Available online at www.sciencedirect.com
SCIENCE DIRECT
Behavioural Brain Research 169 (2006) 111–119
BEHAVIOURAL BRAIN RESEARCH
www.elsevier.com/locate/bbr

Research report

Cerebral processing of food-related stimuli: Effects of fasting and gender

Rudolf Uher*, Janet Treasure, Maike Heining, Michael J. Brammer, Iain C. Campbell

King's College London, Institute of Psychiatry PO59, DeCrespigny Park, London SE5 8AF, UK

Received 30 October 2005; received in revised form 17 December 2005; accepted 23 December 2005
Available online 30 January 2006

Abstract

To maintain nutritional homeostasis, external food-related stimuli have to be evaluated in relation to the internal states of hunger or satiety. To examine the neural circuitry responsible for integration of internal and external determinants of human eating behaviour, brain responses to visual and complex gustatory food-related stimuli were measured using functional magnetic resonance imaging in 18 healthy non-smokers (10 women, 8 men). Each individual was studied on two occasions, the order of which was counterbalanced; after eating as usual and after 24 h fasting. Raised plasma free fatty acids and lower insulin and leptin concentrations confirmed that participants fasted as requested. When fasted, participants reported more hunger, nervousness and worse mood and rated the visual (but not gustatory) food-related stimuli as more pleasant. The effect of fasting on hunger was stronger in women than in men. No circuitry was identified as differentially responsive in fasting compared to satiety to both visual and gustatory food-related stimuli. The left insula response to the gustatory stimuli was stronger during fasting. The inferior occipito-temporal response to visual food-related stimuli also tended to be stronger during fasting. The responses in the occipito-temporal cortex to visual and in the insula to gustatory stimuli were stronger in women than in men. There was no interaction between gender and fasting. In conclusion, food reactivity in modality-specific sensory cortical areas is modulated by internal motivational states. The stronger reactivity to external food-related stimuli in women may be explored as a marker of gender-related susceptibility to eating disorders.

Keywords: Human; Eating behaviour; Hunger; Satiety; Gender; Neuroimaging; Gustatory; Physiology

1. Introduction

To maintain energy balance, an organism has to find and recognise food in the environment and to evaluate it according to its current metabolic needs. While external food-related cues are perceived through the visual, olfactory and gustatory sensory systems, the organism's internal energy status is sensed in the hypothalamus [27]. In non-human primates, the internal and external information are integrated in the amygdala and the orbitofrontal cortex, where the representation of food-related cues is dependent on the current metabolic needs [25,38].

In humans, decisions on what, when and how much to eat may be more complex and involve higher brain centres, including prefrontal and temporal cortical circuits [7,24,29,34]. Several functional neuroimaging studies have implicated the orbitofrontal cortex [14,16,22,23,28], the amygdala [14,20] but also the insula [14,28], the anterior cingulate [14] and the fusiform gyrus [20] as parts of circuits integrating external and internal determinants of eating behaviour in humans. However, the agreement between studies is limited: for example, activity in the lateral orbitofrontal cortex has been found to correlate positively with hunger in one study [22] but increase with satiation in another [28]. Such inconsistencies may be due to differences in sample selection, variations in regional sensitivity of neuroimaging techniques [35], different sensory modalities of stimuli presentation or the fixed temporal order of fasting and satiation.

Gender is another factor to be considered in studies of eating behaviour as women are more prone to develop eating disorders and gender differences in food-preferences and in neurohumoural regulation of eating behaviour have been observed [37]. To date, only one functional neuroimaging study has explored gender differences in the neural regulation of eating [10]. This study found a more tonic increase in the perfusion of subcortical structures during fasting in men, and a more prefrontal and occipitoparietal perfusion increase with satiation in women. The possibility of differences in reactivity to food-related stimuli between men and women has not been previously investigated.

* Corresponding author. Tel.: +44 20 7848 0183; fax: +44 20 7848 0182.
E-mail address: r.uher@iop.kcl.ac.uk (R. Uher).

0166-4328/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.bbr.2005.12.008

We investigated the neural mechanisms of food-related information processing in states of fasting and satiety using functional magnetic resonance imaging (fMRI), while addressing several major methodological issues. Firstly, to separate the effect of hunger and satiety from scan-order effects, we scanned each participant on two occasions, the order of fasting and satiety being counterbalanced. Secondly, we conducted two separate experiments one with visual and one with gustatory food-related stimuli to evaluate the effect of sensory modality. Finally, we studied both men and women to explore gender differences in food processing.

The following hypotheses were tested:

1. Food-related cues will be more motivationally salient in the fasted state and will lead to increased activation of an orexigenic circuitry, including the insular and orbitofrontal cortices.
2. Activity in this orexigenic circuitry will be independent of the mode of presentation of food-related stimuli (visual and taste).
3. Reactivity to food in this orexigenic circuitry will be greater in women than in men, independent of the states of fasting and satiety.

2. Materials and methods

2.1. Participants

Eighteen healthy volunteers (10 women and 8 men) were recruited by poster advertisement from the local community. Inclusion criteria were age between 18 and 45 and right-handedness. Exclusion criteria were current use of any medication, smoking, psychiatric or neurological illness, diabetes mellitus, pregnancy/lactation, metal implants, history of head injuries, claustrophobia, food allergies, vegetarianism or other pattern of selective eating.

The mean age was 28.4 (S.D. 8.4; range 20–44) for women and 29.4 (S.D. 7.8; range 23–42) for men. The mean body mass index (BMI; body weight in kilograms divided by squared height in metres) was 22.5 kg/m^2 (S.D. 2.8; range 19.9–27.4) for women and 22.4 kg/m^2 (S.D. 2.5; range 17.0–24.7) for men.

On the Three-Factor Eating Questionnaire [30], the participants scored on average 6.0 ± 4.1 on the scale of dietary restraint (range of possible values 0–21), 5.6 ± 2.9 on the scale of hunger (0–14) and 5.0 ± 3.1 on the scale of disinhibition (0–16). These values did not differ from a representative group of 177 healthy volunteers recruited from the same community (all $t[1,193] < 1$; $p > 0.1$) and there were no significant differences between women and men (all $t[1,16] < 1$; $p > 0.1$).

After being given detailed information about the experimental procedures, all participants gave written consent as approved by the Ethical Committee at the Institute of Psychiatry, King's College London.

2.2. Procedures

Participants first attended a screening session, during which they underwent an interview, completed questionnaires and had their height and weight measured. The interview was comprised of the screening items from the Structured Clinical Interview for DSM-IV Diagnosis [12], the diagnostic items from the Eating Disorder Examination [11] and a customised checklist of exclusion criteria. Questionnaires included the Three-Factor Eating Questionnaire [30] and a list of common foods to assess selective eating.

Each participant was randomised for the order of the two experimental sessions: half of the participants (five women and four men) underwent the fasting session first and the other half participated first in the satiated session. All 18 participants attended both experimental sessions. Fasting and satiated sessions were on the same day of the week (Thursday). In most participants, there was a 1-week gap between the two sessions (in four participants this was not possible and there were gaps of 2 or 3 weeks).

For the 24 h preceding each experimental session, the participants recorded their activity, food and fluid intake, mood, nervousness and feeling of hunger every 2 waking hours. Hunger, mood and nervousness were recorded on a seven-point Likert scale with the following prompts: How hungry do you feel? (1 = not at all hungry; 7 = very hungry); How would you describe your mood right now? (1 = very good/high; 7 = very bad/low); Do you feel nervous, restless or irritable? (1 = not at all; 7 = very much so). They were instructed to refrain from strenuous physical activity, to abstain from alcohol for 24 h and from caffeinated beverages on the day of the experimental session.

Before the fasting session, participants were instructed not to eat anything and not to drink beverages other than water for 24 h (starting from 1 p.m. of the preceding day). They were encouraged to admit to any food they had eaten and informed that the blood tests would distinguish fasted and non-fasted states.

Before the satiated session, participants were asked to eat as usual and to have a meal between 9:30 and 10:00 a.m. on the experimental day. All participants reported that they had complied with these requirements.

On the experimental day, the participants arrived at the research centre at 11:30 a.m. Blood samples were drawn between 11:45 and 12:15 (i.e. after an approximately 23 h fast for the fasting session). The fMRI scanning session started at 12:30 and took approximately 60 min. During this session, participants underwent a structural scan and functional experiments with visual and gustatory stimuli.

2.3. Visual experiment

The visual experiment consisted of an event-related paradigm with 20 colour-photographs of foods and 20 of non-edible objects. From a database of images created by the authors and used in previous investigations [32,33], the stimulus photographs were selected based on ratings made by eight healthy volunteers. Photographs of food were selected if these volunteers rated them as easy to recognise, pleasant and appetising (60% or more on a visual analogue scale with anchors: very difficult–very easy to recognise; very unpleasant–very pleasant; not appetising at all–very appetising). The control non-food photographs were individually matched to the food images on visual complexity (very complex–very simple) and on colour composition. The food photographs included savoury and sweet foods (e.g. roast chicken, hamburger, chocolate cake, strawberries). The non-food photographs included various non-edible objects (e.g. an armchair, brushes, car, flower). During the experiment, photographs were presented in a fixed pseudorandom order, using a rear-projecting screen viewed via a double mirror periscope fitted to the headcoil. Each picture was shown for 5 s followed by a screen with a rating question for 3 s and a blank screen for another 8 s. Thus, stimuli were presented at a rate of one picture every 15 s and the total running time of the experiment was 10 min. The rating question was "How do you like this picture?" (1, not at all; 5, like a lot) and subjects responded using thumbs of both hands to press two buttons (right and left) on a customised button box; the initial position of the rating frame was randomised to avoid motor artefacts related to specific ratings.

2.4. Taste experiment

Rather than pure gustatory stimulation, the purpose of this experiment was to effectively administer food-relevant stimuli of a non-visual nature. Hence, liquid stimuli of complex flavour were selected, which also contained an olfactory component and had been readily recognised as common types of foods in a preparatory pilot study. In this block-design experiment, tastes of chocolate milk and chicken broth were compared to a baseline of artificial saliva. The artificial saliva was a tasteless ionic solution prepared with 1.864 g KCl and 0.168 g $NaHCO_3$ per litre of distilled water. Chocolate milk was produced from a commercially available prefabricate and contained 18.0 g sugar, 3.6 g protein and 2.8 g fat per 100 ml of solution. Chicken broth was also produced from prefabricate and contained 3.6 g carbohydrates, 7.2 g protein, 2.8 g fat and 0.5 g salt per 100 ml of solution. The test solutions were delivered to the front half of the tongue via Teflon tubes (inner diameter 1.8 mm) using a purpose-built computer-operated syringe pump at a rate of 0.05 ml per second. We chose to