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Fighting food temptations: The modulating effects of short-term cognitive reappraisal, suppression and up-regulation on mesocorticolimbic activity related to appetitive motivation

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ABSTRACT

The premise of cognitive therapy is that one can overcome the irresistible temptation of highly palatable foods by actively restructuring the way one thinks about food. Testing this idea, participants in the present study were instructed to passively view foods, up-regulate food palatability thoughts, apply cognitive reappraisal (e.g., thinking about health consequences), or suppress food palatability thoughts and cravings. We examined whether these strategies affect self-reported food craving and mesocorticolimbic activity as assessed by functional magnetic resonance imaging. It was hypothesized that cognitive reappraisal would most effectively inhibit the mesocorticolimbic activity and associated food craving as compared to suppression. In addition, it was hypothesized that suppression would lead to more prefrontal cortex activity, reflecting the use of more control resources, as compared to cognitive reappraisal. Self-report results indicated that up-regulation increased food craving compared to the other two conditions, but that there was no difference in craving between the suppression and cognitive reappraisal strategy. Corroborating self-report results, the neuroimaging results showed that up-regulation increased activity in important regions of the mesocorticolimbic circuitry, including the ventral tegmental area, ventral striatum, operculum, posterior insular gyrus, medial orbitofrontal cortex and ventromedial prefrontal cortex. Contrary to our hypothesis, suppression more effectively decreased activity in the core of the mesocorticolimbic circuitry (i.e., ventral tegmental area and ventral striatum) compared to cognitive reappraisal. Overall, the results support the contention that appetitive motivation can be modulated by the application of short-term cognitive control strategies.

Introduction

In most industrialized societies, where food is plenty, people often find themselves eating in the absence of any real hunger and all too often beyond direct energy requirements. This type of eating behavior is thought to be the result of a strong appetitive motivation, which has been linked to activation of the mesocorticolimbic pathway (Alcaro et al., 2007; Kelley and Berridge, 2002). This excessive appetite for particularly palatable high calorie foods would undoubtedly lead to weight gain in the absence of some kind of control. Researchers have therefore proposed that eating behavior is the outcome of an interplay between appetitive motivation and inhibitory cognitive control (Appelhans, 2009; Nederkoorn et al., 2006, 2010).

The suggestion that cognitive control can modulate appetitive motivation is in line with current cognitive interventions for obesity, which propose that food cravings *can* be successfully decreased by actively controlling the way one thinks about foods (Beck, 2007; Stephens, 2007; Werrij et al., 2009a, 2009b). If so, given that appetitive motivation is associated with mesocorticolimbic activity, one would expect that cognitive restructuring – the aim of cognitive therapy – would modulate this activity. There is some indirect evidence for the influence of cognitive control on brain activity within the mesocorticolimbic circuitry. For example, previous neuroimaging studies show that word-level cognitive labels of odors and flavors can modulate activity in the orbitofrontal cortex (OFC; de Araujo et al., 2005; Grabenhorst et al., 2008), and that deliberate suppression of hunger feelings inhibits activity in mesocorticolimbic regions such as the amygdala, the hippocampus, the insula, the OFC, and striatum (Wang et al., 2009). In addition, in a previous study (Siep et al., 2009) increased mesocorticolimbic activity was only found when the task required participants to attend to the palatable taste, smell and texture of a presented visual food cue, but not when they were required to attend to a neutral aspect of the same food cue. These few studies suggest that it is possible that by the way one thinks of a food or the manner in which one deliberately tries to perceive a given food affects mesocorticolimbic activity. As mesocorticolimbic activity is related to appetitive motivation, this in turn might influence how much food is eaten.

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Previous research has identified three types of short-term cognitive control strategies that are known to modulate emotional responses (Gross, 2006); (1) *up-regulation*, which increases the intensity of prepotent responses, (2) *cognitive reappraisal*, which changes the way one thinks about emotion-eliciting cues in a way that changes its emotional impact and (3) *suppression*, which is related to both the active inhibition of thoughts (Wenzlaff and Wegner, 2000) and emotional responses (Gross, 2006). Neuroimaging studies examining the neural bases of up-regulation, cognitive reappraisal and suppression, have found that each strategy differs in the way it influences brain activity in the mesocorticolimbic circuitry. For example, up-regulating negative emotions increases medial prefrontal cortex (PFC) and decreases amygdala activity (Ochsner et al., 2004), while decreasing negative emotion by cognitive reappraisal increases activity in the lateral ventral and orbital PFC and decreases activity in the amygdala, ventral striatum and insula (Ochsner et al., 2004; Wager et al., 2008). In addition, research indicates that suppression and cognitive reappraisal differ in their effects, showing that suppression increases PFC activity, but also increases amygdala and insula responses (Goldin et al., 2008). Taken together, these results show that cognitive strategies are effective in modulating mesocorticolimbic activity involved in emotion processing and suggest that they might also be effective in regulating appetitive motivation.

To further investigate the hypothesized interaction between appetitive motivation and cognitive control, the present functional magnetic neuroimaging (fMRI) study investigates the effects of short-term suppression, cognitive-reappraisal and up-regulation strategies on subjective experiences of food craving and mesocorticolimbic activity in healthy women. Participants were instructed to look at palatable food pictures and 1) imagine the food's palatable smell, texture and taste (i.e., up-regulation), 2) immediately inhibit any thoughts concerning food palatability and/or food cravings (i.e., suppression), or 3) focus on alternative meanings of the presented food cues, for example, the longer term consequences of consuming the food for their health (i.e., cognitive reappraisal). We hypothesized that self-reported food cravings would be higher following the up-regulation strategy, as compared to suppression and cognitive reappraisal. Furthermore, it was hypothesized that the cognitive reappraisal strategy would result in lower self-reported food craving as compared to suppression. Concerning the neuroimaging data, it is expected that activity in mesocorticolimbic regions will be increased by up-regulation compared to both suppression and cognitive reappraisal and that cognitive reappraisal will be more effective in decreasing mesocorticolimbic activity as compared to suppression. Lastly, in line with previous findings suggesting that suppression requires more control resources (Goldin et al., 2008), we hypothesized that suppression would result in larger increases in PFC activity as compared to cognitive reappraisal.

Method

Participants

Undergraduate students were recruited using flyers posted at Maastricht University. Given that women more often engage in nutritional self-assessments and dieting behavior than men do (Davy et al., 2006; Morse and Driskell, 2009), only women were invited for an interview. In this interview height, weight, age, handedness, medication use, (family) history of eating disorders and other psychiatric disorders, dietary restrictions, impulsivity, and reward responsiveness were assessed. Candidates were excluded from participation when they disliked more than four of the foods used as stimuli in this study. Selected participants were 14 right-handed, non-dieting, healthy students with a healthy body weight (body mass index (BMI) between 18.5 and 25 [$M = 21.5$, $SD = 1.9$]), and a score of <15 on the Restraint Scale ($M = 10.7$, $SD = 1.9$; Herman et al., 1978), with a mean age of 21.1 ($SD = 1.5$). Because food intake varies across the menstrual cycle in females (Bryant et al., 2006), participants were selected based on the use of monophasic Combined Oral Contraceptives (COCs). Monophasic COCs inhibit the production of fertility hormones and consequently prevent increases in food intake in the premenstrual phase (Goldzieher, 1994). Further, because the personality characteristics of impulsivity and reward responsiveness are supposed to reflect the sensitivity of the reward system (Davis et al., 2007), participants were screened on reward responsiveness and impulsivity. All participants scored within the normative population range of impulsivity as measured with the Barratt Impulsiveness Scale [Spinella, 2007; Impulsivity score participants: $M = 59.7$, $SD = 4.9$; normative score: $M = 64.2$, $SD = 10.7$]. In addition, participants scored within the normative population range of reward responsiveness as measured with a subscale from the BIS/BAS scale (Carver and White, 1994; participants' score: $M = 16.7$, $SD = 1.5$; normative score: $M = 17.5$, $SD = 1.4$).

Stimuli

In a pilot study, 25 savory and 25 sweet high calorie food pictures were selected as candidate stimuli from an internet database (www.istockphoto.com). Subsequently, these food pictures were rated on 100 mm visual analogue scales (VAS) by 20 healthy, non-dieting female volunteers not participating in the actual study on calorie content (0: very low calorie–100: very high calorie) and palatability (0: very bad tasting–100: very good tasting). Based on these ratings, 14 sweet, palatable, high calorie food pictures [calorie content ratings: $M = 82.06$, $SD = 4.84$; palatability ratings: $M = 65.67$, $SD = 6.85$; e.g., chocolate, cake, cookies, ice cream] and 14 savory, palatable, high calorie food pictures [calorie content ratings: $M = 80.65$, $SD = 4.61$; palatability ratings: $M = 67.20$, $SD = 4.61$; e.g., pizza, fries, crisps, hamburger] were selected. The selected food pictures were projected as pop-out figures on a black canvas to minimize noise input (Rainer et al., 2001). For a more elaborate discussion on pop-out figures and the use of pictures instead of real foods, we refer to a previous fMRI study (Siep et al., 2009). Only pictures of high calorie foods were included, as we assume that healthy, lean women apply cognitive control strategies mainly to high calorie foods and not so much to low calorie foods.

Design and experimental task

This study used a one-way within-subjects design with four levels (cognitive control strategy: cognitive reappraisal, suppression, up-regulation, and passive viewing). To avoid carry-over effects from the cognitive control conditions to the passive viewing condition, all participants started the experiment with a passive viewing task. In the passive viewing task, pictures of food were pseudo-randomly presented in the center of the screen. To ensure that the participant maintained a constant level of attention, she was instructed to press a button with her right index finger as soon as a dot appeared in the center of a food picture. Dots appeared in 13% of the food picture trials and were later removed from analyses.

The passive viewing task was followed by a practice task to familiarize the participant with the cognitive control conditions and the symbols representing the conditions: eye, stop sign, and upward arrow (see Fig. 1 for an overview). Training of the participant included initial instructions, followed by practice as the investigator observed and shaped her technique. The participant was specifically instructed not to look away from the images, or to close her eyes. The eye symbol indicated that the participant should think about the negative consequences of eating the presented food for her weight, health, and bodily appearance (i.e., cognitive reappraisal). This type of reappraisal has also been referred to as situation-focused reappraisal (Ochsner et al., 2004), in which the participant

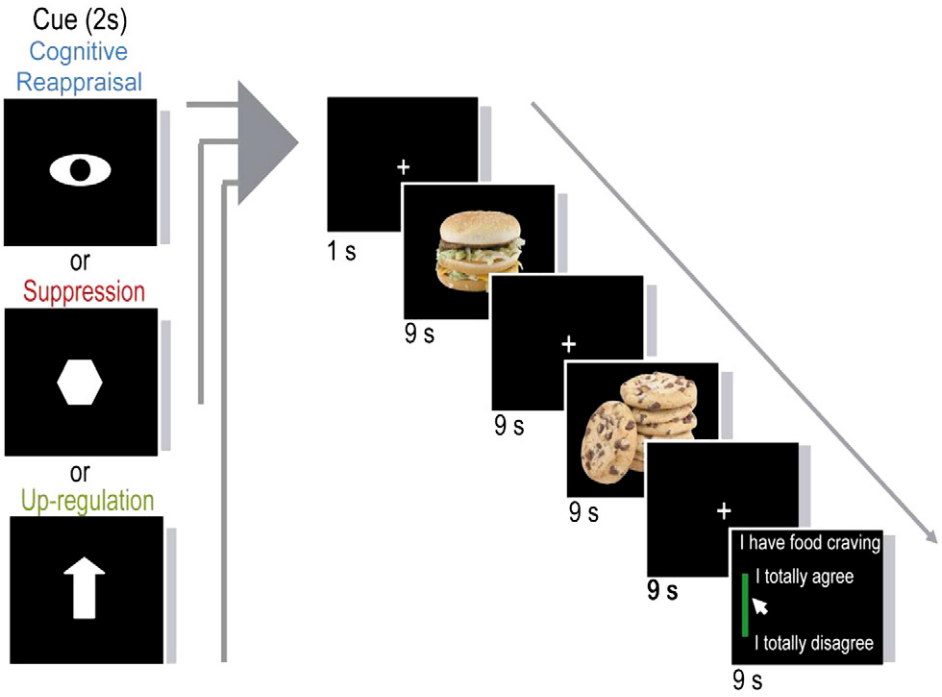

Fig. 1. Graphical outline of the stimulation protocol. Stimuli were presented in a slow-event-related design and involved three cognitive control conditions: up-regulation, cognitive reappraisal and suppression. During the tasks participants focused on the screen center as indicated by the white fixation cross. Stimuli were presented in the center of the participants' visual field. At the beginning of each block a cue was presented indicating the task.

has to re-interpret the actions and outcomes for a given image. The stop sign indicated that the participant should look at the presented food cue in a neutral way and immediately inhibit any thoughts (Wenzlaff and Wegner, 2000) or cravings, which can also be behavioral, (Gross, 2006) related to the palatability of the presented food, without looking away from the picture (i.e., suppression). The upward arrow indicated that the participant should increase their cravings for the presented food cues by actively thinking about the delicious smell, taste, and texture of the presented food cue in a way that would make her mouth water (i.e., up-regulation).

Once the participant had mastered the technique to the satisfaction of the experimenter, two experimental runs followed in which the participant applied the cognitive control strategies. In these two runs, the participant was always first shown the symbol, cueing which type of cognitive control strategy she should apply. To make the application of the three cognitive control strategies less difficult and confusing, two food pictures were presented sequentially, during which the participant applied the same cognitive strategy. The presentation of the two food pictures was followed by a vertical 100 mm VAS, assessing experienced craving (item: "I have cravings for one or more specific foods", top: I totally agree (100)–bottom: I totally disagree (0)). This item was taken from the Food Craving Questionnaire (Moreno et al., 2008).

Stimulation protocol

The experiment consisted of a total of three experimental runs in which food pictures were presented in a slow event-related fashion, and one anatomical scan. During the passive viewing run, the presentation of each food picture trial lasted 9 s, followed by a white fixation cross (9 s). In four of the food picture trials a white dot appeared for 200 ms after a variable time length from the first presentation of the food picture. The participant was instructed that fixation should be maintained throughout the passive viewing run. In total, the passive viewing run lasted approximately 9 min. For each participant, the order of the 14 savory and 14 sweet food pictures within the passive viewing run was randomized and comprised 32 trials including the 4 "dot trials". Identical pictures were presented in all conditions and each picture was presented once per condition.

In the two cognitive control runs, each cognitive control strategy was presented 7 times in a pseudo-randomized order. During each type of cognitive control condition (see Fig. 1), an initial cue appeared (2 s), indicating which cognitive control strategy the participant should apply, followed by a white fixation cross (1 s). Then two food picture trials were presented sequentially, lasting 9 s each, followed by fixation (9 s). Presentation of the two food pictures was followed by a VAS (9 s). Although the duration of the VAS trial remained constant, the VAS disappeared as soon as the participant made her choice. Throughout one cognitive control run, each condition was repeated seven times. Each cognitive control run lasted approximately 20 min.

The order of the three cognitive control conditions was randomized per run and then manually checked for repetitions to avoid fMRI adaptation effects (Grill-Spector and Malach, 2001). For each participant, the order of food stimuli per condition, within each run, was fully randomized. The order of the two cognitive control runs was balanced across participants. The total fMRI session lasted 75 min.

Procedure

All imaging sessions took place around lunch-time (i.e., between 1 and 3 pm). Participants were instructed not to consume any food or beverages (except water) four hours prior to the imaging session. Upon arrival, written informed consent and ethical approval were obtained from the participant. Next, hunger was assessed with 100 mm VAS (Friedman et al., 1999; translated into Dutch), which showed that participants were moderately hungry at the start of the fMRI experiment [$M = 48.7$, $SD = 19.53$]. After completing the questionnaire, the participant entered the scanner. The participant did not receive any instructions about the different experimental tasks, to avoid influences from the cognitive control instructions on the passive viewing task. After completion of the passive viewing task, an anatomical scan was performed during which the participant received

the instructions for the cognitive control tasks. Once the participants had mastered the different techniques to satisfaction of the researcher, two experimental runs were presented in which the participant applied the practiced cognitive control techniques. At the end of the fMRI session, the participant completed an exit questionnaire inquiring about the strategies she applied during the cognitive control conditions and the experienced difficulties. After completing the study, the participant received € 15 compensation.

fMRI data acquisition

Images were acquired with a 3 T Siemens Magnetom Allegra Head-only Scanner at the Maastricht Brain Imaging Centre (MBIC) using a birdcage volume coil. Gradient-echo planar imaging (EPI) volumes were acquired (50 slices, TR = 3000 ms). Imaging parameters were optimized to minimize susceptibility and distortion artifacts in the OFC (see: Weiskopf et al., 2006). The relevant factors included oblique axial imaging with a negative (i.e., backward) tilt angle of 30°, minimizing voxel size ($2\times2\times2.5$ mm) in the plane of imaging, a short echo time of 25 ms, and a high imaging bandwidth (2790 Hz over the field of view, echo spacing = 0.4 ms). The voxel matrix size was 128×104 mm, and the field of view (FoV) was 256×208 mm. Acquisition of functional images yielded 200 volumes during the passive run and 409 during each cognitive modulation run. One high-resolution whole-brain anatomical T1-weighted scan was acquired: an optimized MPRAGE sequence (TR = 2250 ms, TE = 2.6 ms, flip angle = 9°, $1\times1\times1$ mm).

fMRI data preprocessing

All processing and analyses of the fMRI data were performed using BrainVoyager QX version 1.9 (Brain Innovations, Maastricht, The Netherlands). The first two volumes of the T2* weighted functional images were discarded due to magnetic saturation effects. Preprocessing comprised slice scan timing correction (using sinc interpolation), motion correction (using a 3D rigid-body transformation of each volume to the first volume of each run and using sinc interpolation) and high-pass filtering to remove low-frequency noise (up to 3 cycles in the single run time-course). Individual functional data were smoothed using a 6 mm full-width-at-half-maximum isotropic Gaussian Kernel. The anatomical scan and the functional data were then spatially normalized using Talairach transformation procedures (Talairach and Tournoux, 1988). For group analysis, the normalized individual functional data were averaged accounting for both scan-to-scan and participant-to-participant variability.

fMRI analysis

A whole-brain, voxel-wise Random Effects (RFX) ANOVA was used to test for differences in BOLD signal across cognitive control strategies. Because our hypothesis concerned the modulation of mesocorticolimbic activity by the three modulation conditions, only the suppression, cognitive reappraisal, and up-regulation conditions were included at this stage of the analysis.

For the resulting F-map of the RFX ANOVA, *F*-test main effect of cognitive control strategy, a significance level of $p<0.01$ was used. To correct for multiple comparisons, a minimum cluster size of 9 contiguous voxels was adopted (determined by a cluster size threshold estimator plug-in implemented in BrainVoyager), yielding a whole-brain corrected statistical rejection criteria of 5%.

To test our three hypotheses, we used the *functional region of interest* (fROI) approach, which involves identifying a priori hypothesized candidate regions in the PFC and mesocorticolimbic from the corrected whole-brain F-map and then calculating the overall summary measure of response in each region (see: Saxe et al., 2006). This method allowed us to decrease the influence of noise that varies between voxels and make inferences about the response profile of each fROI as a whole, rather than particular voxels within the region.

Our corrected F-map comprised a total of 24 fROIs (Table 1), of which 14 fROIs were located in the a priori hypothesized PFC and mesocorticolimbic circuitry. The beta weights for each condition, including passive viewing, were averaged across participants and across all voxels within each of these 14 fROIs. Bar-plots were made to visualize the response profiles of all fROIs (Fig. 2). Following our hypothesis, fROIs were divided into two groups: regions located in mesocorticolimbic circuitry but outside the PFC (Fig. 2A), and regions located in the PFC (Fig. 2B). A functional region of fROI analysis was performed to evaluate differences in the magnitude of the MR signal change between conditions, using pairwise *t*-tests. *T*-tests were considered statistically significant at $\alpha = 0.01$ and planned comparisons at $\alpha = 0.05$. Results of these *t*-tests are depicted in Fig. 2, and are the focus of the discussion.

Results

Manipulation check

To test whether the participants followed the instructions, they were asked to describe their applied cognitive control strategies in an exit questionnaire. From these reports we concluded that *all* participants did indeed follow our instructions as intended, as their description matched the practice task instructions.

At the end of the fMRI session, the participants completed an exit questionnaire that contained 100 mm VAS questions, inquiring about experienced difficulties during scanning. One of these questions was: "What do you think of the time you spent inside the scanner?" (0: not long at all–100: much too long). Participants scored 48.79 ± 13.86 ($M \pm SD$). Another question asked whether participants were able to maintain their concentration throughout the experiment (0: not at all–100: very well). The participants scored 56.21 ± 18.13 ($M \pm SD$). Together these self-report results indicate that the impact of the scanning duration on the participants' mental state was limited and did not raise major concerns.

Table 1
Results of whole brain RFX ANOVA, *F*-test: main effect of cognitive control strategy.

Functional region of interest	L/R	Talairach coordinates (x,y,z)	BA	*F*-score	*p*-value
Anterior temporal cortex	L	−43, 5, −30	21	8.48	<.001
Cerebellum	L	−31, −81, −27	–	9.32	<.001
Medial orbitofrontal cortex	L	−12, 19, −7	11	3.33	0.03
Inferior temporal gyrus	R	58, −47, −11	20	6.28	0.001
Ventral tegmental area	L	−5, −14, −7	–	6.22	0.002
Fusiform gyrus	L	−29, −56, −15	37	9.51	<.001
Anterior prefrontal cortex	R	23, 65, 11	10	10.06	<.001
	L	−22, 61, 17	10	8.49	<.001
Ventromedial prefrontal cortex	L	−9, 24, −1	24	4.74	0.007
Lateral orbitofrontal cortex	L	−46, 49, 4	11	10.71	<.001
Ventral striatum	L	−11, −2, −3	–	6.22	0.002
Parastriatal cortex	R	22, −94, 12	18	9.50	<.001
	L	−14, −95, 14	18	7.02	<.001
Operculum	L	−58, −19, 26	41	10.94	<.001
Posterior short insular gyrus	R	73, −8, 11	13	10.71	<.001
	L	−38, −6, 11	13	12.33	<.001
Posterior cingulate cortex	L	−9, −53, 8	30	8.65	<.001
Dorsolateral prefrontal cortex	R	41, 53, 33	9	10.71	<.001
Somatosensory cortex	R	−55, −11, 31	3	11.14	<.001
	L	−56, −4, 34	3	10.94	<.001
Inferior parietal cortex	R	41, −47, 43	40	4.66	0.007
Frontal eye field	R	28, −10, 55	6	3.64	0.02
Extrastriate cortex	R	17, −82, 40	19	5.08	0.004

Note: L = left, R = right, BA = Brodmann area; fROIs in *italic*.

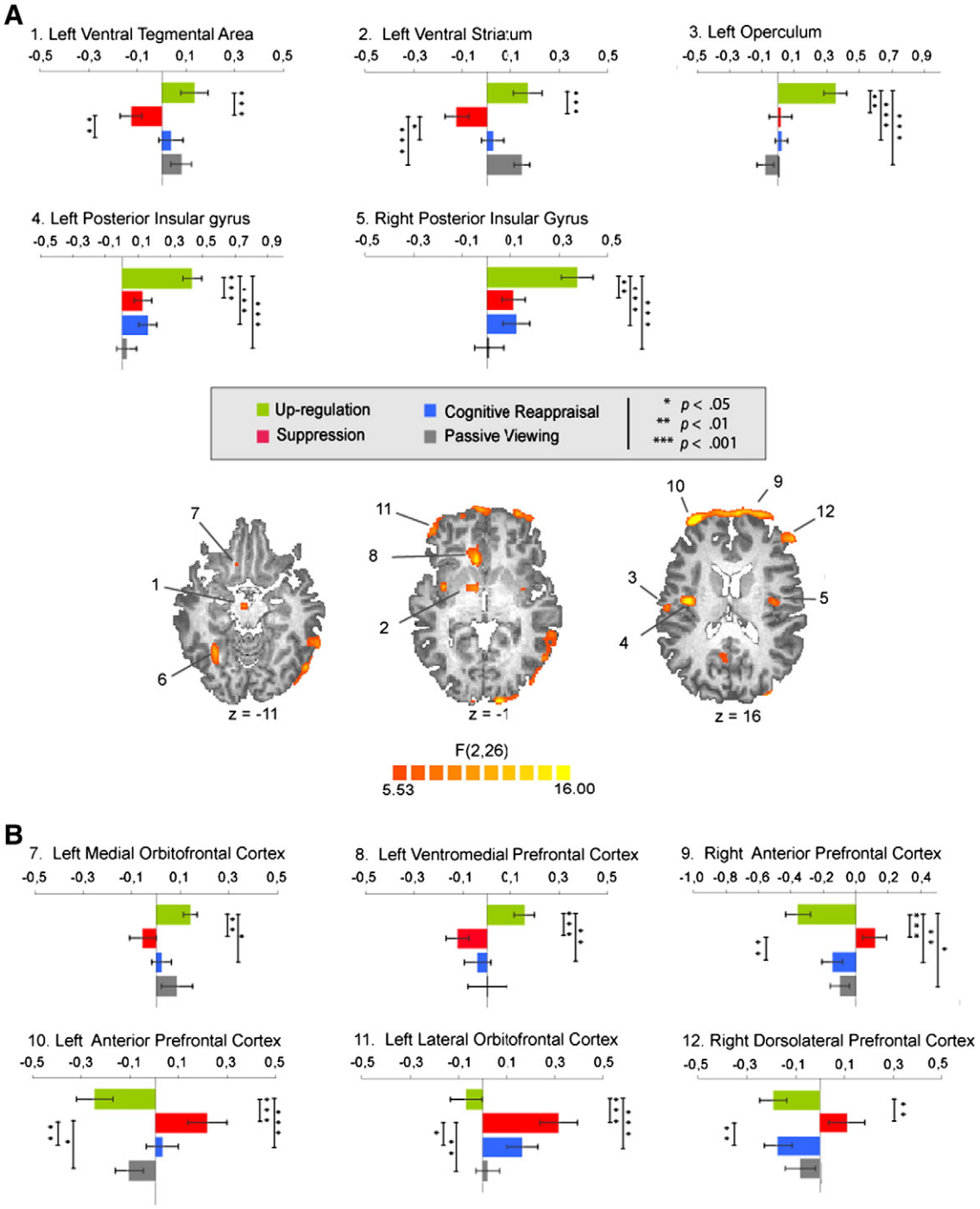

Fig. 2. Results of RFX ANOVA, *F*-test: cognitive control strategy, $p<0.01$. fROI bar-plots represent BOLD signal change in z-scores, ±SEM. A: Results for fROIs located outside the PFC. B: Results for fROIs located in the PFC.

Self-reported food craving

The food craving VAS ratings during the two fMRI runs were averaged over participants, for each cognitive control strategy separately. There was a significant main effect of cognitive control strategy on experienced food craving [$F(2, 26) = 43.37$, $p<.001$; cognitive reappraisal: $M = 50.06$, $SD = 17.98$; suppression: $M = 52.09$, $SD = 18.76$; up-regulation: $M = 70.34$, $SD = 18.27$]. Pairwise comparisons showed that subjective food craving after the up-regulation trials was significantly increased as compared to that following the cognitive reappraisal ($p<.001$) and suppression ($p<.001$) trials, which is in line with the hypothesis of increased food craving after up-regulation compared to up-regulation and suppression. In contrast to what was expected, however, subjective ratings of craving did not differ between the cognitive reappraisal trials and suppression trials ($p = .83$).

fMRI results

The whole brain analysis of the effect of cognitive control strategy (up-regulation, suppression vs. cognitive reappraisal) on BOLD activity revealed a network of fROIs showing significant effects (Table 1). The resulting F-map included six fROIs located within the mesocorticolimbic system, including the left ventral tegmental area (VTA;

Duzel et al., 2009), the left ventral striatum (VS; Kreitzer, 2009), the left operculum (Schweinhardt et al., 2009) and bilateral posterior insular gyrus (PIG; Craig, 2009). See Fig. 2A. In addition, six fROIs were located in the PFC: the left medial orbitofrontal cortex (OFC), the left ventromedial prefrontal cortex (vmPFC), bilateral anterior prefrontal cortex (aPFC), the left lateral orbitofrontal cortex (lOFC) and the right dorsolateral prefrontal cortex (dlPFC). See Fig. 2B.

In line with the hypothesis of increased mesocorticolimbic activity during up-regulation compared to both suppression and cognitive reappraisal, results showed that up-regulation increased activity as compared to suppression in all six mesocorticolimbic fROIs located outside the PFC [VTA: $t(13)=5.88$, $p<.001$; VS: $t(13)=5.47$, $p<.001$; operculum: $t(13)=3.39$, $p<.01$; left PIG: $t(13)=5.30$, $p<.001$; the right PIG: $t(13)=4.03$, $p<.01$] and two regions located in the PFC [mOFC: $t(13)=3.65$, $p<.01$; vmPFC: $t(13)=6.54$, $p<.001$]. Up-regulation showed increased activity as compared to cognitive reappraisal in the left operculum [$t(13)=5.55$, $p<.001$], the left posterior short insular gyrus [$t(13)=5.13$, $p<.001$], the right posterior short insular gyrus [$t(13)=4.48$, $p<.001$]. However, up-regulation did not significantly differ from cognitive reappraisal in the VTA [$t(13)=0.66$, $p=.52$] and the left VS [$t(13)=0.59$, $p=.67$]. Up-regulation did significantly increase activity as compared to cognitive reappraisal in the mOFC [$t(13)=2.50$, $p<.05$] and vmPFC [$t(13)=3.89$, $p<.01$]. In addition, results showed that the up-regulation strategy resulted in greater activity compared to passive viewing in all fROIs, except for the left VTA [$t(13)=0.43$, $p=.76$] and left VS [$t(13)=0.54$, $p=.69$]. For the fROIs located in the PFC (Fig. 2B) results showed that up-regulation significantly decreased activity in the right anterior PFC [aPFC; $t(13)=2.63$, $p<.05$] compared to passive viewing.

Surprisingly, in contrast to the second hypothesis of more successful inhibition of mesocorticolimbic activity during cognitive-reappraisal compared to suppression, results showed that suppression significantly inhibited activity in the left VTA [$t(13)=3.45$, $p<.01$] and the left ventral striatum [$t(13)=2.77$, $p<.05$] relative to cognitive reappraisal. Suppression also resulted in significantly lower activity compared to passive viewing in the left VTA [$t(13)=2.93$, $p<.05$] and left VS [$t(13)=4.54$, $p<.001$]. None of the fROIs showed a change in activity during cognitive reappraisal compared to passive viewing. These findings suggest that short-term suppression is more successful at inhibiting mesocorticolimbic activity as compared to cognitive reappraisal.

In line with the third hypothesis of increased PFC activity during suppression compared to cognitive reappraisal, results showed that suppression significantly increased activity in the right anterior PFC [aPFC; Fig. 2B; $t(13)=3.43$, $p<.01$], the left aPFC [$t(13)=3.07$, $p<.01$], the left lateral OFC [lOFC; $t(13)=2.79$, $p<.05$], and the right dorsolateral PFC [dlPFC; $t(13)=4.49$, $p<.01$] relative to cognitive reappraisal. Suppression also significantly increased activity in the left aPFC [$t(13)=2.78$, $p<.05$] and left lOFC [$t(13)=3.43$, $p<.01$] compared to passive viewing.

Discussion

In this study self-report measures and fMRI were used to examine the regulatory short-term effects of up-regulation, cognitive reappraisal, and suppression on mesocorticolimbic activity related to appetitive motivation. Self-report results indicated that up-regulation increased food craving, which was supported by fMRI results showing that this increase was accompanied by an increase in activity in mesocorticolimbic regions, including the VTA, VS, operculum, PIG, mOFC and vmPFC. Self-report results did not show differences between the cognitive reappraisal and suppression strategy on food craving, but the fMRI results did. Surprisingly, suppression decreased activity in the VTA and VS more successfully than cognitive reappraisal. Both the VTA and the VS play a key role in mediating incentive salience to environmental stimuli that is predictive of behaviorally relevant events (Everitt and Robbins, 2005). This is illustrated by studies showing that lesions or pharmacological manipulation of these two regions prevent the acquisition and expression of Pavlovian approach behavior (Cardinal et al., 2002; Day and Carelli, 2007). The decrease in VTA and VS activity by suppression can therefore be interpreted as the inhibition of the behavioral expression of reward processing. However, results also indicate that suppression increases activity in the bilateral aPFC and dlPFC as compared to cognitive reappraisal, which is in line with the notion that suppression requires increased self-regulatory effort (Gross and John, 2003). An additional observation is that both suppression and cognitive reappraisal resulted in increased activity in the lOFC, while up-regulation resulted in increased activity in the left vmPFC and the left mOFC. This finding is in line with previous neuroimaging research suggesting that the lOFC, together with the mOFC/vmPFC, forms separate neural pathways for the up- versus down-regulation of reward (O'Doherty et al., 2001).

The present findings are in line with previous studies indicating that cognitive control strategies can modulate food cravings by changing activity within the mesocorticolimbic circuitry. For example, Kober et al. (2010) showed that the instruction to think about the long-term consequences associated with eating high-fat foods increased activity in prefrontal regions and successfully decreased activity within the striatum. Wang et al. (2009) showed that the instruction to inhibit hunger feelings decreased activity in the VS, insula and OFC, in men but not in women. The present study shows that women *can* successfully modulate mesocorticolimbic activity related to appetitive motivation by the application of up-regulation, suppression and cognitive reappraisal, and that the specific effects of these strategies on brain activity depend on the type of cognitive control strategy applied: although suppression seems more effective at inhibiting mesocorticolimbic activity compared to cognitive reappraisal as indicated by decreased VS and VTA activity, results also indicate that suppression requires more self-regulatory effort as indicated by the increase in aPFC and dlPFC activity.

The results of this study identify neural mechanisms by which cognitive strategies reduce food craving, and in turn, a potential mechanism by which cognitive therapies can successfully decrease food craving. There is now considerable support that obese people show abnormalities in the mesocorticolimbic circuitry, which – as some researchers believe – may cause them to overeat (Rothemund et al., 2007; Stice et al., 2008; Stoeckel et al., 2008; Volkow and Wise, 2005; Wang et al., 2001). One could argue that the treatment of obesity should target and restore these brain abnormalities. Results of drug treatments targeting mesocorticolimbic neurotransmission (Astrup et al., 2007; Hu et al., 2009) show that they are indeed effective at reducing weight. However, due to their non-specificity, they seem to affect reward processing in general, which increases the risk of adverse psychiatric events (e.g., depression, anxiety, and suicidal ideation). Therefore, it is necessary to find alternative methods to target abnormalities in the mesocorticolimbic circuitry of obese people. One such method may be some form of cognitive behavioral therapy with a focus on training cognitive control strategies such as cognitive reappraisal of palatable foods and suppression of strong food cravings.

A limitation of this study is that the current design cannot test whether suppression or reappraisal significantly lowered subjectively experienced craving compared to passive viewing, because participants were not required to provide subjective craving ratings during passive viewing. As a result we cannot be sure what happened during the passive viewing condition. Although there was no BOLD response in most fROIs, important reward region like the VS, VTA and mOFC did show significant activity during the passive viewing condition. This suggests that some type of reward processing was present during the passive viewing condition. However, without self-reported food craving ratings one cannot be sure whether the observed

changes in activity were also related to changes in the subjective experience of craving. At the time of designing the experiment it was concluded that asking participants to rate their experienced food craving during the passive viewing condition might bias the participants to focus on the palatability of the presented food stimuli. For that same reason, the passive viewing condition was presented in a separate run; intermixing the passive viewing condition with the other conditions would have the disadvantage of carry-over effects from the cognitive modulation conditions to the passive viewing condition. However, future food craving modulation studies could try to mix the passive viewing task with the cognitive control strategies and have participants rate their food cravings during the passive viewing task to get a baseline measure of subjectively experienced craving.

Another important point to keep in mind, while interpreting the present results, is that the participants in this study were required to apply the cognitive control strategies for only a short time period. There is a great deal of evidence suggesting that control strategies may, in the long run, be counterproductive and even provoke paradoxical overeating (Wardle, 1988). Hofmann et al. (2007) showed that instructing high dietary restrained participants to suppress their emotions while watching an emotional movie clip, significantly increased candy consumption afterwards compared to non-dietary restraint controls and high dietary restrained participants who were allowed to let their emotions flow. In addition, it can be speculated that people with high levels of baseline food craving use more energy when applying cognitive control strategies and are therefore more easily depleted, running the risk of overeating when having to apply these strategies for a longer period of time (e.g. while on a diet), compared to people with low levels of food craving. Future neuroimaging research should therefore focus on the more long-term consequences of cognitive control strategies on mesocorticolimbic activation and identify circumstances in which these processes are compromised.

In conclusion, the present study indicates that healthy women can modulate activity within the mesocorticolimbic circuitry using short-term cognitive control strategies. This finding is in agreement with previous studies indicating that eating behavior can be successfully inhibited by actively restructuring the way one thinks about foods (Beck, 2007; Stahre and Hallstrom, 2005; Werrij et al., 2009a). The present results provide additional insight into neurobiological mechanisms underlying appetitive motivation, which might aid in development of effective abnormal eating behavior treatment. For example, considering the observed hypoactivity in the PFC of obese individuals (Volkow et al., 2008), one might suppose that they are less effective in suppressing food reward processing. Therefore, cognitive reappraisal might be a more effective strategy. The present findings also indicate that short-term suppression is more effective at directly inhibiting activity in the VTA and VS, the core of the mesocorticolimbic circuitry. It can also be hypothesized that training self-regulatory abilities, for example by training working memory (Hofmann et al., 2008) might increase the ability to effectively inhibit appetitive motivation and restriction of food intake. However, previous research indicates that cognitive control might be highly vulnerable to disruptions (Baumeister, 2002) and may even drain the very resources necessary for their sustainment (Gailliot and Baumeister, 2007). Future research should therefore focus on the long-term consequences of cognitive control strategies on mesocorticolimbic activation and identify circumstances in which these processes are compromised. Present study should be considered as a baseline upon which future studies of cognitive control strategies and their role in modulating corticomesolimbic activation may be compared.

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