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An Examination of Homeostasis And Food Desires In Obesity Using Functional Mri

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ABSTRACT

It has been discovered that food intake in obesity is less dependent on homeostatic demands and more reward-based. Therefore, abnormal processing in reward- and control-related brain areas was found in obesity in earlier research on the neural processing of food signals. This study examined the impact of glucose metabolism on the neural response during the control of food seeking in obese people in order to better explore the relationship between homeostasis and food intake. A nasogastric tube was used to deliver either water or glucose directly into the stomach of twenty-five normal-weight and twenty-five obese women, who were then checked twice. Before each visit, participants had to abstain from eating for sixteen hours and were blinded to the kind of infusion. The impact of intestinal glucose load on the neural response during the control of food appetite was examined using an event-related fMRI paradigm. When comparing individuals with obesity to healthy controls, a 2 × 2 mixed-model ANOVA showed that desire modulation was linked to increased activity in fronto-parietal areas. Nonetheless, this impact was noted apart from homeostatic satiety. Regression analysis showed that after receiving a water infusion, those with obesity saw a decrease in food cravings and a rise in lingual gyrus activity. In persons with obesity, the neuronal response during the regulation of food appetite is connected with greater neural cognitive top-down control and higher visual food processing. Our findings suggest that homeostasis has less of an impact on brain processing during food cravings in obesity since this discovery was unaffected by satiety state.

KEYWORDS: Biochemical analysis of glucose, Stimuli and task & Functional MRI image acquisition.

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INTRODUCTION

Over 1.9 billion adults are overweight, and 650 million of them are obese, making it one of the biggest dangers to world health (WHO, 2020). In order to successfully prevent and cure obesity, it is crucial to comprehend the neurophysiological mechanisms behind prolonged and excessive consuming, as mortality and morbidity grow progressively with excess body weight (Orzano and Scott, 2004). According to earlier studies, increased food intake in obesity may be caused by changes in neural reward processing, cognitive control, and energy balance (Makaronidis and Batterham, 2018).

In order to explain the neurobiological mechanisms linked with overeating, it is crucial to study body weight regulation in its totality since it includes the integration of homeostatic, reward-, and cognitive control-related processes. Peripheral metabolic signaling abnormalities are linked to the genesis of obesity and have been identified as both a predisposing factor and a result of excessive weight gain (Cai, 2013). For instance, baseline plasma ghrelin concentrations have been reported to be lower in obese persons compared to lean individuals, and the "hunger hormone" ghrelin encourages the onset of eating (Tschöp et al., 2001). Unlike ghrelin, circulating leptin levels are elevated in obese people, who usually become resistant to leptin signaling (Klok et al., 2007). Long-term overeating can have detrimental consequences on the hypothalamus, a part of the brain essential for controlling food intake, leading to the development of leptin-resistance (Hoebel and Teitelbaum, 1962). As a result, the hypothalamus loses its sensitivity to leptin, which causes leptin levels to rise steadily and increases appetite (Fruhther et al., 2018).

Food consumption is influenced by hedonic cues and volitional control in addition to nutritional demands, even if metabolic signals have a significant influence on eating behavior (Berthoud, 2011). Studies using neuroimaging have shown that appetitive food signals encourage hedonic eating and that obese people have an increased brain reaction to high-calorie meal cues (Stoeckel et al., 2008). The enhanced motivational significance of food cues may be explained by a hyperresponsive neural reward system, which includes brain regions such the orbitofrontal cortex, striatum, amygdala, and nucleus accumbens. Hypoactivation of frontal areas, which are frequently linked to reaction inhibition and cognitive control, further enhances increased sensitivity to food cues (Yokum and Stice, 2013). Additionally, there is a significant correlation between subsequent weight gain and the level of brain activity in response to high-calorie foods. In instance, people with obesity have greater activity in response to visual food cues in the dorsal striatum, a region frequently linked to reward anticipation and habit building (Rothemund et al., 2007). Furthermore, dorsal striatal functional connectivity is positively correlated with food cravings and is elevated in obese persons (Contreras-

Rodríguez et al., 2017). Food cues can cause stimulus-response-learned behavior caused by altered dopamine neurocircuitry because of the increased sensitivity to food rewards in obesity, which has been demonstrated to be somewhat independent from physiological hunger (Novelle and Diéguez, 2018). Obesity and compulsive overeating are linked to these changes.

To understand the pathophysiology of obesity, it is essential to examine the interplay of homeostatic, hedonic, and cognitive systems. Prior research using functional magnetic resonance imaging (fMRI) has largely ignored the interaction between metabolic signals and the neural response of cognitive control in favor of concentrating on neuronal responses to visual or taste food cues (Morys et al., 2020). However, food intake and choice are also influenced by emotional and cognitive variables. It has been shown that some sensory features of eating, such sight or scent, can set off learned behaviors or conditioned reward expectancies, which in turn affect how much food is valued and how one feels about it (McCrickerd and Forde, 2016). In particular, the hedonic response to certain meals can be influenced by memories of past eating episodes and expectations about the consequences of eating (i.e., fullness, hedonic, or nutritional value) (Davidson et al., 2019). Therefore, by excluding the anticipatory effects of visual, olfactory, and oral cues, the current study focuses on the impact of metabolic state on the neural control of food seeking. We believe that persons with obesity exhibit less responsiveness to glucose injection compared to the normal-weight group because obesity is linked to lower sensitivity toward food reward and metabolic signaling (Cui et al., 2017). This study intends to further investigate the neural mechanisms underlying cue-induced food wanting and the modulation of craving in persons with obesity, as food cravings are a driving factor for overeating and the development of overweight and obesity (Verzijl et al., 2018). More precisely, we will investigate how intestinal glucose injection affects the neural response in obese individuals to self-regulation of exteroceptive food signals. The link between cognitive, homeostatic, and hedonic signals of food seeking regulation in obesity can be better understood thanks to this work.

METHODS

Participants

Twenty-five female participants were obese, with a body mass index (BMI) of >30 and 19 and 2 mm; one healthy control participant (NCON) and three obese participants (NADI) were eliminated. The Structured Clinical Interview for DSM-IV was used to screen all individuals for mental illnesses (Wittchen et al., 1997). Except for a history of severe depressive illness in those who were obese (NADI = 3), all axis I and II disorders were eliminated. Participants did not use any central nervous system-affecting medications at the time of the research. Left-handedness, MRI contraindications, psychiatric medication, pregnancy, and male gender were additional exclusion factors. The present study was approved by the ethics committee of the University of BBAU, Satellite Centre, Tikarmafi, Amethi, Uttar Pradesh, India and it was in accordance with the ethical standards and participants had to provide written consent in order to participate in the current study.

Questionnaires

Participants completed the German version of the Eating Disorder Examination Questionnaire (EDEQ) (Hilbert et al., 2007) and Beck's Depression Inventory (BDI) (Hautzinger et al., 2006) at the start of the first fMRI session. Participants were required to rate their level of hunger on a 100 mm visual analog scale both before to and following each fMRI session. Participants were instructed to predict which liquid—water or glucose—they were given following each fMRI session.

Procedure

Previous reports have described the task, stimuli, and technique (Simon et al., 2020). All individuals had fasted for at least 16 hours prior to both research sessions, and fMRI scanning began at 12 p.m. All participants were required to complete questionnaires and participate in a clinical interview at the initial research session. A fine-bore nasogastric tube (Flocare Nutrisoft, Nutricia GmbH, Erlangen, Germany) was then inserted into the gastric ventricle and affixed to the participant's face. After a five-minute baseline scan, each fMRI session began with the nasogastric tube being used to administer either 300 ml of water or 75 g of glucose dissolved in 300 ml of water (Accu-Chek® Dextrose O.G.-T., Roche, Basel, Switzerland). The Oral Glucose Tolerance Test, a common technique for evaluating glucose sensitivity, served as the basis for the 75 g glucose dosage. Prior research has shown that 75 g of glucose is adequate to cause neuronal reactions (van Opstal et al., 2020). During the initial fMRI session, individuals were randomly assigned to receive either water or glucose in a counterbalanced sequence. In order to evaluate the hypothalamus's responsiveness to glucose/water infusion, subjects received 30 minutes of fMRI scanning after liquid infusion (Simon et al., 2020). The experimental task, which lasted around 17 minutes, came next. Results from both healthy volunteers and anorexic patients have previously been published. Three blood samples were obtained in order to guarantee a suitable physiological reaction to glucose: 30 minutes before entering the scanner, and 30 and 60 minutes following the infusion of either water or glucose.

Table 1. lists the participants' clinical and demographic details.

Variables	Normal weight Controls (N=26)	Participants with Obesity (N=20)	P
Age in years, mean (SD)	23.83 (4.99)	27.69 (6.25)	0.234
BMI, mean (SD)	21.78 (1.48)	36.07 (3.58)	<0.001
Education in years, mean (SD)	12.89 (0.62)	11.89 (1.18)	0.061
BDI, mean (SD)	4 (3.81)	11.75 (8.13)	<0.001
EDEQ total score, mean (SD)	11.18 (9.19)	56.17 (21.24)	<0.001
EDEQ restraint, mean (SD)	2.39 (3.18)	10.54 (6.18)	<0.001
EDEQ eating concern, mean (SD)	0.5 (0.72)	5.92 (4.17)	<0.001
EDEQ weight concern, mean (SD)	2.64 (2.12)	13.27 (5.65)	<0.001

EDEQ shape concern, mean (SD)	5.85 (4.29)	26.5 (9.82)	<0.001

BDI Beck Depression Inventory, BMI body mass index, EDEQ Eating Disorder Examination Questionnaire.

Biochemical analysis of glucose

At the University BBAU, Satellite Centre, Tikarmafi, Amethi, Uttar Pradesh, India central laboratory, glucose concentrations were measured using the hexokinase technique on a Siemens Advia 2400 system. A repeated-measures ANOVA with infusion method and time point as within variables and group as between factors was used to evaluate variations in blood glucose levels.

Stimuli and task

Participants had to select eight out of 85 pictures that showed foods high in calories throughout each fMRI session. More precisely, participants were asked to select the pictures that they were now wanting. As a control condition, eight pictures that weren't of food were utilized. A modified version of an emotion management task used as the experimental paradigm (Kanske et al., 2011). The paradigm, which had two instructions, was applied in an event-related design. Participants were instructed to either focus intently on the pictures (the watching condition) or use an arithmetic calculation to divert their attention from their cravings (the distraction condition). The food or nonfood picture was shown for 1000 ms following a fixation cross (jittered interval of 30 00–4500 ms). The arithmetic equation was shown as a semitransparent overlay on the picture for 6000 ms after the induction in the distraction condition. In order to indicate whether the equation (for example, 4 + 8 − 2 = 11) was solved properly or wrongly, participants were encouraged to answer the problem as quickly as possible by pressing a button. After viewing instructions for 1000 ms, the picture was presented for 5000 ms to start the viewing condition. For an additional 4000 milliseconds, each experimental condition was followed by a 9-point Likert scale yearning assessment for the previously shown food picture (or a want rating in the case of nonfood things). Each image was shown twice throughout the 64 trials that made up the experimental paradigm.

Functional MRI image acquisition

At the University Hospital Symbiosis Medical College for Women & Symbiosis University Hospital India, a 3 Tesla Siemens Trio MRI scanner (Siemens Medical Solutions, Erlangen, Germany) was used to gather functional MRI pictures. A total of 523 functional T2*-weighted images with a voxel size of 3 × 3 × 4 mm, repetition time (TR) = 2000 ms, echo time (TE) = 30 ms, and flip angle (FA) = 80° were obtained in an interleaved slide order for each research session. Each volume has a field of view (FOV) of 192 × 192 × 120 mm and 30 axial slices. Additionally, we obtained a 192-slice T1-weighted structural picture with TR = 1900, TE = 2.52 ms, and FOV = 256 × 256 × 256 mm.

Data analysis

Statistical Parametric Mapping (SPM8, Wellcome Department of Imaging Neuroscience, London, UK) using MATLAB Version 7.13 (Mathworks, Inc.) was used to evaluate functional MRI data. Slice-time correction, realignment, spatial normalization to a standard stereotactic space, and spatial smoothing using an 8 mm full-width at half maximum Gaussian smoothing kernel comprised the pre-processing pipeline. After co-registration with the mean T2* image, structural images were spatially normalized to the Montreal Neurological Institute standardized space and divided into gray matter, white matter, and cerebrospinal fluid partitions. The duration of each experimental trial and the stimulus start determined the experimental conditions (food distraction, nonfood distraction, food watching, and nonfood viewing) at the single-subject level. The hemodynamic response function was modeled and convolved with experimental circumstances. The ratings, the induction phase, and six movement characteristics were included as uninteresting regressors. Low-frequency noise was eliminated using a high-pass filter with a cutoff of 128 s. A General Linear Model was used to compute the following contrasts of interest: (1) distraction from food—seeing food, and (2) watching food—viewing nonfood things. Using the results from the contrast "distraction from nonfood objects—viewing nonfood objects" as an exclusive mask in all subsequent second-level analyses, we controlled for distraction-specific brain activation, unlike our earlier studies with the same group of healthy participants (Stopyra et al., 2020). In particular, a disjunction analysis (exclusive masking) was carried out using a binary mask constructed from the combined group results (thresholded at $P < 0.05$ cluster level family-wise error (FWE) corrected with a clusterdefining threshold of $P < 0.001$ uncorrected and minimal cluster size of $k > 50$) to exclude activation in brain regions observed during both the distraction from nonfood objects and the distraction from food. A 2 × 2 mixed-model ANOVA (flexible factorial design) was used for the group-level analysis, with liquid type (water, glucose) as a within factor and group (participants with obesity, healthy controls) as a between-subjects factor. To account for dependencies, subject constants were represented using a between factor "subject." As a result, we excluded nuisance factors from this model. The effects of glucose and water infusion were examined separately in persons who were obese and normalweight controls using paired t-tests. Additionally, we modeled variations in craving ratings (desiring ratings during distraction from food vs. craving ratings while sight of food) as a covariate of interest in a whole-brain regression analysis for the contrast "distraction from food—viewing food." Regression analysis was performed independently for both groups and for the infusion of water and glucose, and depression scores were added as variables of no interest. The mean gray matter image of each participant was used to inclusively mask the findings of all fMRI studies (mean binarized image computed with ImCalc in SPM). Additionally, only findings that are significant at the $P < 0.05$ cluster level FWE corrected are shown, with a minimum cluster size of $k > 50$ and a cluster-defining criterion of $P < 0.001$ uncorrected. SPSS (Version 25; SPSS Inc., Chicago, IL, USA) was used to analyze behavioral data. Independent two-sample t-tests were used to evaluate group differences in demographic factors and psychometric scores. A repeated-measures ANOVA was used to evaluate differences in pre-post hunger ratings across groups, with group acting as a between factor and infusion type (water vs. glucose) and time point (before vs. after scanning) acting as within factors. A repeated-measures ANOVA with infusion type as a within factor and group as a between factor was used to evaluate craving ratings during the task.

RESULTS

Behavioral results

Age and years of schooling did not differ across the groups, however individuals who were obese had higher BMI, BDI, and EDEQ scores (Table 1). Because both groups guessed at the chance level at the first visit (normal-weight controls: $\chi 2 = 0.044$, P = 0.799, participants with obesity: $\chi 2 = 0.210$, P = 0.619) and second visit (normal-weight controls: $\chi 2 = 2.191$, P = 0.14, participants with obesity: $\chi 2 = 0.168$, P = 0.625), participants were kept in the type of liquid given during each session.

Hunger ratings

We failed to observe a significant interaction effect in our repeated-measures ANOVA (group × infusion type × time point, P = 0.769). Furthermore, we did not observe a significant change in hunger ratings pre–post scanning during water or glucose infusion in the whole sample (Ps > 0.061). When assessed separately, only participants with obesity displayed a significant increase in hunger ratings following water infusion (t(21) = 2.47, P = 0.019, see Table 2).

Table 2. Descriptive statistics for hunger/craving ratings and blood glucose levels.

Variables	Normal weight Controls (N=26)	Participants with Obesity (N=20)	P
Hunger before water infusion	50.68 (25.95)	51.06 (22.21)	0.941
Hunger after water infusion	52.38 (27.15)	61.41 (20.29)	0.220
Hunger before glucose infusion	56.18 (23.42)	50.89 (25.35)	0.511
Hunger after glucose infusion	51.00 (26.01)	52.42 (23.68)	0.833
Craving during food distraction—water	7.27 (0.74)	6.33 (1.06)	0.220
Craving during food viewing—water	7.28 (0.68)	7.21 (0.98)	0.558
Craving during food distraction—glucose	7.01 (0.97)	6.39 (1.59)	0.279
Craving during food viewing—glucose	7.04 (0.94)	6.85 (1.45)	0.814
Blood glucose prior water infusion	79.73 (6.22)	81.45 (7.75)	0.713
Blood glucose 30 min post water infusion	81.45 (5.19)	80.40 (6.29)	0.539
Blood glucose 60 min post water infusion	82.82 (5.86)	81.95 (6.11)	0.646
Blood glucose prior glucose infusion	83.09 (4.61)	83.59 (7.57)	0.723
Blood glucose 30 min post glucose infusion	144.50 (19.28)	131.52 (26.15)	0.056
Blood glucose 60 min post glucose infusion	139.80 (29.34)	134.77 (37.42)	0.629

Craving ratings

When assessing food photographs for cravings, there was no interaction between group, infusion type, or experimental condition (viewing vs. distraction) (F(1,43) = 0.076, P = 0.765). Additionally, there was no group influence on the kind of infusion or the experimental condition when assessing cravings (Ps > 0.065). In the entire sample, there was no main effect of infusion type on craving ratings (F(1,43) = 1.61, P = 0.201), but there was a main effect of experimental condition on craving ratings (F(1,42) = 7.43, P = 0.009), with lower ratings during distraction compared to viewing in the combined sample (t(91) = −2.56, P = 0.011, see Table 2).

Blood glucose analyses

Some participants' blood glucose levels could not be measured at all three test sites due to technological issues. The corresponding test results are accompanied by information concerning missing values. There was no significant group effect on the infusion type × time point interaction (P = 0.291), but we did find a significant interaction between infusion type (glucose vs. water infusion) and time point (before, during, and after scanning; F(2,73) = 103.9, P < 0.001, missing values in healthy controls: 2, missing values in participants with obesity: 3). Following glucose infusion, blood glucose levels in both groups significantly increased (blood glucose after scanning compared to baseline, normal-weight controls: t(21) = 8.56, P < 0.001, missing values: 2 persons with obesity: t(21) = 4.3, P < 0.001, missing values: 0). Baseline blood glucose levels for both fMRI measures did not differ between the two groups (Ps > 0.613, missing data in both groups: 0). Additionally, both groups showed baseline blood glucose levels that are normally seen in healthy persons who are fasting (Phillips, 2012). See Table 2 for comprehensive descriptive statistics.

FMRI results

Group differences

For both of the relevant comparisons, we found no evidence of a significant interaction between group and liquid type. However, we found a significant group impact in the right dorsolateral prefrontal cortex (DLPFC), medial occipital cortex, bilateral inferior parietal lobule, anterior prefrontal cortex, and middle frontal gyrus for the contrast distraction from food as opposed to watching food (Table 3). Participants who were obese showed higher activity in these areas, according to a post hoc analysis comparing the two groups. It should be mentioned, nonetheless, that because we included two contrast photos for each subject (for both the water and glucose condition), this analysis was artificially overdone. We found a substantial group effect in the occipital cortex for the difference between viewing food and nonfood objects, which was more pronounced in normal-weight controls (Table 3). Crucially, since there was no interaction between group and liquid type, these benefits were seen regardless of the kind of infusion. As a consequence, there were no significant findings from post hoc testing comparing groups during the infusion of water and glucose.

Table 3. Repeated-measures mixed-model ANOVA results; significant effect of "group" on BOLD response during distraction from food and viewing of food.

Contrast/brain regions	z value	P value	k	x	y	z
Distraction from food compared to viewing food						
Dorsolateral prefrontal cortex	5.92	<0.001	182	44	40	25
Medial occipital cortex	5.31	0.001	180	−6	−85	6
Right inferior parietal lobule	5.39	0.001	321	34	−43	32
Left inferior parietal lobule	5.15	0.003	225	−48	−45	54
Anterior prefrontal cortex	5.08	0.004	94	−3	62	14
Middle frontal gyrus	4.81	0.009	80	34	8	62
Viewing food compared to viewing nonfood objects						
Medial occipital cortex	5.17	0.002	147	−14	−83	−2

k = cluster size (voxels). Results significant at PFWE < 0.05 are reported, with a cluster-defining threshold of P < 0.001 uncorrected and minimal cluster size of k > 50.

Within group results

For all contrasts of interest, we found no differences between glucose and water infusion in obese patients. The brain stem (t = 5.04, k = 86, PFWE = 0.041, x = −9, y = −34, z = −21) and bilateral nucleus caudatus (t = 4.74, k = 91, PFWE = 0.033, x = 9, y = 17, z = −2) showed increased activation after glucose infusion when compared to water infusion for the contrast distraction from food.

Regression analysis

After both water and glucose infusion, we found no correlation between brain activity during food-related distraction and evaluations of desire in healthy individuals. Following glucose infusion, there was no correlation between craving ratings and brain activation in obese participants. However, after water infusion, we found a positive correlation between differences in craving ratings (i.e., craving during food viewing vs. craving following food distraction) and activation in the lingual gyrus (t = 4.98, k = 96, PFWE = 0.024, x = 24, y = −52, z = 2).

DISCUSSION

Bypassing eating-related cognitions, the current investigation investigated the impact of intestinal glucose injection on the neural modulation of cue-induced food appetite in obese women. In women who were obese, we found no changes in the neural control of food cravings between glucose and water infusion. On the other hand, after water infusion, we found a favorable correlation between the lowering of food cravings and activity in the lingual gyrus during the distraction from food imagery.

During the diversion from meals, we found that the normal-weight group's neurons differed depending on whether they were infused with water or glucose. More precisely, the delivery of glucose enhanced bilateral nucleus caudatus and brain stem activity. The caudate nucleus is engaged in reward expectancy (Haruno and Kawato, 2006), whereas the brain stem gets projections from the hypothalamus and so greatly contributes to several aspects of energy balance (Roh et al., 2016). As a result, our results suggest both sufficient communication from the hypothalamus to the rest of the brain and a satiety-dependent interplay between glucose signaling and hypothalamic activity. The neural modulation of food cravings in obese individuals was independent of metabolic state, in contrast to women of normal weight. This finding is consistent with our research group's earlier study, in which we examined the same subjects and discovered that obesity is linked to a blunted hypothalamic reactivity in response to glucose infusion, suggesting a reduced or desensitized neuronal reactivity to glucose metabolism. These results are extended to the neural top-down regulation of food cravings in the current investigation. When compared to individuals of normal weight, those who are obese do not show the anticipated drop in leptin and ghrelin production after eating (le Roux et al., 2005). In a similar vein, our results may suggest that after glucose infusion, neural regulation of appetite is compromised, which in turn promotes greater food consumption and weight gain. Neuro-endocrinological signals like ghrelin and leptin most likely underlie the neuronal desensitization to metabolic changes in blood glucose levels. Therefore, faulty desire control in obesity may be related to impairment in central satiety signaling.

As anticipated, subjective judgments of satiety were unaffected by glucose infusion. The lack of cognitive processing and sensory signals, which have been linked to reduced satiety responses in the past, might be the reason for this discovery. We cannot rule out the possibility that a larger glucose dosage had a major impact on subjective satiety. The current study, however, sought to examine how homeostatic satiety—which is distinct from subjective satiety—affects neural responsiveness. Our results highlight the significance of nutritional content and the cephalic phase of gastric secretion as crucial contributing elements to the subjective sense of fullness and related neural responses. Indeed, Crézé and associates contend that in order to elicit a physiological and behavioral satiety response, congruent taste signals and caloric value are required (Crézé et al., 2018).

After being distracted, food cravings decreased similarly in both groups. When comparing water and glucose infusion separately, we found no group differences in neural processing during distraction; however, when pooling the data across conditions (i.e., water and glucose), the distraction from food cravings for pictures of appetizing foods was linked to increased activation in fronto-parietal regions (including the DLPFC) related to self-regulation in obese individuals. According to earlier research, the DLPFC is implicated in the down regulation of appetitive impulses and is a key brain area in dietary self-control (Lowe et al., 2019). Our findings may thus suggest that obese people need more cognitive resources to reduce their cravings to the same extent as

participants of normal weight. However, these results should be interpreted cautiously since pooling across circumstances artificially boosts statistical power, and group differences were only observed when pooling across conditions.

Furthermore, a greater decrease in food cravings in obese women was linked to enhanced lingual gyrus activity. When compared to nonfood stimuli, the lingual gyrus has been shown to be engaged in visual processing of food cues, but its primary function is attentional processing (Huerta et al., 2014). Additionally, a study by Aviram-Friedman and colleagues (2018) discovered that when individuals with binge eating disorder watch pictures of high-calorie and low-calorie foods, their lingual gyrus becomes more activated. The authors talked about how involuntary attention to food might be indicated by the activation of visual areas. Furthermore, visual signals that elicit cravings for things like food, alcohol, cigarettes, narcotics, and video games stimulate the lingual gyrus (Zhou et al., 2019). The demand for more cognitive processing during desire reduction in obesity may be indicated by an enhanced allocation of attentional resources during food craving regulation, albeit this is hypothetical. It is unclear, nonetheless, whether the correlation between lingual gyrus activity and desire reduction in individuals with obesity is suggestive of an increased need for neural resources to reduce seeking, given we did not find any differences in craving reduction across our groups.

This study has a number of shortcomings. Since executive functioning was not evaluated in this investigation, our neuroimaging results may have been impacted by potential variations in executive functioning between people of normal weight and those who are obese. Furthermore, since sadness may alter how rewarding stimuli are processed, variations in depressed symptoms between the two groups may have complicated the fMRI results. Additionally, we only looked at women, and our findings should be interpreted cautiously because sex-related variations in neural food processing have previously been noted. The fact that we did not account for the menstrual cycle, despite evidence showing variations in progesterone and estradiol affect brain food processing, may be another drawback (Arnoni-Bauer et al., 2017). Furthermore, we did not gather information on energy requirements and expenditures, so we cannot completely rule out the possibility that this might have had an impact on glucose metabolism. Additionally, because participants could only select eight food pictures, we cannot completely rule out the impact of habituation effects on our findings. Only one method of controlling food cravings was examined in this study. Nonetheless, it seems that various techniques are preferred by different individuals (Giuliani et al., 2013). Finally, since people with obesity frequently have a history of dieting, which may affect cognitive evaluation of food pictures, it should be noted that participants may have also (explicitly or implicitly) controlled their food cravings during the viewing condition (Myers et al., 2018). Therefore, future studies should examine the impact of previous dieting experiences on regulation strategies during food craving.

CONCLUSION

When considered collectively, our findings lend credence to the idea that neuronal processing during the control of food cravings in obese persons occurs independently of physiological fullness. These results highlight the significance of homeostatic changes for the maintenance of obesity and add to the observation of a central neuronal resistance to glucose signaling in obesity. Additionally, our findings point to enhanced visual attentional processing and neural top-down regulation during the lowering of cravings in obesity. To improve our understanding of the connection between food cravings, craving management, and homeostatic signaling, further research is required. In order to develop innovative therapies for obesity and overweight, it is crucial to comprehend the relationship between eating behavior and neural activity.

REFERENCES

1. Al-Zubaidi A, Heldmann M, Mertins A, Brabant G, Nolde JM, Jauch-Chara K, et al. Impact of hunger, satiety, and oral glucose on the association between insulin and resting-state human brain activity. Front Hum Neurosci. 2019;13:1–15.
2. Arnoni-Bauer Y, Bick A, Raz N, Imbar T, Amos S, Agmon O, et al. Is it me or my hormones? Neuroendocrine activation profiles to visual food stimuli across the menstrual cycle. J Clin Endocrinol Metab. 2017;102:3406–14.
3. Aviram-Friedman R, Astbury N, Ochner CN, Contento I, Geliebter A. Neurobiological evidence for attention bias to food, emotional dysregulation, disinhibition and deficient somatosensory awareness in obesity with binge eating disorder. Physiol Behav. 2018;184:122–8.
4. Berthoud HR. Metabolic and hedonic drives in the neural control of appetite: is the boss? Curr Opin Neurobiol. 2011;21:888–96.
5. Cai D. Central mechanisms of obesity and related metabolic diseases. Rev Endocr Metab Disord. 2013;14:309–10.
6. Contreras-Rodríguez O, Martín-Pérez C, Vilar-López R, Verdejo-Garcia A. Ventral and dorsal striatum networks in obesity: link to food craving and weight gain. Biol Psychiatry. 2017;81:789–96.
7. Crézé C, Candal L, Cros J, Knebel JF, Seyssel K, Stefanoni N, et al. The impact of caloric and non-caloric sweeteners on food intake and brain responses to food: a Randomized Crossover Controlled Trial in healthy humans. Nutrients. 2018;10:1–17.
8. Cui H, López M, Rahmouni K. The cellular and molecular bases of leptin and ghrelin resistance in obesity. Nat Rev Endocrinol. 2017;13:338–51.
9. Davidson TL, Jones S, Roy M, Stevenson RJ. The cognitive control of eating and body weight: it's more than what you "think". Front Psychol. 2019;10:1–22.
10. English PJ, Ghatei MA, Malik IA, Bloom SR, Wilding JP. Food fails to suppress ghrelin levels in obese humans. J Clin Endocrinol Metab. 2002;87:2984.
11. Fruhwürth S, Vogel H, Schürmann A, Williams KJ. Novel insights into how overnutrition disrupts the hypothalamic actions of leptin. Front Endocrinol. 2018;9:89.
12. Giuliani NR, Calcott RD, Berkman ET. Piece of cake. Cognitive reappraisal of food craving. Appetite. 2013;64:56–61.
13. Haruno M, and Kawato M. Different neural correlates of reward expectation and reward expectation error in the putamen

and caudate nucleus during stimulusaction-reward association learning. J Neurophysiol. 2006;95:948–59.
14. Hautzinger M, Keller F, Kühner C. Beck depressions-Inventar: BDI II. Revision. Harcourt Test Services: Frankfurt/Main; 2006.
15. Hilbert A, Tuschen-Caffier B, Karwautz A, Niederhofer H, Munsch S. Eating Disorder Examination-Questionnaire. Diagnostica. 2007;53:144–54.
16. Hoebel BG, and Teitelbaum P. Hypothalamic control of feeding and self-stimulation. Science. 1962;135:375–7.
17. Huerta CI, Sarkar PR, Duong TQ, Laird AR, Fox PT. Neural bases of food perception: coordinate-based meta-analyses of neuroimaging studies in multiple modalities. Obesity. 2014;22:1439–46.
18. Kanske P, Heissler J, Schonfelder S, Bongers A, Wessa M. How to regulate emotion? Neural networks for reappraisal and distraction. Cereb Cortex. 2011;21:1379–88.
19. Klok MD, Jakobsdottir S, Drent ML. The role of leptin and ghrelin in the regulation of food intake and body weight in humans: a review. Obes Rev. 2007;8:21–34.
20. le Roux CW, Patterson M, Vincent RP, Hunt C, Ghatei MA, Bloom SR. Postprandial plasma ghrelin is suppressed proportional to meal calorie content in normalweight but not obese subjects. J Clin Endocrinol Metab. 2005;90:1068–71.
21. Lowe CJ, Reichelt AC, Hall PA. The prefrontal cortex and obesity: a health neuroscience perspective. Trends Cogn Sci. 2019;23:349–61.
22. Makaronidis JM, and Batterham RL. Obesity, body weight regulation and the brain: from fMRI. Br J Radiol. 2018;91:20170910.
23. McCrickerd K, and Forde CG. Sensory influences on food intake control: moving beyond palatability. Obes Rev. 2016;17:18–29.
24. Morys F, García-García I, Dagher A. Is obesity related to enhanced neural reactivity to visual food cues? A review and meta-analysis. Soc Cogn Affect Neurosci. 2020;nsaa113:1–11.
25. Myers CA, Martin CK, Apolzan JW. Food cravings and body weight: a conditioning response. Current Opinion Endocrinol, Diabetes, Obes. 2018;25:298–302.
26. Orzano JA, and Scott JG. Diagnosis and treatment of obesity in adults: an applied evidence-based review. J Am Board Fam Pract. 2004;17:359–69.
27. Phillips PJ. Oral glucose tolerance testing. Aust Family Phys. 2012;41:391–3.
28. Roh E, Song DK, Kim M-S. Emerging role of the brain in the homeostatic regulation of energy and glucose metabolism. Exp Mol Med. 2016;48:e216.
29. Rothemund Y, Preuschhof C, Bohner G, Bauknecht HC, Klingebiel R, Flor H, et al. Differential activation of the dorsal striatum by high-calorie visual food stimuli in obese individuals. NeuroImage. 2007;37:410–21.
30. Simon JJ, Stopyra MA, Mönning E, Sailer S, Lavandier N, Kihm LP, et al. Neuroimaging of hypothalamic mechanisms related to glucose metabolism in anorexia nervosa and obesity. J Clin Investig. 2020;130:4094–103.
31. Stoeckel LE, Weller RE, Cook EW, Twieg DB, Knowlton RC, Cox JE. Widespread reward-system activation in obese women in response to pictures of high-calorie foods. NeuroImage. 2008;41:636–47.
32. Stopyra MA, Friederich H-C, Mönning E, Lavandier N, Bendszus M, Herzog W, et al. The influence of homeostatic mechanisms on neural regulation of food craving in anorexia nervosa. Psychol Med. 2020;51:1011–19
33. Tschöp M, Weyer C, Tataranni PA, Devanarayan V, Ravussin E, Heiman ML. Circulating ghrelin levels are decreased in human obesity. Diabetes. 2001;50:707–9.
34. van Opstal AM, Hafkemeijer A, van den Berg-Huysmans AA, Hoeksma M, Blonk C, Pijl H, et al. Brain activity and connectivity changes in response to glucose ingestion. Nutr Neurosci. 2020;23:110–7.
35. Verzijl CL, Ahlich E, Schlauch RC, Rancourt D. The role of craving in emotional and uncontrolled eating. Appetite. 2018;123:146–51.
36. Wittchen H, Zaudig M, Fydrich T. SKID. Strukturiertes Klinisches Interview für DSM-IV: Achse I und II (SCID. Structured Clinical Interview for DSM-IV: axis I and II.). 1997.
37. World Health Organization. Obesity and overweigt. [Fact sheet]. 2020.
38. Yokum S, and Stice E. Cognitive regulation of food craving: effects of three cognitive reappraisal strategies on neural response to palatable foods. Int J Obes. 2013;37:1565–70.
39. Zhou Y, Gao X, Small DM, Chen H. Extreme spicy food cravers displayed increased brain activity in response to pictures of foods containing chili peppers: an fMRI study. Appetite. 2019;142:104379.