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Diabetes dietary management alters responses to food pictures in brain regions associated with motivation and emotion: an fMRI study

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ABSTRACT

(1) Aims/hypothesis. We hypothesised that living with type 2 diabetes would enhance responses to pictures of foods in brain regions known to be involved in learnt food sensory motivation and that these stronger activations would relate to scores for dietary adherence in diabetes and to measures of potential difficulties in adherence.

(2) Methods. We compared brain responses to food images of 11 people with type 2 diabetes and 12 healthy control participants, matched for age and weight, using functional Magnetic Resonance Imaging (fMRI).

(3) Results. Having type 2 diabetes increased responses to pictured foods in the insula, orbitofrontal cortex (OFC) and basal ganglia and within these regions, the effect of fat content of the foods was larger in participants with type 2 diabetes than in healthy controls. Furthermore, increased activation to food within the insula and OFC positively correlated with external eating, dietary self-efficacy and dietary self-care. In contrast, responses within subcortical structures (amygdala and basal ganglia) were positively correlated with emotional eating and rated appetite for the food stimuli and negatively correlated with dietary self-care.

(4) Conclusion/interpretation. Type 2 diabetes is associated with changes in brain responses to food that were modulated by dietary self-care. We propose that this is linked to the need to follow a life-long restrictive diet and these changes are related to dietary self-care.

Key words: Type 2 diabetes; food pictures; fMRI; Orbitofrontal cortex; Amygdala; insula; basal ganglia; self-efficacy; dietary restraint; dietary self-care

Abbreviations: BOLD: blood-oxygen-level dependent; DEBQ: Dutch Eating Behaviour Questionnaire; fMRI: functional Magnetic Resonance Imaging; OFC: orbitofrontal cortex

INTRODUCTION

Dietary self-care is the cornerstone of self-management in people with type 2 diabetes. To reduce the risk of developing both short- and long-term physical complications, patients are encouraged to reduce their caloric intake and to adopt a well balanced healthy diet, low in fat and sugar and high in fibre. However, many individuals with diabetes have difficulty in following this advice [1]. Moreover, those who do adhere to their dietary recommendations often report feeling deprived and having to deal with cravings for foods [2;3]. The disposition and incentive to eat not only increases during temporary deprivation of food but chronic restrictions on the diet in healthy people result in motivational, emotional and attitudinal changes that can lead to consumption of greater amounts of food and consequent weight gain [2;4;5].

Neuroimaging studies have shown that food stimuli elicit responses in regions of the human brain associated with motivation and/or emotion, such as the orbitofrontal cortex (OFC) [6-9], insula [6-10], basal ganglia and amygdala [6;7;10-12]. In particular, sensory stimuli in foods that are rated as pleasant to eat or are high in calories elicit larger neural responses in these regions [6;13-18].

However, these studies were carried out in healthy individuals. To our knowledge, there has been no investigation of the effects of living with type 2 diabetes on brain responses to food stimuli specifically in areas associated with motivation and emotion. Therefore, the main aim of the current study was to use functional magnetic resonance imaging (fMRI) to compare people with type 2 diabetes with a group of healthy matched controls for their responses to pictures of foods varying in contents of fat, sugar and size of portion and of non-foods visually matched pictures (Figure 1). In addition, as there is limited understanding of influences on the ability of individuals with type 2 diabetes to adhere to their dietary recommendations, we examined whether brain responses to food stimuli were related to measures of dietary self-care[19] and potential difficulties in adherence, in particular dietary self-efficacy [20] and dietary restraint [21].

Self-efficacy is the belief in one's ability to follow given courses of action – in this case, following dietary recommendations -- which has been shown to predict dietary self-care behaviour [20]. Dietary restraint is the conscious effort to limit food intake [21]. However, restrained eaters who lack effective strategies are liable to give up their efforts when faced with a challenge [4]. Such lapses could come from susceptibility to temptations to eat [external eating [4;22]] or from habits of using food in attempts to reduce distress [emotional eating [23]].

We hypothesised that the group with type 2 diabetes would show larger neural responses than the non-diabetic controls to the pictures of foods in brain regions known to be involved in learnt food sensory motivation and in diet-related emotionality and that these stronger activations would relate to scores for dietary self-care in diabetes and to measures of potential difficulties in dietary self-care such as external and emotional eating.

METHODS

Participants

Twelve participants with type 2 diabetes mellitus (1 left handed) and 12 age and BMI matched healthy controls without diabetes (1 left handed; see table 1 for details) were recruited through the diabetes clinic of the Endocrinology Department of the University Hospital Tübingen. None of the participants had a history of any neurological or psychiatric disorders. Selection criteria for participants with type 2 diabetes included: 1) being diagnosed with type 2 diabetes for at least 3 years, 2) no major changes in diabetes-related medication for the past 6 months, 3) no other major health problems. One participant with diabetes had an almost complete agenesis of the corpus collosum and the data collected from this participant were excluded from analysis.

To avoid peak postprandial hyperglycaemia occurring while in the scanner, we asked all participants not to eat for at least 3 hours before the scheduled scanning. They were fully informed about the nature of the study and signed a written consent form before participation. The study was approved by the Medical Ethics committee of the University of Tübingen.

Stimuli, task and procedure

Physical and psychological measures

Prior to fMRI scanning blood glucose levels were measured by finger prick method using an Accu-Check Aviva (Roche Diagnostics, Mannheim, Germany). Each participant's weight and height were measured in order to calculate BMI. Then each participant's current disposition to eat food was assessed by rating hunger on an analogue scale from not at all (scored 0) to very much (scored 10) and participants indicated time since last meal. HbA1c and treatment modality were obtained from the patient's hospital records (Table 1).

Patterns of emotional eating (desire to eat when in an emotional state), external eating (how tempted one is by food) and dietary restraint (how restrained one feels about eating) were assessed using the Dutch Eating Behaviour Questionnaire [21]. Participants with diabetes were assessed for dietary self-efficacy (DSE; [20]) and for dietary self-care activities over the 7 days preceding the study (DSCA; [19]).

Following scanning, participants rated the pictures of foods and non-foods (described below) on valence and arousal on a 1 (low) to 5 (high) self-assessment Manneken scale. The food pictures were also rated for desire to eat (appetite) on visual analogue scale ranging from 1 (not appetizing) to 5 (very appetizing).

Differences between two groups of participants concerning age, BMI, blood glucose, hunger ratings, DEBQ scores and post-scanning ratings (appetite, valence and arousal) were calculated using two-tailed independent samples t-test, assuming unequal variance. We used Matlab 7.2 and SPSS15 for statistical analysis.

fMRI experiment

Stimuli. 36 various food pictures and 36 non-food visually matched control pictures were used. Each food picture was paired with a non-food control picture matched for shape, complexity, brightness and colour (Figure 1). Non-food control pictures included images of

objects not related to food (e.g., plants, car, pillow, ball, furniture, etc.). Food pictures included images of fries, fried chicken, cakes, salads and fresh fruits for example. The healthy diet recommended for individuals with type 2 diabetes is based on decreased sugar, fat and overall food intake. Therefore, in order to test whether these factors modulate brain responses the foods depicted in the pictures varied in their contents of fat, sugar and in volume (portion size), these variations were quantified based on German food composition tables and validated by a dietician from the Diabetes Clinic at the University Hospital Tübingen.

Experimental procedure. During scanning the food and non-food stimuli were presented in a pseudo-random order using an event-related design. Each stimulus was presented for 2 sec followed by an inter-stimulus interval varied between 6 and 12 sec. Each stimulus was presented once. The experiment was split into 3 scanning sessions. Participants were instructed to look carefully at each presented picture during the scanning.

fMRI data acquisition. A Siemens 1.5 T scanner (Siemens Vision, Erlangen, Germany) equipped with a standard head-coil was used to acquire blood oxygenated level dependent (BOLD) contrast weighted echo-planar images (EPI) during the functional scans. 39 axial slices (4 mm thick with 1mm gap) were acquired with 64x64 pixels matrix and in-plane resolution of 3x3x5 mm^3, 90º flip-angle, 40ms echo time (TE) and 2 sec repetition time (TR). Subsequently to the functional scans, a high-resolution T1-weighted structural image (1*1*1 mm resolution) was acquired for co-registration and display of the functional data. The time of scanning was variable across participants though with no differences between groups ($p > 0.1$); diabetes time of testing ranged from 10:45 till 19:15, and controls ranged from 9:45 till 19:05.

Analysis of fMRI data. EPI volumes were spatially realigned and unwrap to correct for movement artefacts, transformed to the MNI standard space using and advanced segment-normalize procedure [24], and smoothed using a 9mm Gaussian kernel to account for residual inter-subject differences using SPM5 (Wellcome Department of Imaging Neuroscience, London;

www.fil.ion.ucl.ac.uk/spm). Finally, to improve signal-to-noise ratio an ICA analysis was performed using Melodic FSL(FMRIB, Oxford, UK) in order to identify artefacts that could not be explained by movement parameters with a frequency that was outside the stimuli frequency range (2-8Hz; [25]). For each session one ICA component was selected and used as a regressor of no interest in the subsequent analyses.

A whole-brain voxel-based analysis was performed with SPM5. For each participant we used general linear model to estimate the response for each condition. The experimental design matrix included a regressor depicting the onset of each condition (food/non-food) and covariates for the individual rating of arousal and valence for each picture. For the food condition we also included covariates that describe the fat content, sugar content, volume and individual appetite ratings. All these regressors were convolved with the canonical HRF (Haemodynamic Response Function, [26]) and their derivatives. Regressors of no interests included the movement parameters, the ICA component and harmonics that capture low frequency changes in the signal (i.e., high pass filtering 1/128Hz).

For each participant we computed contrast images representing the effect of stimuli (food versus non-food), main effect of volume, fat, sugar content, and of appetite ratings. In order to generalise to the population level, the resulting contrasts were used in a second level whole brain analysis with two sample t-test (type 2 diabetes versus control participants), with participants as random variables. Note, that in order to control for the possibility of diabetes-related vascular deteriorations, which could significantly affect the estimated BOLD responses, and for non specific effects of medication in participants with diabetes [27], comparison between groups were done only using interactions (i.e. the contrasts reflecting the differences between conditions within each participant, for example: food *versus* non-food, effect of the amount of fat in the food pictures). Finally, we also tested for correlations between brain responses that were modulated by self-reported adherence to dietary recommendations (DSCA), self-efficacy (DSE), DEBQ scores,

time since last meal and current disposition to eat, rated as 'hunger'. For the latter measure we used BMI and blood glucose levels as covariates. Unequal variance and independent sample were assumed in these models.

In accord with previous work on food-related stimuli, our regions of interest were OFC , insula , basal ganglia (putamen, caudate, nucleus accumbens) and amygdala . Note that for simplicity we did not differentiate substructures within our regions of interests. We report and interpret results based on the gross anatomical definition of these regions. We used a combined peak and cluster size threshold[28] with peak significance of $Z > 3$ ($P<0.0017$) at cluster size larger than 45mm at $P < 0.005$. Effects outside our region of interests and above our threshold are reported in the supplementary materials.

RESULTS

Eating pattern traits, current disposition to eat and appetite for pictured foods

Healthy controls and participants with diabetes did not differ significantly in scores on the DEBQ scales of emotional, external or restrained eating, or current disposition to eat rated as 'hunger' and in time since last meal ($p > 0.1$ in all cases).

Ratings of the visual stimuli after scanning differed between pictures of foods and non-food controls. Positive valence and arousal were both greater for food than for non-food, valence, $t(42.5) = -4.9$, $p < 0.0001$; arousal, $t(42.8) = -4.8$, $p < 0.0001$, but there were no significant differences between two groups.

In contrast, eating-specific ratings of food pictures showed an effect of group. Participants with type 2 diabetes rated food pictures as less appetizing, $t(17.7) = -2.3$, $p < 0.05$ (Table 1), with no difference in SD between groups (both 1.2 ± 0.3) (Table 1).

Blood glucose and BMI

Participants with diabetes had significantly higher levels of blood glucose than did controls who were matched in age and BMI, $t(12.7) = -3.15$, $p < 0.01$ (Table 1). This degree of hyperglycaemia has been found not to affect the BOLD contrast [29].. Blood glucose was not correlated with any of the above psychological measurements (all ps > 0.1), nor with the neural response to food versus no-food. BMI did not significantly differ between groups nor correlated with any of the above behaviour measurements (p > 0.1) and nor did it modulate brain responses to food (versus no-food) within our region of interests.

Activation of brain regions

Across all participants, larger responses to food stimuli when contrasted with non-food stimuli were observed in the right insula/operculum, left orbital frontal cortex (and at a lower threshold of significance (LTS) in the right OFC [33 54 -15], Z=2.62) and right basal ganglia (Table 2, Figure 2a-c) that extended to the left at lower threshold (MNI:[-6 12 -3], Z = 1.93). Interestingly, these food-specific responses within each of these regions were significantly greater in participants with type 2 diabetes than in controls (Table 2; Figure 2a-c). Exclusion of the two left-handed participants (1 control and 1 diabetes) did not alter these results, which concurs with the lack of significant lateralisation in brain responses when threshold was lowered. Therefore the results presented includes all participants regardless of handedness.

In addition, the fat content of the pictured foods had a larger effect on brain responses in participants with type 2 diabetes than in controls. This was observed in the left medial OFC extended bilaterally, left insula/operculum (and in the right, LTS [45 -15 15], Z=1.9), the left caudate (and in the right LTS, [24 -27 9], Z= 2.17) (Table 2) - regions partly overlapping with those showing the effect for food generally. Taking the two groups together, fat content had no reliable effect above threshold.

In contrast, across the groups, increased levels of sugar in the pictured foods correlated with increased responses in the right medial OFC and right caudate (Table 2) but the groups did not differ reliably in modulation by sugar content.

The volume of food did not modulate responses within our regions of interest, either across or between the groups, although volume greatly affected responses in visual cortex in both groups (Supplementary Table S2).

Across all participants, rated appetite for each food in the pictures correlated positively with responses to the food (versus no-food) stimuli, within the basal ganglia (putamen and nucleus accumbens; Table 2). This effect was larger for participants with diabetes than for controls in the caudate bilaterally (Table 2). In contrast, time since last meal did not modulate neural responses to food versus no-food in our pre specified regions of interest.

Relationships of brain activation to dietary management

To examine the role of food motivation in general and in dietary management in diabetes, we correlated the food-specific responses in the regions of interest with the psychological measures. Again for completeness we report results of whole brain voxel-based analysis in the supplementary materials (Tables S3-S6).

Responses to the food stimuli in the OFC, insula and left amygdala correlated positively across the two groups with ratings of current disposition to eat This effects was mostly pronounced in bilateral insula (left:MNI: [-42 -12 24], Z=3.21,cluster = 48mm; right:MNI: [42 -15 -6], Z= 2.96, cluster = 60mm; left OFC (MNI: [-15 36 -21], Z = 3.91, cluster > 900mm) and left amygdala (MNI: [-30 -3 -24], Z = 3.37, cluster = 228mm). Furthermore, responses of the bilateral medial OFC (MNI: [-9 60 -15], Z = 3.89, cluster = 360mm, Figure 3a) correlated with external eating, while activation by food stimuli in the right caudate (MNI: [18 0 9], Z = 3.4, cluster = 417mm) correlated with emotional/comfort eating (Figure 3b).

Finally, in participants with type 2 diabetes, food specific responses in the right OFC (r = 0.6) and left insula (r = 0.8) were positively correlated with dietary self-efficacy, i.e., confidence in ability to follow the dietary recommendations for type 2 diabetes (Table 3; Supplementary Figure 2a-b). In addition, responses of the right lateral OFC were positively correlated with scores for dietary self-care (r = 0.69; Table 3, Figure 4C), whereas the right amygdala (r = -0.79), left putamen (r = -0.83) and left nucleus accumbens (r = -0.78) each showed a negative correlation with dietary self-care (Table 3, Supplementary Figure 2d-e).

DISCUSSION

Our data indicate that people with type 2 diabetes show stronger activation to food pictures in the insula, OFC and basal ganglia structures than do non-diabetic controls. In addition, within these regions we found that the fat content of food stimuli had a larger effect on responses in participants with type 2 diabetes. An important finding of this study is that this increased activation to food within the insula and OFC correlated positively with dietary adherence, dietary self-efficacy and also with external eating. In contrast, activation in subcortical structures including amygdala, caudate, putamen and nucleus accumbens was positively correlated with emotional eating scores and rated appetite for the pictured foods and negatively correlated with dietary adherence. Such results indicate that type 2 diabetes is associated with changes in brain responses to food stimuli. These changes are associated with dietary self-care activities.

Involvement of insula and OFC and basal ganglia in responses to food pictures reported in this study and the correlation of this activity with rated hunger is consistent with previous reports. The insular cortex is a primary gustatory area [30;31]. and is also activated by the thought of tasting food, as evoked by deprivation of food [9;18;32;33]. Similarly, the OFC is well known as a secondary taste area and involved in the learnt integration of visual, gustatory and olfactory input

[30;31;34;35] and shows a decline of activation with eating ("sensory specific satiety"). Single cell recording studies show that neurons in the OFC (and in the amygdala) respond to the sight, taste and smell of food. This food-related neuronal activity varied with hunger and its satiation, implicating these cells in motivational processing of stimuli in foods [36-39].

Numerous neuroimaging studies also indicate that activation of regions within the basal ganglia (putamen, caudate and nucleus accumbens) is associated with food pleasantness and hunger-induced changes in desirability of foods [7;12;40;41]. Previous studies measuring brain responses in healthy participants have shown increases in responses in the insula, basal ganglia and OFC that are greater to high calorie food than to low calorie food [6;42;43]. This accords with our finding that the sugar content of the pictured foods modulated responses in the basal ganglia and medial OFC.

The most innovative contribution of the present study is analysis of relationships between food-specific activation and psychological processes relevant to healthy eating by participants with type 2 diabetes. Activation by the sight of food in the insular and OFC was positively correlated with external eating, predisposition to eat, dietary self-efficacy and dietary adherence. That is to say, these regions showed a larger response to food in individuals who were more tempted by food and yet also were more confident that they can deal successfully with dietary restrictions and hence adhered better to the recommended diet. The simplest interpretation of this pattern is that the strong response to food in the OFC and insula is associated with successful resistance to temptations to eat and better dietary adherence in consequence. This is in line with the proposal that the medial OFC restrains immediate desires in favour of long term outcomes [44-46]. In contrast, food-specific activation in subcortical structures including amygdala (greater in diabetes), caudate, putamen and nucleus accumbens was negatively correlated with dietary adherence. The activation in these structures correlated positively with rated appetite for the pictured foods and scores for emotional eating. Strong desire for food, and especially emotional

overeating, would be expected to disrupt adherence to dietary recommendations and so the obvious conclusion is that the amygdala and basal ganglia are critical to such difficulties in dietary self-management.

One line of interpretation is that success at dietary adherence, thereby boosting dietary self-efficacy, depends, in part, on inhibiting emotionally based eating responses to thoughts of the sensory attractions of foods, particularly items that reduce the healthiness of the diet because they are high in fat or sugar. Thus, success in diet adherence may depend on OFC inhibiting responses to food in subcortical structures, a role that is consistent with reports of OFC functions (cf.[47;48]. Support for such potential inhibition processes in diabetes comes from the finding that the ratings of appetite for food were lower in participants with type 2 diabetes than in the healthy group while BOLD responses to food were greater in many regions of the brain. This is readily explicable by appetite for food being more than the sensory and somatic motivation reflected in those activations. Some of the social motivation of eating those foods, especially of refusing them, is likely not to be captured by those brain responses. These findings may also point to differences between explicit and implicit food preferences in individuals with type 2 diabetes.

It is worth noting that participants in the control group had a longer period since their last meal than the participants with diabetes. Although this difference was not statistically significant and there were no differences in subjective hunger ratings between the groups, there remains the possibility that these time differences may have influenced the results and explain, in part, that the participants in the control group rated the food images as more appetising than those in the diabetes group. However, as mentioned above, despite differences in subjective report, brain activations to food stimuli in regions associated with reward were stronger in the diabetes group than in the control group. Together with the finding that brain activations were not found to be modulated by time since last meal, the pattern of results suggest that the impact of the differences in time since last meal may have been limited.

It is also important to note that our diabetes participants had a less than adequate control of their diabetes. Although blood glucose levels were not significantly related to any of the ratings or BOLD response within our regions of interest, it is possible that higher blood glucose levels may have affected the results. Further we note that previous literature have only indicated effects of reduced BOLD responses following hypoglycaemia[49]. In addition, participants with diabetes used a variety of different medications to control their diabetes and we cannot role out the possibility that these medications exert a specific effect on the BOLD responses. To our knowledge, there are no studies examining how various medications and hyperglycaemia affect the BOLD response and specifically whether it affects neural response to food stimuli. Further research is needed to examine these possible effects.

In summary, activation in response to food pictures in brain regions known to be involved in motivation and in emotion processing are stronger in participants having type 2 diabetes than in healthy participants. These regions also mediate adherence to dietary recommendations and dietary self-efficacy in diabetes, in particular the struggle to keep a healthy diet, especially by reducing fat intake. The observed pattern of activation relates in specific ways to the motivational, emotional and attitudinal changes that known to be associated with chronic restrictions on diet [4;5]. Further work on regional activation and connectivity, coupled with psychological investigation of the particular affective processes involved, is likely to improve understanding of difficulties in dietary adherence in type 2 diabetes. We suggest that similar alterations in motivation and emotion involved in eating could occur in other chronic disorders that require long-term dietary adjustments, such as cardiac disease and obesity and so could be barriers to successful management of the disease.

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Table 1.
Participants' characteristics and behavioural scores. Values are means (SD).

	Type 2 Diabetes N=11 (7M, 4F)	Control N=12 (9M, 3F)
Age (years)	55.4 (14.9)	46.6 (15.6)
BMI (kg/m^2)	32.9 (4.9)	30.4 (4.2)
Blood glucose (mmol/L)	7.70 (2.2)*	5.45 (0.86)
HbA1c (%)	7.59 (1.65)	N/A
Duration of diabetes (years)	6.3 (4.3)	N/A
Diabetes treatment		N/A
Tablets	N = 5	
Insulin	N = 2	
Insulin + tablets	N = 4	
Time since last meal (hours)		
Mean	2.7 (0.9)	4.3 (3.3)
Median	2.5	3.0
Current disposition to eat	5.55 (4.93)	7.24 (8.68)
DEBQ:		
Emotional Eating	0.88 (0.50)	1.14 (1.05)
External Eating	1.77 (0.41)	2.00 (0.78)
Restraint Eating	2.01 (0.58)	1.91 (0.59)
DSE	55.2 (25.2)	N/A

DSCA (*z*-scores)	-0.13 (0.60)	N/A
Food Pictures Ratings:		
Desire to Eat/Appetite	2.60 (0.74)**	3.22 (0.52)
Valence	2.99 (0.63)	3.27 (0.52)
Arousal	2.48 (0.58)	2.91 (0.57)
Control Pictures Ratings:		
Valence	2.34 (0.66)	2.23 (0.60)
Arousal	1.94 ± 0.68	1.93 ± 0.54

*P < 0.008; **P < 0.03; current disposition to eat = rated hunger; DSE= dietary self-efficacy [50]; [20] ; DSCA= dietary self-care adherence (based on SDSCS, [19]; DEBQ=Dutch Eating Behaviour Questionnaire [21].

Table 2. Brain responses for the main contrast of interests: food versus non-food, positive modulation by fat and sugar content, volume and appetite ratings

CONTRAST	BRAIN REGION																					
	INSULA					Med OFC					Lat OFC					Basal Ganglia					Amygdala				
	H	MNI			z-score	CS	H	MNI			z-score	CS	H	MNI			z-score	CS	H	MNI			z-score	CS
FOOD>NON-FOOD																								
Across groups	R	39	0	–21	3.44	150	L	-3	39	-27	3.57	90	L	-24	36	-21	4.22	579	R	6	12	-3	3.08 (NAc)	162
	R	48	-9	0	4.37	135																		
Diabetes>Control	R	48	-12	0	3.42	108	L	-9	36	-24	3.29	36	L	-36	27	-21	3.12	417	R	21	-3	27	3.26 (CA)	63
FAT MODULATION																								
Diabetes>Control	L	-48	-15	-3	2.79‡	15	L	-9	36	-24	3.29	36							L	-21	-24	21	3.38 (CA)	99
SUGAR MODULATION																								
Across groups							R	12	30	-18	3.11	111							R	18	3	24	3.20 (CA)	66

APPETITE MODULATION (rated appetite for food pictures)					
Across groups	R	30	-6	6	2.98‡ (PU)	48
	R	15	6	-12	2.86‡ (NAc)	48
Diabetes > Control	R	27	-6	30	3.53 (CA)	837
	L	-24	-30	18	3.11 (CA)	120
	L	-9	18	21	3.43 (CA)	408

Brain regions are based on the Duvernoy Human Brain Atlas and brain coordinates from the standardized MNI space; H-hemisphere; CS-cluster size (mm^3); Basal Ganglia: CA, caudate, PU, putamen, NAc, nucleus accumbens; All clusters of activation reported were threshold at $P < 0.005$ uncorrected, with clusters size larger than $45mm^3$ and z-score larger/equal than 3.00 (unless specified otherwise for clusters marked with ‡).

Table 3. Correlations between brain responses to food versus non-food and behavioural indices of dietary self-efficacy and dietary adherence

CONTRAST	BRAIN REGION																			
	INSULA					Med OFC				Lat OFC				Basal Ganglia				Amygdala			
	H	MNI			z-score	CS	H	MNI		z-score	CS	H	MNI		z-score	CS	H	MNI			z-score	CS
DSE (dietary self-efficacy)																						
Positive correlation	L	-27	21	-24	3.18	93	R	18	63	6	3.26	129						L	-30	-3	-24	3.37	22
							R	9	45	-18	2.93‡	102										
DSCA (dietary self-care adherence)																						
Positive correlation												L	-30	39	9	3.80	120						
Negative																		L	-12	6	-3	3.59	210	R	21	0	-18	3.01	48

correlation					(PU)	
	L	-24	-12	0	3.37 (PU)	123
	L	-6	12	-12	3.06 (NAc)	30

Brain regions are based on the Duvernoy Human Brain Atlas and brain coordinates from the standardized MNI space; H-hemisphere; CS-cluster size (mm^3); Basal Ganglia: CA, caudate, PU, putamen, NAc, nucleus accumbens; All clusters of activation reported were threshold at $P < 0.005$ uncorrected, with clusters size larger than $45mm^3$ and z-score larger/equal than 3.00 (unless specified otherwise for clusters marked with ‡).

FIGURE CAPTIONS

Figure 1. Examples of visually matched food (top panel) and non-food (bottom panel) pictures used as stimuli in fMRI experiment and associated measures used as covariates in data analysis.

Figure 2a-c. Left column coronal view of SPMs showing food versus non-food within OFC(a), insula (b) and basal ganglia (c). Yellow clusters show reliable increase responses for food versus no-food across groups; red clusters show larger responses in diabetes to food (versus no food) compared with controls. The plots on the right column represent the effects size of the difference between food versus no-food BOLD response in each region.

Figure 3a-b. Left column, coronal view of SPMs depicting significant correlations across groups between brain responses to food versus non-food and external eating behaviour within OFC (a) and with emotional eating behaviour in the basal ganglia (b). In the right column the brain responses (food *minus* no-food) of the above regions are plotted against the behavioural indices black triangles- control participants, red circles- participants with type 2 diabetes. LH- left-handed participants.

SUPPLEMENTARY FIGURES

Supplementary Figure 1a-c. In each group i.e. control participants and participants with type 2 diabetes there was one left-handed person. (a) Examining individual responses in the main results showed that the results were not driven by two left-handed participants as shown here for

main contrast of interest food versus no-food in left lateral OFC and right insula. Data analysis after excluding the two left-handed participants showed on changes in the main results. (b) Responses for food versus no-food across groups in OFC and insula: comparison between all participants and right-handed participants (data analysis excluding two left handed participants). (c) Increased responses for food versus no-food in type 2 diabetes in OFC and insula: comparison between all participants and right-handed participants (data analysis excluding two left handed participants).

Supplementary Figure 2a-e. Left column, coronal view of SPMs depicting significant positive correlations (red) with type 2 diabetes between brain responses to food versus non-food and self efficacy (DSE) in OFC (a) and insula (b); and with self adherence (DSCA) in OFC (c) and negative correlation with he latter (yellow) in putamen (d) and in amygdala (e). In the right column the brain responses (food *minus* no-food) of the above regions are plotted against the behavioural indices. LH- left handed participant.