3000
1000
500
RT<3000
1000

Efficacy of a Food Response and Attention Training Treatment for Obesity: A Randomized Placebo Controlled Trial

Eric Stice[a1]

Stanford University

Sonja Yokum[b]

Jeff Gau[b]

Oregon Research Institute

Harm Veling[c]

Radboud University Nijmegen

Natalia Lawrence[d2]

University of Exeter

Eva Kemps[e2]

Flinders University

1: corresponding author.
2: joint last authors.
a. Department of Psychiatry and Behavioral Sciences, Stanford University, 401 Quarry Road, Stanford CA 94305 USA; estice@stanford.edu
b. Oregon Research Institute, 1776 Millrace Drive, Eugene OR 97403 USA
c. Behavioural Science Institute, Radboud University Nijmegen, PO Box 9104 6500 HE Nijmegen, The Netherlands
d. School of Psychology, University of Exeter, Exeter EX4 4QG, UKe. School of Psychology, Flinders University, GPO Box 2100, Adelaide, SA 5001, Australia

Supplemental Methods

Genotyping. Participants provided saliva at baseline. Epithelial cells were collected using a commercial product (Oragene, DNA Genotek Inc, Ottawa, Ont). Each 96-well plate included non-templates, DNA standards of known genotype, and 10% sample replication for accuracy (100% concordance). DNA was extracted using standard salting-out and solvent precipitation methods. Genotypes were determined using the Taqman allelic discrimination assay (ThermoFisher Scientific, Waltham, MA). Assays were done using a fluorogenic 5' nuclease method on a StepOne Plus quantitive PCR instrument (Applied Biosystems Inc, Foster City, CA). Reactions contained 10 ng of DNA in a volume of 10 ul, which were amplified using the TaqMan Genotyping Master Mix and standard cycling conditions. Three genotype groups were defined for *TaqIA*: A1 homozygotes (n = 10), A1/A2 heterozygotes (n = 48), and A2 homozygotes (n = 93). For the *COMT* val^{158}met assay, forward and reverse primers, and allele specific probes were kindly provided by Dr. Daniel Weinberger (Mattay et al., 2003; and personal communication). We defined three genotype groups for *COMT* val^{158}met assay: Met homozygotes (n = 33), Val/Met heterozygotes (n = 81), and Val homozygotes (n = 36). For one participant, the *COMT* val^{158}met assay was undetermined. We defined three genotype groups for *DRD2*-141C Ins/Del assay: Ins homozygotes (n = 113), Ins/Del (n = 36) heterozygotes, and Del homozygotes (n = 2). The assay for the 48-base pair (bp) exon 3 VNTR polymorphism in the *DRD4* gene was based on the method used by Anchordoquy et al. (Anchordoquy, McGeary, Liu, Krauter, & Smolen, 2003). The assay for the 40-bp *DAT1* VNTR in the 3' untranslated region of the gene was based on the method used by Anchordoquy et al. (Anchordoquy et al., 2003). PCR reactions contained 1 µl of genomic DNA (20 ng), 10% DMSO (Hybra-Max® grade; Sigma, St. Louis, MO), 1.8 mM $MgCl_2$, 180 µM deoxynucleotides, with 7'-deaza-2'-deoxyGTP (Roche

Applied Science, Indianapolis, IN) substituted for one half of the dGTP, 400 nM forward and reverse primers (IDT, Coralville, IA) and 1 unit of AmpliTaq Gold® polymerase (ABI, Foster City, CA), in a total volume of 20 µl. Amplification was performed using touchdown PCR (Don, Cox, Wainwright, Baker, & Mattick, 1991). A 95°C incubation for 10 min was followed by two cycles of 95°C for 30 s, 65°C for 30 s, and 72°C for 60 s. The annealing temperature was decreased every two cycles from 65°C to 57°C in 2°C increments (10 cycles total), and a final 30 cycles of 95°C for 30 s, 55°C for 30 s, and 72°C for 60 s and a final 30-min incubation at 72°C. After amplification, an aliquot of PCR product was combined with loading buffer containing size standard (Rox1000, Gel Company, San Francisco, CA) and analyzed with an ABI PRISM® 3130xl (Genetic Analyzer, Foster City, CA) using company supplied protocols. Allele sizes were scored independently by two investigators; inconsistencies were reviewed and rerun when necessary. Based on studies suggesting that the 7 repeat allele confers a functional difference in D4 receptors (Asghari et al., 1995), participants were classified as having the *DRD4* 7-repeat or longer allele (*DRD4*-L; n = 65) versus shorter alleles (*DRD4*-S; n = 86). We defined three genotype groups for the *DAT1* assay: 10-repeat/10-repeat homozygotes (10R/10R; n = 85), 10-repeat/9-repeat heterozygotes (9R/10R; n = 55), and 9-repeat/9-repeat homozygotes (9R/9R; n = 10). For one participant, the *DAT1* assay was undetermined.

Supplemental Statistical Analysis

Multilocus genetic composite score. We calculated a multilocus genetic composite reflecting the total number of the five genotypes (Stice, Yokum, Burger, Epstein, & Smolen, 2012; Yokum, Marti, Smolen, & Stice, 2015). Genotypes putatively associated with high dopamine (DA) signaling received a score of 1 and those putatively associated with low DA signaling received a score of 0. Further, genotypes associated with intermediate signaling

strength received a score of 0.5. Specifically, *TaqIA* A2/A2, *COMT* Val/Val genotypes, *DRD2*-141C Ins/Del and Del/Del, *DRD4*-S, and *DAT1*-S were assigned a score of 1 ('high'); *TaqIA* A1/A1, *COMT* Met/Met genotypes, *DRD2*-141C Ins/Ins, *DRD4*-L, and *DAT1*-Lwere assigned a score of 0 ('low'), and *TaqIA* A1/A2 (Noble, Blum, Ritchie, Montgomery, & Sheridan, 1991) and *COMT* Met/Val genotypes (Egan et al., 2001) received a score of 0.5. The scores were then summed to create the multilocus composite risk score (M= 2.23 ± 0.82).

Supplemental Results

Training task performance: Evidence for associative learning and improvement over time

Go reaction time (RT) and commission errors were computed separately for each relevant stimulus category, e.g. in the go/no-go task low-calorie foods vs. water filler images (or their control task equivalents) for go RT, and all foods vs. water filler images (or their control task equivalents) for commission errors. Note, commission errors on go (i.e. pressing the wrong button) and no-go (i.e. pressing anything) filler trials in the go/no-go task could not be dissociated therefore commission errors for go and no-go trials were combined and compared between food and filler categories.

The analyses of RT and commission errors enabled comparison of responses to stimuli that were consistently associated with go (low-calorie foods or birds) or inhibit signals (high-calorie foods or flowers) relative to stimuli that were inconsistently (10% in dot probe or 50% in go/no-go) associated with go or inhibit signals (e.g. filler images in the go/no-go task). The performance difference between these image categories is thought to reflect associative (stimulus-response) learning in the tasks and is shown in Table 2 in the manuscript under "Category effect".

In the go/no-go task evidence for associative learning was mixed. The control group showed evidence of stimulus-response learning in the commission error data. However, this was lacking in the intervention group, who showed very similar rates of commission errors for food (go and no-go) and filler trials. Both the intervention and control groups showed faster responses to the 100% predictive stimuli than the 50% predictive (filler) stimuli indicating associative learning of go responses and replicating prior research (Lawrence et al., 2015). A similar measure of associative learning in the dot-probe tasks is indicated by the relative speeding to respond to targets following a consistent versus inconsistent predictive stimulus; data suggested improved associative learning over time in these tasks, replicating previous findings (Kakoschke, Kemps, & Tiggemann, 2014).

In the go/no-go task, commission error rates were very low (on average 2.71% in session 1 and 1.88% in session 4) and did not change significantly over time (F [1, 70] = 1.72, p = .2, η2p = .024) or differ as a function of group (F [1, 70] = 0.07, p = .79, η2p = .001) or group x time (F [1, 70] = 0.02, p = .89, η2p < .001). There was a main effect of stimulus category (F [1, 70] = 15.17, p < .001, η2p = .18) and a significant group x category interaction (F [1, 70] = 10.18, p = .002, η2p = .13). This was due to a strong effect of stimulus category in the control group (p < .001), with fewer commission errors to the 100% predictive stimuli (1.47% errors) than to the 50% filler stimuli (3.32% errors) as expected. However, there was no difference (p = .5) in commission errors to foods (2.11%) vs. filler stimuli (2.29%) in the intervention group. The category effect did not significantly interact with time (F [1, 70] = 0.002, p = .96, η2p < .001) and there was no category x group x time interaction (F [1, 70] = 0.04, p = .85, η2p = .001). Go RT became significantly faster over time (F [1, 70] = 30.58, p < .001, η2p = .3) but did not differ as a function of group (F [1, 70] = 0.55, p = .46, η2p = .008) or group x time (F [1, 70] = .04, p =

.85, η2p = .001). The main effect of stimulus category on Go RT was significant (F [1, 70] = 23.86, $p < .001$, η2p = .25), and there was an interaction between stimulus category and time (F [1, 70] = 5.79, $p = .019$, η2p = .08). There was no interaction between group and category (F [1, 70] < .01, $p = .99$, η2p < .001) or three-way interaction between stimulus category, group and time (F [1, 70] = .008, $p = .93$, ηp2 < .001). The faster RTs to the 100% go stimuli (low-calorie food or their control equivalents) than to the 50% go filler stimuli suggested that stimulus-go learning occurred as expected in both conditions (category effect in Table 2). However the lack of category effect for commission errors in the intervention group casts doubt on whether stimulus-inhibition learning occurred.

In the stop-signal task stopping error rates were also very low (on average 1.1% in session 1 and 2.6% in session 4). These error rates increased over time (F [1, 136] = 47.18, $p < .001$, η2p = .26), perhaps because the first session was conducted in the scanner, with longer inter-trial intervals, slower responses and fewer trials, leading to fewer commission errors (Table 2). The differences in stop errors between groups was not quite significant (F [1, 136] = 3.68, $p = .06$, η2p = .026) nor was the interaction group x time (F [1, 136] = 0.59, $p = .44$, η2p = .004). Go RT in the stop-signal task became significantly faster over time (F [1, 136] = 635.43, $p < .001$, η2p = .82), differed as a function of group (F [1, 136] = 5.31, $p = .02$, η2p = .038) but there was no group x time interaction (F [1, 136] = .001, $p = .98$, η2p < .001). The control group was faster (M = 499.04, SE = 4.67) than the intervention group (M = 482, SE = 5.73). There was only one category of go (low-calorie food or control task equivalent) and stop (high-calorie food or control equivalent) in the stop-signal task so it was not possible to assess category-specific learning.

In the dot-probe task, responses became faster over time and, as expected, were faster when probes appeared behind images that were consistently (90% of the time) associated with the probe location relative to images that were infrequently (10% of the time) associated with the probe location. This is reflected in the positive attentional bias score (RT difference) in Table 2. There was a main effect of group (F [1, 144] = 35.69, $p < .001$, $\eta 2p = .20$), whereby the intervention group showed a larger attentional bias than the control group. Attentional bias scores also increased over time (F [1, 144] = 10.39, $p < .01$, $\eta 2p = .07$). However, there was no group × time interaction (F [4, 144] = .08, $p = .772$), suggesting similar learning of the attentional bias over sessions in both groups.

In the visual-search task, the mean RT to correctly identify the one low-calorie food (or its control task equivalent) in the array of high-calorie foods showed significant improvement over time (F [1, 136] = 15.68, $p < .001$, $\eta 2p = .10$). There was also a main effect of group (F [1, 136] = 289.02, $p < .001$, $\eta 2p = .68$), with control participants responding faster than the intervention group (ps < .001; Table 2), and a group × time interaction (F [1, 136] = 23.60, $p < .001$, $\eta 2p = .15$), due to significant improvements in response speed in the intervention group ($p < .001$) but not in the control group ($p = .531$). There was only one category of target image (low-calorie food or control task equivalent) in the visual-search task so it is not possible to assess category-specific learning.

References

Anchordoquy, H. C., McGeary, C., Liu, L., Krauter, K. S., & Smolen, A. (2003). Genotyping of three candidate genes after whole-genome preamplification of DNA collected from buccal cells. *Behav Genet, 33*(1), 73-78. doi:10.1023/a:1021007701808

Asghari, V., Sanyal, S., Buchwaldt, S., Paterson, A., Jovanovic, V., & Van Tol, H. H. (1995). Modulation of intracellular cyclic AMP levels by different human dopamine D4 receptor variants. *J Neurochem, 65*(3), 1157-1165. doi:10.1046/j.1471-4159.1995.65031157.x

Don, R. H., Cox, P. T., Wainwright, B. J., Baker, K., & Mattick, J. S. (1991). 'Touchdown' PCR to circumvent spurious priming during gene amplification. *Nucleic Acids Res, 19*(14), 4008. doi:10.1093/nar/19.14.4008

Egan, M. F., Goldberg, T. E., Kolachana, B. S., Callicott, J. H., Mazzanti, C. M., Straub, R. E., . . . Weinberger, D. R. (2001). Effect of COMT Val108/158 Met genotype on frontal lobe function and risk for schizophrenia. *Proc Natl Acad Sci U S A, 98*(12), 6917-6922. doi:10.1073/pnas.111134598

Kakoschke, N., Kemps, E., & Tiggemann, M. (2014). Attentional bias modification encourages healthy eating. *Eat Behav, 15*(1), 120-124. doi:10.1016/j.eatbeh.2013.11.001

Lawrence, N. S., O'Sullivan, J., Parslow, D., Javaid, M., Adams, R. C., Chambers, C. D., . . . Verbruggen, F. (2015). Training response inhibition to food is associated with weight loss and reduced energy intake. *Appetite, 95*, 17-28. doi:10.1016/j.appet.2015.06.009

Mattay, V. S., Goldberg, T. E., Fera, F., Hariri, A. R., Tessitore, A., Egan, M. F., . . . Weinberger, D. R. (2003). Catechol O-methyltransferase val158-met genotype and individual variation in the brain response to amphetamine. *Proc Natl Acad Sci U S A, 100*(10), 6186-6191. doi:10.1073/pnas.0931309100

Noble, E. P., Blum, K., Ritchie, T., Montgomery, A., & Sheridan, P. J. (1991). Allelic association of the D2 dopamine receptor gene with receptor-binding characteristics in alcoholism. *Arch Gen Psychiatry, 48*(7), 648-654. doi:10.1001/archpsyc.1991.01810310066012

Stice, E., Yokum, S., Burger, K., Epstein, L., & Smolen, A. (2012). Multilocus genetic composite reflecting dopamine signaling capacity predicts reward circuitry responsivity. *J Neurosci, 32*(29), 10093-10100. doi:10.1523/JNEUROSCI.1506-12.2012

Yokum, S., Marti, C. N., Smolen, A., & Stice, E. (2015). Relation of the multilocus genetic composite reflecting high dopamine signaling capacity to future increases in BMI. *Appetite, 87*, 38-45. doi:10.1016/j.appet.2014.12.202

Figure S1. Participant Flow Diagram.