Visual food cues decrease postprandial glucose concentrations in lean and obese men without affecting food intake and related endocrine parameters

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Abbreviations:

cephalic phase insulin release, CPIR

Abstract

The abundance of highly palatable food items in our environment represents a possible cause of overconsumption. Neuroimaging studies in humans have demonstrated that watching pictures of food increases activation in brain areas involved in homeostatic and hedonic food cue processing. Nevertheless, the impact of food cues on actual food intake and metabolic parameters has not been systematically investigated. We tested the hypothesis that watching high-calorie food cues increases food intake and modifies anticipatory blood parameters in lean and especially in obese men. In 20 normal-weight and 20 obese healthy fasted men, we assessed the effects of watching pictures of high-calorie food items versus neutral contents on food intake measured during a standardized test buffet and subsequent snacking as well as on glucose homeostasis and endocrine parameters. Compared to neutral pictures, viewing food pictures reduced postprandial blood glucose concentrations in lean ($p = 0.016$) and obese ($p = 0.044$) subjects, without any differences in insulin or C-peptide concentrations (all $p > 0.4$). Viewing food pictures did not affect total calorie intake during the buffet (all $p > 0.5$) and snack consumption (all $p > 0.4$). Concentrations of ghrelin, adrenocorticotropic hormone (ACTH), cortisol, and glucagon also remained unaffected (all $p > 0.08$). These data indicate that preprandial processing of food cues curbs postprandial blood glucose excursions, without immediately affecting eating behavior in normal-weight and obese men. Findings indicate that exposure to food cues does not acutely trigger calorie overconsumption but rather improves the glucoregulatory response to food intake.

Keywords: Visual cues; Food pictures; Food intake; Glucose homeostasis; Cephalic phase response; Anticipation

Introduction

The current obesity epidemic is a major problem for health care. The abundance of high-calorie food, rich in sugar and fat, may contribute to overconsumption and development of overweight. Moreover, pictures of palatable foods shown e.g. for advertising purposes are a ubiquitous part of everyday life in western societies (Mink, Evans, Moore, Calderon, & Deger, 2010). Exposure to food (slices of pizza) in the laboratory has been demonstrated to increase rated desire to eat this particular food in both men and women (Marcelino, Adam, Couronne, Koster, & Sieffermann, 2001). Furthermore, showing food pictures increased the size of pizza portions normal-weight women intended to eat as well as subsequent actual intake, suggesting that food cues increase the amount of food that people will consume (Ferriday & Brunstrom, 2008). In contrast, a recent study in women failed to demonstrate any stimulating effects of food pictures on snack intake (van Nee, Larsen, & Fisher, 2016).

Neuronal effects of exposure to food cues have been examined in studies using functional magnetic resonance imaging (fMRI). Watching food pictures activates a large bilateral brain network which is typically involved in food cue processing (Kroemer, Krebs, Kobiella, Grimm, Vollstadt-Klein, et al., 2013). Visual cues of high-fat food stimulate neural circuits engaged in energy homeostasis and reward processing, like the hypothalamus and the striatum, in healthy lean women (Schur, et al., 2009). In contrast to lean women, obese women react to high-calorie food cues in particular with an activation of the dorsal striatum, a brain region involved in reward anticipation and habit learning (Rothemund, et al., 2007).

Visual food cues also affect metabolic and endocrine parameters. The sight of appetizing food was sufficient to increase gastric acid and serum gastrin levels (Feldman & Richardson, 1986) and, moreover, to increase the concentrations of the

orexigenic hormone ghrelin (Schussler, et al., 2012). These anticipatory changes in metabolism are regarded as cephalic phase responses, i.e. metabolic reflexes whose afferent signals originate in the head and which are thought to prepare the body for the processing of absorbed nutrients (Power & Schulkin, 2008).

In our study in lean and obese men, we investigated the effects of watching pictures of food or non-food items on hunger- and reward-driven eating behavior by analyzing calorie intake from a standardized test buffet (including the analysis of separate macronutrients) and a subsequent snack test (with three different types of cookies). Furthermore, we scrutinized blood glucose and blood parameters of energy metabolism as well as subjective mood, hunger and the desire to eat. We tested the hypotheses that watching high-calorie food cues increases food intake from the test buffet and the snack test as well as ratings of hunger and the desire to eat. Because mood and impulsivity might affect food intake, these variables were measured using questionnaires. In addition, because food cues might affect glucose metabolism by increasing anticipatory responses such as ghrelin and insulin/C-peptide, we measured the glucoregulatory hormones ACTH, cortisol, and glucagon. We expected the stimulatory effect of food cues to be observable in lean men and – to an even greater extent – in obese men. In a supplementary experiment, the same food items were both visually presented as food cues and subsequently offered for actual consumption, inasmuch as recent studies have stressed the importance of this aspect (Blechert, Klackl, Miedl, & Wilhelm, 2016).

Subjects and Methods

***Subjects*.** Twenty normal-weight and twenty obese healthy men participated in the study (mean age ± SEM, 24.1 ± 3.7 vs. 25.2 ± 3.7 years, $p \geq 0.35$; BMI, 22.4 ± 1.5 vs. 34.9 ± 3.6 kg/m^2, $p < 0.001$). Sample size was calculated with G*Power (version

3.1.9.2) according to previous studies on related effects on food intake and endocrine parameters (Kroemer, Krebs, Kobiella, Grimm, Pilhatsch, et al., 2013; Ott, et al., 2013). Body composition was assessed by bioelectrical impedance analyses (Nutriguard-M, Data Input, Darmstadt, Germany) at the start of each experimental session. Body composition was different between both weight groups with regard to lean body mass ($F(1,35) = 51.98$; $p < 0.001$ for between-subjects comparisons) and fat mass ($F(1,35) = 76.68$; $p < 0.001$), but remained comparable across conditions (both $p > 0.4$ for "condition"). In detail, obese compared to lean participants had more body fat (39.44 ± 2.61 kg vs. 13.78 ± 0.79; $p < 0.001$) and lean body mass (79.32 ± 1.78 kg vs. 61.75 ± 1.61; $p < 0.001$). The health of participants was evaluated by clinical examination, medical history including abuse of alcohol, nicotine or any drugs, and routine laboratory tests during screening. All participants submitted written informed consent and the study was approved by the ethics committee of the University of Lübeck, Germany.

***Experimental procedure of the main experiment*.** Experiments were carried out in the Center for Brain, Behavior and Metabolism at the University of Lübeck, Germany during August 2014 and February 2016. They were performed in a within-subject comparison. Each participant attended two different conditions (food pictures vs. non-food (neutral) pictures). There was a 14-day interval between sessions with the order of conditions balanced across subjects. All subjects were instructed to be fasted (with exception of drinking water) after 2200h on the day preceding each session.

Participants arrived at the lab at 0900h. After a brief history and physical examination, a venous cannula was inserted into the non-dominant lower arm or cubital fossa to enable blood sampling during experiments. Blood was sampled at 0950h for baseline assessments of hormonal parameters and blood glucose, as well

as at defined intervals throughout the session. As a cover story, participants were told that the experiment aimed at investigating the impact of visual cues on gustatory perception, tested at the end of the experiment by gustatory questionnaires referring to the implemented snack test. At 1010h and 1130h (just before the test buffet and the snack test), a set of 50 pictures of food items or – in the other condition – non-food items was shown on a notebook computer. Each picture was displayed for ten seconds, amounting for eight minutes and twenty seconds for the whole set of pictures. This set comprised high-resolution images of food from a standardized database, showing high-calorie meals (caloric values rated above > 300 kcal for each of the items), e.g. chocolate cake, pasta or ice-cream. Neutral images originated from the database of Brooks and colleagues and depicted non-food items like books or pencils (Brooks, et al., 2011).

Immediately after watching the picture set, participants ate from an ad libitum test buffet until satiated. Without the knowledge of participants, the offered food was weighed before and after the test buffet to assess spontaneous food intake in the fasted state. The test buffet consisted of bread rolls, brown bread, cheese, smoked salmon, meat salad, salami, cream cheese, butter, chocolaty hazelnut spread, meatballs, potato chips, peanuts, chocolate, muffins, wine gums, custard, lemonade, chocolate-flavored milk, orange juice, condensed milk, sugar, fruit tea, coffee (decaffeinated), and water (about 10,000 kcal were offered; **Supplemental Table 1**). After the second run of picture exposure at 1130h, subjects underwent a snack test with three different types of snacks (salty, sweet and neutral) in a paradigm addressing the hedonic component of eating behavior in the relative absence of hunger (Hallschmid, Higgs, Thienel, Ott, & Lehnert, 2012; Higgs, Williamson, & Attwood, 2008). Here, participants filled out questionnaires assessing their gustatory perception with ratings of the items “salty”, “sweet”, and “sour” for different snacks, so

that our cover story was corroborated. Again, subjects were instructed to eat as much as they like and total intake of macronutrients in kilocalories was protocolled.

Mood was rated on the Multidimensional Mood Questionnaire on a 5-point scale containing items of the categories good/bad mood, alertness/sleepiness, and calmness/agitation (Hinz, Daig, Petrowski, & Brahler, 2012). For the assessment of subjective feelings of hunger, satiety, or desire to eat something sweet or savory, visual analogue scales (0–100 mm) were used (Flint, Raben, Blundell, & Astrup, 2000). Participants performed the set of questionnaires at five times in each session (0940h, 1025h, 1110h, 1145h and 1210h).

To assess impulsivity, participants performed a 27-item Monetary Choice Questionnaire (MCQ) at the end of each session (1215h), which measures delayed discounting by asking individuals to choose between smaller rewards available immediately and larger rewards available after a delay (Gray, Amlung, Palmer, & MacKillop, 2016; Kirby, Petry, & Bickel, 1999). Individual indifference points were determined and discounting rates (overall k-values) calculated. Logarithmic transformations of k-values were used to approximate normal distribution to enable use of parametric statistical analyses.

Supplementary experiment

As recent studies have shown that stimulatory effects of food presentation might critically depend on the visual presentation of food items that are actually consumed later on (Blechert, et al., 2016), we conducted an additional experiment in which food pictures were repeatedly shown and subjects could eat exactly the type of food depicted on the pictures. Also, the offered buffet was typical for German lunch habits and comprised warm dishes to include a strong olfactory cue that might also be important for hedonic stimulation. The aim of this additional experiment was to

corroborate our findings in an enhanced, but otherwise comparable paradigm of food picture presentation in ten normal-weight healthy men (mean age 25.1 ± 1.9 years; BMI 22.6 ± 1.3 kg/m^2). The experimental procedure was the same as described above but did not include blood sampling since we wanted to focus on the main parameters of food intake and reduce the experimental burden for our subjects.

The set of food pictures was modified to include 20 pictures (10 food, 10 non-food items). Each picture was shown for 7 seconds and was repeated three times (total time of picture set 8 min). Food pictures were taken from a standardized high-resolution picture database (Blechert, et al., 2016) and depicted salami pizza, vegetable pasta, currywurst, pancakes, rice pudding with cherries, chocolate-covered cornflakes (Choco Crossies®, Nestle), orange juice, tortilla chips with two different dips (mexican and cheese), cashew nuts and custard (**Supplemental Table 2**). After watching the picture set, participants received a test buffet composed exactly of the food shown on the pictures (amounting to a total of about 4,000 kcal). After the second run of the picture set, subjects underwent the same snack test as described above.

***Metabolic and endocrine parameters*.** All blood samples were centrifuged and supernatants were stored at -80°C. For the measurements of glucagon, tubes were prepared with aprotinine (370 kIU/ml; Roth GmbH, Karlsruhe, Germany). Plasma glucose and lactate were measured in fluoride plasma (Roche-Diagnostic, Grenzach, Germany). Routine assays were used for the measurement of insulin, C-peptide, cortisol and adrenocorticotropic hormone (ACTH) (all Immulite, Siemens, Erlangen, Germany), glucagon (RIA, IBL International, Hamburg, Germany), as well as active and total ghrelin (RIA, Biotrend, Cologne, Germany).

***Statistical analyses*.** Data were analysed with SPSS statistical software (SPSS 24.0, Inc., Chicago, USA) and are presented as mean absolute values ± SEM. Baseline-adjusted values of the blood parameters and questionnaires were obtained by subtracting the individual baseline value (at 09:50h) from subsequent individual measurements. Statistical comparisons were based on analyses of variance (ANOVA) with the between-subjects factor "group" (normal-weight vs. obese) and the within-subject factors "condition" (food vs. non-food pictures) and "time" (comprising six baseline-corrected time points) as appropriate. Greenhouse-Geisser procedure was used for correction of degrees of freedom. Post-hoc comparisons of blood parameters and food intake (macronutrients and snack types) were performed by t-tests or by Wilcoxon tests in case of non-normal distribution (total ghrelin, insulin, C-peptide). Note that for illustrative purposes, results of the main parameters are also presented separately for the two individual groups (normal-weight and obese) when ANOVA did not indicate group-related differences. A p-value <0.05 was generally considered significant but adjusted by Bonferroni correction as appropriate (yielding significance levels of $p < 0.007$ for blood parameters and $p < 0.016$ for test buffet macronutrients and snack test cookies in post-hoc comparisons).

Results

Calorie intake. Total calorie consumption was in general comparable between groups ($F(1,38) < 1$; $p > 0.7$) without any influence of food cue stimulation ($p > 0.8$ for "condition × group"; $F(1,38) < 1$; $p > 0.5$ for "condition"). In group-specific analyses, viewing food pictures in comparison to non-food pictures did not affect total calorie intake from the test buffet either in lean (1469 ± 81 kcal vs. 1428 ± 78 kcal, $t(19) = 0.59$; $p > 0.5$ for t-test comparison) or in obese participants (1510 ± 128 kcal vs. 1490 ± 147 kcal, $t(19) = 0.29$; $p > 0.7$; **Figure 1A**). With regard to macronutrients, obese

men ingested higher amounts of proteins ($F(1,38) = 17.42$; $p < 0.001$) and fat ($F(1,38) = 10.44$; $p = 0.003$) than normal-weight participants, but this effect was not influenced by visual cues (both $p > 0.1$ for "group × condition; both $p > 0.2$ for "condition"). Intake of carbohydrates was comparable between groups and conditions (all $p > 0.1$).

In analyses focusing on the most hedonic food items (potato chips, peanuts, chocolate, muffins, wine gums, chocolaty hazelnut spread, lemonade, chocolate-flavored milk), we neither found differences in food intake between groups or conditions (all $p > 0.2$). Thus, intake of these foods did not differ between conditions in lean men (258 ± 55 vs. 309 ± 45 kcal, $t(19) = 1.00$, $p = 0.33$) or in obese men (242 ± 67 vs 276 ± 60 kcal, $t(19) = 0.60$, $p = 0.56$). The total weights of solid foods and the total volumes of liquid food neither differed between groups or conditions (all $p > 0.1$). After watching food cues compared to neutral cues, normal-weight men ingested 509 ± 28 vs. 492 ± 27 g solid food ($t(19) = 0.67$, $p = 0.51$) and 295 ± 41 vs. 266 ± 49 ml liquid food ($t(19) = 0.86$, $p = 0.40$). Obese men ingested 507 ± 40 vs. 475 ± 45 g solid food ($t(19) = 1.28$, $p = 0.22$) and 287 ± 65 vs. 296 ± 57 ml liquid food ($t(19) = 0.19$, $p = 0.85$).

Total calorie intake from snacks was not different between weight groups ($F(1,38) < 1$; $p > 0.7$) nor influenced by food cues ($F(1,38) = 1.0$; $p = 0.31$ for "condition × group"; $F(1,38) < 1$; $p > 0.5$ for "condition"). Lean men ingested comparable amounts of total calories in both conditions (149 ± 13 kcal vs. 158 ± 13 kcal, $t(19) = 0.72$, $p > 0.4$; **Figure 1B**), as did obese men (158 ± 30 kcal vs. 139 ± 21 kcal, $t(19) = 0.86$, $p > 0.4$). Similarly, comparisons of salty, sweet or neutral snacks did not reveal any differences between lean and obese men (all $p > 0.1$) nor influences by food cues (all $p > 0.1$).

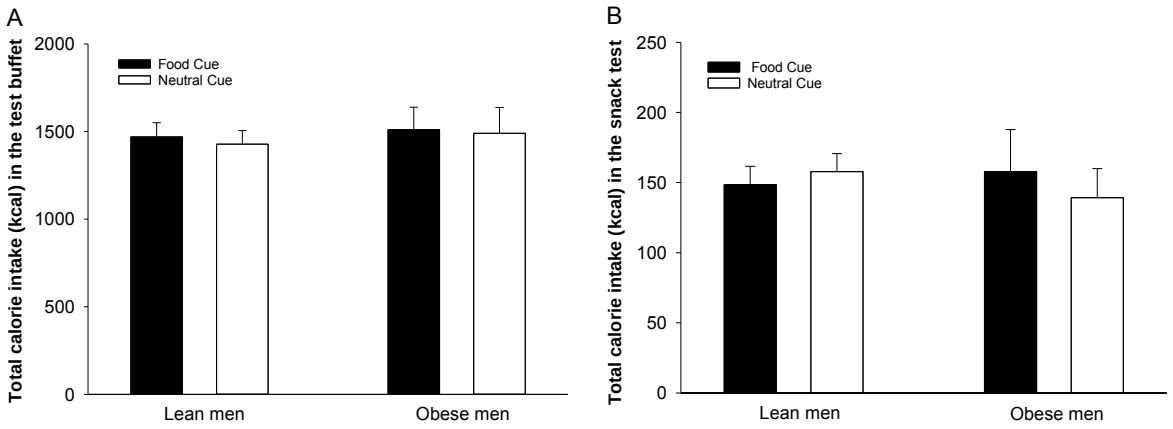

Figure 1: Total calorie intake in the test buffet and snack test. *Mean ± SEM total intake of kilocalories in the test buffet (**A**) and snack test (**B**) after watching pictures of palatable food (black bars) or neutral items (white bars) in lean and obese men.*

In the additional experiment, where lean men were presented with pictures of high-calorie food items that were offered for consumption later on or with control pictures, we did not find differences in total calorie intake between conditions (1781 ± 109 kcal vs. 1711 ± 105 kcal, $t(9) = 0.66$, $p > 0.3$). In the subsequent snack test, participants ingested comparable amounts of total calories in both conditions (183 ± 40 kcal vs. 191 ± 52 kcal; $t(8) = 0.78$, $p > 0.7$).

Ratings and impulsivity. ”Hunger”, “satiety” and “desire to eat” were rated on visual analogue scales by our participants. There were no differences in ratings of “hunger” between groups ($F(1,38) < 1$; $p > 0.5$) or due to food cues ($F(1,38) < 1$; $p > 0.7$ for “condition × group”; $F(1,38) < 1$; $p > 0.9$ for “condition”). Ratings of “satiety” and “desire to eat” were likewise comparable, with no differences between groups or conditions (all $p > 0.2$). Subjective ratings of mood neither differed between weight groups or conditions in the categories “good/bad mood” (all $p > 0.2$), “alertness/sleepiness” (all $p > 0.3$) and “calmness/agitation” (all $p > 0.08$). In the

additional experiment, visual analogue scale ratings were comparable for “hunger” ($F(1,9) < 1$; $p > 0.4$ for “condition”), “satiety” ($F(1,9) < 1$; $p > 0.6$) and “desire to eat” ($F(1,9) < 1$; $p > 0.4$).

Impulsiveness of participants was measured by the Monetary Choice Questionnaire. In both conditions, obese in comparison to lean men displayed higher delay discounting-rates (logarithmic k values) ($F(1,37) = 5.45$; $p < 0.03$), but food cues had no impact on these differences or on impulsivity in general (both $p > 0.2$). Supplementary analyses indicated that delay discounting-rates were statistically unrelated to total calorie intake from the test buffet in the food cue condition ($r = 0.201$; $p = 0.2$, Pearson’s coefficient) as well as in the non-food condition ($r = 0.110$; $p > 0.2$).

***Glucose homeostasis*.** Baseline concentrations of glucose, insulin and C-peptide were comparable between conditions and groups ($p > 0.1$ for all comparisons). Glucose concentrations did not differ between groups ($F(1,38) < 1$; $p > 0.5$), but displayed a marked dependence on preceding food cue presentation ($F(1,38) = 6.07$; $p = 0.018$ for “condition”; $F(3,116) = 2.74$; $p = 0.046$ for “condition × time”; $p = 0.083$ for “condition × group”). In detail, watching food as compared to neutral pictures decreased postprandial blood glucose concentrations in lean subjects ($F(1,19) = 8.56$; $p = 0.018$ for “condition”; $F(3,55) = 2.63$; $p = 0.061$ for “condition × time”; $F(1,19) = 7.04$; $p = 0.016$ for “condition” in the postprandial period (“$\text{condition}_{t55\text{-}115}$”); **Figure 2A**). Also in the obese participants, postprandial glucose concentrations were lower after watching pictures of food than neutral items ($F(3,50) = 2.38$; $p = 0.088$ for “condition × time”; $F(1,19) < 1$; $p > 0.5$ for “condition”; $F(2,39) = 3.36$; $p = 0.044$ for postprandial “$\text{condition} \times \text{time}_{t55\text{-}115}$”; **Figure 2B**). The picture stimulation-induced decreases in postprandial glucose concentrations were still evident when including

306 the consumed calories in the test buffet as a covariate in the respective analysis
307 ($F(1,37) = 5.64$; $p = 0.023$ for “condition”).

308 Obese men as expected displayed higher serum insulin concentrations than
309 lean men ($F(1,38) = 6.47$; $p = 0.015$; **Figures 2C + 2D**). Watching food cues did not
310 affect serum insulin concentrations (all $p > 0.2$). Similarly C-peptide concentrations
311 showed a trend towards higher concentrations in obese compared to lean subjects
312 ($F(1,38) = 2.89$; $p = 0.09$; **Figures 2E + 2F**) with no difference regarding conditions
313 (all $p > 0.1$).

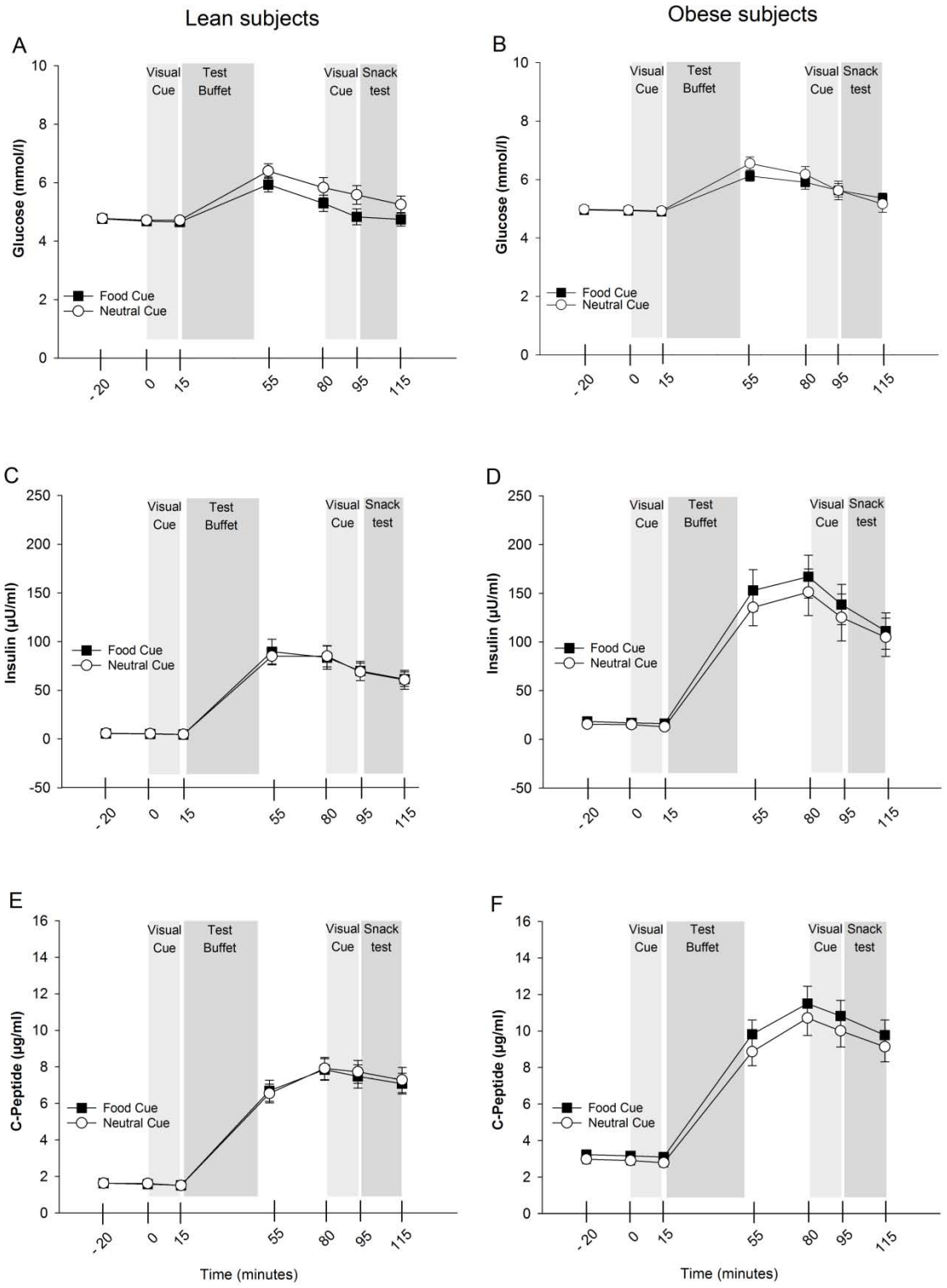

Figure 2: Parameters of glucose homeostasis. *Mean ± SEM plasma or serum concentrations of glucose (**A, B**), insulin (**C, D**) and C-peptide (**E, F**) during baseline and after watching food pictures (black squares) or neutral items (white circles). Baseline concentrations of glucose, insulin and C-peptide were comparable between conditions and groups (all p > 0.1). Blood samples were drawn at 0950h (-20min), 1010h (0min), 1025h (15min), 1105h (55min), 1130h (80min), 1145 (95min), and 1205h (115min).*

Ghrelin concentrations. Baseline concentrations of total ghrelin were comparable between conditions in both groups (both $p > 0.7$). In group comparisons, lean men displayed higher total ghrelin concentrations than obese men ($F(1,38) = 14.44$; $p = 0.001$; **Figures 3A + 3B**). Food cues did not affect the time course of total ghrelin concentrations in any weight group ($p > 0.6$ for all comparisons). Baseline concentrations of active ghrelin were likewise comparable between conditions in lean men as well as in obese men (all $p > 0.5$). Consistent with total ghrelin, concentrations of active ghrelin were higher in lean compared to obese men ($F(1,38) = 21.11$; $p < 0.001$; **Figures 3C + 3D**), but viewing food pictures did not affect active ghrelin concentrations ($F(1,38) = 1.90$; $p > 0.1$ for "condition"; $p > 0.09$ for "condition × group").

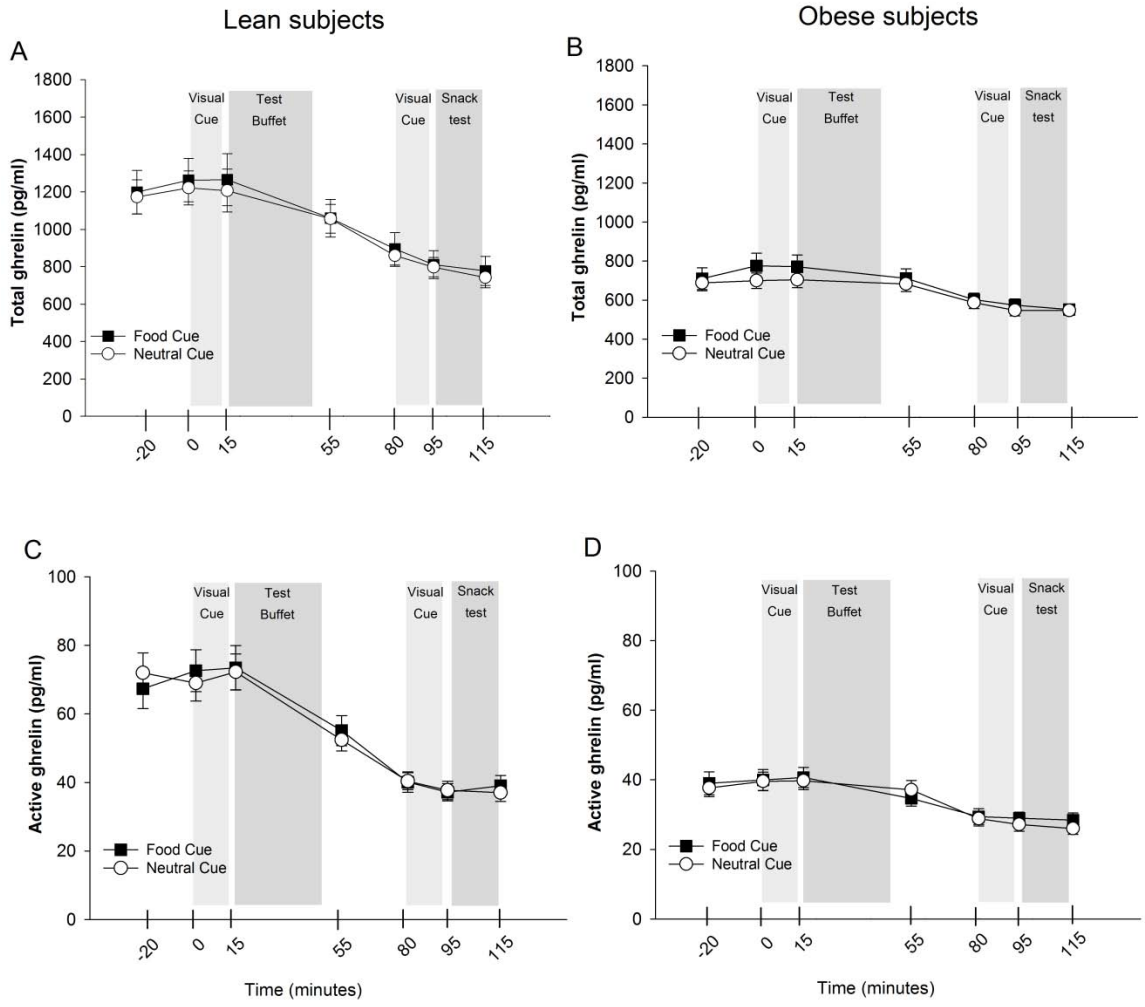

Figure 3: Total and active ghrelin concentrations. *Mean ± SEM plasma concentrations of total ghrelin (**A, B**) and active ghrelin (**C, D**) after watching food cues (black squares) or neutral pictures (white circles) in lean and obese men. Blood samples were drawn at 0950h (-20min), 1010h (0min), 1025h (15min), 1105h (55min), 1130h (80min), 1145 (95min), and 1205h (115min).*

Additional endocrine parameters. Baseline concentrations of ACTH, cortisol and glucagon did not differ between conditions in both groups (all $p > 0.3$). In ACTH concentrations, there were no differences between groups ($F(1,38) < 1$; $p > 0.3$) or conditions ($F(1,38) < 1$; $p > 0.5$ for "condition"; $p > 0.9$ for "condition × group"). Cortisol concentrations were slightly higher in lean than in obese men ($F(1,38) = 4.22$; $p = 0.047$) but comparable between conditions ($F(1,38) < 1$; $p > 0.4$ for "condition"; $p > 0.1$ for "condition × group). Glucagon concentrations showed no group differences ($F(1,38) < 1$; $p > 0.7$) and were comparable after watching food cues or non-food cues ($F(1,39) < 1$; $p > 0.5$ for "condition"; $p > 0.4$ for "condition × group").

Discussion

Contrary to our hypotheses, preprandial exposure to visual food cues did not influence calorie intake from a buffet and the consumption of snacks in the postprandial period. Moreover, our participants did not report increases in feelings of hunger or desire to eat, and relevant hormones (ghrelin, ACTH, cortisol, glucagon, insulin, and C-peptide) were neither affected by exposure to food cues. However, watching food pictures induced a consistent reduction in postprandial blood glucose concentrations in lean as well as obese men.

The observed impact of food cues on glucose regulation might have been due to so-called anticipatory or cephalic phase insulin release (CPIR), which is defined as swift insulin release occurring in response to sensory stimulation prior to nutrient

absorption (Teff, 2011). Early increments in circulating insulin emerging between three and nine minutes after olfactory and visual exposure to a standard meal were described in normal- and overweight subjects some thirty years ago (Simon, Schlienger, Sapin, & Imler, 1986). Such insulin responses to the sight and smell of food appeared to be stronger in obese than lean subjects (Sjostrom, Garellick, Krotkiewski, & Luyckx, 1980). However, in the present study, we did not observe a significant increase in insulin or C-peptide concentrations immediately after exposure to food pictures. Considering that CPIR peaks about four minutes after stimulation, we might have missed the optimal time frame, although blood sampling was conducted directly after the presentation of pictures which took about eight minutes. Notably, CPIR is of small magnitude, reaching only approximately 1% of normal postprandial insulin release, and exhibits a large variability in humans (Teff, 2011). Snel and colleagues (2012) investigated the effect of visual and odorous stimulation on different endocrine and metabolic parameters after a 60h-fast in healthy men. They demonstrated increased glucose and insulin concentrations in response to an oral glucose tolerance test due to the prolonged fasting period, but these effects were not modified by food cues (Snel, et al., 2012). Nevertheless, the very long period of fasting might have provoked a ceiling effect that could have masked any stimulatory effects of food cues. Further studies should focus on the interaction of food cues and glucose metabolism in a more controlled setting to confirm whether the effects on postprandial glucose concentrations observed in our study are mediated by anticipatory responses to food cues.

Beside the effects on glucose metabolism in response to food pictures, we did not observe any differences in ghrelin concentrations, a hormone important for meal initiation (Cummings, et al., 2001). Total ghrelin concentrations are inversely associated with BMI and waist circumference (Monti, Carlson, Hunt, & Adams, 2006),

387 which was confirmed by our study demonstrating higher total and active ghrelin
388 concentrations in lean than in obese men, irrespective of the content of pictures.
389 Neuroimaging studies have demonstrated that food pictures presented in a satiated
390 state can increase ghrelin concentrations in normal-weight volunteers (Schussler, et
391 al., 2012). Moreover, labeling a milkshake as energy-dense and delicious is sufficient
392 to induce a stronger postprandial decline in ghrelin concentrations compared to the
393 response the same milkshake elicits when bearing a low-calorie label (Crum, Corbin,
394 Brownell, & Salovey, 2011). Fittingly, postprandial suppression of ghrelin
395 concentration is markedly stronger in men who anticipate food intake than in men
396 who expect to remain fasted (Ott, et al., 2012). Although the effects of food pictures
397 on glucose metabolism hint at a central stimulation, our results did not corroborate
398 food cue-induced anticipatory processes acting on active and total ghrelin
399 concentrations.

400 The lack of stimulatory effects of food cues on ingestive behavior contrasts
401 with the results of fMRI studies measuring brain activation patterns. Watching food
402 pictures stimulated activity in brain areas typically involved in reward-processing and
403 responses to food stimuli in lean women (Kroemer, Krebs, Kobiella, Grimm, Vollstadt-
404 Klein, et al., 2013; Schur, et al., 2009). This effect was even more pronounced in
405 obese compared to normal-weight humans (Martens, et al., 2013; L. E. Martin, et al.,
406 2010; Murdaugh, Cox, Cook, & Weller, 2012; Puzziferri, et al., 2016; Rothemund, et
407 al., 2007). In contrast to these results in neuroimaging studies, there are different
408 outcomes of studies in adults investigating actual food intake after viewing food
409 pictures; most of them focused on women, groups including members of both sexes,
410 and children (Boswell & Kober, 2016). In 1989, Cornell and her team demonstrated
411 that the sight of food stimulated the intake of pizza or ice cream in normal-weight
412 men and women who had been previously satiated (Cornell, Rodin, & Weingarten,

1989). Moreover, the exposure to slices of pizza increased rated desire to eat this pizza afterwards in men and women (Marcelino, et al., 2001). In contrast to these studies, but in line with our results in men, a neuroimaging study showed that brain responses to food cues did not predict total caloric intake at the buffet in a group of normal-weight men and women (Mehta, et al., 2012). Additionally, recent behavioral studies in women did not demonstrate stimulatory effects of food cues on energy intake. Thus, food cues in advertisements did not influence total energy intake and even decreased chocolate intake in young women compared to subjects who watched the same TV program without food cues (van Nee, et al., 2016). Also in obese women, watching food cues did not stimulate total calorie consumption (C. K. Martin, Coulon, Markward, Greenway, & Anton, 2009; Schyns, Roefs, Mulkens, & Jansen, 2016). However, it should be noticed that there are signs of sex differences in brain stimulation by visual food cues, with women showing higher activation in the fusiform gyrus than men while viewing high-calorie pictures in the hungry state (Frank, et al., 2010). A recent meta-analysis suggests that acute exposure to food advertising increases food intake in children but not in adults (Boyland, et al., 2016).

While the lack of effects on food intake observed in our study is in line with recent findings, we cannot specify with our design whether there are still some stimulatory effects on central nervous structures, especially on reward-processing areas. Thus, our stimulation might not have been strong enough or of sufficient duration to translate such changes to the behavioral level, i.e., to actual food intake. Interestingly, our additional experiment revealed that the missing effects on food intake were independent of the type of food presented in the pictures, i.e., there were still no effects if participants were offered exactly the food presented on the pictures. The discrepancy of the presented food pictures and the offered foods are therefore unlikely to be responsible for the lack of effects in our main study, although recent

studies demonstrated that foods are particularly rewarding when they are immediately available (Blechert, et al., 2016) and that restrained eaters only eat more when the food on offer concurs with prior food cues (Fedoroff, Polivy, & Herman, 2003).

Another interesting factor with relevance for the reactivity towards food cues might be impulsivity. Impulsive women seem to be more vulnerable to conditioned context-induced overeating (van den Akker, Jansen, Frentz, & Havermans, 2013). In our study, obese participants displayed higher impulsivity rates than lean men, which is in line with recent research (Bickel, et al., 2014; Ikeda, Kang, & Ohtake, 2010). However, there was no correlation between impulsivity rates and food intake, suggesting that impulsivity did not contribute to the lack of food intake effects in the present study.

Conclusions

While our study demonstrates a dampening effect of exposure to hedonically salient food pictures on postprandial glucose concentrations, effects on actual food intake did not emerge. Our results therefore suggest that although food pictures might induce anticipatory effects that affect postprandial blood glucose homeostasis, they do not necessarily trigger changes in ingestive behavior. These results are in line with recent studies on short-term stimulation with food cues in women, and challenge the assumption that the overall abundance of food cues contributes to overconsumption and the development of overweight. However, the nature of our study does not allow any conclusions on long-term consequences of the omnipresence of food. Further investigation of these effects is crucial when bearing in mind potential links between the increasing number of environmental food stimuli and the rising prevalence of obesity.

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