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Research report

Neural predictors of chocolate intake following chocolate exposure ☆

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ABSTRACT

Previous studies have shown that one's brain response to high-calorie food cues can predict long-term weight gain or weight loss. The neural correlates that predict food intake in the short term have, however, hardly been investigated. This study examined which brain regions' activation predicts chocolate intake after participants had been either exposed to real chocolate or to control stimuli during approximately one hour, with interruptions for fMRI measurements. Further we investigated whether the variance in chocolate intake could be better explained by activated brain regions than by self-reported craving. In total, five brain regions correlated with subsequent chocolate intake. The activation of two reward regions (the right caudate and the left frontopolar cortex) correlated positively with intake in the exposure group. The activation of two regions associated with cognitive control (the left dorsolateral and left mid-dorsolateral PFC) correlated negatively with intake in the control group. When the regression analysis was conducted with the exposure and the control group together, an additional region's activation (the right anterior PFC) correlated positively with chocolate intake. In all analyses, the intake variance explained by neural correlates was above and beyond the variance explained by self-reported craving. These results are in line with neuroimaging research showing that brain responses are a better predictor of subsequent intake than self-reported craving. Therefore, our findings might provide for a missing link by associating brain activation, previously shown to predict weight change, with short-term intake.
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Introduction

Self-reports of attitudes and intentions rely on introspection, and it is well known that people do not have introspective access to all causes that underlie their behaviour (Nisbett & Wilson, 1977) and that these self-reports can be distorted by socially desirable answering tendencies (Schwarz & Oyserman, 2001). Recently, neuroimaging research showed that brain responses have added value in the prediction of behaviour. For example, in participants who were exposed to persuasive messages regarding the value of regular sunscreen use or the benefits of quitting smoking, brain activation was a better predictor of subsequent behaviour than were self-reports of intentions (Falk, Berkman, Mann, Harrison, & Lieberman, 2010; Falk, Berkman, Whalen, & Lieberman, 2011). Likewise, in addicted participants, the brain response to pictures or videos of cues of the particular drug was a better predictor for relapse than were subjective craving reports (Grüsser et al., 2004; Kosten et al., 2006). Studies investigating the neural responsivity to high-calorie food cues also found that this activation in brain reward regions was correlated with weight gain after one year (Stice, Yokum, Bohon, Marti, & Smolen, 2010; Yokum, Ng, & Stice, 2011) or with less success in losing weight in a subsequent weight-loss program (Murdaugh, Cox, Cook, & Weller, 2012). Further, long-term weight gain was negatively correlated with activation of regions involved in the inhibition of food reward (Kishinevsky et al., 2012; Stoeckel, Murdaugh, Cox, Cook, & Weller, 2013).

Although many studies in the last few years have investigated the differences between healthy-weight and overweight people with regard to neural correlates of food reward (e.g., Batterink, Yokum, & Stice, 2010; Frankort et al., 2012; Rothemund et al., 2007; Stoeckel et al., 2008), the neural correlates in response to visual food cues or taste cues that predict subsequent food intake or food choice in the short term have so far been studied only recently (Hare, Malmaud, & Rangel, 2011; Lawrence, Hinton, Parkinson, & Lawrence, 2012; Mehta et al., 2012; Spetter, de Graaf, Viergever, & Smeets, 2012;

Abbreviations: CERP, cue exposure with response prevention; PFC, prefrontal cortex; BMI, body mass index; VAS, visual analogue scale; OFC, orbitofrontal cortex; ROI, region of interest.

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Van der Laan, De Ridder, Viergever, & Smeets, 2012). The study by Lawrence et al. (2012) for example found that snack consumption after the scanning session was predicted by activation of the nucleus accumbens in response to food cues. Prediction of the amount of food intake is interesting because weight gain is ultimately the result of a sustained positive energy balance, that is, total energy intake minus total energy expenditure (Swinburn et al., 2009). The goal of the current study was to examine whether neural correlates of food reward and inhibition could predict food intake during an alleged taste-test. The predictive validity of these neural correlates was studied under two conditions: during a session of exposure to the smell of chocolate without eating and during a control exposure (no food). Neural responses to chocolate pictures versus neutral pictures were measured using functional magnetic resonance imaging (fMRI).

Prolonged exposure is a well-known treatment strategy in the clinical practice of mental health care. During food cue exposure with response prevention (CERP), one is exposed to food cues, like the smell or taste of foods, or contexts, like eating places, that predict food intake, while at the same time eating is not allowed (response prevention). In bulimia nervosa and binge eating patients, as well as in obese children, CERP has been shown to be effective in reducing the urge to binge or the frequency of bingeing (Boutelle et al., 2011; Jansen, Broekmate, & Heymans, 1992; Kennedy, Katz, Neitzert, Ralevski, & Mendlowitz, 1995; Martinez-Mallén et al., 2007; Toro et al., 2003). The exposure aims to disrupt the conditioned link between the food cue (sight, smell or context of food intake) and one's learned response to this cue (eating). Actually, during repeated prolonged effective exposure it is learned that the food cue or context does not predict intake anymore (see e.g., Jansen, Havermans, & Nederkoorn, 2011). During the exposure which ranged from 45 min to 90 min in the different studies, levels of self-reported craving first increased during prolonged exposure, peaked and then slowly decreased to the end. After several sessions (ranging from 1 to 36 sessions), the self-reported craving and/or physiological indices of craving did not go up anymore and almost fully extinguished (see, e.g., Jansen, Van den Hout, De Loof, Zandbergen, & Griez, 1989; Jansen et al., 1992; Martinez-Mallén et al., 2007; Toro et al., 2003; Van Gucht et al., 2008). In our lab, we measured the effect of prolonged exposure to the smell of chocolate, without eating, on self-reported cravings and brain responses to neutral and chocolate pictures (Frankort et al., 2013). It was found that self-reported chocolate craving in a group that was exposed to chocolate increased over a one-hour session, reaching a peak just before the end of the session, followed by a tendency towards a decrease (for a graph of craving over time, please see Frankort et al., 2013). Contrary to expectations, chocolate cravings did not extinguish within the hour. However, activation in brain reward regions in response to chocolate versus neutral pictures rose from the start to the middle of the session. At the end of the session the brain reward activation returned to control levels again, indicating that craving on a neural level did extinguish. Therefore, brain reward activation was considered to be a precursor of self-reported craving (Frankort et al., 2013).

The current study follows up on these results and focuses specifically on chocolate intake during a bogus taste-test that was performed after the fMRI scanning session. We expected that chocolate exposure would lead to reduced intake as compared to the neutral control exposure, because a prolonged exposure usually leads to a decrease in craving. Further it was expected that brain activation in response to chocolate versus neutral pictures in regions associated with food reward would show predictive validity with regard to subsequent intake above and beyond the variance explained by self-reported craving. Brain regions commonly accepted to be involved in food reward are the amygdala, striatum, hippocampus, insula, ventral tegmental area and substantia nigra, as well as the anterior cingulate, posterior fusiform, orbitofrontal and prefrontal cortices (for reviews see: Berridge, Ho, Richard, & DiFeliceantonio, 2010; Berthoud, Lenard, & Shin, 2011; Carnell, Gibson, Benson, Ochner, & Geliebter, 2012; Kringelbach, 2009; Rolls, 2011; Small, 2009; Smeets, Charbonnier, Van Meer, Van der Laan, & Spetter, 2012; Van der Laan, De Ridder, Viergever, & Smeets, 2011). Regions that appear to be involved in the inhibition of food reward, in the sense that less activation in a delay discounting task or a lower grey matter volume of these regions predicted more long-term weight gain in women, are subdivisions of the prefrontal cortex (PFC) like ventrolateral, dorsolateral and medial PFC, as well as posterior parietal cortex (Kishinevsky et al., 2012; Stoeckel et al., 2013; Yokum, Ng, & Stice, 2012). More specifically, because previous papers found that brain activation was a better predictor of behaviour than were self-reports (Falk et al., 2010, 2011; Grüsser et al., 2004; Kosten et al., 2006), we expect activation in these regions to explain variance in chocolate intake (as measured directly after the scanning session), on top of what is predicted by self-reported craving.

Method

Part of these data have been published in a previous paper (Frankort et al., 2013), which focused on the course of brain activation during the cue exposure session. In contrast, the current paper investigates the prediction of short-term chocolate intake after the session by brain activation.

Participants

34 female undergraduate students of Caucasian ethnicity from Maastricht University participated with full informed consent: 17 in an exposure group and 17 in a control group. They were right-handed, not currently on a weight-loss diet and had a low score (total score < 14) on the Restraint Scale (Herman & Polivy, 1980). Exclusion criteria were a self-reported mental disorder history or family history of eating disorders. Both groups had similar age and scores of hunger, restraint and trait chocolate craving, but body mass index (BMI) tended to differ between the groups (see Table 1 for participant characteristics). Seven additional participants were excluded from analyses due to scanner problems or excessive head movement. Participation was remunerated with € 30 or course credits. The local ethical committee approved the study.

Assessment

Self-reported chocolate craving

Self-reported chocolate craving was measured repeatedly with a visual analogue scale (VAS) item asking "how much do you crave chocolate at this moment", ranging from 0 (*not at all*) to 100 (*very much*).

Trait chocolate craving

To assess the trait craving for chocolate and the degree of compulsive behaviour elicited by chocolate, the craving subscale of the Attitudes to Chocolate Questionnaire (Benton, Greenfield, & Morgan, 1998) was used. All items addressed preoccupation with chocolate, with the scale for each item ranging from 0 (*this does not apply to me at all*) to 100 (*this very much applies to me*). The subscale is considered valid and reliable (Cramer & Hartleib, 2001; Müller, Dettmer, & Macht, 2008). The total score was computed by averaging the ten VAS items (0 to 100).

Hunger

A VAS item asking "How hungry do you feel at this moment?", ranging from 0 (*not hungry at all*) to 100 (*very hungry*), was used to assess hunger.

Table 1
Characteristics and self-report data of participants.

	Exposure group ($n = 17$)		Control group ($n = 17$)			
	M	SD	M	SD	$t(32)$	p
Age (yrs)	19.8	1.4	20.2	1.5	.89	.38
BMI	22.8	1.7	21.6	1.8	1.94	.06
Time between lunch and scan (min)	86.5	14.4	82.6	20.9	.62	.54
Hunger[a]	18.6	14.5	14.9	14.1	.74	.46
Restraint[b]	10.6	2.6	10.8	4.7	.18	.86
Trait chocolate craving[c]	38.3	19.1	35.0	13.2	.58	.56
Overall chocolate intake (g)	19.6	15.8	24.7	16.4	.92	.36
Overall chocolate intake (kcal)	108.8	88.3	136.7	91.3	.91	.37

Note: Reprinted with permission from Frankort et al. (2013) *Cerebral Cortex.*
Abbreviations. BMI = Body Mass Index.
[a] Scored on 100 mm VAS, ranging from 0 (*not hungry at all*) to 100 (*very hungry*).
[b] Scored on the Restraint Scale (Herman & Polivy, 1980), with a minimum total score of 0 (*no restraint*) and a maximum of 35 (*high restraint*).
[c] Scored on the craving subscale of the Attitudes to Chocolate Questionnaire (Benton et al., 1998), with a minimum total score of 0 (*no trait chocolate craving*) and a maximum of 100 (*high trait chocolate craving*).

Restraint

The participant's intention to restrain her food intake, her concern about body weight and weight fluctuations were measured with the Restraint Scale (Herman & Polivy, 1980), with a minimum total score of 0 and a maximum of 35. A higher score reflects a higher level of restraint. The scale is sufficiently valid and reliable (Scagliusi et al., 2005; Van Strien, Herman, Engels, Larsen, & Van Leeuwe, 2007; Williamson et al., 2007).

Bogus chocolate taste test

The bogus taste test was adapted from Herman and Mack (1975) and is an accepted measure of food intake that is frequently used in eating research. In a bogus chocolate taste test, participants were asked to taste four kinds of chocolate buds (white, milk, dark, extra dark; Barry Callebaut Belgium N.V., Wieze, Belgium). Chocolate types differed in calorific value (in kcal per 100 g: white, 569; milk, 560; dark, 535; extra dark, 514). The separate bowls in which they were presented were weighed prior to the test and contained approximately 250 g of chocolate each. Participants were instructed that they could taste as many chocolate buds as needed to complete the taste ratings, and that they were free to consume chocolate buds after they had finished. The chocolate's smell, taste, intensity, appearance, taste persistence and sweetness were rated with six VAS items (0 to 100). The overall intake of chocolate was measured by adding up the consumed weights of the four different chocolate types.

Experimental design

The experimental design was a mixed design with an exposure group (exposure to the smell of chocolate) versus a control group (exposure to the smell of a control stimulus), with repeated measures of both self-reported chocolate craving and the brain response to chocolate pictures versus neutral control pictures (i.e., visual chocolate stimuli). Chocolate intake was measured after the session. For the current study, only brain responses in the last run (run 7) were analysed because they were closest in time to subsequent intake.

Stimuli

56 pictures of (products containing) chocolate and 56 neutral pictures of office supplies and utensils not related to food were used as stimuli. Only chocolate pictures without festive associations (such as Valentine, Easter and birthday) were used. Pictures were predominantly purchased online (www.istockphoto.com). Stimuli covered a visual angle of approximately 12° and were presented in the centre of the screen as pop-out figures on a light grey background. Each picture was presented four times in the course of the scanning session.

Stimulation protocol (visual chocolate and neutral stimuli)

A blocked design with a block duration of 14.8 s[1] was used to present the stimuli (E-Prime version 2.0.8.90 (PST, 1996)). All blocks consisted of eight pictures with a duration of 1850 ms each, which were chosen randomly without replacement. Half of the stimulus blocks were followed by a question block of 3 s duration with a yes/no question about the depicted picture having been presented in the preceding stimulus block. This was done to maintain the attention of the participant, who responded with a button press. A black fixation cross on a light grey background preceded all blocks, with a duration of either 12 s (before stimulus blocks) or 6 s (before question blocks). After the last block an additional fixation cross was shown for 12 s.

One run consisted of four chocolate blocks, four neutral blocks, and four question blocks. The order of stimulus blocks was randomised for each of the seven runs, with the constraint that a maximum of two stimulus blocks of the same category would occur subsequently. Question blocks were then inserted randomly, with the constraint that twice they followed a chocolate block and twice a neutral block. This resulted in seven fixed run orders that lasted on average for 270 s[2]. For each participant, the sequence of these seven runs was randomised.

Session protocol

The session of 65 min duration started with the first functional run, after which the first exposure to smell (chocolate versus pencil) took place (for a session diagram, please see Frankort et al., 2013). Functional runs and exposures to smell were alternated during the scanning session. For exposure, the participant remained in the scanner and was handed a piece of chocolate (in the exposure group)

[1] Some blocks in the first two runs were presented up to 15.1 s, probably due to the time it took E-Prime to retrieve the pictures from the local hard disk for the first time and write them to the cache. To synchronise with image acquisition, blocks always started with the reception of a trigger pulse by the scanner indicating the MRI scanner's radiofrequency pulse.
[2] The average run duration was longer than the anticipated 264 s because some of the trigger pulses of the scanner were missed, leading to a prolongation of fixation times between blocks, as waiting times for trigger pulses between blocks were filled with fixation.

or a pencil (in the control group), with the instruction to hold it under her nose and smell it. The piece of chocolate (approximately 4 cm × 2 cm × 1 cm) was partly wrapped in an odourless tissue to prevent it from melting. Participants in the chocolate exposure group were instructed to try to crave the chocolate as much as possible, by imagining eating it and feeling it melting in their mouth. The objects were taken back at the end of each exposure. Therefore, there was no exposure to real chocolate or to the pencil during functional runs. Habituation to the smell of the cue was counteracted by instructing the participant to ask for a different one of in total eight brands of milk and dark chocolate (in the exposure group) or a different one of eight pencils (in the control group). In practice, this led to a replacement of the cue at least every few minutes. Every functional run started and ended with a VAS item about the participant's chocolate craving, which could be scored using a joystick on her abdomen. Chocolate craving was additionally assessed every five minutes in the final prolonged exposure cycle, which lasted 20 min. The other exposures were rather short and amounted to 1, 1, 2, 3 and 3 min respectively. The anatomical measurement was done after the last functional run.

Procedure

The scanning sessions took place in the afternoon and consisted of seven functional runs and one anatomical measurement. On the scanning day, participants were asked to refrain from eating chocolate products and from drinking coffee or tea (Koppelstaetter et al., 2010). They had to consume a regular lunch 1 to 1.5 hours before the start of the scanning session. Upon arrival, the participant's hunger, restraint, trait craving for chocolate, weight and height were measured. After the participant gave informed consent the scanning session started. After the scanning session, the participant did the bogus chocolate taste test and filled in an exit form in an adjacent room. Then she was thanked and compensated for participation. Debriefing was done by e-mail at the end of the study.

fMRI data acquisition

A 3T Siemens Magnetom Allegra head-only scanner was used for image acquisition.

Functional T2*-weighted images (50 slices, TR = 3000 ms) were acquired using gradient-echo planar imaging parameters, optimised for reducing susceptibility and distortion artefacts in the OFC (Deichmann, Gottfried, Hutton, & Turner, 2003; Weiskopf, Hutton, Josephs, Turner, & Deichmann, 2007): TE = 25 ms, oblique axial slices acquired in interleaved order with a negative (i.e. backward) tilt angle of 30°, voxel size = 2 mm × 2 mm × 2.5 mm, field of view (FoV) = 256 mm × 192 mm, imaging bandwidth = 2790 Hz/pixel, echo spacing = 0.42 ms, flip angle = 90°. Each run contained 88 volumes. An optimised anatomical T1-weighted magnetisation-prepared rapid gradient-echo sequence (Deichmann, Good, Josephs, Ashburner, & Turner, 2000; Mugler & Brookeman, 1990) was used after the last run, with the following settings: TR = 2250 ms, TE = 2.6 ms, flip angle = 9°, voxel size = 1 mm × 1 mm × 1 mm, echo spacing = 6.9 ms.

Data pre-processing

Pre-processing and first-level analyses were conducted with BrainVoyager QX version 2.4.1.2052 (BrainInnovation, 2001). The first two volumes of each functional run were excluded due to T1 saturation effects. Pre-processing involved slice scan time correction with cubic spline interpolation, low-frequency noise removal with high-pass temporal filtering (0.0075 Hz cut-off), and three-dimensional motion correction, using trilinear interpolation for alignment and sinc interpolation for final resampling. Pre-processed data were then aligned to the anatomical scan, resulting in co-registered three-dimensional space data with a voxel resolution of 2 mm × 2 mm × 2 mm over the course of time for each run. These data were subsequently spatially normalised using Talairach transformation procedures (Talairach & Tournoux, 1988) and spatially smoothed with a 6 mm full-width-at-half-maximum isotropic Gaussian Kernel. For group-level analyses, anatomical Talairach-standardised participant data sets were averaged. On this basis a whole-brain mask was generated.

Data analysis

Regarding chocolate characteristics and overall chocolate intake, group differences were analysed with *t*-tests. In addition, Pearson correlations were calculated between chocolate intake and self-reported chocolate craving, restraint scale scores, trait chocolate craving scores, hunger and time passed between lunch and the start of the scanning session. For brain responses boxcar predictors were set for chocolate, neutral, and question blocks of the last run (run 7). Question block predictors were considered as confounds. A standard haemodynamic response function (Friston et al., 1998) was used to convolve all predictors. The design matrix of the general linear model was generated after adding *z*-transformed motion correction parameters. This modelling approach considers the response to fixation times between blocks as a baseline.

In three separate whole-brain regression analyses, brain responses in the last run (run 7) to chocolate pictures minus neutral pictures were correlated with the total chocolate intake for the whole sample (first analysis) as well as separately for the exposure group (second analysis) and the control group (third analysis). Only voxels with a p value below 0.05 were considered significant, corrected for multiple comparisons at the cluster level by using a Monte Carlo simulation based approach, with 1000 iterations and a voxel size of 2 mm × 2 mm × 2 mm (Forman et al., 1995; Goebel, Esposito, & Formisano, 2006). In total 191,443 voxels were contained in the Talairach-standardised whole-brain mask. As a result of these calculations, the minimal cluster size of regions of interest (ROIs) was set to 328 mm^3 or 41 functional voxels (first analysis, whole sample), 336 mm^3 or 42 functional voxels (second analysis, exposure group only), and 352 mm^3 or 44 functional voxels (third analysis, control group only). The Talairach Client (www.talairach.org) (Lancaster et al., 2000) was used to indicate the anatomical localisation of the ROIs. To obtain activation characteristics of these ROIs, average β values were extracted for each ROI, run, picture category and participant and were entered into SPSS version 19 for visualisation purposes.

Regression model

To test the added value of neural activation in run 7 to self-reported chocolate craving for the prediction of chocolate intake, three hierarchical regression models were tested: one for the whole sample, one for the exposure group, and one for the control group. In each model, in step 1, self-reported craving was entered in the model, and in step 2, neural activation that correlated with chocolate intake was added. The self-reported chocolate craving was the average of the craving ratings obtained at the beginning and end of run 7. The neural activation was centred before it was entered into the model. Centering was done across participants, so that each statistical predictor would have a mean of zero. Neural activation was based on the response to chocolate pictures versus neutral pictures that correlated with chocolate intake, in clusters larger than the threshold in each regression analysis (whole sample, exposure group and control group).

Table 2
Correlations of overall chocolate intake with participant characteristics and measurements of state craving.

		Whole sample (n = 34)	Exposure group (*n* = 17)	Control group (*n* = 17)
Hunger[a]		–.17	–.10	–.20
Time between lunch and scan session		.10	–.02	.22
Restraint[b]		.24	.23	.25
Trait chocolate craving[c]		.17	.18	.21
Self-reported chocolate state craving[d]				
Run 1	Before	.05	.01	.05
	After	.11	.24	.04
Run 2	Before	.09	.26	.01
	After	.14	.25	.09
Run 3	Before	.10	.36	.01
	After	.19	.32	.14
Run 4	Before	.16	.53*	–.03
	After	.08	.35	–.05
Run 5	Before	.07	.46	–.10
	After	.07	.36	–.08
Run 6	Before	.07	.52*	–.15
	After	.08	.46	–.08
During prolonged exposure (20 min)	At 5 min	.12	.61**	–.14
	At 10 min	.06	.53*	–.16
	At 15 min	.10	.57*	–.12
Run 7	Before	.06	.50*	–.20
	After	.09	.42	–.10

Note: Significance indications: *$p < .05$; **$p < .01$ (uncorrected).
[a–c] See notes of Table 1.
[d] Scored on 100 mm VAS, ranging from 0 (*not craving chocolate at all*) to 100 (*craving chocolate very much*).

Results

Chocolate intake and self-reported craving

Overall chocolate intake did not differ between groups (see Table 1), although it had been expected that chocolate CERP would lead to reduced intake as compared to the neutral control exposure. Chocolate intake was not correlated with restraint scale scores, trait chocolate craving scores, hunger, or time passed since lunch was eaten, in either the exposure or the control group, or the whole sample (see Table 2). No significant correlations were found between self-reported chocolate craving and subsequent intake in the whole sample or just the control group. However, within the exposure group, chocolate craving showed significant correlations with overall chocolate intake (Table 2).

Chocolate characteristics

Chocolate characteristic ratings, as measured in the bogus taste test, did not differ between groups, except for the smell of milk chocolate (Table 3).

Neural predictors of chocolate intake

The whole-brain regression analysis (for the whole sample) yielded one ROI larger than the minimal cluster size, in which the activation (response to chocolate pictures versus neutral pictures) of all individual voxels was positively correlated with intake. This ROI was located in the right anterior PFC (cluster A in Fig. 1 and Table 4). The second analysis, performed with only the exposure group, resulted in two ROIs (clusters B and C in Fig. 1 and Table 4) with a positive correlation of activation and subsequent chocolate intake. These were located in the right caudate and the left lateral frontopolar cortex. The third regression analysis with only the control group produced two ROIs (clusters D and E in Fig. 1 and Table 4) with a negative correlation between activation and intake, in the left dorsolateral and the left mid-dorsolateral PFC surrounding the inferior frontal sulcus. Independent samples *t* tests showed that within each cluster, groups did not differ on average activation, all *t*s < .67, all *p*s > .51.

Table 3
Chocolate characteristics.

	Exposure group (*n* = 17)		Control group (*n* = 17)			
	M	SD	M	SD	*t*(32)	*p*
Extra dark chocolate						
Visual attractiveness	29.4	22.0	31.5	20.2	.30	.77
Smell	50.1	27.1	59.2	28.3	.95	.34
Taste	52.1	25.7	46.2	32.2	.58	.56
Sweetness	19.8	11.6	25.4	18.3	1.06	.30
Intensity	75.5	11.5	80.5	19.4	.91[a]	.37[a]
Taste persistence	77.8	18.1	75.4	17.5	.40	.70
Dark chocolate						
Visual attractiveness	33.2	21.3	33.8	22.1	.09	.93
Smell	57.3	24.7	59.0	25.2	.20	.84
Taste	56.9	25.5	53.1	27.5	.42	.68
Sweetness	32.5	19.6	38.2	13.9	.98	.34
Intensity	70.4	16.0	72.9	16.1	.46	.65
Taste persistence	69.2	18.0	75.6	12.5	1.21	.24
Milk chocolate						
Visual attractiveness	76.4	13.6	81.2	20.2	.82	.42
Smell	64.2	19.4	78.4	12.7	2.53[b]	.02*[,b]
Taste	80.1	16.2	77.2	24.1	.40	.69
Sweetness	68.0	17.8	73.6	10.1	1.13	.27
Intensity	56.9	21.4	59.9	22.2	.41	.69
Taste persistence	54.5	20.0	65.0	17.8	1.61	.12
White chocolate						
Visual attractiveness	82.2	7.9	83.1	12.1	.25	.80
Smell	60.5	22.7	67.2	24.4	.83	.41
Taste	84.6	12.4	79.7	12.5	1.14	.26
Sweetness	80.5	15.3	80.8	10.8	.07	.95
Intensity	64.1	17.7	53.9	23.0	1.45	.16
Taste persistence	62.4	10.7	56.2	14.4	1.42	.17

Note: Significance indications: *$p < .05$ (uncorrected).
[a] Variances of this rating could not be considered equal between groups, degrees of freedom = 25.99.
[b] Variances of this rating could not be considered equal between groups, degrees of freedom = 27.54.

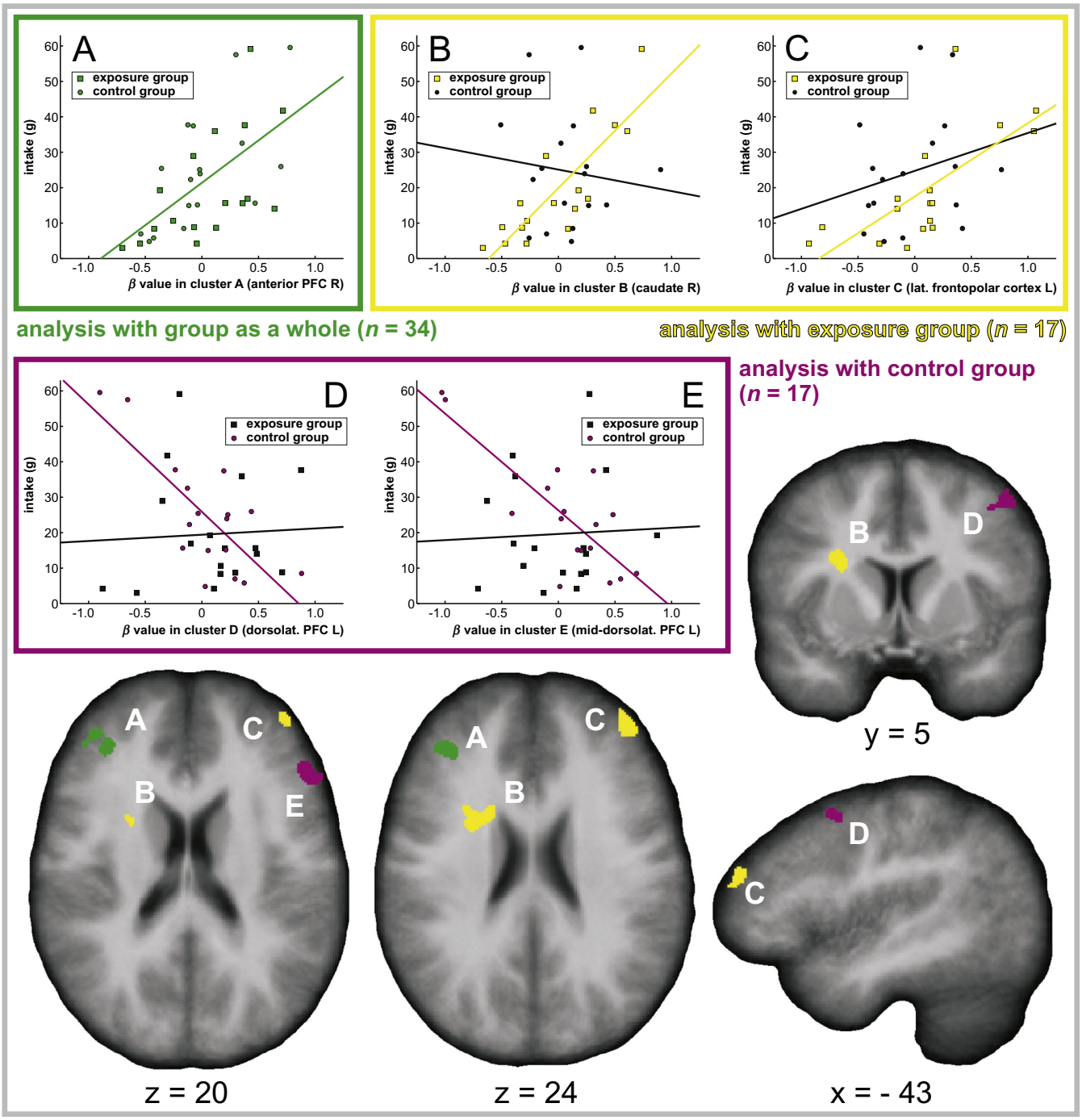

Fig. 1. Upper part: Scatter plots of clusters resulting from three regression analyses of average β values on overall chocolate intake. Average β values were extracted from neural activation of all voxels in the corresponding cluster in response to chocolate pictures versus neutral pictures. Lower part: Locations of clusters that significantly correlated with overall chocolate intake after the scanning session, overlaid on a brain averaged from all participants (radiological convention). One cluster (A, green) resulted from the regression analysis of the whole sample; the regression analysis of the exposure group (B and C, yellow) and the control group (D and E, purple) yielded two clusters each. Only clusters A, B and E were significant predictors of intake in the regression model. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

Regression model with self-reported craving and neural correlates of intake

Step 1 of the regression models showed that the regression of self-reported craving on intake was not significant, neither in the whole sample nor in the separate groups (Table 5). After adding neural activation to the model in step 2, all three regression analyses (one with the whole sample, one with only the exposure group and one with only the control group) were significant. Variance explained by neural activation was above and beyond the variance explained by self-reported craving alone in all three regression analyses. Significant contributions to explained variance were made by the right anterior PFC (cluster

Table 4
ROIs: Clusters larger than the calculated minimal cluster size of the respective analysis (whole sample, exposure group or control group). In these clusters, all voxels significantly correlated with overall chocolate intake in terms of their activation in response to chocolate pictures minus neutral pictures.

ROI	Anatomical label	p[a]	Sign of correlation	Estimated BA[b]	Size (mm^3)	Peak voxel values[c]				
						x	y	z	$r_{intake\text{-}beta}$[d]	$r_{craving\text{-}beta}$[e]
Whole sample (n = 34)										
A	Anterior PFC (MFG) R	.0002	+	10, 9	412	35	38	23	.57**	.24
Exposure group (n = 17)										
B	Caudate body, claustrum R	.00003	+		501	19	11	23	.76**	.39
C	Lateral frontopolar cortex (MFG/SFG) L	.002	+	10, 9, 46	412	–40	53	23	.75**	.38
Control group (n = 17)										
D	Dorsolateral PFC (MFG) L	.0004	–	6	379	–46	7	51	–.88**	.09
E	Mid-dorsolateral PFC surrounding the IFS (MFG/IFG) L	.00009	–	46, 45	433	–55	25	19	–.78**	.02

Note: Significance indications: *p < .05; **p < .01; ***p < .001 (uncorrected).
Abbreviations. BA = Brodmann Area; R = right hemisphere; L = left hemisphere; SMA = supplementary motor area; IFG = inferior frontal gyrus; IFS = inferior frontal sulcus; MFG = middle frontal gyrus; SFG = superior frontal gyrus.
[a] This is the significance indication of averaged beta values of the cluster as a single predictor of intake.
[b] Identified with the "nearest grey matter" option in the Talairach Client (www.talairach.org) (Lancaster et al., 2000).
[c] Voxel coordinates are reported in Talairach space.
[d] This is the correlation between intake and the beta value of the peak voxel in response to chocolate pictures versus neutral pictures in run 7. This correlation coefficient should be interpreted with caution, because these clusters were extracted based on high correlation (double dipping).
[e] This is the correlation between average self-reported chocolate craving immediately before and after run 7 and the beta value of the peak voxel in response to chocolate pictures versus neutral pictures in run 7.

A in the analysis with the whole sample), the right caudate (cluster B in the exposure group analysis) and, with a negative sign, the left mid-dorsolateral PFC (cluster E in the control group analysis).

Discussion

Building on a previous study (Frankort et al., 2013), the current study investigated the self-reported and neural predictors of chocolate intake after having been exposed during approximately one hour to chocolate (exposure group) or to a control stimulus (control group). In three regression models it was tested if there are neural correlates in brain regions associated with reward that predict intake, and if the variance explained by these neural correlates is above and beyond the variance explained by self-reported craving. For the whole sample, self-reported chocolate craving did not correlate at any point in time with subsequent intake, which was unexpected. Interestingly, activation in the right anterior PFC was positively correlated with intake and significantly contributed to the explained variance of intake. There was no group difference in average activation levels in this region. Although the function of this region is not very specific as it is active during multiple and diverse cognitive tasks (Ramnani & Owen, 2004), a systematic review of brain lesions in eating disorders (Uher & Treasure, 2005) found a consistent association of right frontal lobe lesions with weight loss. The same region's taste response to appetising food versus water (at MNI coordinates 45, 45, 9) was found to correlate positively with BMI (Stice et al., 2010). Moreover, the activation of this part of the PFC (at TAL coordinates 24, 47, 11) elicited by alcohol-associated cues compared with affectively neutral and abstract pictures has been associated with the intake of alcohol in abstinent alcoholics who subsequently relapsed compared with control subjects (Grüsser et al., 2004). Therefore, the predictive validity of this region's activation on intake is in line with existing literature.

The control group showed no correlation between self-reported craving during the session and chocolate intake after the session. On a neural level, two brain regions in the left dorsolateral and mid-dorsolateral PFC correlated with intake, with the latter contributing significantly to explained variance of intake. Correlation with chocolate intake was negative in both regions, which is not surprising, given the fact that both have been associated with cognitive control, self-control and inhibition (Coutlee & Huettel, 2012; Figner et al., 2010; Petrides, 2005). More specifically, an increase in regional cerebral blood flow in the vicinity of these regions (at Talairach coordinates –28, 17, 50 and –48, 30, 3) was associated with a decrease in reward value (Small, Zatorre, Dagher, Evans, & Jones-Gotman, 2001) and in a prospective study, activation in both regions (at MNI coordinates 44, 10, 52 and –48, 26, 14) in response to food versus control stimuli was predictive of subsequent weight loss after 12 weeks (Murdaugh et al., 2012). Moreover, a voxel-based morphometry study showed that a reduction of grey matter in almost exactly the same region (at MNI coordinates –48, 9, 51) in the left dorsolateral PFC was predictive of an increase in BMI after one year (Yokum et al., 2012). The negative correlations in our study with the control group intake confirm that these regions are implicated in the inhibition of food reward. Slightly surprising

Table 5
Hierarchical multiple regression analysis predicting chocolate intake from self-reported craving and neural correlates. Variances explained (ΔR^2) by neural correlates are listed for comparative purposes only.

Predictor	ΔR^2	β	Significant contribution of neural correlates?
Whole sample (n = 34)			
Step 1: self-reported craving only	.006		
Average of craving ratings before and after run 7		.08	
Step 2: self-reported plus neural correlates	.36***		Yes
Average of craving ratings before and after run 7		–.06	
Activation in cluster A in run 7		.60***	
Exposure group (n = 17)			
Step 1: self-reported craving only	.22		
Average of craving ratings before and after run 7		.47	
Step 2: self-reported plus neural correlates	.77***		Yes
Average of craving ratings before and after run 7		.22	
Activation in cluster B in run 7		.57*	
Activation in cluster C in run 7		.27	
Control group (n = 17)			
Step 1: self-reported craving only	.02		
Average of craving ratings before and after run 7		–.16	
Step 2: self-reported plus neural correlates	.72***		Yes
Average of craving ratings before and after run 7		–.22	
Activation in cluster D in run 7		–.21	
Activation in cluster E in run 7		–.66*	

Note: Significance indications: *p < .05; **p < .01; ***p < .001 (uncorrected).

was the fact that only *inhibitory* brain regions predicted intake in the control group (instead of brain *reward* regions). It appeared that, at the end of the session, inhibitory activation in response to chocolate versus neutral pictures did predict subsequent intake whereas activation in reward regions did not, although the average activation in the inhibitory ROIs did not differ from the average activation in these regions in the exposure group. Considering that our participants scored low on a measure of dietary restraint, it may be expected that these results would be more pronounced in a sample of participants scoring high on dietary restraint. However, this remains for future research.

In the exposure group, self-reported craving was related to chocolate intake at certain moments during the session. However, the average of the craving ratings immediately before and after run 7 did not significantly contribute to the explained variance in the regression analysis. Regarding the BOLD response, intake did correlate with neural activation in the right caudate and the left lateral frontopolar cortex, with a significant contribution of the caudate activation to explained variance of intake, above and beyond the variance explained by self-reported craving. The more active these regions were, the more the chocolate-exposed participants ate after the session. Although the frontopolar cortex has been found to exercise control over highly abstract plans, goals, and response strategies (Coutlee & Huettel, 2012), regions in the left lateral frontopolar cortex close to that identified here have also been implicated in reward and craving, like monetary reward (at TAL coordinates –33, 51, 27) (Pochon et al., 2002) and craving for cocaine (at MNI coordinates –36, 42, 28) (Gorelick et al., 2005), but it is also active during many complex cognitive tasks (Ramnani & Owen, 2004). Activation of the other cluster in this exposure group analysis, the caudate, has been correlated with the reward value of chocolate (Small et al., 2001), although this was a more anterioventral part of the caudate (at TAL coordinates 15, 20, 9) and with meal pleasantness in general (at TAL coordinates 12, 10, 20) (Small, Jones-Gotman, & Dagher, 2003). In obese participants, the caudate nucleus has been found to be more activated than in healthy-weight controls in response to pictures of food versus neutral pictures, even though other parts of the caudate were active than the one we found (Rothemund et al., 2007; Stoeckel et al., 2008). The increased caudate activation predicting increased chocolate intake after chocolate exposure fits with these findings.

It must be noted that intake was predicted by different brain regions in the exposure group as compared to the control group, even though no group differences in absolute level of activation were found between the groups in any of these regions. Only activation in reward regions correlated with intake in the exposure group, and only activation in inhibitory regions correlated with intake in the control group. We speculate that the exposure group experienced a greater focus on palatability, and, as a consequence, activation in reward regions was mostly predictive of intake. So, the consumption of these participants may have been driven mostly by palatability considerations. It may also explain why only in the exposure group a correlation between self-reported craving during the session and intake was found. That is, a greater correspondence between self-reported craving and intake was found because both measures may have been mostly driven by palatability considerations. In the control group, health considerations may have been more relevant, presumably resulting in a negative correlation between activation in inhibitory brain regions and intake, and in a lack of correlation between self-reported craving and intake. One should keep in mind that the measurement of chocolate craving was measured with a single VAS question. If a more comprehensive chocolate craving measure would have been used, correlations between craving and intake might have been larger. Regarding the ratings of chocolate characteristics, the groups did not differ except for the rating of the smell of milk chocolate. The exposure group rated this smell as less pleasant than the control group. This may be the result of the exposure with real chocolate in the exposure group. However, no group differences were found regarding the smell of the other chocolate types, so the effect can be considered small.

As these results show, the CERP manipulation did influence the predictive validity of the neural correlates of chocolate craving on intake. However, the CERP manipulation was not as effective as it was expected to be, because overall chocolate intake was similar in both groups, although it was expected to be smaller in the exposure group as compared to the control group. One explanation for the lack of an effect of exposure on chocolate consumption could be the specific demands of the bogus taste test. Maybe the exposure only affected the decision to eat or not, but not so much the amount eaten, which is the dependent variable in the bogus taste test. Alternatively, the lack of an effect on intake may be due to the fact that extinction of craving was not attained in the chocolate exposure group, which may have been the result of the olfactory exposure being interrupted too often by scans (see Frankort et al., 2013). In addition, extinction may not have been attained because the bond between the conditioned stimulus (CS) and the unconditioned stimulus (US) is likely particularly strong for chocolate, as this food is generally very much liked and people typically have had many exposures to chocolate, resulting in many opportunities for the CS-US bond to strengthen. So, it is likely that one session is not enough to attain extinction. Another possibility is that the exposure procedure did break the link between the olfactory cues and consumption, but not between the visual cues and consumption.

In summary, all three regression analyses suggest that neural correlates predict subsequent behaviour (i.e., chocolate intake) above and beyond self-reported chocolate craving, which confirmed our hypothesis. Self-reported craving did not significantly contribute to the prediction of subsequent intake. In contrast, the BOLD response to chocolate pictures versus neutral pictures in the caudate, which has been associated with long-term weight gain in previous studies, was a significant predictor of intake for the chocolate exposure group. Also the activation in the mid-dorsolateral PFC negatively predicted subsequent chocolate intake in the control group. This region has been linked to weight loss in previous studies. Further, the response in the right anterior PFC significantly predicted intake in the whole sample. Lesions in this region have been associated with weight loss. Therefore, even though we did not measure weight change, our findings might provide a missing link between brain activation and long-term weight change by showing an association between brain activation and subsequent intake. Furthermore, only reward regions correlated with intake in the exposure group, and only inhibitory regions correlated with intake in the control group. In other words, the prevailing influence on subsequent intake in the exposure group was reward. In the control group, this prevailing influence was inhibition. In conclusion, neural correlates were more predictive of subsequent intake than was self-reported craving, for the chocolate exposure group, the control group and the whole sample. However, the brain regions found to be predictive differed between groups, both in location and in assumed functionality (reward in the exposure group versus inhibition in the control group). This can be considered as an effect of the CERP manipulation, which is noteworthy because of the fact that brain correlates were a better predictor of subsequent intake than self-reported craving. It remains to be investigated if the same results would be achieved after addition of other self-reported measures to the craving measure, like eating behaviour risk factors and emotion regulation abilities. Also it would be interesting to explore if, after an effective CERP, reward region activation would still be predictive of subsequent intake and if activation in reward regions would extinguish together with craving.

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