Functional connectivity in obesity during reward processing

I. García-García a,b, M.A. Jurado a,b,c,⁎, M. Garolera c,d, M. Segura a,c, I. Marqués-Iturria a,b, R. Pueyo a,b,c, M. Vernet-Vernet e, M.J. Sender-Palacios e, R. Sala-Llonch a,c, M. Ariza a,b,c, A. Narberhaus a, C. Junqué a,c,f

a Department of Psychiatry and Clinical Psychobiology, University of Barcelona, Barcelona, Spain
b Institute for Brain, Cognition and Behaviour (IR3C), University of Barcelona, Barcelona, Spain
c Grup de Recerca Consolidat en Neuropsicologia (SGR0941), University of Barcelona, Barcelona, Spain
d Neuropsychology Unit, Hospital de Terrassa, Consorci Sanitari de Terrassa, Terrassa, Spain
e CAP Terrassa Nord, Consorci Sanitari de Terrassa, Terrassa, Spain
f Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

A R T I C L E   I N F O
Article history:
Accepted 12 October 2012
Available online xxxx

Keywords:
Obesity
Reward
Connectivity
Functional magnetic resonance imaging

A B S T R A C T
Obesity is a health problem that has become a major focus of attention in recent years. There is growing evidence of an association between obesity and differences in reward processing. However, it is not known at present whether these differences are linked exclusively to food, or whether they can be detected in other rewarding stimuli. We compared responses to food, rewarding non-food and neutral pictures in 18 young adults with obesity and 19 normal-weight subjects using independent component analysis. Both groups modulated task-related activity in a plausible way. However, in response to both food and non-food rewarding stimuli, participants with obesity showed weaker connectivity in a network involving activation of frontal and occipital areas and deactivation of the posterior part of the default mode network. In addition, obesity was related with weaker activation of the default mode network and deactivation of frontal and occipital areas while viewing neutral stimuli. Together, our findings suggest that obesity is related to a different allocation of cognitive resources in a fronto-occipital network and in the default mode network.

© 2012 Published by Elsevier Inc.

Introduction

Obesity is a health problem that has received a great deal of attention in recent years. There is evidence that it may be related to abnormal processing of rewarding stimuli (Kenny, 2011). A growing body of research into the neurobiological bases of reward suggests that distinct, but interconnected, neural systems work together to support sensory, cognitive and emotional processes associated with stimulus valuation (Haber and Knutson, 2010; Ikemoto, 2010).

The literature on obesity has focused mainly on the neural responses to food by using functional neuroimaging. The response to visual food stimuli is of particular interest. The sight of food activates a set of preparatory physiological responses that will likely determine intake. Studies comparing individuals with obesity and normal-weight controls have found functional alterations in the obese persons in several brain structures. A large core of evidence points to the existence of enhanced activity of basal ganglia, amygdala, insula and orbitofrontal cortex (Nummenmaa et al., 2012; Rothemund et al., 2007; Stoeckel et al., 2008), as well as inhibited responses in lateral and medial prefrontal areas (Batterink et al., 2010; McCaffery et al., 2009; Nummenmaa et al., 2012; Page et al., 2011). However, some of the results are contradictory. For example, at least one study did not find any differences in the neural response between obese subjects and controls (Murdaugh et al., 2012), and other studies failed to find an exacerbated (Cornier, 2009) or blunted responses (Stoeckel et al., 2008) associated with obesity. Methodological differences in the paradigms used, as well as the intrinsic heterogeneity attributed to obesity, may account for the discrepancies in the results; in general, more research is needed to elucidate the effects of rewarding responses to food on overeating and obesity.

So far, only one study has examined the neural response to rewarding stimuli other than food associated with obesity. Stice et al. (2011) compared the activation of reward circuitry in response to receipt and anticipated receipt of food and monetary reward in two groups of normal-weight young people: a group at high risk for obesity (defined as having two parents with excess weight) and a low risk group (participants with two lean parents). They found that individuals at risk for obesity showed hypersensitivity of the striatum to reward in general, and elevated activity in somatosensory regions in response to palatable, energy-dense food. To date, however, no studies have compared the response of participants with obesity and normal-weight individuals to rewarding non-food stimuli.

Functional MRI (fMRI) is well suited to the study of patterns of brain activity. Interestingly, and specifically with regard to Independent Component Analysis (ICA), fMRI is able to capture hidden,
underlying and statistically independent source signals among the hypercomplex organization of the human brain (Beckmann, 2012; Calhoun et al., 2009). This method allows obtaining spatial patterns of networks consisting in sets of brain regions that share common functional activity measured with BOLD signal fluctuations. ICA is a data-driven method, and the obtained patterns do not depend on the model specification by the user. Therefore, this characteristic makes it appropriate in studies where the task contains an elevated number of conditions (i.e. sources of activity). The ICA technique has been shown to provide similar results to standard model-based general linear model approaches (Calhoun et al., 2001) and in some cases it can isolate patterns of activation that cannot be generated by general linear model approaches (Beckmann and Smith, 2004). ICA has been used for a variety of task-fMRI studies including those investigating recognition memory (Barret et al., 2011), verbal generation (Karunanayaka et al., 2010), verbal comprehension (Karunanayaka et al., 2007; Schmithorst et al., 2006), working memory (Palacios et al., 2012) and music perception (Schmithorst, 2005).

Close to the present study, two works have examined differences in the connectivity of functional networks related to Body Mass Index. The first study found that, compared with lean subjects, obese participants had increased connectivity of the default mode network (DMN) in a visual activation task (Tregellas et al., 2011). The DMN includes cortical midline regions such as the anterior medial prefrontal cortex, posterior cingulate cortex, precuneus and inferior parietal cortex (Fox et al., 2005). The second study tested the effect of stimulus category (food versus non-food stimuli) and body-weight (overweight and obese versus lean individuals) on the functional connectivity of networks (Kullmann et al., 2012). They found that the extrastriate visual network, which includes the cuneus, calcarine gyrus and inferior parietal cortex, showed higher correlation for the food than for the non-food condition. Moreover, its connectivity was decreased in the group of participants with excess weight. In addition, the salience network, which is formed mainly by the insula and the anterior cingulate cortex, showed an increased response to food stimuli in participants with excess weight. The previous evidence thus suggests the existence of alterations in functional connectivity networks in food reward tasks. However, it is unknown whether the differences observed are exclusively associated with food stimuli, or whether rewarding stimuli other than food may be related to differences between functional networks in obese and normal-weight participants.

The aims of this paper were twofold: 1) to examine whether participants with obesity and normal-weight controls differ in brain activity patterns associated with rewarding stimuli, by using task-based independent component analysis; 2) to investigate whether the differences depend on the type of reward; specifically, to examine whether or not the differences are exclusive to food stimuli.

Materials and Methods

Participants

Thirty-seven participants (participants with obesity = 18; normal-weight participants = 19) aged 21–40 years (64.8% women) were included in the study (see reasons for exclusion below). They were recruited from public medical centers belonging to the Consorci Sanitari de Terrassa. The study was approved by the institutional ethics committee (Comissió de Bioètica de la Universitat de Barcelona (CBUB); Institutional Review Board IRB 00003099 assurance number: FWA00004225, http://www.ub.edu/recerca/comissiobioetica.htm) and was conducted in accordance with the Helsinki Declaration. Written informed consent was obtained from each participant prior to taking part in the study.

As described in a previous study which shared a large part of the sample (Garcia-Garcia et al., 2012) potential participants were excluded from the study if they had a history of any neurological or psychiatric disorder, a history of any disorder that could be related to obesity, such as thyroid pathology, if they presented diabetes, hypertension, hyperglycemia, high levels of triglycerides or cholesterol, and if they showed global cognitive impairment (estimated IQ below 85, assessed with the Vocabulary subtest of the Wechsler Adult Intelligence Scale 3rd edition [WAIS-III]). The presence of anxiety, depression or binge-eating disorder was also an exclusion criterion; these were evaluated with the Hospital Anxiety and Depression Scale (HADS) and the Bulimia Inventory Test of Edinburgh (BITE) respectively. A cut-off score of 11 was applied to each scale of the HADS (Herrero et al., 2003), and a cut-off of 20 was used in the BITE (Henderson and Freeman, 1987). Pathological use of alcohol and/or drugs was evaluated using the Structural Clinical Interview for DSM-IV (SCID-I), and tobacco habits were also recorded. Participants were excluded if alcohol and/or drug abuse were detected.

Finally, participants were included in the obesity group if their Body Mass Index (BMI) was equal to or higher than 30 and in the normal-weight group if their BMI was between 18.5 and 25.

Three subjects were not entered in the analysis: two who had not completed the fMRI task successfully, and one for presenting outlying scores which compromised the consistency of the Independent Component Analysis results.

Motivation variables were closely controlled. First, to ensure that all participants were in a similar state of motivation, they were asked to refrain from eating or drinking for between three and five hours previously. Second, prior to the scan, participants rated their subjective hunger perceived on a 10 cm visual analogue scale (VAS). Time fasting (hours) was recorded, and they were asked to describe their last meal before the scan session. We determined the mean caloric intake prior to scanning by an Internet-based database (http://www.bedca.net). Other data related to their regular diet, such as frequency of fruit and vegetable intake, were also recorded. For female participants we calculated the current phase of the menstrual cycle. Third, immediately after the scan, participants were asked to rate all images presented during the fMRI in terms of how much they liked it, on a 1–10 Likert scale, with higher scores indicating greater liking.

MRI acquisition

Data were acquired on a 3 Tesla TIM TRIO 3 T scanner (Siemens, Germany) at the Hospital Clinic in Barcelona. During the fMRI protocol, 210T2-weighted volumes were obtained using multi-slice gradient-echo EPI sequence [repetition time (TR): 2000 ms; echo time (TE): 30 ms; 36 × 3 mm axial slices providing whole brain coverage].

A T1-weighted structural image was also acquired for each subject with the MP-RAGE 3D protocol (TR: 2300 ms; TE: 2.98 ms; inversion time: 900 ms; FOV: 256 mm × 256 mm, 1-mm isotropic voxel).

Task

Our protocol was inspired by typical designs of food reward (e.g. Killgore et al., 2003; Rothemund et al., 2007), but included modifications, such as number of categories, related to our aims. Visual stimuli consisted of 128 color photographs classified in four categories: food stimuli (both salty and sweet flavor), and subdivided in two categories: high-calorie food [n = 32] and low calorie food [n = 32], neutral non-food stimuli [n = 32; e.g. furniture, and office objects] and rewarding non-food stimuli (n = 32; e.g., puppies, babies, beautiful landscapes and images showing social reward, like people hugging).

Stimuli were selected from an initial pool of 400 photographs. We performed a previous experiment in students of Psychology (n = 39, 206
-aged 22.36 ± 4.44 years, 90% women) who voluntarily rated each picture on a 1–7 Likert scale (with scores of 1 considered as neutral and 7 considered as highly rewarding). For rewarding pictures, that is, pictures included in the high calorie food, low calorie food, and rewarding non-food stimuli categories, we selected the ones which were most positively rated. For the neutral non-food stimuli category we selected the pictures rated most neutral.

Functional imaging was performed while the two groups viewed visual stimuli. Images were presented inside the scanner with VisualStim digital MRI Compatible High Resolution Stereo 3D glasses (Resonance Technology, Inc) and Presentation® software (http://www.neurobs.com) running on Windows XP. We used a block paradigm in which each block corresponded to one category of stimuli, which was repeated four times. The blocks contained eight pictures, and each picture was displayed for two seconds. A fixation cross appeared for ten seconds between blocks. Total task duration was seven minutes (Fig. 1).

To ensure that participants paid attention to the task, they were told to press a button located on the right hand side if the image contained a red element, and to press a button on the left hand side if there were no red elements in the image. Percentage of correct responses, number of errors and reaction time were recorded. Participants were excluded from the study if they did not achieve a minimum of correct responses.

The rates for liking obtained after the MRI scan were also analyzed. In addition, a 4 (conditions of the task) x 2 (group) repeated measures ANCOVA was carried out to examine differences in conditions and their interaction with the group. Post-hoc analyses were conducted using the Sidak adjustment for multiple comparisons. Degree of hunger was controlled in all analyses. Statistical analyses were performed using PASW® Statistics v.18.

fMRI analysis with MELODIC

A tensor-ICA (TICA) decomposition of the fMRI datasets was conducted as implemented in MELODIC tool (Beckmann and Smith, 2004) version 3.05, part of the FSL software (http://www.fmrib.ox.ac.uk/fsl/) in order to find common spatio-temporal patterns of signal oscillations.

First, each fMRI dataset was corrected for motion using MCFLIRT (Jenkinson et al., 2002). Then, non-brain voxels were removed using BET (Smith et al., 2002), spatial smoothing with a Gaussian kernel of FWHM = 6.0 mm was applied, and the entire 4D dataset was normalized using the grand mean intensity. High pass temporal filtering (sigma = 208 s) was used in order to restrict for task-related temporal patterns, and 4D sets were finally registered to the MNI152 template.

After this preprocessing, fMRI analysis of the task was carried out using TICA. MELODIC decomposes data into a set of Independent Components (ICs), where each IC is composed of three-dimensional sets of vectors which describe signal variation across the temporal domain (time-series), the spatial domain (spatial maps) and the subject domain (subject modes).

A general linear model matrix was introduced in order to model the task time-series and to evaluate components related to each of the eight following contrasts: 1) High calorie food > Low calorie food; 2) High calorie food < Low calorie food; 3) All food stimuli > Neutral non-food stimuli; 4) All food stimuli < Neutral non-food stimuli; 5) All food stimuli > Rewarding non-food stimuli; 6) All food stimuli < Rewarding non-food stimuli; 7) Rewarding non-food stimuli > Neutral food stimuli; 8) Rewarding non-food stimuli < Neutral non-food stimuli.

Spatial maps of each IC were then thresholded using a Gaussian/ gamma mixture model and represented on the MNI standard template. While spatial maps include regions of synchronous activations and deactivations, subject modes reveal the strength of both these activations and deactivations. Higher subject mode values indicate higher activations and higher deactivations of the positive and negative parts of an IC respectively (Beckmann and Smith, 2004).

In order to examine differences between groups, we introduced a general lineal model matrix modelling the two groups of participants (obese and normal-weight). Post-hoc analyses were performed by regression of the individual scores against the defined subject’s general lineal model. Thus, the subject score obtained with MELODIC refers to the whole large-scale brain network represented by each component.

fMRI analysis with FEAT

The same pre-processing of the fMRI data as described in the previous section was effectuated. Then, model-based fMRI data processing was carried out using FEAT (FMRI Expert Analysis Tool) part of the FSL. Higher-level analysis was carried out using FLAME (FMRI’s Local Analysis of Mixed Effects) (Beckmann et al., 2003; Woolrich et al., 2004). This analysis was carried out in order to prove validity of the ICA results, thus, only the contrasts All food stimuli > Neutral non-food stimuli and Rewarding non-food stimuli > Neutral non-food stimuli were modelled. Statistic images were considered significant at a corrected cluster threshold of p ≤ .05.

Results

Demographical data

Demographical characteristics of the sample are summarized in Table 1. Groups were similar in age, gender, years of education, vocabulary subtest score from the WAIS-III, anxiety, depression and toxic habits. Focusing on participants who smoke or who drink alcohol, the frequency of cigarettes per day and frequency of alcoholic units per day was also similar between the groups of obese and normal-weight participants (cigarettes per day: obese, 13.67 ± 8.12; normal-weight, 15.00 ± 5.77; p = .79; alcohol units per week: obese, 2.57 ± 1.72; normal-weight: 5.91 ± 4.76; p = .10).

They differed in Body Mass Index and on the symptom scale from the BITE test.

![Fig. 1. Schema of the task design.](dx.doi.org/10.1016/j.neuroimage.2012.10.035)
Motivational variables

Participants with obesity reported a lower subjective feeling of hunger than normal-weight participants. In addition, two normal-weight participants reported having fainted more than five hours. Nonetheless, we did not find differences in number of hours fasting between groups, nor in the estimated calorie intake of the last meal (Table 2). To control for the possible effect of this confounding factor, subjective degree of hunger was included as a covariate in all analyses.

The frequency of female participants in each menstrual phase was similar in the two groups (p = 0.26). Additionally, we calculated the frequency of participants scanned before (09:00–13:00 a.m.), during (13:01–16:00), and after (16:01–20:30) regular lunch time in Spain. The Chi squared test did not identify differences between participants with obesity and normal-weight participants for this variable (p = 0.483).

Using a multivariate analysis of variance, we also tested for the possible effect of time of the day in which the scanner was performed (before, during and after lunch time) and its interaction with the group (obesity and normal-weight) on the following appetite-related variables: degree of hunger perceived, liking of high calorie food and liking of low calorie food. Neither time of the day nor its interaction with group were significant (not even marginally in either case, p > 0.1) (Table S1).

Performance on fMRI activation task

The percentage of correct responses in both groups was high (around 91%), indicating that participants were attentive to the task (see Fig. 2 and supplementary material table S2). The two groups behaved similarly on the task. An effect of condition was found for the following variables: errors in the task, reaction time and rate for liking of low calorie food. Neither time of the day nor its interaction with group were significant (not even marginally in either case, p > 0.1) (Table S1).

fMRI results: MELODIC

Decomposition of the fMRI dataset produced 17 different activation patterns of connectivity. We selected the first three components, IC1, IC2 and IC3, based on the following criteria: first, these components had the highest correspondence with the temporality of the stimuli and the highest Z value; second, they showed a consistent effect across the group because their standardized subject scores were not likely to be driven by outliers; third, they did not represent known artifacts such as noise, motion or venous pulsation (see Fig. 3 and supplementary material table S3 for information on each component).

The TICA analysis revealed a main task-related component, IC1, which was associated with the following contrasts of interest: High calorie food > Low calorie food (p = 0.006); All food stimuli > Neutral non-food stimuli (p < 0.001); All food stimuli > Rewarding non-food stimuli (p = 0.004); Rewarding non-food stimulus > Neutral non-food stimuli (p < 0.001).

The spatial map of the IC1 included bilateral activation of the occipital lobe, lateral prefrontal cortex, medial prefrontal cortex and precentral gyrus. It also included deactivation of precuneus and lateral occipital cortex bilaterally. Deactivation was labeled as posterior DMN.

We found differences between groups in this component, with the IC1 being stronger in normal-weight participants than in obese participants (p = 0.016).

The second activation pattern, IC2, was associated with the following contrasts: All food stimuli > Neutral non-food stimuli (p = 0.015) and Rewarding non-food stimuli > Neutral non-food stimuli (p = 0.010).

The spatial map of the IC2 seemed to show an inverse pattern of activity with respect to the IC1. It included activation in the paracingulate gyrus and anterior cingulate gyrus, precuneus, posterior or cingulate cortex and lateral occipital cortex. We labeled this pattern as DMN. It also included deactivation in lateral occipital cortex, precentral gyrus and inferior frontal gyrus. This component was stronger in normal-weight participants than in participants with obesity (p = 0.024).

The time series of the IC3 were associated with the following contrasts: High-calorie food > Low calorie food (p = 0.036); All food stimuli > Neutral stimuli (p = 0.001); Rewarding non-food stimuli > Neutral stimuli (p < 0.001). Activated regions included lateral occipital cortex and fusiform gyrus. There were no group differences in this component.

Table 2

<table>
<thead>
<tr>
<th></th>
<th>Participants with obesity (n = 18)</th>
<th>Normal-weight participants (n = 19)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hr fasting</td>
<td>3.86 ± 0.82 (3–5.5)</td>
<td>4.49 ± 2.74 (3–12)</td>
<td>−0.932</td>
<td>0.358</td>
</tr>
<tr>
<td>Caloric content (kcal) of the last meal</td>
<td>373.53 ± 250.87 (63–948)</td>
<td>419.37 ± 231.51 (35–780)</td>
<td>−0.578</td>
<td>0.567</td>
</tr>
<tr>
<td>Hunger perceived (kcal)</td>
<td>2.78 ± 2.32 (0–7.3)</td>
<td>4.76 ± 2.53 (0.1–8.4)</td>
<td>−2.482</td>
<td>0.018</td>
</tr>
<tr>
<td>Frequency of ingestion of high calorie food per week</td>
<td>3.56 ± 1.95 (1–7)</td>
<td>3.37 ± 2.39 (0–9)</td>
<td>0.338</td>
<td>0.737</td>
</tr>
<tr>
<td>Frequency of ingestion of fruits and vegetables per week</td>
<td>18.22 ± 9.94 (1–47)</td>
<td>18.59 ± 6.53 (9–33)</td>
<td>−0.130</td>
<td>0.907</td>
</tr>
</tbody>
</table>

Note: All values are mean ± SD (range).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Participants with obesity (n = 18)</th>
<th>Normal-weight participants (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34.78 ± 4.45 (22–39)</td>
<td>32.00 ± 5.87 (21–40)</td>
</tr>
<tr>
<td>Gender (women/men)</td>
<td>13/5</td>
<td>11/8</td>
</tr>
<tr>
<td>Years of education</td>
<td>13.22 ± 2.84 (10–20)</td>
<td>14.32 ± 2.34 (10–18)</td>
</tr>
<tr>
<td>Vocabulary (scalar score)</td>
<td>11.56 ± 2.36 (8–16)</td>
<td>11.68 ± 1.53 (9–15)</td>
</tr>
<tr>
<td>Body Mass Index**</td>
<td>34.89 ± 4.78 (30.1–48.58)</td>
<td>22.44 ± 1.93 (19.53–24.97)</td>
</tr>
<tr>
<td>Symptom scale BITE***</td>
<td>9.22 ± 4.58 (1–18)</td>
<td>2.47 ± 2.08 (0–8)</td>
</tr>
<tr>
<td>Anxiety scores (HADS)</td>
<td>4.00 ± 2.57 (1–10)</td>
<td>4.95 ± 3.24 (0–10)</td>
</tr>
<tr>
<td>Depression scores (HADS)</td>
<td>1.06 ± 1.31 (0–5)</td>
<td>1.00 ± 1.41 (0–8)</td>
</tr>
<tr>
<td>Use of tobacco (smokers /non-smokers)</td>
<td>6/12</td>
<td>4/15</td>
</tr>
<tr>
<td>Intake of alcohol (drink alcohol /do not drink alcohol)</td>
<td>7/11</td>
<td>11/8</td>
</tr>
<tr>
<td>Sporadic use of drugs (use drugs / do not use drugs)</td>
<td>1/17</td>
<td>1/18</td>
</tr>
</tbody>
</table>

Note: Except for sex, use of tobacco, intake of alcohol and sporadic use of drugs all values are mean ± SD (range).

** p < 0.01.
The pattern of activation by group on the contrasts All food stimuli > Neutral non-food stimuli and Rewarding non-food stimuli > Neutral non-food stimuli can be consulted in the supplementary material Fig. S1 and Table S4. In the first contrast, participants with obesity showed activation of the occipital lobe, superior frontal gyrus, paracingulate gyrus and superior frontal gyrus. Controls showed a similar pattern of activation also extended to cerebral stem. Regarding the activation pattern of the second contrast, participants with obesity show regional activation in the occipital lobe and angular gyrus. The normal-weight group showed a similar pattern also involving the inferior frontal gyrus, paracingulate gyrus, medial prefrontal cortex, cerebral stem and frontal pole. The group comparison using model-based fMRI analysis did not yield significant differences between groups.

Discussion

The present study compared behavioural and neural responses to food stimuli, non-food rewarding stimuli and neutral stimuli between participants with obesity and normal-weight subjects. In both groups, we identified activation of visual and frontal areas and deactivation of the DMN in response to rewarding stimuli, both food and non-food. However, the overall strength of connectivity within these networks was weaker in participants with obesity. Conversely, the presentation of neutral stimuli was linked with activation of the DMN and deactivation of occipital and frontal areas. Strength of connectivity within these networks was reduced in participants with obesity. The findings are novel and add evidence for the effect of obesity on brain activity in a reward-related network and in the DMN.

There is compelling evidence that emotion, which as a concept comprises reward, facilitates and potentiates perceptual processes and attention (Bocanegra and Zeelenberg, 2009; Dominguez-Borras et al., 2009; Phelps et al., 2006). In the present paper, processing of rewarding stimuli was associated with a higher connectivity of the IC1, a network involving frontal and occipital areas. More specifically, areas fundamental for basic processing of the environment were implicated, such as occipital areas, structures involved in selective attention, working memory, preparatory set and monitoring such as the inferior frontal gyrus (Fuster, 2002) and areas with an important role in appraisal and decision-making processes such as the paracingulate cortex (Barbeau and Patterson, 2011). The spatial map of the IC1 (Fig. 3 and supplementary Table S3) was in coherence with the regional maps of activity obtained when contrasting rewarding versus neutral stimuli (supplementary Fig. S1 and supplementary Table S4). However, unlike the ICA analysis, the regional analysis failed to detect differences between groups. With model-based analyses (e.g. analysis with FEAT), activation may be underestimated, whereas the model-free techniques (e.g. analysis with MELODIC) provide richer description of the data showing additional processes of interest (Beckmann and Smith, 2004). In agreement with previous studies (e.g. Ilharretxe-Bilbao et al., 2011), our results show that ICA analysis is more sensitive than regional model-based methods.

The processing of reward was also related to connectivity deactivation in prefrontal and lateral occipital gyri, which together form the posterior part of the DMN (Grecius et al., 2004). This pattern is highly consistent with the finding that reductions in the DMN typically occur in association with increased activation in task-relevant regions (Fox et al., 2005).

Participants with obesity showed weaker connectivity in the IC1, that is, blunted activation in frontal and occipital areas and less deactivation of the posterior part of the DMN. On the one hand, this result is consistent with a previous report of decreased strength of connectivity in the extrastriate network in subjects with excess weight (Kullmann et al., 2012). The extrastriate network and the IC1 obtained here shared involvement of visual areas. However, the IC1 included also lateral and medial frontal areas. On the other hand, a previous study of connectivity also reported a failure in deactivation of the DMN in participants with obesity during a visual activation task (Tregellas et al., 2011). Activity in the DMN is thought to underlie task-irrelevant thoughts (McKiernan et al., 2003) as well as self-referential thoughts (Raichle et al., 2001). Taken together, our findings support previous reports that obesity may be related to a lower level of recruitment of cerebral regions that subserve basic and higher perceptual processes. These results may suggest an alteration in processing of reward in obesity not only linked to food but extending to other types of positive reinforcements. Given that the functional network IC1 involves activation in regional areas with an important role in attentional processes, it is tempting to speculate that obesity may be associated with differences in the integration of attention resources in response to reward; however, this hypothesis needs to be tested with specific methodologies, such as the attention network task (Fan et al., 2005).

Studies examining behavioural responses to rewarding stimuli other than food in obese and normal-weight subjects may provide additional support to the hypothesis of a generalized abnormal processing of reward in obesity. These papers suggest that participants with obesity have more difficulty in delaying gratification (Davis et al., 2010; Verdejo-Garcia et al., 2010). Regarding behavioural bias to food cues in obesity, the results are somewhat contradictory (for a review see Nijs and Franken, 2012). Some studies reported that participants with obesity paid greater visual attention to food images than to non-food images (Castellanos et al., 2005). However, results...
reported by Loeber et al. (2005) indicate that not only obese but also normal-weight controls showed an approach bias for food stimuli, without differences between groups. Thus, behavioural data suggest that obesity may be associated with cognitive bias towards food and non-food rewarding stimuli, although some of the results are contradictory. Caution should be taken when comparing results in our behavioral task with previous literature examining emotional bias, since our task was a relatively simple attention test and was used to demonstrate that participants were attentive to stimuli rather than to investigate cognitive bias per se. However, in agreement with Loeber et al. (2005), the behavior in the two groups was equivalent. High and low calorie food conditions elicited more errors in both groups. There were more errors in the rewarding non-food blocks compared with neutral stimuli, but fewer than for high-calorie food. Reaction times were also slower for food and rewarding non-food pictures.
than for neutral stimuli, and slower too for rewarding stimuli than for food. There were no differences between groups. These results are perhaps indicative that, when viewing rewarding cues, participants sacrificed the detection of fine visual details (identification of the red color) for the processing of coarse information, an effect described in other papers on emotional bias (Bocanegra & Zeelenberg, 2009).

Perhaps surprisingly, participants with obesity showed a lower hunger perceived than normal-weight controls (Table 2), and this result was independent of the time of the day in which the scanner was performed (supplementary Table S1). This difference in hunger perceived is in agreement with several studies indicating that the excess of energy intake in obesity is partly explained by the behaviour of eating in the absence of hunger (e.g. Hill et al., 2005; Tanofsky-Kraff et al., 2008). The subjective degree of hunger was included as a covariate in all analyses, thus, differences observed in obesity seem to be independent from this factor. In addition to this, it might seem logical that participants with obesity would show increased subjective rating of food stimuli liking. However, the analysis showed no group differences (supplementary Table S2). By reviewing other works in obesity close to the one presented here that included subjective rates for liking, appetite or pleasure of food stimuli, we found that the majority of papers did not report group differences (e.g. Dimitropoulos et al., 2012; Frank et al., 2005; Nummenmaa et al., 2012; Rothmund et al., 2007; Scharmüller et al., 2012). Only Stoeckel et al. (2008) found a group x category interaction, which showed that obese’s individual ratings for high calorie foods were higher than their ratings of low calorie foods. So, previous literature seems to be inconsistent on this issue, perhaps due to the large amount of confounders inherent to research on obesity (e.g. differences in age, gender or the presence of other vascular risk factors). We understand that the results presented here are suggestive of differences in reward processing associated to obesity but evident only at the neural level.

Compared with rewarding stimuli, viewing neutral pictures was associated with activation of the DMN and deactivation in lateral frontal areas and the visual cortex. Participants with obesity also obtained weaker connectivity in this component. This result probably suggests that obesity is associated with differences in a task-relevant network and in the DMN when shifting attention to rewarding and neutral pictures. Difficulties in recruiting the task-relevant and DMN regions in an efficient manner have been detected in neuropsychiatric disorders associated with disturbances in impulse-control, such as drug addiction (Roberts and Garavan, 2010) and attention deficit hyperactivity disorder (Christakou et al., 2012).

The current study does have a number of limitations that need to be acknowledged. Although we discussed on the functions developed by the elements that conform the functional networks IC1 and IC2, we do not have direct evidences on the contribution the individual parts of these networks. However, the main conclusion of the paper refers to the global components obtained with the ICA analysis and not to its regional elements. Studies have previously reported evidences for differences in somatosensory processing in obese subjects (Wang et al., 2002). However, we did not evaluate visual sharpness systematically, which could have biased results. Nevertheless, we excluded pathological processes related to severe obesity that can impair vision, such as thyroid pathology or presence of diabetes.

Conclusions

In summary, we present the first fMRI study comparing the response to food, rewarding non-food stimuli and neutral stimuli in young adults with obesity and normal-weight participants using independent component analysis. The groups behaved similarly on the task and modulated activity in visual and frontal areas and in the DMN in a plausible way. However, in response to both food and non-food rewarding stimuli, participants with obesity showed weaker connectivity in a network involving activation of frontal and occipital areas and deactivation of the posterior part of the DMN. This finding has two implications. First, obesity seems to be associated with differences in the integration of cognitive resources in response to reward. Second, the differences may be generalized to positive reinforcements other than food. In addition, neutral stimuli elicited weaker connectivity in a network involving activation of the DMN and deactivation of frontal and occipital areas in obesity. Taken together, the findings suggest that obesity is related to differences in the allocation of cognitive resources in visual and frontal areas and in the DMN.

Conflicts of interest statement

None to declare.

Acknowledgments

The authors thank all the participants in the study without whose support the work would not have been possible. They also thank Encarnación Tor for her invaluable help in performing all blood analyses. This work was supported by the grant PSI2008-05803-C02-01/PSIC to Dr. María Ángeles Jurado Luque from the Ministerio de Ciencia e Innovación, and a FI-DGR 2011 grant to Isabel García-García from the Generalitat de Catalunya.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.neuroimage.2012.10.035.

References

Christakou, A., Murphy, C.M., Chantilucu, R., Cubillo, A.I., Smith, A.B., Ciampietro, V., Daly, E., Ecker, C., Robertson, D., MRC AIMS consortium, et al., 2012. Disorder-specific functional abnormalities during sustained attention in youth with attention deficit hyperactivity disorder (ADHD) and with autism. Mol. Psychiatry http://dx.doi.org/10.1038/ mp.2011.185.

Please cite this article as: García-García, I., et al., Functional connectivity in obesity during reward processing, NeuroImage (2012), http://dx.doi.org/10.1016/j.neuroimage.2012.10.035


Kullmann, S., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumoto, M., Matsumoto, K., Matsumot