NeuroImage 55 (2011) 296–303

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

The first taste is always with the eyes: A meta-analysis on the neural correlates of processing visual food cues

L.N. van der Laan [a,*], D.T.D. de Ridder [b], M.A. Viergever [a], P.A.M. Smeets [a,c]

[a] Image Sciences Institute, University Medical Center Utrecht, The Netherlands
[b] Department of Clinical and Health Psychology, Utrecht University, The Netherlands
[c] Division of Human Nutrition, Wageningen University and Research Centre, The Netherlands

ARTICLE INFO

Article history:
Received 26 July 2010
Revised 8 October 2010
Accepted 16 November 2010
Available online 25 November 2010

Keywords:
Food
Pictures
Meta-analysis
fMRI
Hunger
Energy

ABSTRACT

Food selection is primarily guided by the visual system. Multiple functional neuro-imaging studies have examined the brain responses to visual food stimuli. However, the results of these studies are heterogeneous and there still is uncertainty about the core brain regions involved in the neural processing of viewing food pictures. The aims of the present study were to determine the concurrence in the brain regions activated in response to viewing pictures of food and to assess the modulating effects of hunger state and the food's energy content.

We performed three Activation Likelihood Estimation (ALE) meta-analyses on data from healthy normal weight subjects in which we examined: 1) the contrast between viewing food and nonfood pictures (17 studies, 189 foci), 2) the modulation by hunger state (five studies, 48 foci) and 3) the modulation by energy content (seven studies, 86 foci).

The most concurrent brain regions activated in response to viewing food pictures, both in terms of ALE values and the number of contributing experiments, were the bilateral posterior fusiform gyrus, the left lateral orbitofrontal cortex (OFC) and the left middle insula. Hunger modulated the response to food pictures in the right amygdala and left lateral OFC, and energy content modulated the response in the hypothalamus/ventral striatum.

Overall, the concurrence between studies was moderate: at best 41% of the experiments contributed to the clusters for the contrast between food and nonfood. Therefore, future research should further elucidate the separate effects of methodological and physiological factors on between-study variations.

Introduction

In modern societies people are continuously exposed to food cues since there is an abundant availability of palatable food at virtually every moment of the day. Like other primates, humans have a highly developed visual system. Food selection, like many other behaviors, is primarily guided by the visual system (Laska et al., 2007; Linne et al., 2002). Not without reason, an ancient quote attributed to Apicius (first century) states that "the first taste is always with the eyes."

The sight of food elicits a wide range of physiological, emotional and cognitive responses. Firstly, it is a cue for the body to prepare itself for subsequent food ingestion with accompanying anticipatory physiological responses, such as a cephalic phase release of insulin and changes in heart rate (Drobes et al., 2001; Wallner-Liebmann et al., 2010). Secondly, it can elicit emotional responses like a desire to eat (Ouwehand and Papies, 2010). It is thought that positive emotions, such as pleasure, evolved as a biological mechanism to promote behaviors that support survival, like eating (Berthoud and Morrison, 2008; Van den Bos and De Ridder, 2006). Thirdly, the sight of a food gives rise to cognitive processes, such as memory retrieval and hedonic evaluation, based on information that was stored during previous experience(s) with the food (Berthoud and Morrison, 2008; Shin et al., 2009). In addition, exposure to food cues can trigger inhibitory cognitive processes like self-regulation, e.g. processes involved in resisting the temptation of palatable foods in order to maintain a healthy body weight (Kroese et al., 2009; Van den Bos and De Ridder, 2006).

Multiple neuro-imaging studies have investigated the brain mechanisms subserving the response to visual food cues in order to provide insight in the neural correlates of eating behavior (e.g., Cornier et al., 2009; Fuhrer et al., 2008; Santel et al., 2006; Simmons et al., 2005; St-Onge et al., 2005). These studies have shown that a diverging network of brain regions is activated in response to viewing

Abbreviations: ALE, Activation Likelihood Estimation; LOC, Lateral Occipital Complex; MA, Modeled Activation; OFC, Orbitofrontal cortex; FDR, False Discovery Rate.

* Corresponding author. Heidelberglaan 100, room Q0S.459, 3584 CX Utrecht, The Netherlands.
E-mail address: nynke@isi.uu.nl (L.N. van der Laan).

1053-8119/$ – see front matter © 2010 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2010.11.055

food pictures (compared to viewing pictures of nonfoods). Although there seems to be fair concurrence among studies in some regions (e.g., the occipital cortex and insula), other regions are only reported by a few studies (e.g., the hippocampus) (Cornier et al., 2009; Fuhrer et al., 2008; Santel et al., 2006; Simmons et al., 2005; St-Onge et al., 2005). Hence, it is still unclear which are the core brain regions that are activated in response to viewing food pictures.

A principal reason for this may be that between-study variability is high: study designs, tasks and stimuli differ between studies, and the sample sizes are generally small. In addition, the acquisition and analysis of neuro-imaging data is affected by many factors such as the particular scan sequence and the type of preprocessing algorithms used (Bennett and Miller, 2010). Given the high between-study variability caused by these factors it would be advantageous to identify the brain responses that are concurrent across studies, i.e., those responses that are relatively unaffected by between-study differences.

Novel meta-analysis techniques allow for integrating findings from multiple studies more precisely compared to previously employed methods like counting anatomical labels. In this study we employed the Activation Likelihood Estimation (ALE) meta-analysis technique (Eickhoff et al., 2009). This is a quantitative voxel-wise meta-analysis technique that compares the results of neuro-imaging studies using reported coordinates in a standardized 3D atlas space.

The inconsistencies among studies have also served as a basis to investigate a wide range of factors that might modulate the brain response to viewing food pictures. Two of the most frequently investigated factors are the food's energy content and the hunger state of the individual. Behavioral studies have shown that these factors influence eating behavior, e.g., people have a higher preference for energy-rich foods (Drewnowski and Greenwood, 1983), and foods are rated as more pleasant when people are hungry (Cabanac, 1979). This suggests that energy content and hunger state will modulate the neural responses to viewing food pictures. However, the neuro-imaging studies that have addressed these factors have not yielded consistent results (e.g., Fuhrer et al., 2008; Killgore and Yurgelun-Todd, 2005b; LaBar et al., 2001b; Passamonti et al., 2009). Therefore, we included these two primary modulators in our meta-analysis.

Evidently, there are more potential modulating factors. These include individual differences in age, gender, mood, genotype and behavioral traits like reward sensitivity, disinhibition, dietary restraint and the tendency toward external eating behavior (Kaurijoki et al., 2008; Beaver et al., 2006; Coletta et al., 2009; Martin et al., 2009; Passamonti et al., 2009; Killgore and Yurgelun-Todd, 2005a; 2005b; 2006; Stoeckel et al., 2008; Uher et al., 2006). However, research into these factors is relatively young, i.e., only (very) few studies have specifically investigated these factors. Therefore, it is not yet possible to do a meta-analysis on these factors.

In summary, our aims were to determine the concurrence in the brain regions activated in response to viewing pictures of food in normal-weight individuals and to assess the modulating effects of hunger state and the food's energy content.

Methods

Study and experiment selection

Studies were selected by searching the Pubmed database (www.pubmed.org) using the following keyword search (all fields): (brain OR neural) AND (food OR nutrition) AND (pictures OR images). Additional studies were found by examining references of relevant articles. The inclusion criteria were that studies 1) were published in a peer-reviewed journal, 2) employed a task involving the visual presentation of pictures of food, 3) reported the coordinates in Montreal Neurological Institute (MNI) (Evans et al., 1993) or Talairach space (Talaraich and Tournoux, 1988), 4) reported coordinates of activation in the whole brain (i.e., not only selected regions of interest) and 5) included healthy normal-weight participants (Body Mass Index between 18.5 and 25 kg/m^2). Experiments from these studies were selected as follows: to be included in the meta-analysis for the contrast between food and nonfood, the data had to be analyzed using a contrast between food and nonfood pictures (e.g., tools, scenery, flowers, animals). For experiments to be included in the meta-analysis on the modulation of neural responses to food by hunger state, coordinates of activation in response to food pictures had to be reported for a contrast between a hungry and a satiated state. For the meta-analysis on the contrast between high and low energy foods, coordinates for a contrast of neural activation in response to viewing foods high versus low in fat, sugar or energy content had to be reported.

Table 1 shows an overview of the studies and experiments included in the three meta-analyses. All studies used functional MRI. For the contrast between food and nonfood pictures, 18 experiments from 17 studies, with a total of 246 participants (133 females) and 189 reported coordinates were included. For the interaction with hunger state, five experiments (from five studies) with 57 participants (27 females) and 48 foci remained. These studies reported the contrast of activation by viewing food pictures between a hungry and a satiated state. The duration of fasting in the hungry state ranged between 4 and 14 hours across the included studies. In the satiated state, subjects were scanned within 1 hour following the last consumption. For the meta-analysis on the contrast between high and low energy foods, seven experiments (seven studies) with 112 participants (70 females) and 90 foci remained. Three of these studies reported a contrast between high- and low-calorie foods, two studies contrasted appetizing with bland foods, and one study contrasted foods with a high and a neutral hedonic value. The appetizing or high-hedonic food category typically contained foods high in energy (e.g., hamburgers, ice cream) and the bland or neutral-hedonic food category consisted of foods lower in energy (e.g., whole grain products, potatoes, vegetables). Thus, the bland or neutral-hedonic food categories did not only contain very low-energy foods, such as fruit and vegetables, but also some low-/moderate-energy foods, such as bread and potatoes. Still, these foods are less calorie-dense than the foods in the highly appetizing and high-hedonic value category.

The statistical thresholds employed in the different experiments ranged between $p<0.001$ uncorrected and $p<0.01$ corrected for multiple comparisons. Some of the included studies involved patient groups (e.g., anorectic patients) and/or pharmacological interventions. However, of these studies, only experiments concerning healthy participants in the control condition were included in the meta-analyses.

ALE meta-analyses

To determine the concurrence in reported coordinates across studies, we conducted three ALE meta-analyses, using the Brainmap GingerALE software. We used the revised version of the ALE approach (Eickhoff et al., 2009) for coordinate-based meta-analysis of neuro-imaging results (Turkeltaub et al., 2002; Laird et al., 2005b). The input for the first meta-analysis consisted of the coordinates of brain regions that were activated in response to viewing pictures of foods compared to pictures of nonfoods. For the second meta-analysis, coordinates of brain regions that were modulated by hunger status were used. The third meta-analysis included coordinates of the contrast between high and low-energy foods.

We converted coordinates reported in Talaraich space to the standard space of the Montreal Neurological Institute (MNI) using the Brainmap GingerALE software. ALE modeling uses reported coordinates as the center of a 3-dimensional Gaussian kernel function to create a modeled activation (MA-) map for each individual experiment. Because the uncertainty of the spatial localization can be due to between-template and to between-subject variance, both these

Table 1
Studies and experiments included in the ALE meta-analyses.

	Study (author/year of publication)			*n*	No. of Foci
Experiments: food>nonfood		Nonfood stimuli	Time fasted		
1	Simmons et al., 2005	Locations, buildings	Not reported	9	6
2	Labar et al., 2001b	Tools	>8 hours and<1 hour	17	3
3	Killgore et al., 2003	Rocks, trees, flowers	>1,5 hours, median 3,9 hours	13	12
4	Killgore and Yurgelon-Todd, 2005b	Rocks, trees, flowers	>1 hour	8	14
5	Rothemund et al., 2007	Rocks and flowers	>1,5 hours	13	1
6	Beaver et al., 2006	Objects (videocassettes, iron, etc.)	>2 hours	12	16
7	Cornier et al., 2007	Animals, trees, furniture, buildings	Overnight fast	25	2
8	Fuhrer et al., 2008	Objects (watch, pen, calculator, etc.)	1 hour and 14 hours	12	20
9	Schienle et al., 2009	Household articles	>12 hours	19	12
10	Santel et al., 2006	Objects (tools, make-up, pencils, etc.	12 hours and 1 hour	10	7
11	Uher et al., 2006	Objects (brushes, car, flower, etc.)	>3 hours (mean 3.5)	18	5
12	Miller et al., 2007	Animals, tools	10 min after oral glucose load of 75 g	8	2
13	Cornier et al., 2009	Animals, trees, furniture, buildings.	Overnight fast *(not exactly reported)*	22	23
14	Holsen et al., 2005	Animals	<1 hour and 4 hours	9	17
15	Davids et al., 2009	Landscapes, work-related sceneries	7 participants within 2 hours, 15>2 hours after meal	22	15
16a	Malik et al., 2008 (control condition of control/ghrelin group	Scenery, landscapes	3 hours (standardized breakfast after 12 h fast)	12	11
16b	Malik et al., 2008 (control/control group)	Scenery, landscapes	3 hours (standardized breakfast after 12 h fast)	8	10
17	Holsen et al., 2006	Animals	<1 hour and 4 hours	9	13
			Total:	*246*	*189*
Experiments: hungry>satiated state		Nonfood stimuli	Time fasted: hungry vs. satiated state	*n*	No. of foci
1	Fuhrer et al., 2008	Objects (watch, pen, calculator, etc.)	14 hours vs. 1 hour	12	7
2	LaBar et al., 2001b	Tools	>8 hours vs. <1 hour	17	5
3	Santel et al., 2006	Objects (tools, make-up, pencils, etc.	12 hours vs. 1 hour	10	3
4	Holsen et al., 2005	Animals	4 hours vs <1 hour	9	24
5	Mohanty et al., 2008	Tools	>8 hours vs. <1 hour	9	9
			Total	*57*	*48*
Experiments: high>low energy foods		Food stimuli: high and low energy content	Time fasted	*N*	No. of foci
1	Killgore et al., 2003	High calorie: french fries, ice cream, etc. Low calorie: salads, whole grain cereals, etc.	>1,5 hours, median 3,9 hours	13	7
2	Killgore and Yurgelon-Todd, 2005b	see Killgore et al, 2003	>1 hour	8	5
3	Beaver et al., 2006	Appetizing: chocolate cake, ice cream, etc. Bland: uncooked rice, potatoes	>2 hours	12	16
4	Passamonti et al., 2009	see Beaver et al., 2006	>2 hours	21	13
5	Cornier et al., 2007	High hedonic value: waffles with whipped cream, cake, plate of egg and bacon Neutral hedonic value: fruit, bread, cereals, etc.	Overnight fast	25	7
6	Goldstone et al., 2009	High calorie: burgers, cakes, chocolate Low calorie: salads, fruits, fish	Overnight fast (mean 15,9 hours), fed (mean 1,6 hours)	20	42
7	Rothemund et al., 2007	High calorie: Hamburgers, pancakes Low calorie: Fruit, vegetables	>1.5 hours	13	0
			Total:	*112*	*90*

components are used to compute the parameters of the Gaussian kernel function. The algorithm takes differences in sample size into account by weighing the between-subject variance by the number of subjects in the experiment. Subsequently, the MA-maps are combined to calculate an experimental ALE map. This experimental ALE map is tested against an ALE null distribution map. This map represents the null-hypothesis that there is a random spatial association between the results of the experiments, while regarding the within-experiment distribution as fixed. The ALE analysis implements a random effects inference, i.e., the inference is focused on the above-chance concurrence between experiments, and not on the clustering of coordinates within experiments. The null distribution map is derived from a permutation procedure and is created on basis of the same number of experiments and reported coordinates as the experimental map. We used a statistical threshold of $p<0.05$ False Discovery Rate (FDR) corrected for multiple comparisons and a minimum cluster size of 100 mm^3 (Genovese et al., 2002). ALE maps were overlaid onto an MNI anatomical template using the MRIcroN software (http://www.cabiatl.com/mricro/mricron/index.html).

Because our aim was to identify the most concurrent regions, i.e., those that are most robustly activated across experiments with different designs and tasks, we initially applied an extra criterion to the results, namely that clusters would only be reported if 50% or more of the included experiments contributed to them. This cutoff value seemed reasonable given the inherently low reproducibility of fMRI results (Bennett and Miller, 2010). However, because there were no clusters for the contrast between food and nonfood with 50% or more experiments contributing, this criterion was liberalized such that the results section now reports all significant ALE clusters. In the discussion only the clusters with 33% or more contributing experiments are discussed.

Results

Significant ALE clusters for the contrast between viewing food and nonfood pictures

The ALE analysis revealed 16 significant clusters for the contrast between viewing food pictures and viewing nonfood pictures (Figs. 1, 2, Table 2), i.e., regions responding stronger to pictures of food than to pictures of nonfoods. However, only four of these clusters met the 33% contributing experiments criterion. The three most concurrent clusters, which were contributed by seven of the 17 experiments (41%), were located in the posterior fusiform gyrus

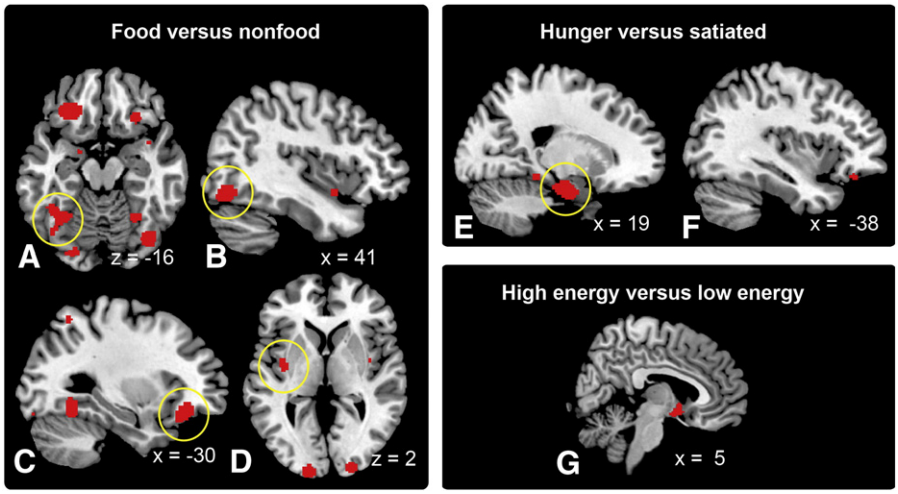

Fig. 1. Results of the ALE meta-analysis showing clusters with significant ALE maxima ($p<0.05$, FDR-corrected for multiple comparisons, cluster size>100 mm^3). Clusters to which at least 33% of the experiments contributed are indicated with a circle and anatomical labels of these clusters are given. (A–D) ALE clusters for the contrast food>nonfood: (A) A cluster stretching from the left posterior fusiform gyrus to the middle occipital gyrus, (B) right posterior fusiform gyrus, (C) left lateral OFC (inferior frontal gyrus) and (D) left middle insula; (E–F) ALE clusters for the contrast of viewing food pictures in a hungry versus a satiated state: (E) a cluster stretching from the right parahippocampal gyrus to the right amygdala, (F) left lateral OFC (inferior frontal gyrus); (G) ALE cluster for the contrast of viewing pictures of high versus low energy foods stretching from the hypothalamus to the caudate.

(bilaterally) (left ALE peak at MNI (−30, −56, −10), ALE value = $2.37*10^{-3}$, volume = 3056 mm^3; right ALE peak at MNI (38, −74, −14), ALE value = $2{,}78*10^{-3}$, volume = 2592 mm^3) and the left lateral orbitofrontal cortex (OFC, inferior frontal gyrus; ALE peak at MNI (−26, 32, −14), ALE value = $3{,}15*10^{-3}$, volume = 2440 mm^3). Concurrence was also found in the left middle insula (ALE peak at MNI (−38, −4, 6), ALE value = 1.96×10^{-3}, volume = 1264 mm^3) with six contributing experiments (35%).

Significant clusters that did not meet the criterion of 33% contributing experiments are listed in Table 2.

Modulation by hunger state and the energy content of the food

Table 3 and Fig. 1 show the results of the meta-analysis on the modulation by hunger state and the energy content of the food. The meta-analysis on the modulation by hunger state revealed two significant ALE clusters which also met the "33% contributing experiments" criterion. In these two regions neural activation during viewing of food pictures was stronger in the hungry compared to the satiated state. The largest cluster was located in the right parahippocampal gyrus and extended to the amygdala and was contributed by three (60%) of the five studies (ALE peak at MNI (18, -12, -22), ALE value = $1.96*10^{-3}$, volume = 2224 mm^3). A second cluster with two contributing studies (40%) was located in the left lateral OFC (inferior frontal gyrus; ALE peak at MNI (-36, 42, -20), ALE value = 0.88×10^{-3}, volume = 224 mm^3).

For the contrast between high- and low-energy foods the meta-analysis yielded five clusters where neural activation was higher during viewing of high- compared to low-energy foods. Only one cluster met the "33% contributing experiments" criterion. This cluster was contributed by three of the seven studies (43%) and was located in a region stretching from the right hypothalamus to the right ventral striatum (ALE peak at MNI (6, 6, -6), ALE values = 1.21×10^{-3}, volume = 448 mm^3). The other four clusters are listed in Table 3.

A conjunction map of the contrasts "hunger versus satiated" and "high versus low-energy foods" did not show overlapping brain regions between the contrasts (results not shown).

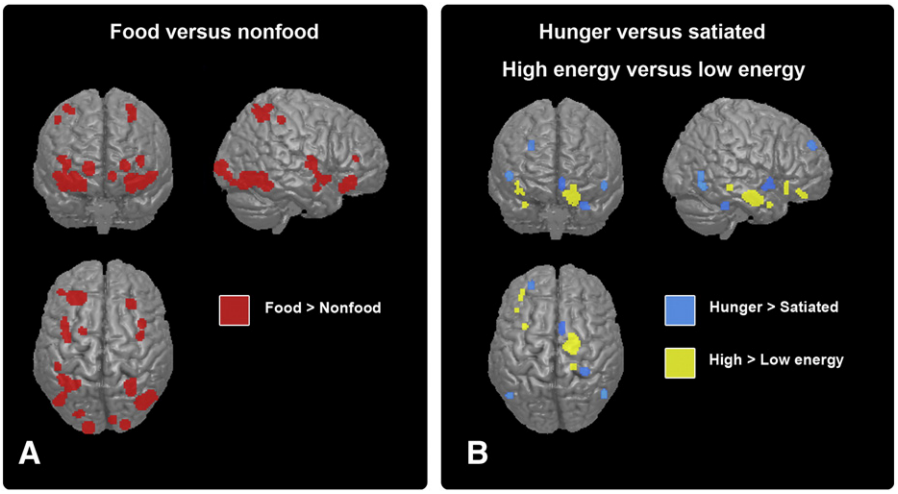

Fig. 2. The results of the ALE meta-analysis shown as a projection of significant ALE clusters ($p<0.05$, FDR-corrected for multiple comparisons, cluster size>100 mm^3) on a 3-D rendering of a single-subject brain in MNI space. (A) ALE clusters for the contrast food>nonfood. (B) ALE clusters for the contrast of viewing food pictures in a hungry>satiated state and for viewing high>low energy foods.

Table 2
Locations (MNI) of clusters with significant ALE values for the contrast of food versus nonfood[a].

Cluster	Anatomical label[b]	Peak voxel coordinates[c]			Cluster size (mm^3)	ALE value ($\times 10^{-3}$)	No. of contributing experiments	
		x	*y*	*z*				%
1	Posterior fusiform gyrus L	−30	−56	−10	3056	2.37	7	41
	Inferior occipital gyrus L	−46	−72	−6		1.98		
	Posterior fusiform gyrus L	−40	−52	−18		1.87		
2	Posterior fusiform gyrus R	38	−74	−14	2592	2.78	7	41
3	Inferior frontal gyrus L / lateral OFC	−26	32	−14	2440	3.15	7	41
4	Middle Insular cortex L	−38	−4	6	1264	1.96	6	35
	Middle Insular cortex L	−40	4	−10		1.63		
	Middle Insular cortex L	−38	−2	−4		1.35		
5	Superior parietal gyrus R	28	−62	60	992	1.85	5	29
	Inferior parietal gyrus R	30	−54	52		1.63		
6	Middle occipital gyrus L	−16	−100	0	1120	2.43	3	18
7	Superior parietal gyrus L	−38	−50	62	456	1.71	3	18
	Superior parietal gyrus L	−32	−58	58		1.45		
8	Middle insular cortex R	38	−8	10	360	1.49	3	18
9	Amygdala L	−20	−2	−20	280	1.51	3	18
	Amygdala L	−18	0	−14		1.18		
10	Fusiform gyrus L	28	−56	−12	968	2.8	2	12
11	Calcarine gyrus L	22	−96	4	592	2.35	2	12
12	Lingual gyrus L	10	−92	−8	360	1.81	2	12
13	Middle Insular cortex R	38	6	−12	352	2.08	2	12
14	Middle occipital gyrus L	−24	−84	−14	280	1.54	2	12
15	Inferior parietal gyrus L	−46	−38	50	248	1.59	2	12
16	Inferior frontal gyrus L	−42	38	10	144	1.38	2	12

[a] Reported ALE clusters were thresholded at $p<0.05$ (FDR-corrected for multiple comparisons), cluster size>100 mm^3.
[b] L, left hemisphere; R, right hemisphere.
[c] Voxel coordinates are in the Montreal Neurologic Institute (MNI) space.

Discussion

We determined the most concurrent brain regions activated in response to viewing pictures of food in healthy normal-weight individuals. Our ALE meta-analysis yielded a diverging range of concurrent brain regions in terms of ALE values. However, despite highly significant ALE values, the percentage of contributing experiments can be regarded as moderate: at best 41% (seven out of 17) of the included experiments contributed to the clusters for the contrast between food and nonfood. Most meta-analyses base their conclusions only on the significance of the concurrence, i.e., on the proximity between reported coordinates. However, one can argue that the percentage of contributing experiments is equally important, e.g., when only two out of 17 experiments report that a particular brain region is activated in response to viewing foods, this response is probably very specific to the design characteristics (e.g., details of the fMRI task design and stimuli) of those experiments. It would then not be appropriate to draw conclusions about the neural process of interest as a whole, in this case food perception. Compared to other meta-analyses (e.g., Turkeltaub and Coslett, 2010; Wiener et al., 2010), the maximum percentage of contributing experiments in our study (41%) can be regarded as moderate.

The moderate concurrence in brain activation that we found is in line with recent findings of Bennett and Miller (2010) who showed that the reproducibility of fMRI results was only 50%, even for the same task and stimuli in the same group of participants. Reproducibility of studies with different tasks, study populations and stimuli can be expected to be lower. In addition, some brain regions are more prone to signal loss (OFC) or habituation (OFC, amygdala) than others, which might result in an underestimation for these structures (LaBar

Table 3
Locations (MNI) of clusters with significant ALE maxima for the modulation by hunger state and the food's energy content.[a]

Cluster	Anatomical label[b]	Peak voxel coordinates[c]			Cluster size (mm^3)	ALE ($*10^{-3}$)	No. of contributing experiments	
		x	*y*	*z*				%
Experiments: hungry>satiated state								
1	Parahippocampal gyrus L/ Amygdala	18	−12	−22	2224	1.96	3	60
2	Inferior frontal gyrus / lateral OFC L	−36	42	−20	224	0.88	2	40
	Inferior frontal gyrus / lateral OFC L	−36	36	−16		0.86		
Experiments: high>low energy foods								
1	Hypothalamus	6	6	−6	448	1.21	3	43
	Ventral striatum	6	0	−12		1.19		
2	Cerebellum R	30	−40	−32	392	1.51	2	29
3	Frontal middle gyrus L	−26	50	32	352	1.43	2	29
4	Middle occipital gyrus, L	−48	−66	0	280	1.37	2	29
5	Inferior temporal gyrus, R	50	−64	−10	256	1.25	2	29

[a] Reported ALE clusters were thresholded at $p<0.05$ (FDR-corrected for multiple comparisons), cluster size>100 mm^3.
[b] L, left hemisphere; R, right hemisphere.
[c] Voxel coordinates are in the Montreal Neurologic Institute (MNI) space.

et al., 2001a; Weiskopf et al., 2006). Furthermore, there are several sources of between-study variation which are specific to food perception. The present meta-analysis showed that the brain responses to viewing food pictures are indeed modulated by the food's energy content and by the hunger state of the participant. Moreover, other studies have shown that several other factors, like serum leptin concentration, gender, age and mood, can modulate the brain response to viewing food pictures (Killgore and Yurgelun-Todd, 2005a; 2005b; 2006; Stoeckel et al., 2008; Uher et al., 2006). Additional modulating factors are personality characteristics and behavioral traits like reward sensitivity, disinhibition, dietary restraint and a tendency toward external eating behavior (Beaver et al., 2006; Coletta et al., 2009; Martin et al., 2009; Passamonti et al., 2009). Also individual differences in genotype have been shown to modulate the neural response to viewing food pictures: Kaurijoki et al (2008) showed that subjects that are homozygous for the long allele of the serotonin transporter gene show stronger posterior cingulate activation when viewing pictures of food compared to the persons that are heterozygous or homozygous for the short allele.

Another important modulating factor is body weight. Multiple neuroimaging studies showed that overweight and obese subjects respond differently to food pictures compared to normal-weight subjects (e.g., Martin et al., 2009; Rothemund et al, 2007; Stoeckel et al., 2008). Killgore and Yurgelon-Todd (2005a) showed that, even within the normal range of BMI, differences in BMI can alter the OFC responses to viewing pictures of food, that is, OFC activation correlates negatively with BMI. So although we included only studies with participants in the normal range of BMI, this suggests that BMI may still have affected our meta-analysis results, in particular in the OFC.

Apart from the above-mentioned subject-specific factors, additional variance can arise from differences in task instruction and the experimental paradigm. For example, Siep et al. (2009) showed that explicit evaluation of the food, i.e., attending to the food and judging the palatability, is essential for detecting activation in the amygdala and medial OFC. Of the studies included in the meta-analysis on the contrast between food and nonfood pictures, seven used an event-related design and ten used a block-design. Further inspection showed no bias related to the type fMRI design. The task instructions were diverse and ranged from specific instructions like memorizing or categorizing the stimuli to no instruction at all. There was too much variation in the type of instructions to be able to attribute any effects to that factor.

In conclusion, multiple modulating factors and sources of variability may explain the moderate concurrence we found. However, because information on many factors is not reported (and usually also not measured, especially genotypic and personality characteristics), it was not possible to account for these factors in our analyses. Therefore, in order to elucidate the modulating effects of such factors on the neural response to viewing food pictures, many more studies are needed, along with more advanced (e.g., multivariate) meta-analysis techniques.

In the following sections we discuss the most concurrent brain regions, i.e., significant clusters that met the additional "33% contributing experiments" criterion.

Lateral OFC

The highest ALE value for the contrast between viewing food and nonfood pictures, and thus the most dense concentration of activation foci, was found in the left lateral OFC (left inferior frontal gyrus). Multiple studies have shown that activation in the lateral OFC correlates with the subjective pleasantness ratings of the taste and smell of food (Kringelbach et al., 2003; Rolls and Grabenhorst, 2008). For example, Kringelbach et al. (2003) showed that activation in a cluster located near the cluster found in the present study (MNI (−22, 34, −8)) correlated with pleasantness ratings of liquid food stimuli. A study of O'Doherty et al. (2002) showed that the lateral OFC was not only activated during exposure to a pleasant taste, but also during anticipation to receiving this taste.

In summary, the activation of the lateral OFC in response to food pictures may reflect the expected pleasantness of the food. This is also supported by the significant ALE cluster for the modulation by hunger state, which was located at the same location as the cluster for the contrast between food and nonfood pictures. This cluster may thus reflect the higher desirability of food in the hungry state (Cabanac, 1979). This finding also implies that variability in hunger state in the studies included for the contrast between viewing food and nonfood pictures can induce variability in OFC activation and thereby lowers the convergence across studies. Therefore, it is important to take hunger status into account.

Lateral occipital complex (LOC)

The two other most convergent clusters, both with seven contributing experiments (41%) for the contrast between food and nonfood pictures, were located in the LOC (bilaterally) and stretched from the posterior fusiform gyrus to the inferior occipital gyrus. The LOC is part of the visual association cortex, which is mainly known for its role in object recognition (Grill-Spector et al., 2001). The clusters in the LOC cannot be explained by a difference in visual characteristics between the food and nonfood stimulus categories, since in the majority of studies that contributed to this cluster the different stimuli were matched on visual characteristics like color, luminance and visual complexity. An alternative, and more likely, explanation why food pictures elicit a stronger activation in the LOC is that emotionally salient stimuli like food lead to heightened attention and thereby more extensive visual processing (Killgore and Yurgelun-Todd, 2007). The amygdala and anterior cingulate have been proposed as the mediators of this top-down regulation of visual processing, as these structures are sensitive to the motivational salience and project back to the visual cortex (Lang et al., 1998). The cluster that we found in the LOC may reflect this attention effect. The high concurrence in this area is also in line with multiple studies (e.g., Harrington et al., 2006; Peelen and Downing, 2005) that showed a relatively high (compared to other brain regions) within- and between-subjects reproducibility of activation in the fusiform gyrus and other visual areas.

Middle insular cortex

We found convergent regions of activation for the contrast between food and nonfood pictures in the bilateral middle insula. The cluster in the left middle insula also survived the additional "33% contributing experiments" criterion. Whereas functions of the anterior insula (i.e., taste processing) and the posterior insula (i.e., cephalic phase responses such as gastric distention) are well documented (e.g., Small, 2006; Tomasi et al., 2009), the function of the middle insula is less well understood. A diverse range of food-related processes has been associated with activation of the middle insula, including imagining the taste of food, craving for food, and the mouthfeel of water and oil (de Araujo et al., 2003; de Araujo and Rolls, 2004; Pelchat et al., 2004). In addition, several studies have suggested that activation of the middle insula represents memory retrieval of previous experiences with the food (Levy et al., 1999; Pelchat et al., 2004). Hence, the middle insula ALE cluster we found might also reflect the latter.

Amygdala

With only three of the 17 experiments contributing to the ALE cluster in the left amygdala, this was one of the least concurrent (yet significant) clusters for the contrast between food and nonfood pictures. However, the meta-analysis on the interaction with hunger state yielded a significant cluster in the right amygdala/parahippocampal

gyrus with more than 33% contributing experiments. The amygdala is often a region of interest because of its role in reward processing. It is thought to be involved in weighing the importance and arousal-evoking potential of both positive and negative stimuli (Baxter and Murray, 2002; Bechara et al., 1999). The stronger amygdala activation in response to food pictures compared to nonfood pictures could thus be the result of the higher arousal by or the higher salience of foods compared to nonfoods. In line with this, we found that hunger, which induces a higher motivational salience of foods, increases amygdala activation by viewing food pictures.

Striatum

Our meta-analysis yielded a convergent region of activation stretching from the ventral striatum to the hypothalamus for the contrast between high- and low-energy foods. The hypothalamus is a key region involved in the regulation of food intake, whereas the ventral striatum plays a prominent role in reward processing (Blevins and Baskin, 2010; Carlezon and Thomas, 2009). The ALE cluster in the ventral striatum might reflect the greater (metabolic) reward value of the high energy foods. However, in most studies the stimuli were not matched on palatability (the high energy foods were rated higher in tastiness or appeal than the low-energy foods). Therefore, future studies should try to disentangle effects of expected (metabolic) reward and hedonic value (expected palatability).

For the contrast between viewing food and nonfood pictures, no significant concurrent clusters were identified in the striatum. This has previously been explained by arguing that passively viewing pictures may not be rewarding enough to elicit a striatal response, i.e., for striatal activation actual reward receipt or anticipation to a real impending reward is required (Piech et al., 2009). However, the results of this meta-analysis suggest that the mere sight of food can elicit a striatal response, albeit only in response to high (versus low) energy foods.

Strengths and limitations

To our knowledge this is the first study that employed a voxel-based method to systematically determine concurrence across studies on the response to viewing food pictures. An ALE meta-analysis has a greater level of spatial accuracy compared with the previously employed more global characterization method of counting anatomical labels (Laird et al., 2005a). The principal strength of a quantitative meta-analysis is that it is based on multiple peer-reviewed studies, in our case with a total of almost 300 participants. Thus, the results from the present food-related brain activation maps are more robust than those of any individual imaging study. A limitation of the ALE analysis is that it only includes reported local maxima and does not take into account the level of statistical significance and the cluster size. However, we do not think that the variation in statistical thresholds has significantly biased our results because false positives from a single study will be averaged out when multiple studies are combined.

Conclusions

In conclusion, concurrence between studies on the brain response to viewing pictures of food was moderate: at best 41% of the experiments contributed to the clusters for the contrast between food and nonfood. The most concurrent brain regions activated in response to viewing pictures of food in normal-weight individuals were the lateral OFC, the LOC and the left middle insula. This study provides evidence for the modulation by hunger state (lateral OFC and amygdala) and by the food's energy content (hypothalamus/ventral striatum) in specific brain regions. Future research should further elucidate the separate effects of methodological and physiological factors on between-study variations.

Findings from this study can be used to support hypothesis-driven neuroimaging studies on the responses to visual food cues and eating behaviors like food selection.

Disclosure statement

The authors declare no conflict of interest.

Acknowledgments

This work was supported by a (governmental) research grant of Agentschap NL.

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