Running Head: RESPONSE AND ATTENTION TRAINING OBESITY TREATMENT

Efficacy of a Combined Food Response Inhibition and Attention Training for Weight Loss

Eric Stice¹

Stanford University

Sonja Yokum

Oregon Research Institute

Timothy D. Nelson

University of Nebraska-Lincoln

Elliot Berkman

University of Oregon

Harm Veling

Radboud University Nijmegen

Natalia Lawrence

University of Exeter

¹: corresponding author. Department of Psychiatry and Behavioral Sciences, Stanford University, 401 Quarry Road, Stanford CA 94305 USA; estice@stanford.edu

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Abstract

This Current Opinion in Behavioral Sciences article reviews trials that evaluated an obesity treatment that combines response inhibition training with high-calorie foods and training designed to reduce attention for high-calorie foods. Two randomized controlled trials suggest that food response inhibition and attention training produced significant body fat loss, along with a reduction in valuation of, and reward region response to, high-calorie foods. However, these effects did not emerge in a third trial, potentially because this trial used more heterogeneous food images, which reduced inhibition learning and attentional learning. Collectively, results suggest that food response inhibition and attention training can devalue high-calorie foods and result in weight loss, but only if a homogenous set of high-calorie and low-calorie food images are used.

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

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The increasing worldwide prevalence of obesity continues to be a primary health concern as it accounts for over 2.8 million deaths annually and is the second leading cause of mortality [1]. Unfortunately, the most common treatments, behavioral weight loss programs, almost never produce lasting weight loss [2], suggesting that it would be useful to evaluate treatments that use a different approach. Herein we discuss the conceptual rational for dually improving inhibitory control in response to high-calorie foods and reducing attentional bias for high-calorie foods to produce weight loss and trials that have evaluated this combined training. (See Veling et al.; Lawrence et al.; Chambers et al.; etc, this issue, for reviews of studies focusing on only response inhibition training).

Neural Vulnerability Factors that Predict Future Weight Gain

It is posited that obesity results from elevated reward and attention brain region response to high-calorie foods and their cues coupled with lower recruitment of inhibitory regions that modulate food reward and attention responsivity [3-5]. In support, prospective research has found that individuals who exhibit greater activity in brain regions implicated in reward processing (striatum, orbitofrontal cortex) in response to high-calorie food images show elevated future *ad lib* caloric intake [6] and future weight gain [7-10]. Attentional bias for high-calorie food also predicts elevated future *ad lib* intake [11, 12] and future weight gain [13]. Moreover, lower dorsolateral prefrontal cortex activity, an inhibitory region, in response to high-calorie food images predicted elevated future *ad lib* intake [14]. Further, lower recruitment of inhibitory control regions (inferior, middle, and superior frontal gyri) during a delay-discounting task predicted elevated future weight gain [15], converging with evidence that lower inhibitory control in response to high-calorie foods predicted elevated future weight gain [16-19]. However,

another study did not find a relation between N2 event-related potential data, a neural indicator of inhibitory control, and future weight gain over 12-week follow-up [20].

Cognitive Science Tools for Reducing Neural Vulnerability Factors for Excess Weight Gain

Data suggest that an intervention that reduces responsivity of reward and attention regions to high-calorie foods and increases responsivity of inhibitory regions may reduce overeating prompted by high-calorie food images and cues, and promote weight loss. There is evidence that manipulations of motor responses to food images reduce reward valuation of high-calorie foods and produce weight loss. Randomized experiments show that relative to control training, computerized go/no-go and stop-signal training in which participants are signaled to repeatedly respond with a button press to low-calorie food or non-food images, and repeatedly refrain from pressing a button to high-calorie food images (which we refer to as food response inhibition training) produced decreased palatability ratings for the high-calorie foods paired with response inhibition signals and less *ad lib* intake of those foods [21-24] and reduced reward region (mid-insula) response to the high-calorie foods [24]. Food response inhibition training has also been found to produce weight loss among overweight individuals in some trials [22, 25, 26], but not others [20, 24, 25, 27, 28; see for a review 29].

There is also evidence that attention training can reduce attentional bias toward high-calorie food cues, which should decrease the potential for these cues to induce eating in the absence of hunger. Randomized experiments found that dot-probe training in which attentional bias for high-calorie foods is reduced and attentional bias for low-calorie foods is increased reduces attentional bias for and intake of high-calorie foods relative to control trainings that increase attention for high-calorie foods and reduce attention for low-calorie foods [30-32]. However, an attention modification task lacking a behavioral response element [12] 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. Additionally, a recent metaanalysis found no differences between obese and lean individuals in attention bias to palatable foods, suggesting that targeting attention bias training alone might be insufficient to change eating behavior [33].

Combined Food Response Inhibition and Attention Training

We hypothesized that combining food response inhibition training and food attention training might make the training more engaging and effective in reducing high-calorie food intake [34]. We therefore conducted a randomized pilot trial that tested the hypothesis that a multifaceted training protocol including both food response inhibition training and attention training would produce greater reductions in body fat compared to a parallel placebo response inhibition and attention training with non-food images [35]. Participants in the intervention were trained to respond to and direct attention toward low-calorie foods and to inhibit responses to and direct attention away from high-calorie foods. Training consisted of 4 weekly 50-minute visits in the lab during which participants completed stop-signal training, go/no-go training, respond-signal training, dot-probe training, and visual search training. We used high-calorie and low-calorie foods that were tailored to the preferences of participants, making this a personalized precision medicine intervention. Overweight or obese adults who completed the intervention showed greater body fat loss from pretest to posttest than controls who completed placebo training. Intervention versus control participants also showed greater reductions in brain reward (putamen; mid insula) and attention (inferior parietal lobe) region response to, and palatability ratings and monetary valuation of, high-calorie foods, consistent with the thesis that training reduces valuation of high-calorie foods.

A follow-up trial found that adding this food response inhibition and attention training to a dissonance-based obesity prevention program, which produced significant reductions in body weight and reduced future onset of overweight and obesity [36], resulted in significantly greater body fat loss from pretest to posttest versus completing the obesity prevention program and placebo response and attention training with non-food images [37]. Training consisted of 6 weekly 20-minute training visits in the lab during which participants completed stop-signal training, go/no-go training, dot-probe training, and visual search training. High-calorie and low-calorie food images were again tailored to participants preferences. However, we did not observe significant reductions in palatability or monetary valuation of the high-calorie food images or attentional bias for those images, providing mixed support for the thesis that response and attention training reduces valuation of high-calorie foods.

Given the growing evidence that this multifaceted food response inhibition and attention training produced body fat loss in two trials, we conducted a large randomized trial to examine whether food response and attention training would produce significantly greater reductions in body fat compared to placebo response and attention training involving non-food images over a longer follow-up in a larger sample. We also tested the hypothesis that the food response inhibition 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. Participants were 179 community-recruited adults with overweight/obesity who completed assessments at pretest, posttest, 3-, 6-, and 12-month followups. The training consisted of 4 weekly visits in the lab during which participants completed stop-signal training, go/no-go training, dot-probe training, and visual search training [38]. Similar to our randomized pilot trial, we used high-calorie and low-calorie foods that were tailored to the preferences of participants. Participants randomized to the intervention showed significantly greater increases in palatability ratings of low-calorie foods compared to placebo controls. However, participants who completed the intervention did not show body fat loss, reductions in palatability ratings and monetary valuation, or brain reward and attention region response, to high-calorie foods compared to placebo controls.

The lack of effects in this third trial appear to be related to weaker learning in the training evaluated in this trial versus the earlier trials. Specifically, there was no difference in commission errors in the go/no-go task between foods (100% predictive of a response) and filler stimuli (50% predictive) in the intervention group, suggesting that participants did not form an association between high-calorie foods and inhibition. Participants in the current trial also made 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 [39, 40], the weaker learning may have contributed to the null findings. Further, the increase in attentional bias from pre to post-test was less pronounced relative to our earlier pilot, both in the intervention and control groups.

One explanation for the weaker learning in the present trial versus the past two trials that produced body fat loss effects [35, 37] is that we used more diverse food images in both the lowand high-calorie food categories than in the trainings for those earlier trials. In the earlier trials, we included only images of fruits and vegetables in the low-calorie (go/attend) category and fewer categories of unhealthy food images. In the current trial, we included other types of lowcalorie foods taken from ten different categories, including whole grain foods, sushi, eggs, fish and lean meats. The high-calorie foods also encompassed a more diverse range of 10 subcategories, including sweet foods, pizza, meats, fast food, and drinks. It is possible that the boundaries may have been 'blurred' by the diversity of food images included in both the lowand high-calorie food categories, resulting in weaker associative learning at the category-level. Although some studies have demonstrated associative learning and devaluation of food at the item-specific level, these have generally included fewer food items (e.g. 20) compared to the number of items (80) in the current trial [21]. We therefore 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 [41]. 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. Alternatively, a recent metaanalysis found that interleaved practice (i.e., category items presented in an interleaved fashion with items of other categories) with labeled category items can improve learning of heterogeneous categories [42]. 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 verses fillers [22] or memory for stimulus-response contingencies [43] to check that the target mechanisms have been successfully modified [44].

The COVID-19 pandemic may also have made it more difficult to detect body fat loss effects in the third trial because the lockdown contributed to much higher attrition at the 3-, 6-, and 12- month follow-ups than we observed in past trials of obesity interventions, making it impossible to evaluate the longer-term effects of the intervention. Moreover, lockdowns have been related to increased unhealthy food consumption and reduced physical activity, particularly among overweight individuals [45, 46], which may further reduce the ability to find long-term effects.

Interestingly, the *d* effect size for body fat loss effects from pretest to 12-month follow-up based on the observed means was .32, 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.

Conclusions

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. Findings from cognitive psychology suggest that combining food response inhibition and attention training might prove useful in reducing neural vulnerability factors that predict future weight gain. Two randomized controlled trials suggest that food response inhibition and attention training produced significant body fat loss, along with a reduction in valuation of the high-calorie foods. However, these effects did not emerge in a third trial, most likely because this trial used a more heterogeneous set of the food images, which attenuated learning. It will be important for future research to test whether using more homogenous sets of images of high-calorie and low-calorie foods results in larger reductions in valuation of the high-calorie foods and body fat. It would also be useful for future research to evaluate adaptations to food response and attention training that contribute to larger and more reliable intervention effects (e.g., such as gradually fading the response and inhibition cues [28]). Finally, it would be valuable for additional prospective brain imaging studies to identify individual differences in neural responsivity that predict future weight gain, which may isolate additional neural vulnerability factors to target in future experimental therapeutics trials.

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