



## Pilot test of a novel food response and attention training treatment for obesity: Brain imaging data suggest actions shape valuation



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### 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 ( $p = 0.009$ ,  $d$ 's = 0.92), and greater body fat loss over a 4-week period ( $p = 0.009$ ,  $d = 0.90$ ), 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.

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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, & Schiöth, 2013; Stice, Yokum, Bohon, Marti, & Smolen, 2010; Stoeckel et al., 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, Photos, 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 dorso-lateral PFC response to high-calorie food images predicted greater subsequent *ad lib* intake (Cornier, Salzberg, Endly, Bessesen, & Tregellas, 2010). Further, adults who showed less inhibitory

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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 gray 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, 2014; 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, Veling, Dijksterhuis, & Holland, 2016; Folkvord et al., 2016; Houben, 2011; Houben & Jansen, 2011; Lawrence et al., 2015a, Lawrence, Verbruggen, Morrison, Adams, & Chambers, 2015; Veling, Aarts, & Stroebe, 2013a; Veling, Aarts, & Stroebe, 2013b). 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 ( $p = 0.01$ ;  $d = 0.48$ ). 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, Tiggemann, & Hollitt, 2014). 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 et al., 2014a). 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, Kemps, & Tiggemann, 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  $d = 0.61$ , 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,

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