Running Head: RESPONSE AND ATTENTION TRAINING OBESITY TREATMENT

# Pilot Test of a Novel Food Response and Attention Training Treatment for Obesity: Brain Imaging Data Suggests Actions Shape Valuation

Eric Stice[a1]

Sonja Yokum[a]

Oregon Research Institute

Harm Veling[b]

Radboud University Nijmegen

Eva Kemps[c2]

Flinders University

Natalia Lawrence[d2]

University of Exeter

1: corresponding author.
2: joint last authors.
a. Oregon Research Institute, 1776 Millrace Drive, Eugene OR 97403 USA; e-mail estice@ori.org
b. Behavioural Science Institute, Radboud University Nijmegen, PO Box 9104 6500 HE Nijmegen, The Netherlands; e-mail: h.veling@psych.ru.nl
c. School of Psychology, Flinders University, GPO Box 2100, Adelaide, SA 5001, Australia; e-mail: eva.kemps@flinders.edu.au
d. School of Psychology, University of Exeter, Exeter EX4 4QG, UK; e-mail Natalia.lawrence@exeter.ac.uk

Abstract

Elevated brain reward and attention region response, and weaker inhibitory region response to high-calorie food images have been found to predict future weight gain. These findings suggest that an intervention that reduces reward and attention region response and increases inhibitory control region response to such foods might reduce overeating. We conducted a randomized pilot experiment that tested the hypothesis that a multi-faceted food response and attention training with personalized high- and low- calorie food images would produce changes in behavioral and neural responses to food images and body fat compared to a control training with non-food images among community-recruited overweight/obese adults. Compared to changes observed in controls, completing the intervention was associated with significant reductions in reward and attention region response to high-calorie food images (Mean Cohen's $d$ = 1.54), behavioral evidence of learning, reductions in palatability ratings and monetary valuation of high-calorie foods ($p$ = .009, *d's* = .92), and greater body fat loss over a 4-week period ($p$ = .009, $d$ = .90), though body fat effects were not significant by 6-month follow-up. Results suggest that this multifaceted response and attention training intervention was associated with reduced reward and attention region responsivity to food cues, and a reduction in body fat. Because this implicit training treatment is both easy and inexpensive to deliver, and does not require top-down executive control that is necessary for negative energy balance obesity treatment, it may prove useful in treating obesity if future studies can determine how to create more enduring effects.

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

**Pilot Test of a Novel Food Response and Attention Training Treatment for Obesity: Brain Imaging Data Suggests Actions Shape Valuation**

Obese versus lean humans show greater responsivity of brain regions implicated in reward (striatum, amygdala, orbitofrontal cortex [OFC]), attention (anterior cingulate cortex [ACC]), and motor processes (precentral gyrus, cerebellum) to high-calorie food images (Brooks, Cedernaes, Schioth, 2013; Stice, Yokum, Bohon, Marti, Smolen, 2010; Stoeckel, Weller, Cook, Twieg, Knowlton, & Cox, 2008) and attentional bias for high-calorie food images (Castellanos et al., 2009; Nijs, Muris, Euser, & Franken, 2010). Critically, elevated reward region response to high-calorie food images and cues predicts future weight gain (Demos, Heatherton & Kelley, 2012; Stice, Burger, Yokum, 2015; Yokum, Gearhardt, Harris, Brownell & Stice, 2014; Yokum, Ng & Stice, 2011). Attentional bias for high-calorie food also predicts greater *ad lib* intake (Nijs et al., 2010; Werthmann, Field, Roefs, Nederkoorn, & Jansen, 2014) and future weight gain (Calitri, Pothos, Tapper, Brunstrom & Rogers, 2010). These cross-sectional and prospective relations are consistent with the theory that obesity may result from increased reward sensitivity to high-calorie food-cues (Boswell & Kober, 2016) that is coupled with a weak ability to inhibit impulses (Nederkoorn, Houben, Hofmann, Roefs, & Jansen, 2010).

Obese versus lean humans also show less inhibitory control region (ventral medial prefrontal cortex [vmPFC]) response to high-calorie food advertisements (Gearhardt, Yokum, Stice, Harris & Brownell, 2014) and less activation of prefrontal regions (dlPFC, ventral lateral PFC) when trying to inhibit responses to high-calorie food images (Batterink, Yokum & Stice, 2010), and lower dorsolateral PFC response to high-calorie food images predicted greater subsequent *ad lib* intake (Cornier, Salzberg, Endly, Bessesen & Tragellas, 2010). Further, adults who showed less inhibitory region (inferior, middle, and superior frontal gyri) recruitment during a delay-discounting task showed elevated future weight gain (Kishinevsky et al., 2012). Individuals with less grey matter volume in inhibitory regions (superior frontal gyrus, middle frontal gyrus) also showed marginally greater future weight gain (Yokum, Ng & Stice, 2012).

These data suggest the hypothesis that an intervention that decreases reward and attention region response to high-calorie foods and increases inhibitory region response may reduce overeating rooted in exposure to omnipresent food cues. Auspiciously, experiments indicate that training people to inhibit a behavioral response to high-calorie food and to direct their attention away from high-calorie foods, which might reduce these neural vulnerability factors, reduces intake of high-calorie foods and produces weight loss (e.g., Kemps, Tiggemann, Orr & Grear, 2014a; Lawrence et al., 2015a; Veling, van Koningsbruggen, Aarts & Stroebe, 2014), suggesting that food response and attention training may prove efficacious in treating obesity.

Experiments show that relative to control training, go/no-go, stop-signal, and respond-signal computer training in which participants are signaled to repeatedly respond behaviorally with a button press to low-calorie food or non-food images, and to repeatedly inhibit behavioral responses to high-calorie food images, is associated with decreased palatability ratings for the foods paired with response inhibition signals and less *ad lib* intake of those high-calorie foods versus high-calorie foods not paired with inhibitory signals (Chen et al., 2016; Folkvord et al., 2016; Houben, 2011; Houben & Jansen, 2011; Lawrence et al., 2015a, 2015b; Veling et al., 2013). As these paradigms directly train participants to inhibit a behavioral approach response to the high-calorie training foods, while training them to make a behavioral response to the non-training foods/images, we conceptualize this as *response training*. Relatively overweight adults who completed stop-signal response training in 4 15-min weekly sessions, in which stop-signals were consistently (100% of the time) paired with 100 images of high-calorie foods and go-signals were consistently paired with 100 non-food images, showed significantly greater directly-measured pre-post weight loss than those who completed a stop-signal paradigm in which non-food images were paired with go and stop signals on a 50:50 basis (Veling et al., 2014). Participants who completed 4 10-min go/no-go training sessions in which high-calorie food images were consistently paired with no-go-signals and low-calorie food images were not, likewise showed greater directly-measured weight loss and reduced caloric intake per 24-hr food diary measure versus controls who completed parallel response inhibition training with non-food images (Lawrence et al., 2015a); critically, the weight loss effects (2.2 kg) persisted through 6-month follow-up ($p = .01$; $d = .48$). Similar effects emerged in a trial that used a stop-signal training task (Allom & Mullan, 2015), though this effect did not replicate in a second study, likely because the high-calorie foods were not as consistently paired with an inhibitory response, as was the case in the other experiments, and because participants were not overweight or obese, as in the other trials (Jones et al., 2016). Respond-signal training, in which people are trained to make a quick behavioral response for certain food images consistently paired with an auditory respond signal (for 25% of the foods), and to inhibit responses for other food images consistently not paired with the respond signal, was associated with increased choice for the foods paired with the respond signal versus those not paired with the respond signal, with effects persisting over 2-month follow-up (Schonberg et al., 2014). Of note, removing the behavioral responses from the respond-signal training abolished the effects on food choice, implying that the motor response element is essential for its efficacy.

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 among people with greater reward region responsivity to such cues. In a food-specific dot-probe paradigm, participants were shown images in which pairs of foods are shown side-by-side and are asked to respond as quickly as possible to indicate whether a visual probe subsequently appears behind the left or right image. In critical trials, chocolate foods are shown on one side of the screen and non-chocolate foods on the other. In non-chocolate attention training the probe appears behind non-chocolate foods 90% of the time and behind chocolate foods 10% of the time; this directly trains people to make a response to non-chocolate foods while indirectly training them to withhold a response to chocolate foods. In chocolate attention training the contingencies are reversed. Completion of the former versus the latter training was associated with greater reductions in attentional bias for chocolate foods, chocolate craving, and chocolate food intake (Kemps et al., 2014a). Obese participants who completed attention training for an array of low-calorie foods showed a reduction in attentional bias for high-calorie food images used in the training paradigm versus those who completed attention training for high-calorie foods (Kemps, Tiggeman & Hollit, 2014). Completing attention training for low-calorie food images was associated with reduced attentional bias for the high-calorie food images used in the training and less consumption of high-calorie foods in a taste test versus completion of attention training for high-calorie foods (Kakoschke et al., 2014). However, the results from this study could be explained by the response-facilitation training to high-calorie foods in the control condition, suggesting it is vital to use neutral control conditions in these types of studies. It is noteworthy that a training paradigm lacking a behavioral response element (Werthmann et al., 2014) did not produce the significant shift in attentional bias that emerged in the dot-probe training that included behavioral responses, implying that the motor response element of attention training may also be essential.

The response training interventions that reduced weight showed an average Cohen's $d = .61$, a medium effect size. We therefore conducted a randomized trial to test the hypothesis that a more intensive 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. We reasoned that making the training multifaceted might improve participant engagement and treatment compliance. We also reasoned that it might be useful to train responses to and attention toward low-calorie foods while at the same time training response inhibition to and attention away from high-calorie foods, as this should be more effective than using non-food images for the former training and would increase the credibility of the treatment, though there is little evidence that such training would increase consumption of low-calorie foods. We used high-calorie and low-calorie foods that were tailored to the preferences of participants, as there seemed little value in training response inhibition and attention from high-calorie foods that participants did not like.

We also investigated three theories regarding the mechanism of effect for the multifaceted food response and attention training. First, response training may result in automatic elicitation of an *inhibitory response*, which replaces the automatic approach response to high-calorie foods (Verbruggen & Logan, 2008), consistent with evidence that stop-signal response training slows button press response to high-calorie training foods versus high-calorie non-training foods (Veling, Aarts & Papies, 2011). Second, response training may *reduce valuation* of high-calorie training foods (Veling, Holland & van Knippenberg, 2008), leading to reduced intake, consistent with evidence that pairing foods with response inhibition reduces appetitive valuation of the training foods (Veling et al., 2013a; Lawrence et al., 2015a). Third, training attention away from high-calorie foods may reduce *attention* for such foods, which should decrease cravings for and intake of high-calorie foods (Kemps et al., 2014b), consistent with evidence that participants who complete dot-probe training showed reduced attentional bias for and intake of foods consistently not paired with the dot probe (Kemps et al., 2014a; Kakoschke et al., 2014).

It is important to acknowledge that by combining the response inhibition and attention training tasks it is not possible to examine the unique contributions of these training tasks in changing value and neural response to foods. However, our aim was to test whether the multifaceted training as a whole influences these outcomes. To examine the mechanism of effect, we assessed pre-post changes in palatability and monetary value ratings of the food images to index valuation. In addition, we measured errors and response times during training to index improvements in stimulus-specific learning, attention, and inhibition. We also used functional magnetic resonance imaging (fMRI) to test whether completing food response training was associated with pre-to-post increases in inhibitory region response to high-calorie food images and reductions in reward and attention region response to these images compared to completing training with non-food images. We used fMRI because it is uniquely suited to simultaneously evaluate whether training is associated with changes in inhibitory, attention, and reward valuation region responsivity and because it would provide a novel objective neuroscience test of the mechanisms of effect for this new multifaceted treatment, in line with recent work that has used neuroscience to inform psychological treatment (Craske, 2014). Thus, our joint objectives were to evaluate the effects of our novel multifaceted food response and attention training intervention on body fat loss and to identify potential mechanisms associated with the intervention.

## Methods

**Participants and procedures**.

We recruited 47 overweight/obese adults (91% female; 82% European-American; M % body fat = 44.9 ± 8.5; M BMI = 36.6 ± 8.7) for a weight loss trial and randomly assigned them to a food response and attention training condition or a parallel generic response and attention training comparison condition involving non-food images. Recruitment material (mass email messages and advertisements) invited individuals with weight concerns to participate in a weight control trial. Informed consent was obtained for this institutional review board-approved trial. 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 anorexia nervosa, bulimia nervosa, or binge eating disorder. A research assistant used a random number table to randomize participants to condition.

During the first visit to the lab (pretest), participants rated the palatability of 200 color images of high-calorie foods and 200 images of low-calorie foods; they also completed surveys, and height, weight, and body composition measurements. Three to 6 days after their first visit to the lab, participants were scanned and completed the first of their four weekly training sessions (visit #2). Participants returned to the lab for their second (visit #3) and third (visit #4) training sessions. Immediately after their 4th training session (visit #5), participants rated the palatability of the 200 color images of high-calorie foods and 200 images of low-calorie foods again, completed their second scan, and completed surveys, height, weight, and body composition measurements; the latter three outcomes were also assessed at 6-month follow-up (visit #6). Participants received $30/hour for completing assessments.

**Response training intervention.**

Participants (n = 23) completed 4 50-min weekly training visits in the lab wherein they completed 5 training tasks. During each visit they completed 10-min versions of previously validated stop-signal (Veling et al., 2014) and go/no-go training (Lawrence et al., 2015a) to high-calorie food images. As noted, we used low-calorie foods for go trials. We used 100% response contingencies for food images because the more strongly stimuli are associated with response outcomes, the greater the associative learning (Livesey & McLaren, 2007) and the more effective the training (Jones et al., 2016). Participants also completed a 10-min respond-signal training (Schonberg et al., 2014) in which they pressed a button in response to a tone that accompanied presentation of low-calorie food images on 100% of the trials and withheld a button press response 100% of the time in response to all high-calorie foods because no respond tone occurred with any of these images. We did not include the adaptive nature of the original stop-signal and respond-signal tasks because we reasoned that it would decrease the number of correct inhibitory responses toward the high calorie food items, which may reduce efficacy of the training as a whole (Jones et al., 2016). We employed the different tasks for three reasons. First, the go/no-go training, stop-signal training, and respond-signal training involve distinct task sets (the former two emphasise stopping, the latter going) and they have shown different effects on valuation and food intake in prior studies: The former two inhibit intake and cause devaluation of stop foods, the latter does not; the respond-signal task may increase valuation of go foods, the go/no-go and stop tasks do not (e.g., Chen et al., 2016). Second, offering slightly different tasks may make the intervention as a whole more engaging and acceptable. Third, by using different kinds of cues to respond or withhold responding toward the food items across the tasks we aimed to facilitate learning of general go or stop responses to the food items rather than the learning of specific food-signal associations or the learning of responses to the go, no-go or stop cues themselves (Best et al., 2016).

Participants also completed a 10-min dot-probe training that trained attention to low-calorie foods and away from high-calorie foods (90% of the time for both events) (Kakoschke et al., 2014). In addition, participants completed a 10-min visual-search training in which they quickly identified the one low-calorie food image in a larger array of high-calorie food images. Visual-search training has reduced attention for rejection-related words and increased attention for acceptance-related words and reduced exam- and occupational stress previously (Dandeneau & Baldwin, 2004; Dandeneau, Baldwin, Baccus, Sakellaropoulo & Pruessner, 2007). We selected dot-probe training because it targets the orienting attention network and visual-search training because it targets the executive attention network (Posner et al., 2006). All training tasks involved exposure to 80 high-calorie foods/beverages commonly consumed to maximize training generalizability. We used 80 randomly selected images from the 100 high-calorie food images and the 100 low-calorie food images that each participant rated the most palatable to ensure that the images were tailored to participants' tastes (palatability ratings ranged from 1 to 10). They also rated how much they would be willing to pay (<$1 to $10+) for a serving of each of the foods.

**Training paradigms**

**Stop-signal training.** In this 10-minute training task 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. 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. Filler images of glasses of water were also included, and associated with go and no-go signals on a 50:50 basis, which was also done in the go/no-go and respond-signal tasks. The task was divided into 10 blocks of 32 trials (blocks contained 14 low-calorie foods, 14 high-calorie foods, and 4 glasses of water; 320 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 10-minute task 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 fillers images were randomly selected with replacement (300 trials total). The task was divided into 6 blocks of 50 trials each. High-calorie food images were always paired with inhibition signals whereas low-calorie foods were never paired with inhibition signals.

**Respond-signal training.** In this 10-minute task participants were told to make a button press response for images paired with an auditory respond signal and to inhibit a response for images not paired with the respond signal (Fig 1C). The 80 images of low-calorie food were consistently paired with the auditory respond-signal tone, whereas the 80 images of high-calorie foods were not. Each image appeared for 1000ms; participants were told to respond as quickly as possible when they heard the respond-signal tone (between 200ms to 400ms after the image appeared). High- and low-calorie food images were presented twice and water glasses were presented once per training (352 trials), divided into 8 blocks of 44 trials.

**Dot-probe training.** In this 10-minute task participants were trained to direct their attention away from high-calorie food images and to direct their attention toward low-calorie food images (Fig 1D). 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 (320 trials), with each picture presented twice on each side of the screen. The training was divided into 8 blocks of 40 trials.

**Visual-search training.** In this 10-minute task participants searched for one low-calorie food image in a 4 x 4 array of high-calorie food images, touching the low-calorie food as quickly as possible (Fig 1E). 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 4 training blocks containing 30 arrays each (120 trials total), with each array presented for 3000 ms or until the participant responded. 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).

Because food response training is more effective when participants are hungry (Veling, Aarts & Stroebe, 2013a,b), training was done at least 3 hrs since last caloric intake. To increase the likelihood that participants would complete all trainings (including controls), training sessions began with a brief motivational enhancement activity, which we have used in an obesity prevention program (Stice, Rohde, Shaw, & Gau, 2017). For example, in a brief computer-based task participants generated 5 health costs of obesity.

**Generic response training control condition.** Controls (n = 24) 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., 2015a,b; Veling et al., 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, implying that mere exposure to high-calorie foods does not affect weight (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 (e.g., Houben & Jansen, 2011; van Koningsbruggen, Veling, Stroebe & Aarts, 2014). We used 80 images of birds and 80 images of flowers (counterbalanced) for the control response and attention training; we included images of small mammals (chipmunks) 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, Yokum, Burger, Rohde, Shaw, & Gau, 2015). Indeed, pre-to-post change in body fat did not correlate significantly with pre-post change in BMI in the present study ($r$ = .03, $p$ = .837). Further, the goal was to reduce excess body fat, rather than lean muscle mass or bone mass. ADP estimates of percent body fat show high test-retest reliability ($r$ = .92-.99), correlate with DEXA and hydrostatic weighing estimates ($r$ = .98-.99), and have a mean difference of only 1.7% relative to DEXA estimates (Weyers et al., 2002).

**fMRI food image exposure paradigm.** Participants completed a scan assessing neural response to images of high- and low-calorie foods. They consumed their regular meals but refrained from eating or drinking caffeinated beverages for 3-4 hours preceding their scans. During this event-related paradigm, participants were exposed to 40 randomly selected images from the 100 high-calorie foods each participant rated highest in palatability and 40 randomly selected images from the 100 low-calorie foods each participant rated highest in palatability. Half of these images were used in the training and half were not, so as to better assess generalizability of the training effects. Images were presented for 5 secs in a randomized order. A 2-4 sec jitter occurred between each picture during which a blank screen with a crosshair was presented. Stimuli were presented in one scanning run (total duration 20 minutes).

**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. We collected 409 scans for the food image paradigm. Functional scans used a T2* weighted gradient single-shot echo planar imaging (EPI) sequence (TE=30 ms, TR = 2000 ms, flip angle=80°) with an in plane resolution of 3.0 × 3.0 mm2 (64 × 64 matrix; 192 × 192 mm2 field of view). To cover the whole brain, 32 4mm slices (interleaved acquisition, no skip) were acquired along the AC-PC transverse, oblique plane as determined by the midsagittal section. Structural scans were collected using an inversion recovery T1 weighted sequence (MP-RAGE) in the same orientation as the functional sequences to provide detailed anatomic images aligned to the functional scans. High-resolution structural MRI sequences (FOV = 256 × 256 mm2, 256 × 256 matrix, thickness = 1.0 mm, and in-plane resolution of 1 x 1 mm) were acquired. Total scan time was 45 minutes, including the structural scan.

Neuroimaging data was preprocessed and analyzed using previously published procedures (Stice et al., 2015a). We contrasted BOLD activation during high-calorie food images versus low-calorie food images. Condition-specific effects at each voxel were estimated using general linear models. Vectors of the onset for each event of interest were compiled and entered into the design matrix so that event-related responses could be modeled by the canonical hemodynamic response function using SPM12.

Individual maps were constructed to compare the activations within each participant during high-calorie food images versus low-calorie food images and were constructed for pretest and posttest separately (i.e., pretest high-calorie > low-calorie and pretest low-calorie > high-calorie; posttest high-calorie > low-calorie and posttest low-calorie > high-calorie). We then conducted a 2 Group (intervention, control) x 2 Time (pre, post) repeated-measures ANOVA on BOLD responses to examine group differences in change in neural response to high-calorie and low-calorie food images between conditions using these individual maps. Reported hunger before each scan was included as a covariate in analyses. Whole brain analyses were conducted after the binarized DARTEL derived sample-specific gray matter mask was applied. An overall significance level of $p < 0.05$ corrected for multiple comparisons across the grey matter masked whole brain was calculated. The threshold for correcting for multiple testing was calculated by: 1) estimating the inherent smoothness of the masked functional data with the 3dFWHMx module in AFNI (Cox, 1996), and 2) performing 10,000 Monte Carlo simulations of random noise at 3 mm through the masked data using the 3DClustSim module of AFNI (Forman et al., 1995). Simulation results indicated activity surviving a threshold of $p < 0.001$, with a cluster ($k$) $\geq 15$ is statistically significant corrected for multiple comparisons. Data were inspected to insure that outliers did not drive significant effects. Effect sizes ($r$) were derived from the Z-values ($Z/\sqrt{N}$).

**Statistical Analyses of Non-Imaging Data**

Repeated measures ANOVAs with one between-subjects factor with two levels (condition) evaluated change in the behavioral data, neural responses to food images, percent body fat, BMI, and value ratings of food images. The levels of the within-subject factor, time, varied by measure with two time points for the behavioral data (training session 1 on visit #2 vs. training session 4 on visit #5), neural response data (pre-training on visit #2, and post-training on visit #5, scan), value ratings for food images (pretest on visit #1 and posttest on visit #5) and three time points for percent body fat and BMI (pretest at visit #1, posttest at visit #5, and 6-mo follow-up at visit #6). Effects for percent body fat and BMI were examined during the acute phase of the intervention (visit #1 vs. #5) and again including the longer-term follow-up (visit #1 vs. #5 and #6). Eta-square values from the models were converted to a d-statistic and provided as a measure of effect size and interpreted as .2 small, .5 medium, and .8 large.

# Results

## Behavioral data

Intervention and control groups did not statistically differ on demographic factors or study variables at baseline (smallest $p$ = .11), with the exception of monetary valuation of low-calorie foods at baseline, suggesting randomization produced initially equivalent groups (see Table 1). Note that the analyses testing the condition effects on change in monetary valuation of low-calorie foods statistically controlled for baseline differences in monetary valuation of low-calorie foods. Retention was 87% at the posttest assessment and 85% at the 6-month follow-up assessment. Number of completed assessments was not related to condition ($\chi^2[1,47]=1.73$, $p=.422$). Participants showed excellent adherence to the training and reported high acceptability, as indexed by the fact that 100% of participants completed all trainings.

Task performance accuracy in all tasks and training sessions (weekly visits) was high (at least 80%) demonstrating that all participants were engaged in the training. Table 2 displays mean group errors (expressed as a proportion of no-go/stop trials) 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 task performance over time (see Supplementary Material for more details). Repeated measures ANOVAs confirmed that the intervention and control groups showed similar task performance and improvements over time in most tasks. There were very few errors, go RT improved over sessions, and there were only minor differences between groups. Namely, the intervention relative to control group showed a larger attentional bias score from the dot-probe task and slower RT in the visual-search task (potentially reflecting the greater motivational salience of food versus non-food images), significantly greater reductions in RT for intervention versus control participants (which may have emerged because intervention versus control participants showed slower RT at baseline), aand stronger respond-signal learning. Further, both groups showed similar learning of stimulus-specific respond and no-respond associations, as demonstrated by the lower error rates and faster reaction times to the 100% versus 50% associated stimuli. These results suggest that training conditions were generally matched for task demands, stimulus-specific learning, and engagement.

**Intervention effects on neural response to high-calorie versus low-calorie food images**

Forty-one participants completed both pre and post scans (food response training n = 20; control n = 21). Six participants were ineligible due to fMRI contra-indications. Whole brain analyses comparing the food response training and control participants on change in BOLD activity in response to high-calorie food pictures > low-calorie food pictures showed significant group x time interactions in the right postcentral gyrus ($r = 0.73$), right mid insula ($r$'s = 0.61 and 0.57; Fig 2C), left superior temporal gyrus ($r$'s = 0.72 and 0.61), bilateral Rolandic operculum ($r$ left = 0.64; $r$ right = 0.60), left inferior parietal lobe ($r = 0.66$; Fig 2A), and right putamen ($r = 0.61$; Fig 2B) (Table 3). The interactions revealed that the food response-training group showed decreases in BOLD activity in these regions and the generic response-training group showed minor increases in BOLD activity (Fig 2). Post-hoc analyses tested whether changes in these regions were significant within groups. We extracted the main effect parameter estimates at the individual level from the peak coordinates (i.e., right postcentral gyrus [MNI coordinates: 48, -24, 24], left superior temporal gyrus [MNI coordinates: -48, -12, -6], left inferior parietal lobe [MNI coordinates: -57, -39, 27], right putamen [MNI: 33, 0, -6]) at pretest and posttest. Bonferroni tests were used to correct for the number of tests ($p<0.05/4$ peaks = 0.01). The food response training participants showed significant decreases in the right postcentral gyrus ($d$ =

1.41), left superior temporal gyrus ($d$ = 0.82), left inferior parietal lobe ($d$ = 1.09), and right putamen ($d$ = 0.68). The control group showed a significant increase in left superior temporal gyrus ($d$ = 0.74). No other significant changes in BOLD activity occurred in the control group.

The food response training versus generic response training participants did not show significant increases in BOLD activity from pre- to posttest. There were no significant group x time differences in BOLD signal in response to low-calorie > high-calorie food images. There were no significant changes in BOLD activity in the generic response training group compared to the food response training group.

We tested whether pre-post changes in BOLD response correlated with pre-post changes in palatability and monetary valuation ratings of the high-calorie ‘inhibited’ and low-calorie ‘go’ food pictures across all participants. For these analyses, we extracted the parameter estimates of the significant group x time interactions of the significant peaks and tested whether change in parameter estimates correlated with change in palatability and monetary valuation ratings of the high-calorie and low-calorie food pictures. Bonferroni corrections were used to correct for the number of tests. Pre-post reductions in BOLD activity in the right postcentral gyrus ($r$ = 0.43, $p$ = 0.007) and right mid insula ($r$ = 0.43, $p$ = 0.007) correlated positively with pre-post reductions in palatability ratings of the high-calorie food pictures. Pre-post reductions in BOLD activity in the right putamen ($r$ = 0.39, $p$ = 0.01) and mid insula ($r$ = 0.39, $p$ = 0.01) correlated positively with pre-post reductions in monetary valuation ratings of high-calorie food pictures. Changes in BOLD activation did not significantly correlate with changes in palatability and monetary value ratings of low-calorie food pictures.

**Intervention effects on body fat and palatability and monetary value ratings of food images**

Palatability ratings for high calorie foods changed over time (*F* [1, 36] = 42.45, $p < .001$, *d* = 2.08), differed as a function of group (*F* [1, 36] = 5.12, $p = .030$, *d* = .76) and showed significant condition x time differences (*F*[1,36] = 7.59, $p = .009$, *d* = .92; food response training: pretest *M* = 5.1 [*SD* = 1.3], posttest *M* = 3.5 [*SD* = 1.4]; control: pretest *M* = 5.6 [*SD* = 1.5], posttest *M* = 4.9 [*SD* = 1.5]). Follow-up tests of the significant interaction showed intervention participants significantly decreased over time at approximately twice the magnitude (*F* [1, 19] = 37.74, $p < .001$, *d* = 2.81) compared to control participants (*F* [1, 17] = 7.55, $p = .014$, *d* = 1.33). Monetary ratings for high calorie foods changed over time (*F* [1, 36] = 5.00, $p = .032$, *d* = .70), did not differ as a function of group (*F* [1, 36] = 0.78, $p = .384$, *d* = .29) and showed significant condition x time differences (*F*[1,36] = 7.57, $p = .009$, *d* = .92; food response training: pretest *M* = 4.7 [*SD* = 1.4], posttest *M* = 3.5 [*SD* = 1.0]; control: pretest *M* = 4.3 [*SD* = 1.0], posttest *M* = 4.5 [*SD* = 1.5]). Follow-up tests of the significant interaction showed intervention participants significantly decreased over time (*F* [1, 19] = 9.36, $p < .001$, *d* = 1.40) whereas control participants did not (*F* [1, 17] = 0.32, $p = .576$, *d* = .28). No significant condition x time effect was found for palatability or monetary ratings for low-calorie foods.

Results showed that percent body fat from pretest to posttest significantly changed over time (*F* [1, 38] = 4.98, $p = .032$, *d* = .72), did not differ as a function of group (*F* [1, 38] = 1.09, $p = .303$, *d* = .33), but did show a significant condition x time interaction (*F*[1, 38] = 7.64, $p = .009$, *d* = .90; percent body fat: pretest *M* = 45.9 [*SD* = 8.0], posttest *M* = 44.9 [*SD* = 8.3] for response training and pretest *M* = 42.5 [*SD* = 8.9], posttest *M* = 42.6 [*SD* = 9.2] for control participants). Follow-up tests of the significant interaction showed that percent body fat of intervention participants significantly decreased over time (*F* [1, 19] = 9.83, $p = .005$, *d* = 1.44) whereas that of control participants did not change over time (*F* [1, 19] = 0.19, $p = .665$, *d* = .20). Pre to posttest results showed that BMI did not change over time ($F$ [1, 39] = 0.02, $p$ = .877, $d$ = .05), did not differ as a function of group ($F$ [1, 39] = 1.00, $p$ = .324, $d$ = .32) and did not show a significant condition x time interaction ($F$[1, 39] = 0.02, $p$ = .877, $d$ < .01; BMI: pretest $M$ = 37.7 [$SD$ = 9.2], posttest $M$ = 37.7 [$SD$ = 9.2] for response training participants and pretest $M$ = 35.0 [$SD$ = 7.7], posttest $M$ = 35.0 [$SD$ = 7.6] for control participants). Pre-to-post change in body fat showed a marginal correlation with pre-to-post change in palatability ratings for high-calorie foods ($r$ = .31, $p$ = .066) and low-calorie foods ($r$ = -.29, $p$ = .087), but not with pre-to-post change in monetary value ratings for high-calorie foods ($r$ = .04, $p$ = .835) or low-calorie foods ($r$ = .06, $p$ = .747).

When we included data from the 6-month follow-up for body fat and BMI, the time x condition interactions were not significant, signaling that the body fat loss effect did not persist over 6-month follow-up. Specifically, for body fat there was no change over time ($F$ [2, 70] = 0.69, $p$ = .506, $d$ = .06), no difference as a function of group ($F$ [1, 35] = 1.31, $p$ = .260, $d$ = .39) and a non-significant condition x time interaction ($F$[2, 70] = 1.58, $p$ = .214, $d$ = .33). Similarly, for BMI, there was non-significant change over time ($F$ [2, 72] = 1.27, $p$ = .288, $d$ = .25), non-significant group differences ($F$ [1, 36] = 1.36, $p$ = .250, $d$ = .39) and a non-significant condition x time interaction ($F$[2, 72] = 0.02, $p$ = .976, $d$ < .01).

## Discussion

In sum, completion of the food response training intervention versus the generic training intervention was associated with (a) behavioral evidence of learning during the training tasks, (b) a significant reduction in reward and attention region response to high-calorie food images versus low-calorie food images, (c) reduced palatability ratings and monetary valuation of high-calorie foods, but not low-calorie foods, and (d) greater body fat loss over a 4-week period, though this effect was not significant by 6-month follow-up.

Behavioral data from both groups suggested that participants showed the expected stimulus-response learning during the trainings; they showed faster go responses to consistent (vs. inconsistent) go items and responses became faster over sessions. Both groups also showed lower commission errors to consistent (vs. inconsistent) no-go/stop items. Yet there was evidence of larger attentional bias in the food response training vs. generic training for food versus non-food image tasks overall from the dot-probe training and slower RT in the visual-search task for food versus non-food images. The latter might have driven the significantly larger reductions in RT for food response training participants versus generic control training participants. In addition, food response training participants showed greater RT differences for respond versus non-response images on the response-signal task compared to controls. In general, these data replicate past findings from studies that evaluated single modality training interventions (Lawrence et al., 2015a; Kakoschke et al., 2014; Verbruggen & Logan, 2008) and confirm that the training tasks worked as expected, even when the different training tasks were combined.

Critically, completing food response versus generic response training was associated with significantly greater pre-post reductions in neural responsivity to high-calorie versus low-calorie food images in regions that appear to play a role in attention (inferior parietal lobe), reward processing (putamen, mid insula), and sensory processing (postcentral gyrus, superior temporal gyrus), including oral somatosensory processing (Rolandic operculum). Reductions in responsivity in the postcentral gyrus and mid insula were positively associated with the decrease in palatability ratings of the high-calorie ‘inhibited’ foods and reductions in the putamen and mid insula were positively associated with the decrease in monetary value ratings of high-calorie ‘inhibited’ foods. These findings suggest that the reductions in the postcentral gyrus, mid insula, and putamen could have contributed to the decrease in palatability and value of the high-calorie foods. The inferior parietal lobe has been implicated in attentional bias towards high-calorie food images (Fuhrer, Zysset & Stumvoll, 2008) and unhealthy food commercials (Gearhardt et al., 2014). The putamen responds to (food) reward (Stoeckel et al., 2008; Stice, Burger & Yokum, 2013) and may underlie the automatic “go” response towards high-calorie foods (Fuentes-Claramonte et al., 2016), an important component of reward valuation (Guitart-Masip, Duzel, Dolan & Dayan, 2014). The insula integrates perception, emotion, interoceptive awareness, cognition, gustation, as well as information about the salience and reward value of stimuli (Dagher, 2009), though the mid insula is particularly responsive to food cravings (Pelchat, Johnson, Chan, Valdez & Ragland, 2004). Thus, results suggest that the food response training may reduce attention- and reward-related responsivity to high-calorie food cues. Interestingly, there is evidence that surgical weight loss also reduces putamen and insula responsivity to food cues (Bruce et al., 2012; Ochner et al., 2012b). This pattern of findings implies that reducing reward region response to high-calorie food images/cues mediates the effects of two treatments shown to reduce body fat and implies that response and attention training might represent a ”knifeless” method of engaging this intervention target. Collectively, data suggest that response training was associated with reduced activation in attention and reward regions, suggesting that humans automatically devalue stimuli associated with behavioral inhibition and reduce attentional allocation to the trained food images (i.e., actions shape valuation).

Food response training was also associated with greater reductions in the (oral) somatosensory regions (e.g., postcentral gyrus, Rolandic operculum) and the superior temporal gyrus in response to high-calorie food, though the latter effect was equally driven by a reduction in responsivity in intervention participants and an increase in responsivity in control participants. These regions have been implicated in the neural encoding of taste and are activated by high-calorie food cues (Ochner, Laferrere, Afifi, Atalayer, Geliebter, & Teixeira, 2012) as well as high-fat/sugar food receipt (Stice, Figlewicz, Gosnell, Levine & Pratt, 2013).

It was noteworthy that food response training did not increase responsivity of inhibitory regions to high-calorie food images at posttest. However, it is possible that participants in both groups showed increases in general inhibitory control.

The fMRI findings are highly innovative, in that past research has not used brain imaging to evaluate the effects of food response training interventions. The fact that participants were exposed to high-calorie and low-calorie foods that were both used and not used in the response training provides some evidence of generalizability of training effects, though there were too few images of foods not used in the training for separate analyses.

It could be argued that because intervention participants were exposed to images of high-calorie foods more than control participants, that this drove the differential change in BOLD signal. However, this is unlikely because we tested change in BOLD response to high-calorie foods > low-calorie foods; mere exposure would have reduced BOLD response to both types of food images, and therefore cannot logically explain the observed pattern of findings.

Completing the food response training was associated with decreases in palatability and monetary value ratings for high-calorie ‘inhibited’ foods, which were large effects ($d$ = 1.10 and .87, respectively), relative to completing the generic response training. This suggests that response training reduces valuation of high-calorie foods, as found in past trials of single modality training interventions (Veling et al., 2013a; Lawrence et al., 2015a).

Response training and attention training was not associated with increased palatability rates of, and willingness to pay for, low-calorie foods. Although we had participants respond to low-calorie foods because it seemed like it would increase the credibility of the intervention for weight loss purposes, to our knowledge only one study has found evidence of increased valuation of low-valued foods (Chen et al., 2016). One difference is that Chen and associates used an adaptive staircase procedure that made responding correctly more challenging. This pattern of findings suggests that making the trainings adaptive may result in increased attentional engagement that contributes to a change in valuation of stimuli associated with go/respond cues (Schonberg et a., 2014).

Food response training participants also showed greater reductions in body fat than generic response training controls, a large effect (*d* = .90), although effects were non-significant by 6-month follow-up and we did not detect any effects for BMI. The fact that the body fat reduction effects did not persist at follow-up implies that it will be critical for future research to evaluate procedures to improve the persistence of body fat loss effects (e.g., by adding booster training sessions). It is encouraging that our pre- to post-training (one month) body fat loss effect converges with evidence that single modality training has produced weight loss in studies conducted by multiple independent research teams (Veling et al., 2014; Lawrence et al., 2015a, Allom & Mullan, 2015), but it would have been more encouraging if we had also observed effects for BMI. The fact that we detected intervention effects in this and a previous trial with body fat, but not with BMI (Stice et al., 2015) suggests that the former is a more sensitive measure of body fat than is BMI, which reflects height-adjusted overall body density. As has been noted by methodologists, BMI does not differentiate between body fat and muscle mass (e.g., Rothman, 2008).

There are other important factors to consider when interpreting the body fat loss effect. First, our active credible comparison condition represents a more rigorous control than the minimal education or assessment-only control typically used in obesity treatment trials, as it was matched for contact time and should equate expectancy effects. Several behavioral weight loss interventions produced significantly greater weight loss than a minimal intervention exercise condition, but they did not significantly outperform a credible general practice comparison condition matched for clinician contact time (Jolly et al., 2011). Second, the acute effect size for this brief 4-hr intervention ($d$ = .90) compares favorably to the average pre-post weight loss effect from much more intensive 6-month behavioral weight loss treatments ($d$ = .85) (Franz et al., 2007) that are typically 50 hours in duration. Third, unlike the typical behavioral obesity treatment that is delivered by professional clinicians that costs $1400/year per participant (Pellegrini, Hoffman, Collins & Spring, 2014), our response training intervention can be delivered over the Internet (Veling et al., 2014; Lawrence et al., 2015a) to an enormous number of obese/overweight individuals at a minimal expense. Fourth, our pilot treatment lasted only 1-month, versus the typical behavioral obesity treatment that often spans 6 to 12 months.

It is important to consider the limitations of the present study when interpreting the effects. First, the sample size was only moderate, which limited our sensitivity to detecting small to moderate effects. Second, training only took place in 4 brief 50 min sessions, which might have limited the effects on body fat loss and persistence of these effects. Future experiments should test whether increasing training duration or frequency results in larger intervention effects. Third, the relatively small sample size of this pilot did not provide adequate power for formal mediation analyses. Relatedly, because we did not include pre and post measures of inhibitory control to food and attention toward high calorie food items in both groups, we were not able to test whether intervention participants showed a reduced attentional bias and improved inhibitory control compared to controls. Future trials should assess attentional bias for, and inhibitory control in response to, high-calorie versus low-calorie food images in both conditions before and after training to provide a better assessment of the mechanisms of effect. Fourth, the intervention involved both response training and attention training, making it impossible to gauge the relative effects of these two interventions. Fifth, the food response training participants reported slightly higher baseline monetary value ratings for low-calorie foods compared to the generic response training controls. Although the analyses testing the effects of condition effects on change in monetary valuation of low-calorie foods statistically controlled for baseline differences in monetary valuation of low-calorie foods, this baseline difference may have influenced the outcome. Finally, the sample was predominantly European-American, which may limit generalizability to other ethnic groups.

Food response training has advantages over standard weight loss interventions, including the fact that it targets implicit processes, rather than relying on effortful control to affect changes in eating. The treatment-of-choice for obesity - behavioral weight loss interventions – relies on top-down effortful control to reduce food intake. Another drawback of behavioral weight loss interventions is that they involve prolonged caloric deprivation, which ironically increases the reward value of high-calorie foods (Stice et al., 2013a; Leidy, Lepping, Savage & Harris, 2011). This may represent a key rate-limiting factor for the amount and persistence of weight loss from existing behavioral obesity treatment. Response training, which is associated with a reduction in the elevated approach behavior toward high-calorie foods exhibited by obese individuals, relies on implicit training, which is a bottom-up approach – that is most effective for precisely those that need it most – individuals with a pronounced approach tendency for high-calorie foods and low inhibitory control (Batterink et al., 2010; Seeyave et al., 2009). Such computerized training aims to directly change the automatic cognitive motivational processes that drive overeating, such as elevated reward and attention region response to food cues, and should thus result in sustained behavior change (Jansen, Houben & Roefs, 2015; Marteau, Hollands & Fletcher, 2012). It is also a cost-effective intervention that could be used alone or with extant weight loss treatments. However, it will be critical to evaluate procedures for producing body fat loss effects that persist over time, such as refining the trainings to produce greater reduction in valuation of high-calorie foods and greater increases in valuation of low-calorie foods and adding booster trainings in multiple contexts. Future research should also evaluate whether adding food response training to behavioral and surgical weight loss treatments improves efficacy.

**Acknowledgements**

National Institutes of Health grant DK-080760 supported this study. The National Institutes of Health had no role in the study design, collection, interpretation of the data, writing the manuscript, or the decision to submit the paper for publication. The authors thank the Lewis Center for Neuroimaging at the University of Oregon for their assistance with the fMRI scans.

**Conflict of Interest Statement**

The authors declare that there are no conflicts of interest.

**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.

Batterink, L., Yokum, S., & Stice, E. (2010). Body mass correlates inversely with inhibitory control in response to food among adolescent girls: An fMRI study. *Neuroimage, 52*, 1696-1703.

Best, M., Lawrence, N. S., Logan, G. D., McLaren, I. P., & Verbruggen, F. (2016). Should I stop or should I go? The role of associations and expectancies. *Journal of Experimental Psychology: Human Perception and Performance*, *42*, 115-137.

Boswell, R.G., & Kober, H. (2016). Food cue reactivity and craving predict eating and weight gain: a meta-analytic review. *Obesity Reviews, 17*, 159-177.

Brooks, S. J., Cedernaes, J., & Schiöth, H. B. (2013). Increased prefrontal and parahippocampal activation with reduced dorsolateral prefrontal and insular cortex activation to food images in obesity: a meta-analysis of fMRI studies. *PloS ONE, 8*, e60393.

Bruce, J.M., Hancock, L., Bruce, A., Lepping, R.J., Martin, L., ... & Savage, C.R. (2012). Changes in brain activation to food pictures after adjustable gastric banding. *Surgery for Obesity and Related Diseases, 8,* 602-608.

Calitri, R., Photos, E., Tapper, K., Brunstrom, J., & Rogers, P. (2010). Cognitive biases to healthy and unhealthy food words predict change in BMI. *Obesity, 18*, 2282-2287.

Castellanos, E., Charboneau, E., Dietrich, M., Park, S., Bradley, B., Mogg, K., & Cowen, R. (2009). Obese adults have visual attention bias for food cue images: Evidence for altered reward system function. *International Journal of Obesity, 33*, 1063-1073.

Chen, Z., Veling, H., Dijksterhuis, A., & Holland, R.W. (2016). How does not responding to appetitive stimuli cause devaluation: Evaluative conditioning or response inhibition? *Journal of Experimental Psychology: General, 145,* 1687-1701.

Cornier M.A., Salzberg A.K., Endly D.C., Bessesen D.H., & Tregellas J.R. (2010). Sex-based differences in the behavioral and neuronal responses to food. *Physiology & Behavior, 99*, 538–543.

Cox, R.W. (1996). AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research, 29,* 162-173.

Craske, M. G. (2014). Introduction to special issue: How does neuroscience inform psychological treatment?. *Behaviour Research and Therapy, 62,* 1-2.

Dagher, A. (2009). The neurobiology of appetite: hunger as addiction. *International Journal of Obesity, 33,* S30-S33.

Dandeneau, S.D., & Baldwin, M.W. (2004). The inhibition of socially rejecting information among people with high versus low self-esteem: The role of attentional bias and the effects of bias reduction training. *Journal of Social and Clinical Psychology, 23*(4), 584-603.

Dandenau, S.D., Baldwin, M.W., Baccus, J.R., Sakellaropoulo, M., & Pruessner, J.C. (2007). Cutting stress off at the pass: Reducing vigilance and responsiveness to social threat by manipulating attention. *Journal of Personality and Social Psychology, 93,* 651-666.

Demos, K., Heatherton, T., & Kelley, W. (2012). Individual differences in nucleus accumbens activity to food and sexual images predict weight gain and sexual behavior. *Journal of Neuroscience, 32,* 5549-5552.

Folkvord, F., Veling, H., & Hoeken, H. (2016). Targeting implicit approach reactions to snack food in children: Effects on intake. Health Psychology, 35(8), 919.

Forman, S. D., Cohen, J.D., Fitzgerald, M., Eddy, W. F., Mintun, M.A., Noll, D.C. (1995). Improved assessment of significant activation in functional magnetic resonance imaging (fMRI): use of a cluster-size threshold. *Magnetic Resonance in Medicine, 33,* 636–647.

Franz, M., VanWormer, J., Crain, A., Boucher, J., Histon, T., Caplan, W., et al. (2007). Weight-loss outcomes: A systematic review and meta-analysis of weight-loss clinical trials with a minimum of 1-year follow-up. *Journal of the American Dietetic association, 107,* 1755-1767.

Fuentes-Claramonte, P., Ávila, C., Rodríguez-Pujadas, A., Costumero, V., Ventura-Campos, N., Bustamante, J.C., et al. (2015). Characterizing individual differences in reward sensitivity from the brain networks involved in response inhibition. *Neuroimage, 124,* 287-299.

Führer, D., Zysset, S., Stumvoll, M. (2008). Brain activity in hunger and satiety: an exploratory visually stimulated fMRI study. *Obesity, 16,* 945-950.

Gearhardt, A.N., Yokum, S., Stice, E., Harris, J.L., & Brownell, K.D. (2014). Relation of obesity to neural activation in response to food commercials. *Social Cognitive and Affective Neuroscience, 9,* 932-938.

Guitart-Masip, M., Duzel, E., Dolan, R., & Dayan, P. (2014). Action versus valence in decision making. *Trends Cognitive Science, 18,* 194-202.

Houben, K. (2011). Overcoming the urge to splurge: influencing eating behavior by manipulating inhibitory control. *Journal of Behavior Therapy and Experimental Psychiatry, 42,* 384-388.

Houben, K. & Jansen, A. (2011). Training inhibitory control. A recipe for resisting sweet temptations. *Appetite, 56,* 345-349.

Jansen, A., Houben, K., & Roefs, A. (2015). A Cognitive Profile of Obesity and Its Translation into New Interventions. *Frontiers in Psychology, 6,* 1807.

Jolly, K., Lewis, A., Beach, J., Denley, J., Adab, P., Deeks, J.J., Daley, A., & Aveyard, P. (2011). Comparison of range of commercial or primary care led weight reduction programmes with minimal intervention control for weight loss in obesity: Lighten Up randomised controlled trial. *BMJ,* 343:d6500.

Jones, A., Di Lemma, L.C., Robinson, E., Christiansen, P., Nolan, S., . . ., 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.

Kakoschke, N., Kemps, E., & Tiggemann, M. (2014). Attentional bias modification encourages healthy eating. *Eating Behaviors*, *15*, 120-124.

Kemps, E., Tiggemann, M., & Hollitt, S. (2014b). Biased attentional processing of food cues and modification in obese individuals. *Health Psychology, 93*, 1391-1401.

Kemps, E., Tiggemann, M., Orr, J., & Grear, J. (2014a). Attentional retraining can reduce chocolate consumption. *Journal of Experimental Psychology: Applied*, *20*, 94-102.

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.

Lawrence, N.S., O'Sullivan, J., Parslow, D., Javaid, M., Adams, R.C., Chambers, C.D. *et al*. (2015a). Training response inhibition to food is associated with weight loss and reduced energy intake. *Appetite*, *95*, 17-28.

Lawrence, N. S., Verbruggen, F., Morrison, S., Adams, R. C., Chambers, C. D. (2015b). Stopping to food can reduce intake: Effects of stimulus-specificity and individual differences in dietary restraint. *Appetite. 85*, 91-103.

Leidy, H., Lepping, R., Savage, C., Harris, C. (2011). Neural responses to visual food stimuli after a normal vs. higher protein breakfast in breakfast-skipping teens: A pilot fMRI study. *Obesity*, *19*, 2019–2025.

Livesey, E. J., & McLaren, I. P. L. (2007). Elemental associability changes in human discrimination learning. *Journal of Experimental Psychology: Animal Behavior Processes, 33,* 148-159.

Marteau, T.M., Hollands, G.J., & Fletcher, P.C. (2012). Changing human behavior to prevent disease: the importance of targeting automatic processes. *Science, 337,* 1492-1495.

Nederkoorn, C., Houben, K., Hofmann, W., Roefs, A., & Jansen, A. (2010). Control yourself or just eat what you like? Weight gain over a year is predicted by an interactive effect of response inhibition and implicit preference for snack foods. *Health Psychology, 29,* 389-393.

Nijs, I.M., Muris, P., Euser, A.S., & Franken, I.H. (2010). Differences in attention to food and food intake between overweight/obese and normal-weight females under conditions of hunger and satiety. *Appetite, 54,* 243-254.

Ochner, C.N., Laferrere, B., Afifi, L., Atalayer, D., Geliebter, A., Teixeira, J. (2012a). Neural responsivity to food cues in fasted and fed states pre and post gastric bypass surgery. *Neuroscience Research, 74*, 138-143.

Ochner, C.N., Stice, E., Hutchins, E., Afifi, L., Geliebter, A., … & Teixeira, J. (2012b). Relation between changes in neural responsivity and reductions in desire to eat high-calorie foods following gastric bypass surgery. *Neuroscience, 209,* 128-135.

Pelchat, M. L., Johnson, A., Chan, R., Valdez, J., & Ragland, J.D. (2004). Images of desire: food-craving activation during fMRI. *Neuroimage, 23,* 1486-1493.

Pellegrini, C.A., Hoffman, S.A., Collins, L.M., & Spring, B. (2014). Optimization of remotely delivered intensive lifestyle treatment for obesity using the Multiphase Optimization Strategy: Opt-IN study protocol. *Contemporary Clinical Trials, 38,* 251-259.

Posner, M., Sheese, B, Odludas, Y, & Tang, Y. (2006). Analyzing and shaping human attentional networks. *Neural Networks, 19,* 1422-1429.

Rothman, K.J. (2008). BMI-related errors in the measurement of obesity. *International Journal of Obesity, 32,* S56-S59.

Schonberg, T., Bakkour, A., Hover, A.M., Mumford, J. A., Nagar, L., Perez, J., & Poldrack, R. A. (2014). Changing value through cued approach: an automatic mechanism of behavior change. *Nature Neuroscience, 17*, 625-630.

Seeyave, D., Coleman, S., Appugliese, D., Corwyn, R., Bradley, R., Davidson, N., . . . Lumen, J. C. (2009). Ability to delay gratification at age 4 years and risk of overweight at age 11 years. *Archives of Pediatric and Adolescent Medicine, 163,* 303-308.

Stice, E., Burger, K., & Yokum, S. (2013a). Caloric deprivation increases responsivity of attention and reward brain regions to intake, anticipated intake, and images of palatable foods. *Neuroimage*, *67*, 322–330.

Stice, E., Burger, K.S., & Yokum, S. (2015a). Reward Region Responsivity Predicts Future Weight Gain and Moderating Effects of the TaqIA Allele. *Journal of Neuroscience, 35,* 10316-10324.

Stice, E., Figlewicz, D.P., Gosnell, B.A., Levine, A.S., & Pratt, W.E. (2013b). The contribution of brain reward circuits to the obesity epidemic. *Neuroscience Biobehavioral Reviews, 37*(9 Pt A), 2047-2058.

Stice, E., Rohde, P., Shaw, H., & Gau, J. (2017). *An experimental therapeutics test of whether adding dissonance-induction activities improves the effectiveness of a selected obesity and eating disorder prevention program*. Under review.

Stice, E., Yokum, S., Bohon, C., Marti, N., & Smolen, A. (2010). Reward circuitry responsivity to food predicts future increases in body mass: Moderating effects of DRD2 and DRD4. *Neuroimage, 50,* 1618-1625.

Stice, E., Yokum, S., Burger, K., Rohde, P., Shaw, H., & Gau, J. (2015b). A pilot randomized trial of a cognitive reappraisal obesity prevention program. *Physiology and Behavior, 138,* 124-132.

Stoeckel, L.E., Weller, R.E., Cook, E.W., Twieg, D.B., Knowlton, R. C., & Cox, J. E. (2008). Widespread reward-system activation in obese women in response to pictures of high-calorie foods. *Neuroimage, 41,* 636-647.

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. *British Journal of Health Psychology, 19,* 767-782.

Veling, H., Aarts, H., & Papies, E.K. (2011). Using stop signals to inhibit chronic dieters' responses toward palatable foods. *Behaviour Research & Therapy, 49*, 771-780.

Veling, H., Aarts, H., & Stroebe, W. (2013a). Stop signals decrease choices for palatable foods through decreased food evaluation. *Frontiers in Psychology*. 4:857.

Veling, H., Aarts, H., & Stroebe, W. (2013b). Using stop signals to reduce impulsive choices for palatable unhealthy foods. *British Journal of Health Psychology, 18,* 354-368.

Veling, H., Holland, R. W., & van Knippenberg, A. (2008). When approach motivation and behavioral inhibition collide: Behavior regulation through stimulus devaluation. *Journal of Experimental Social Psychology, 44,* 1013-1019.

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

Verbruggen, F., & Logan, G.D. (2008). Response inhibition in the stop-signal paradigm. *Trends in Cognitive Sciences, 12,* 418-424.

Werthmann, J., Field, M., Roefs, A., Nederkoorn, C., & Jansen, A. (2014). Attention bias for chocolate increases chocolate consumption–An attention bias modification study. *Journal of Behavioral therapy and Experimental Psychiatry, 45*, 136-143.

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. *Medicine and Science in Sports and Exercise*, *34,* 497-502.

Yokum, S., Gearhardt, A., Harris, J., Brownell, K., & Stice, E. (2014). Individual differences in striatum activity to food commercials predict weight gain in adolescents. *Obesity, 22*, 2544-2551.

Yokum, S., Ng, J., & Stice, E. (2011). Attentional bias for food images associated with elevated weight and future weight gain: An fMRI study. *Obesity, 19*, 1775-1783.

Yokum, S., Ng, J., & Stice, E. (2012). Relation of regional gray and white matter volumes to current BMI and future increases in BMI: a prospective MRI study. *International Journal of Obesity, 36,* 656-664.

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

| | Intervention | | Control | | Test Statistics |
|---|---|---|---|---|---|
| *Categorical [N, (%)]* | | | | | |
| Female | 21 | 87.5 | 21 | 95.5 | $\chi^2[1,46] = 0.91$, p = .339, *d* = 0.28 |
| Taking medications | 7 | 28.0 | 6 | 27.3 | $\chi^2[1,47] = 0.01$, p = .955, *d* = 0.02 |
| *Continuous [Mean, (SD)]* | | | | | |
| Age | 32.8 | (8.3) | 32.4 | (8.4) | *t*[42] = 0.15, *p* = .882, *d* = 0.04 |
| Body Mass Index | 38.46 | (9.76) | 35.00 | (7.66) | *t*[45] = 1.36, *p* = .181, *d* = 0.40 |
| Percent body fat | 46.89 | (8.25) | 43.10 | (8.41) | *t*[45] = 1.56, *p* = .126, *d* = 0.46 |
| Value ratings for food images | | | | | |
| Palatability rating high calorie foods | 5.14 | (1.30) | 5.14 | (1.46) | *t*[47] = 0.04, *p* = .972, *d* = 0.01 |
| Monetary value rating high calorie foods | 4.80 | (1.38) | 4.36 | (1.16) | *t*[47] = 1.21, *p* = .236, *d* = 0.36 |
| Palatability rating low calorie foods | 4.65 | (1.25) | 5.05 | (1.35) | *t*[47] = 1.08, *p* = .286, *d* = 0.32 |
| Monetary value rating low calorie foods | 4.62 | (1.51) | 3.79 | (0.81) | *t*[47] = 2.35, *p* = .025, *d* = 0.70 |

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 (n = 23) | | Control (n = 24) | |
|---|---|---|---|---|
| Time-point | Session 1 | Session 4 | Session 1 | Session 4 |
| **Go/No-go** | | | | |
| No-Go errors (HC) | .013 (.02) | .007 (.01) | .011 (.01) | .01 (.01) |
| No-Go errors (Filler) | .025 (.09) | .027 (.06) | .043 (.05) | .035 (.04) |
| **Category effect** | **.012 (.07)** | **.02 (.05)** | **.032 (.05)** | **.025 (.03)** |
| Go RT ms (LC) | 512.1 (61.7) | 463.5 (58.6) | 507.2 (73.4) | 433.3 (57.1) |
| Go RT ms (Filler) | 522.3 (78) | 475.8 (74.8) | 508.8 (81.9) | 440 (55.6) |
| **Category effect** | **10.1 (34.8)** | **12.3 (30.6)** | **1.7 (30.2)** | **6.7 (14.3)** |
| **Stop-Signal** | | | | |
| Stop errors (HC) | .006 (.01)[3] | .016 (.02)[3] | .004 (.01) | .013 (.02) |
| Stop errors (Filler) | 0 (0)[3] | .024 (.08)[3] | .015 (.04) | .053 (.09) |
| **Category effect** | **-.006 (0)[3]** | **.008 (.08)** | **.011 (.04)** | **.039 (.09)** |
| SST Go RT ms (LC) | 543.3 (110.7)[3] | 348.8 (32.6)[3] | 499.8 (94.4) | 349.9 (37.5) |
| SST Go RT ms (Filler) | 550.9 (125.4)[3] | 357.9 (29.3)[3] | 519 (102.5) | 359.8 (46.9) |
| **Category effect** | **7.61 (44.4)[3]** | **9.11 (18.4)[3]** | **19.23 (25.7)** | **9.88 (25.1)** |
| **Dot-Probe** | | | | |
| Target RT ms (LC) | 401.6 (64.1) | 305.8 (80.9)[3] | 397.5 (51.4) | 335.7 (70.1)[2] |
| Target RT ms (HC) | 514.4 (65.2) | 461.3 (94.5)[6] | 434.3 (76.1) | 460.3 (65.4)[2] |
| **Attentional bias (ms)** | **112.8 (86.7)** | **155.6(103.8)[6]** | **36.8(56.4)** | **124.6 (75.9)[2]** |
| **Visual-search** | | | | |
| Target RT ms (LC) | 1655.7 (111) | 1440.2 (137)[2] | 928.4 (133)[1] | 909.6 (147)[5] |
| **Respond-Signal** | | | | |
| Go RT ms (LC) | 330.75 (55.3)[9] | 355.55 (89.3)[13] | 359 (64.5)[6] | 323.19 (54.6)[9] |
| Go RT ms (Filler) | 424.19 (75)[9] | 427.31 (90.2)[13] | 402.41 (67.2)[6] | 349 (44.4)[9] |
| **Category effect** | **93.4 (68.8)[9]** | **71.8 (70.2)[13]** | **43.4 (50.2)[6]** | **25.8 (22.1)[9]** |

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. The Category effect (shown in bold font) shows the difference between 100% and 50% associated stimuli – with larger numbers indicating quicker responding and lower inhibition errors to 100% vs. 50% predictive stimuli.

Table 3.

*Significant Condition-by-Stimulus-by-Time Interactions in Brain Activation during Exposure to Food Images: Flexible Factorial 2x2: Intervention (n = 20) vs control (n = 21).*

| Contrasts and regions | *k* | Z-value | MNI coordinates | r |
|---|---|---|---|---|
| ***Intervention> control*** | | | | |
| *High-calorie > low-calorie* | | | | |
| Baseline>follow-up: | | | | |
| Postcentral gyrus | 63 | 4.68 | 48, -24, 24 | 0.73 |
| Mid insula | | 3.66 | 36, -12, 9 | 0.57 |
| Superior temporal gyrus | 100 | 4.60 | -48, -12, -6 | 0.72 |
| Rolandic operculum | | 4.11 | -45, 0, 12 | 0.64 |
| Superior temporal gyrus | | 3.89 | -48, 0, -12 | 0.61 |
| Inferior parietal lobe | 71 | 4.21 | -57, -39, 27 | 0.66 |
| Putamen | 78 | 3.93 | 33, 0 ,-6 | 0.61 |
| Mid insula | | 3.89 | 42, 6, 0 | 0.61 |
| Rolandic operculum | | 3.87 | 51, 0, 6 | 0.60 |

*Notes.* Peaks within the regions were considered significant at $p<0.001$, $k \geq 15$, $p < 0.05$, corrected for multiple comparisons across the entire brain. Hunger was controlled for in the analyses.

## 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 respond-signal training , D) the dot-probe task, and E) the visual-search training

*Figure 2.* Greater pre- to post BOLD response decreases in A) inferior parietal lobe (MNI: -57, -39, 27, Z = 4.21, k = 71), B) putamen (MNI: 33, 0, -6, Z = 3.93, k = 79), and C) mid insula (MNI: 42, 6, 0, Z = 3.89) in response to high-calorie relative to low-calorie food images in the food response training condition versus control condition.

Figure 1.

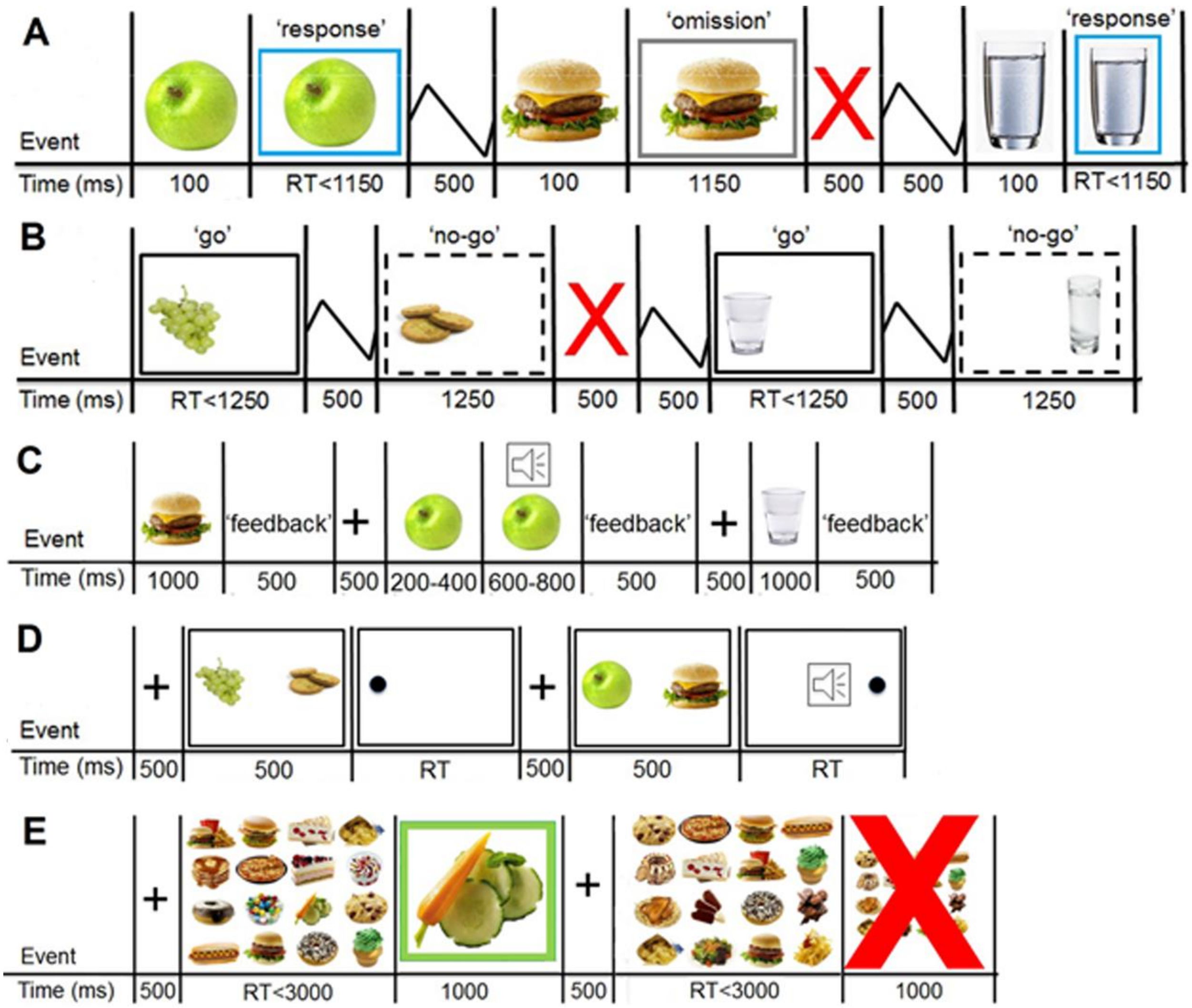
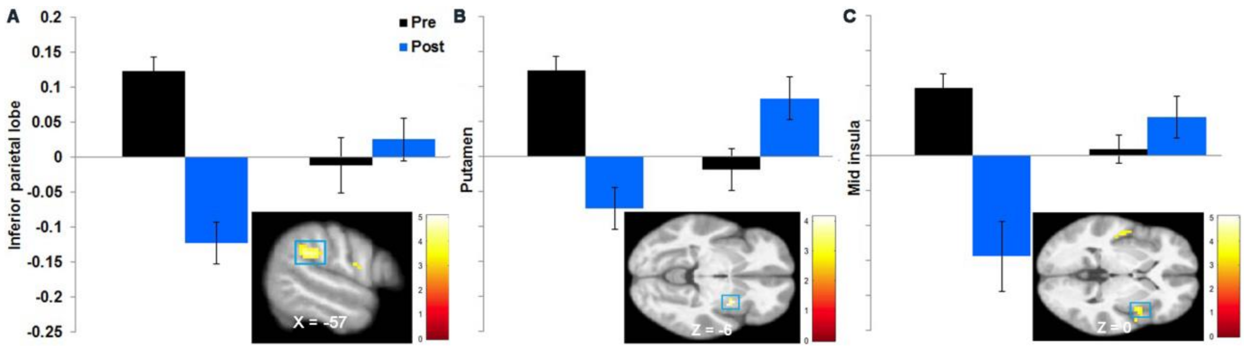

A
Event
Time (ms)
'response'
'omission'
'response'
100
RT<1150
500
100
1150
500
500
100
RT<1150
B
Event
Time (ms)
'go'
'no-go'
'go'
'no-go'
RT<1250
500
1250
500
500
RT<1250
500
1250
C
Event
Time (ms)
'feedback'
'feedback'
'feedback'
1000
500
500
200-400
600-800
500
500
1000
500
D
Event
Time (ms)
500
500
RT
500
500
RT
E
Event
Time (ms)
500
RT<3000
1000
500
RT<3000
1000

Figure 2.


A
B
C
Pre
Post
Inferior parietal lobe
Putamen
Mid insula
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
-0.25
X = -57
Z = -6
Z = 0