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Volitional regulation of brain responses to food stimuli in overweight and obese subjects: A real-time fMRI feedback study

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ABSTRACT

Obese subjects who achieve weight loss show increased functional connectivity between dorsolateral prefrontal cortex (dlPFC) and ventromedial prefrontal cortex (vmPFC), key areas of executive control and reward processing. We investigated the potential of real-time functional magnetic resonance imaging (rt-fMRI) neurofeedback training to achieve healthier food choices by enhancing self-control of the interplay between these brain areas. We trained eight male individuals with overweight or obesity (age: 31.8 ± 4.4 years, BMI: 29.4 ± 1.4 kg/m^2) to up-regulate functional connectivity between the dlPFC and the vmPFC by means of a four-day rt-fMRI neurofeedback protocol including, on each day, three training runs comprised of six up-regulation and six passive viewing trials. During the up-regulation runs of the four training days, participants successfully learned to increase functional connectivity between dlPFC and vmPFC. In addition, a trend towards less high-calorie food choices emerged from before to after training, which however was associated with a trend towards increased covertly assessed snack intake. Findings of this proof-of-concept study indicate that overweight and obese participants can increase functional connectivity between brain areas that orchestrate the top-down control of appetite for high-calorie foods. Neurofeedback training might therefore be a useful tool in achieving and maintaining weight loss.

1. Introduction

The prevalence of overweight and obesity has increased rapidly in less than half a century and the spread of many comorbidities including type 2 diabetes and cardiovascular diseases has followed suit (Finkelstein, Trogdon, Cohen, & Dietz, 2009). Obesity is strongly associated with increased intake of high-calorie and energy-dense palatable food (Berthoud & Zheng, 2012).

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Accordingly, obese in comparison to lean individuals display altered activity of brain areas involved in reward processing, eating motivation, and cognitive control, which may contribute to the persistence of elevated body weight (Carnell, Gibson, Benson, Ochner, & Geliebter, 2012; Ng, Stice, Yokum, & Bohon, 2011; Val-Laillet et al., 2015). These insights rely on neuroimaging as an effective means of investigating the neural networks underlying the regulation of appetite and food preference in normal-weight and overweight subjects (Carnell, Benson, Pryor, & Driggin, 2013). Neuroimaging has moreover turned out to be a potential noninvasive neurotherapeutic tool in the treatment of disorders such as depression (Linden et al., 2012) and eating disorders (Bartholdy, Musiat, Campbell, & Schmidt, 2013). Thus, recent experiments have shown that individuals can learn to voluntarily control their brain activity with the help of real-time functional magnetic resonance imaging (rt-fMRI) providing online feedback of neural activity (Weiskopf, 2012).

Since rt-fMRI paradigms have been found to trigger intended behavioral effects (Caria, Sitaram, Veit, Begliomini, & Birbaumer, 2010) and factors critical for food intake control like self-regulation and impulse control are suitable targets of neurofeedback (Birbaumer, Ruiz, & Sitaram, 2013; Schlogl, Horstmann, Villringer, & Stumvoll, 2016; Val-Laillet et al., 2015), respective interventions might be a promising avenue to the modulation of eating behavior (Frank et al., 2012; Ihssen, Sokunbi, Lawrence, Lawrence, & Linden, 2016). In this context, areas that process reward or mediate inhibitory control can be assumed to be of major relevance (Val-Laillet et al., 2015). Overeating in obese subjects may be conceptualized to stem from hyper-responsivity of reward-processing structures or, rather, from diminished sensitivity triggering surplus calorie intake (Kenny, 2011). Therefore, targeting reward-processing areas by neurofeedback might bear the risk of unintended effects, whereas impairments in impulse control and decision making have been conclusively observed in obese subjects (Rangel, 2013). Neuroimaging studies have indeed indicated that the interplay between the dorsolateral and the ventromedial prefrontal cortices (dlPFC and vmPFC) may be of particular significance in this regard. While the vmPFC is assumed to encode the valence of a stimulus (Hare, O'Doherty, Camerer, Schultz, & Rangel, 2008), the dlPFC rather mediates self-control over consummatory behaviors (Hollmann et al., 2012). Functional connectivity between dlPFC and vmPFC is increased during exposure to food pictures when healthy individuals are satiated as compared to being fasted (Thomas et al., 2015). Accordingly, healthy food choice is positively related to functional connectivity between dlPFC and vmPFC, and dlPFC activity is increased when participants exercise self-control (Hare, Camerer, & Rangel, 2009). In line with these results, individuals who show greater diet-induced weight loss than others exhibit stronger dlPFC-vmPFC functional connectivity (Weygandt et al., 2013). Improving the connectivity between these brain areas may therefore normalize eating behavior and support weight loss in obese subjects. In the present proof-of-principle study we investigated whether rt-fMRI neurofeedback training enables overweight and obese subjects to increase dlPFC-vmPFC functional connectivity during visual stimulation with unhealthy, high-calorie food stimuli and, if so, how such changes relate to food choices and eating behavior.

2. Methods

2.1. Participants

Eight healthy male participants with overweight or obesity participated in the study (age: 31.8 ± 4.4 years, BMI: 29.4 ± 1.4 kg/m^2). Exclusion criteria included weight loss exceeding 5 kg within 3 months before participation, eating disorders, neurological or psychiatric diseases, use of medication, and contraindications for MRI. Prior to participation subjects were informed about the procedure and gave written informed consent. The study protocol was approved by the local Ethics Committee and in accordance with the Declaration of Helsinki.

2.2. Experimental protocol

Within four weeks, subjects participated in six sessions separated by at least two days, a pre-training session in the first week, four neurofeedback training sessions in the second and third week, and one post-training session in the fourth week. Sessions took place in the late morning after at least two hours of post-breakfast fasting.

2.2.1. Pre-training

In the pre-training session, individual regions of interest (ROI) for neurofeedback training (dlPFC and vmPFC) were determined (Hare et al., 2009) (Supplementary Fig. S1). Participants first rated 90 food images (Hare et al., 2009) on tastiness (1 = not tasty at all, 2 = not tasty, 3 = neutral, 4 = tasty, 5 = very tasty) and healthiness (1 = very unhealthy, 2 = unhealthy, 3 = neutral, 4 = healthy, 5 = very healthy) in separate sessions on 5-point scales while they were scanned. One item that was rated as neutral both regarding tastiness and healthiness was selected as the reference image for the subsequent choice task. (If necessary, a tastiness rating of 4 was taken to represent relative neutrality). In that task, participants first saw their personalized reference image and were told that in each of the following trials they would have to indicate if they preferred to eat the food item presented in the trial or their reference food (Hare et al., 2009). This procedure yielded healthy, neutral and unhealthy choices. Food images were displayed for 3 s on a computer screen (Presentation, Neurobehavioral Systems Inc, www.neurobs.com) and ratings during the scan were given via a fMRI-compatible button box (www.curdes.com).

2.2.2. Training sessions

In the training sessions, participants learned to self-control dlPFC-vmPFC functional connectivity. On the first neurofeedback day, the idea of neurofeedback (self-regulation) was explained and suggestions to control the specific brain areas were given (reappraisal techniques (Greer, Trujillo, Glover, & Knutson, 2014); see Supplementary File 1). Subsequently the participant was placed in the scanner and underwent three training runs of 9 min each (see Fig. 1 for neurofeedback set-up). Each run consisted of 6 trials of 30 s up-regulation of functional connectivity between dlPFC and vmPFC and 30 s of passive viewing, including 12 s of rest in-between and between trials. During up-regulation and viewing, an appetitive high-calorie food picture (rated high in tastiness and low in healthiness in the rating task of the pre-training session), two black thermometers on the right and respectively left side of the food image (providing feedback on functional connectivity) and two additional symbols indicating the type of the trial (upward arrow during up-regulation, plus sign during passive viewing) were displayed. The thermometer bars included ten levels which turned from black to grey in an upward, incremental fashion whenever functional connectivity between the ROIs increased by 0.1. Only increases in functional connectivity were fed back to the participants, otherwise the thermometer bars were displayed as empty. Participants received feedback only during up-regulation trials. During passive viewing, participants were instructed to relax, and the same visual cues as during up-regulation were shown without updating the feedback thermometers. During rest, a cross appeared. Stimuli were displayed on a screen through a computer