



Loss of lateral prefrontal cortex control in food-directed attention and goal-directed food choice in obesity



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ABSTRACT

Loss of lateral prefrontal cortex (LPFC)-mediated attentional control may explain the automatic tendency to eat in the face of food. Here, we investigate the neurocognitive mechanism underlying attentional bias to food words and its association with obesity using a food Stroop task. We tested 76 healthy human subjects with a wide body mass index (BMI) range (19–35 kg/m²) using fMRI. As a measure of obesity we calculated individual obesity scores based on BMI, waist circumference and waist-to-hip ratio using principal component analyses. To investigate the automatic tendency to overeat directly, the same subjects performed a separate behavioral outcome devaluation task measuring the degree of goal-directed versus automatic food choices. We observed that increased obesity scores were associated with diminished LPFC responses during food attentional bias. This was accompanied by decreased goal-directed control of food choices following outcome devaluation. Together these findings suggest that deficient control of both food-directed attention and choice may contribute to obesity, particularly given our obesogenic environment with food cues everywhere, and the choice to ignore or indulge despite satiety.

Introduction

Obesity is reaching pandemic proportions and is associated with major health problems. Although many factors contribute to obesity, altered neural regulation of appetite has been repeatedly associated with body mass index (BMI) variation (Dagher, 2012). Through a lifetime of conditioned responses, high caloric foods act as strong rewards. This may lead to loss of control and the automatic tendency to overeat (Papies et al., 2008; Johnson, 2013), particularly in our obesogenic environment with an abundance of high caloric food cues. Individual differences in controlling the automatic tendency to eat when facing food cues, may therefore explain some variation in obesity. Lateral prefrontal cortex (LPFC) has been consistently associated with exercising control over food choices (Hare et al., 2009, 2011; Lopez et al., 2014) and regulating food craving (Giuliani et al., 2014; Silvers et al., 2014; Dietrich et al., 2016). However, obesity-related loss of LPFC-mediated attentional control in the face of food cues has not yet been shown.

In drug addiction, which is suggested to show neurocognitive parallels with obesity (Volkow et al., 2008, 2013; Hebebrand et al.,

2014; but see Ziauddeen et al. (2012)), there is evidence for loss of attentional control in, for example, emotional color-naming Stroop tasks (Field and Cox, 2008; Hester and Lijten, 2014). In these tasks, the simple goal is to name the color of a word as fast and accurately as possible. When words are related to their target of abuse, and thus highly salient, individuals are generally distracted from their goal, resulting in an attentional bias to those words reflected by slower response times. In substance addiction, attentional bias has been found to correlate with craving and drug use severity (Franken, 2003; Field and Cox, 2008), as well as with altered lateral and medial prefrontal and striatal (e.g. putamen) responses (Chase et al., 2011; Hester and Lijten, 2014). In addition, BOLD responses in putamen for smoking-related attentional bias were found to correlate positively with craving in smokers (Lijten et al., 2011). Similar to addiction, using a color-naming Stroop task, attentional bias to palatable food words has been related to (future) obesity in children and adults (Braet and Crombez, 2003; Calitri et al., 2010). However, two other studies have not found a relationship between attentional bias to food words and obesity (Nijss et al., 2010a; Phelan et al., 2011). The neural mechanisms underlying attentional bias to food words and their relation to obesity has not yet

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been investigated, and could shed light on these inconsistent behavioral findings.

Attentional bias is often interpreted as decreased control over the automatic tendency to attend to salient cues, possibly leading to craving and habitual intake (Field et al., 2009). However, the automatic tendency to attend to salient cues is different from automatic, or habitual, choices when faced with these cues. The latter can be measured more directly with instrumental tasks implementing an outcome devaluation procedure. Such tasks have revealed that habitual behavior, as opposed to goal-directed control, in animals and humans is associated with responses in dorsolateral striatum (i.e. putamen) (Tricomi et al., 2009; Balleine and O'Doherty, 2010) and with reduced white matter strength between putamen and premotor cortex in humans (de Wit et al., 2012). However, whether increased food attentional bias is paralleled by the failure to exert goal-directed control during food choices is unknown. Here, we investigated these two types of control as a function of obesity.

Our aim was to investigate the neurocognitive mechanisms underlying food attentional bias and choice. We tested 76 healthy human subjects with a wide body mass index range (19–35 kg/m²) using fMRI, while performing a food Stroop task (Nijs et al., 2010a). We hypothesized that increased obesity would be related to a stronger behavioral and neural attentional bias to food words. Increased neural food attentional bias would be reflected in reduced IPFC-control and perhaps altered IPFC-connectivity with putamen, associated with habitual behavior. In addition, we included a separate behavioral outcome devaluation task (adapted from Hogarth et al. (2012)) to measure the degree to which subjects make goal-directed versus automatic food choices. We hypothesized that enhanced attentional bias effects would be paralleled by decreased goal-directed – and thus increased automatic – food choices with increased obesity.

Materials and methods

Subjects

The reported results are based on data from 76 healthy right-handed subjects (65 women; mean age: 31.5 years old, SD: 10.7, range: 18–53; mean BMI: 26.4 kg/m², SD: 3.8, range: 19–35) with adequate demand of Dutch and with normal or corrected-to-normal vision. Subjects were recruited from Nijmegen and surroundings through advertisement. To be eligible for the study, subjects were required to be motivated to change their eating habits (not per se losing weight, but also targeting unhealthy snacking or irregular eating patterns), as this study was part of a larger protocol including a behavioral intervention program to change eating habits. Here, only data acquired prior to the intervention are presented. Subjects were excluded from participation if they reported any (history of) clinically relevant neurological or psychiatric disorders, current psychological treatment, current use of psychotropic medication, (history of) taste or smell impairments, eating disorders (including binge eating disorder), extremely high restrained eating scores (Dutch Eating Behaviour Questionnaire, males ≥ 4.0 , females ≥ 3.6 ; van Strien et al. 1986), current dieting (i.e. following a strict diet to lose weight and/or being in treatment with a dietitian), changes in body weight > 5 kg during the last two months, and contra-indications for MRI. Following scanning, seven subjects (3 males, 4 females) were excluded from the analyses due to: being extreme outliers in terms of task performance ($n=3$; see Behavioral Analyses below), bad image quality ($n=2$; excessive signal intensity spikes and signal dropout), incidental finding ($n=1$), and no longer meeting the inclusion criteria due to a concussion ($n=1$). All subjects provided written informed consent, which was approved by the regional research ethics committee (Commissie Mensgebonden Onderzoek, regio Arnhem-Nijmegen, Registration Number: 2013/188, Date: 20 June 2013), and received financial compensation for participation.

Obesity score

As a measure of obesity we calculated an obesity score, which reflects common variance in three highly correlated variables that have been related to degree of obesity and the associated health risks: body mass index (BMI), waist-to-hip ratio (WHR) and waist circumference (all r 's > 0.4, all p -values < 0.001) (Huxley et al. 2009). We z-scored these variables and ran principal component analysis on the z-scored variables using the built-in function 'princomp' in MATLAB (version 7.9.0, Mathworks, Natick, MA) for reducing the number of correlated variables under consideration whilst retaining most of the information in the data (Jolliffe 2002). We then selected the first principal component, which explained 80.1% of the common variance in these measures. Finally, to correct the resulting score for gender and age, which are known to co-vary with obesity, we regressed them against the first principal component and saved the unstandardized residuals as the obesity score.

Procedure

Test sessions started at 11 a.m. or 12:30 p.m. and lasted approximately 3.5 h. Subjects were asked to refrain from eating and drinking anything else than water 4 h prior to testing. They were also asked to abstain from recreational drugs one week, and from alcohol 24 h prior to testing. Compliance was assessed by administering a self-report compliance questionnaire. The tasks described below were part of a larger protocol and were performed approximately 1 h after the start of the test session. The order of the tasks was the same across subjects. All tasks were programmed with Presentation software (Version 16, Neurobehavioral Systems, Inc.).

Weight (in kg), height (in cm), and waist and hip circumference (in cm) were measured at the start of the test session. During scanning, subjects performed a color-naming Stroop task to assess attentional bias. Before the task started, they rated how hungry they felt using a visual analogue scale ranging from 0 (not hungry) to 10 (very hungry) on the screen. After scanning, subjects performed a food-choice satiety task to assess the degree of goal-directed control over their choices after outcome devaluation. In between these tasks, subjects also performed an incentive delay task in the scanner in which small monetary and caloric rewards could be earned. This task was programmed such that the accumulative earnings were similar across subjects. Data from the incentive delay task are not reported here. On a separate intake session prior to the test days, subjects were screened for exclusion criteria, rated the Stroop words (see below), and the Dutch version of the National Adult Reading Test (NART) was administered to assess education level ranging from 0 (no degree) to 7 (college degree) (M: 6.3, SD: 0.6, range: 5–7) and verbal IQ (M: 104.7 SD: 9.9, range: 83.0–127.0) (Schmand et al. 1991).

Paradigms

Stroop task

Subjects were instructed in the Stroop task before going into the scanner and were further familiarized with the task by practicing the color-button contingency and performing 10 practice trials with feedback (correct/incorrect) in the scanner. For task details see Fig. 1A. In short, subjects had to indicate the color of the word presented on the screen pressing the button reflecting that color as fast and accurately as possible. Subjects were presented with food, positively valenced emotional and neutral words. All task stimuli were presented with a digital projector on a screen at the back end of the MRI scanner bore, which was visible via a mirror mounted on the head coil. Responses were made using an MRI-compatible button box. Twenty generally high-calorie, palatable food words were selected from word lists reported in previous studies (Nijs et al. 2010a; Phelan et al. 2011). Twenty positively valenced emotional words were selected from the Dutch

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