Does GLP-1 receptor agonist liraglutide alter food-related sensory pleasure in patients with obesity? A randomized controlled trial

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Abstract

Background/Objectives: Obesity is a complex condition and the mechanisms involved in weight gain and loss are poorly understood. Liraglutide, a GLP-1 receptor agonist, has been demonstrated to successfully promote weight loss in patients with obesity (OB). Yet, it is unclear whether the observed weight loss is driven by an alteration of food reward processing. Here we investigated the effects of liraglutide on cerebral correlates of food-related sensory pleasure in OB.

Subjects/Methods: This study was a randomized, single-centre, double-blind, placebo-controlled, parallel group, prospective clinical trial. 73 patients with OB and without diabetes were randomly assigned (1:1) to receive liraglutide 3.0 mg (37.40±11.18 years old, BMI = 35.89 kg ±3.01) or placebo (40.04±14.10 years old, BMI = 34.88 kg ±2.87) subcutaneously once daily, for 16 weeks. They also followed a multidisciplinary weight loss program.

Interventions/Methods: We investigated sensory pleasure during food consumption (i.e., “liking”). Participants reported their hedonic experience while consuming a high-calorie food (milkshake) and a tasteless solution. The solutions were administered inside the scanner with a Magnetic Resonance Imaging (MRI)-compatible gustometer to assess neural responses during consumption. The same procedure was repeated for pre- and post-intervention sessions.

Results: The liraglutide group lost more weight (BMI post-pre = - 3.19 kg/m^2 ±1.28) than the placebo group (BMI post-pre = - 0.60 kg/m^2 ±1.26). The sensory pleasure during food reward consumption was associated with the activation of the ventromedial prefrontal cortex (vmPFC) and the amygdala. We did not find any statistically significant difference in the liraglutide group between the pre and post sessions, neither at a subjective level nor at a neural level in terms of reactivity of the vmPFC to the milkshake.

Conclusions: These results suggest that liraglutide leads to weight loss without self-report or neural evidence supporting a concomitant reduction of food-related sensory pleasure in patients with from obesity.

Introduction

Obesity is a complex condition associated with cognitive, affective, behavioral, cerebral, and metabolic dysfunctions [1–5]. Nevertheless, the mechanisms involved in weight gain and weight loss are poorly understood.

Glucagon–like peptide 1 (GLP-1) analogues, approved for the treatment of type 2 diabetic patients (T2DM) because of their glucose–lowering effects, have shown an additional benefit on weight loss. As of today, the exact mechanisms of GLP-1 agonists on weight loss are poorly understood. GLP-1 analogues have been demonstrated to promote weight loss in patients by exerting anorectic effect [6]. One could speculate that the GLP-1 agonists-related side effects (e.g., nausea, vomiting) are the main responsible for decreased appetite and weight reduction. However, the large majority of treated patients lose weight in absence of clinically significant side effects of the GLP-1 analogs. fMRI studies examining the effects of GLP-1 on reward circuitry in humans with obesity and using food stimuli administered by an fMRI-compatible gustometer are limited. It has been demonstrated that liraglutide may exert central effects by decreasing attention to highly desirable food cues, as illustrated by decreased parietal cortex activation [7]. Farr et al. [8] also showed that liraglutide may increase the right orbitofrontal cortex response to food cues when administrated at a high dose and in a long-term fashion. More recently, Hanssen et al. [9] have shown behavioral evidence of GLP-1 modulation of incentive motivation on food rewards but did not investigate neural correlates of this effect.

Here we investigated whether GLP-1 analogue liraglutide affects food-related sensory pleasure in obesity without diabetes. We measured self-reports as well as brain responses to a milkshake compared to a tasteless solution in two groups of patients with obesity and without diabetes: an intervention group receiving liraglutide injections daily and a control group receiving placebo injections during 16 weeks of treatment period.

Materials And Methods

Trial overview

The data reported here were acquired in the context of a larger study, components of which have been [10] and will be reported separately. More precisely, we conducted this randomized, single-centre, double-blind, placebo-controlled, parallel group, prospective clinical trial from March 7, 2018, through March 18, 2020, in the Geneva University Hospitals (Switzerland), i.e. before the COVID-19 pandemic – we can reasonably exclude COVID-19 loss of smell and taste in the patients recruited. The trial was carried out in accordance with the protocol and with principles enunciated in the current version of the Declaration of Helsinki, the guidelines of Good Clinical Practice (GCP) issued by ICH, and the Swiss Law and Swiss regulatory authority's requirements. The trial was registered on ClinicalTrials.gov (NCT03347890) and the protocol and any subsequent amendments were approved by local ethical committee (Commission Cantonale d'Ethique de la Recherche, CCER, Genève) and by Swiss Agency for Therapeutic Products (Swissmedic). Safety of the participants was monitored throughout the trial by an independent data monitoring committee and was monitored from screening to week 16. Participants were informed about the aims of the study and gave their written consent before the initiation of any trial-related procedures. The trial overview is presented in Fig. 1.

Participants

Multidisciplinary weight loss program: Participants with obesity (Body Mass Index, BMI $\geq$ 30 kg/m^2 and < 45 kg/m^2) were recruited in the Division of endocrinology, diabetology, nutrition and therapeutic patient education in Geneva University Hospitals among patients addressed for a structured and multidisciplinary patient educational weight loss program. This weight loss program based on lifestyle counseling (combining group and individual approach) includes a cognitive behavioral therapy coupled with a diet and physical activity support, as described in detail in Pataky et al. [11]. Patients attended individual and group counseling sessions during the 16-week period, delivered by qualified health care professionals (registered dietician, nurse and physicians specialized in obesity treatment and patient education). The weight loss program was consequently tailored to each patient's needs.

Inclusion and exclusion criteria: The inclusion criteria were defined as age between 18 and 75 years, stable body weight (< 5% reported change within 3 months before screening), right-handedness and being currently non-smoker. The exclusion criteria were based on contraindications to Liraglutide treatment, any drugs interfering with the body weight control (e.g., Orlistat, Phentermine and Topiramate, Buproprion and Naltrexone) or any centrally acting medication, history of any psychiatric disease, heart failure (NYHA II-IV), type 1 and type 2 diabetes mellitus and deficits of smell and taste. The complete list of eligibility criteria is listed in the supplementary information. All participants gave written informed consent and received 200 Swiss Francs (the equivalent of 200 USD$) for their participation in the two sessions.

Trial population: A total of 73 participants with obesity (OB) were screened. After being checked for the study eligibility criteria, 66 participants were included in the trial. Among them, 32 were randomized to liraglutide 3.0 mg combined with lifestyle counseling and 34 to placebo combined with lifestyle counseling (see Fig. 1 in Supplementary Information). Baseline characteristics of the studied population are described in Table 1, Supplementary Information.

In total, 22 participants were excluded from the analysis (10 participants did not complete the second testing session and 12 participants had missing or corrupt MRI data). We report data on the 44 remaining participants (liraglutide group: age 37.4 years ± 11.18, BMI 35.89 kg/m^2 ± 3.01, n = 20; placebo group: age 40.04 years ± 14.1, BMI 34.88 ± 2.87 kg/m^2, n = 24).

Taste stimuli and presentation

We used two types of stimuli in this experiment: a milkshake and a tasteless solution.

We prepared the milkshake by mixing a chocolate flavored milk drink (300 g) with a fior di latte flavored ice cream (60 g) for a total of 71 kcal/100 g.

We prepared a tasteless solution as close as possible to artificial saliva in three steps. First, we diluted potassium chloride (KCl, 1.8g) and sodium bicarbonate (NaHCO3, 0.21g) in 1 L of distilled water. Second, we created three less concentrated versions of this solution. Thus, there were 4 different tasteless concentrated solutions (1/1, ¾, ½ and ¼). Third, patients were invited to taste the 4 solutions. We picked the one that tasted the most neutral to them (i.e., closest to 50 on a scale from 0 to 100) as their tasteless solution. We believe it was better to use one of these 4 tasteless solutions as the control stimulus rather than water because water has an inherent taste [12].

The milkshake and the tasteless solution were kept in the fridge. We took them out simultaneously, 30 minutes before the experiment so that they were delivered at ambient temperature.

The apparatus used to deliver the liquids in the scanner has been described in Muñoz-Tord et al. [10]. In a nutshell, a 3D-printed pacifier-shape fMRI mouthpiece paired with a gustometer was used to deliver liquids while participants were lying down. As demonstrated in Muñoz-Tord et al. [10], this allows a precise, reliable and comfortable liquid delivery. The collection of the responses was controlled by a computer running MATLAB (version R2015a; MathWorks, Natick, USA). The presentation of the visual stimuli was implemented using Psychtoolbox (version 3.0) [13].

Procedures

Participants who fulfilled the randomization criteria were randomly assigned, in a 1:1 ratio, to receive liraglutide 3.0 mg or placebo, after a dose escalation period starting at 0.6 mg q.d., with weekly increments of 0.6 mg, administered subcutaneously by pen injectors. The placebo pen injector was strictly identical to the liraglutide pen injector. Participants were followed-up on a weekly basis during the dose escalation period of 5 weeks and monthly afterwards.

Metabolic measures

Blood samples for study purposes were collected both at baseline and 16-week follow-up. Plasma fasting blood glucose, insulin, plasma lipids and HbA1c were measured by routine biochemistry in fasting conditions.

Experimental Procedure

The experiment consisted of three separate testing days (see Fig. 1). The first time participants came to the laboratory for a pretest (see description below). The second time participants came for a test session before the beginning of the intervention (i.e., baseline testing session). This session took place in the morning. All participants were asked to fast overnight. Afterwards, participants followed the intervention (placebo + counseling vs liraglutide + counseling) and came back to the laboratory a third time at the end of the intervention for a second test session (i.e., 16 weeks follow-up testing session). Both test sessions followed the exact same procedure.

Please note that during the test sessions participants performed multiple experimental tasks, but, here, we only report the results for the hedonic reactivity task.

Pretest. Participants chose the most neutral tasteless solution to them. The 4 solutions were presented to them in shot glasses (= 1dl). Participants self-reported current hunger level and pleasantness, intensity and familiarity levels for their selected tasteless solution and for the milkshake (see Table 2, supplementary information). They also underwent 10–20 minutes of structural scans in the MRI. This small fMRI session allowed them to be more confident and comfortable for the longer functional scans taking place during the test sessions.

Test session. We administered a taste reactivity task while participants were lying in the scanner. The task consisted in the evaluation of the perceived pleasantness, intensity and familiarity of the two different stimuli: the milkshake and the tasteless solution. Participants were instructed to assess the solutions focusing on their current perception of them. During each trial, 1 mL of the solution was administered, and the delivery order of the two conditions was randomized within each participant. Participants were visually guided through the task with on-screen indications. First, they saw a 3 seconds countdown before the solution was delivered, followed by an asterisk presented for 4 seconds and indicating them to keep the solution on their tongue until they saw the indication to swallow: “swallow please” (see Fig. 2). We asked them to wait 4 seconds before swallowing to avoid adding movement noise to the Blood-Oxygen-Level-Dependent (BOLD) response. Since they were lying down, the mouthpiece was placed in such a way that the solution was delivered at the center of the participant’s tongue. We expected that the solution would slide down to the back of their tongue during the 4 seconds period in which they had the solution on it. The experimental trials were intertwined with rinse trials to cleanse the participants’ palates with 1 mL of water. All 40 evaluations (20 per solution) were done on visual analog scales displayed on a computer screen. Participants had to answer through a button-box placed in their hand. The visual scales ranged from “not perceived” to “extremely intense” for the intensity ratings; from “extremely unpleasant” to “extremely pleasant” for the liking ratings; and from “extremely familiar” to “extremely unfamiliar” for the familiarity ratings.

Statistical Analysis

Behavioral and metabolic Data

We analyzed the behavioral and metabolic data with R (version 4.0; R Core Team, 2019).

We build two statistical models. The first model aimed at testing the relationship between weight loss (measured by subtracting the BMI after the intervention from the BMI before the intervention). We entered (1) intervention: placebo or liraglutide as a fixed effect and (2) age and (3) gender as control factors. As a random effect we entered intercepts for participants. We build the model as follows:

$$weightloss \tilde{} intervention + gender + age + (1|id)$$

The second model aimed at testing the relationship between the perceived pleasantness of taste and the intervention. We entered (1) the taste stimulus: milkshake or tasteless, (2) session: pre- or post-intervention, (3) intervention: placebo or liraglutide, and (4) a linear decreasing contrast over trials to account for satiation. As random effects we entered intercepts for participants as well as by-participant random slopes for the effect of the interaction between taste stimulus session and trial. We build the model as follows:

$$pleasantness \tilde{} intervention \times stimulus \times session \times satiation + (stimulus \times session \times satiation|id)$$

We used the lmer4 package [14] and the LmerTest package [15]. We extracted Bayse factors through linear mixed bayesian analysis using brms [16], cmdstanr [17] and baysestestsR [18] packages. The models were estimated using Markov chain Monte Carlo (MCMC) sampling with 4 chains of 5000 iterations and a warmup of 1000. The dependent variables were scaled before being entered in the model. For the first model (weight loss) prior parameters were set as normal (*mean* = 0.00, *SD* = 1.00) distributions. For the second model (perceived pleasantness) prior parameters were set as normal (*mean* = 0.00, *SD* = 1.00) distributions. The Bayes factors reported for the main effects compared the model with the main effect in question versus the null model, while Bayes factors reported for the interaction effects compared the model including the interaction term to the model including all the other effects but the interaction term. Evidence in favor of the model of interest was considered anecdotal (1 < BF10 < 3), substantial (3 < BF10 < 10), strong (10 < BF10 < 30), very strong (30 < BF10 < 100) or decisive (BF10 > 100). Similarly, evidence in favor of the null model could also be qualified as anecdotal (0.33 < BF10 < 1), substantial (0.1 < BF10 < 0.33), strong (0.033 < BF10 < 0.1), very strong (0.01 < BF10 < 0.033) or decisive (BF10 < 0.01).

fMRI Data

Acquisition Parameters. Acquisition parameters were identical to the ones described in Muñoz-Tord et al. [10]. The neuroimaging data were acquired on a 3-Tesla MRI system (Magnetom Tim Trio, Siemens Medical Solutions) supplied with a 32-channel head coil following a gradient echo (GRE) sequence to record data acquisition BOLD signal. We recorded forty echo-planar imaging (EPI) slices per scan with an isotropic voxel size of 3 mm. The scanner parameters were set at: echo time (TE) = 20 ms, repetition time (TR) = 2000 ms, field of view (FOV) = 210×210×144 mm, matrix size = 70×70 voxels, flip angle = 85°, 0.6 mm gap between slices. Structural whole brain T1-weighted (T1w) images (isotropic voxel size = 1.0 mm) were acquired, as well as dual gradient B0 field maps (Fmaps) for each participant to correct for inhomogeneity distortions in the static-field.

Preprocessing. As in Muñoz-Tord et al. [10], we created a pipeline optimized for the preprocessing of our neuroimaging data. More specifically, we combined the Functional Magnetic Resonance Imaging of the Brain (FMRIB) Software Library (FSL, version 4.1) [19] with the Advanced Normalization Tools (ANTS, version 2.1) [20]. The BOLD signal is highly prone to movement artifacts. This characteristic makes our experimental setting particularly challenging to analyze because our participants swallowed solutions in the scanner, which produces major deglutition artifacts. To offset this loss of signal- to-noise ratio (SNR), we followed Griffanti et al. [21]'s protocol. This protocol uses an fMRI independent component analysis (ICA) to remove artifacts. The multivariate exploratory linear optimized decomposition tool (MELODIC) [22] decomposes the raw BOLD signal into independent components (IC). We chose this ICA-based strategy for motion artifact removal because it is more reliable to remove motion-induced signal variations than regressions from motion parameters [23]. Two researchers from our laboratory independently hand classified a sample of 20 participants' IC into two categories: 'potential signal' or 'clear artifact' (e.g., motion/deglutition, blood flow in arteries). The two researchers' categorizations were then compared, and each discrepancy was discussed until an agreement was reached (inter-rater reliability = 93%). This process allowed manually classified components. These components were then used to train a classifier using a random forest machine learning algorithm [24]. We used leave-one-out testing, i.e. we iteratively left one participant out of the training data and tested the classifier accuracy on the left-out participant. Leave-one-out testing at the optimal sensitivity (threshold = 5) resulted in a median 94% true positive rate (i.e., the percentage of 'true signal' accurately classified). We consequently applied the FMRIB's ICA-based X-noiseifier (FIX) to automatize the denoising of our BOLD signal [25]. We then applied field maps to correct geometric distortions. We used ANTS for a diffeomorphic co-registration of the preprocessed functional and structural images in the Montreal Neurological Institute (MNI) space, using the nearest-neighbor interpolation and leaving the functional images in their native resolution. Finally, we applied a spatial smoothing of 8 mm full width half maximum (FWHM).

Statistical analysis. We used the Statistical Parametric Mapping software (SPM, version 12) [26] to perform a random-effects univariate analysis on the voxels of the image times series following a two-stage approach.

For the first-level, we specified a general linear model (GLM) for each participant. We used a high-pass filter cutoff of 1/128 Hz to eliminate possible low-frequency confounds. Each regressor of interest was derived from the onsets of the stimuli and convoluted using a canonical hemodynamic response function (HRF) into the GLM to obtain weighted parameter estimates. The GLM consisted of seven regressors: (1) the onsets of the trial, (2) the onsets of the reception of a taste stimulus modulated by (3) the presence of the milkshake (4) the trial-by-trial ratings of the perceived pleasantness (5) the onsets of the question about pleasantness, (7) the onset of the question about intensity and (8) the onset of the question about familiarity. We extracted the contrast of the taste delivery modulated by the perceived pleasantness for each participant at each session (43 participants x 2 sessions = 86).

For the second-level, we entered the first level contrasts in a mixed measures 2 (session: pre or post) by 2 (treatment: placebo or liraglutide) ANOVA using the multivariate and repeated measures toolbox (MRM) [27]. The MRM toolbox is a MATLAB toolbox allowing to perform mass multivariate group models of neuroimaging data using the summary statistic approach by selecting the correct error term [28]. We extracted F contrasts with a voxel-wise significance threshold set at $p < 0.001$ FDR corrected for multiple comparisons. For display purposes we plotted non-masked and uncorrected statistical p-maps of our group results overlaid on a high-resolution template (CIT 168) in MNI space.

Code and Data accessibility

The computer code used to preprocess and analyze the data is available in a publicly hosted software repository (for preprocessing of the fMRI data: https://github.com/munoztd0/Mouthpiecegusto/tree/main/preprocessing; for data analysis : https://github.com/evapool/GLP1_Pleasure).

Results

Weight loss results

The multilevel model testing the effect of the intervention on the weight loss revealed a main effect of intervention (β = -1.474, SE = 0.219, 95% CI [-1.9179, -1.029], P < 0 .001; BF < 1000; see Fig. 3 and Table 3, supplementary information). There was no significant effect of age (β = 0.173, SE = 0.107, 95% CI [-0.042, 0.389], P = 0.112; BF = 0.384) or gender (β = -0.097, SE = 0.234, 95% CI [-0.570, 0.376], P = 0.680; BF = 0.132).

Sensory pleasure results

The multilevel model testing the effect of the intervention on the perceived pleasantness of a rewarding taste revealed a main effect of taste stimulus (β =-8.739, SE = 1.642, 95% CI [-11.959, -5.520], P < 0.001, BF < 1000; see Fig. 4A), a main effect of satiation (β = 0.271, SE = 0.058, 95% CI [0.157, 0.385], P < 0.001, BF = 94.30; see Fig. 4B) and a interaction effect between satiation and taste stimulus (β =-0.139, SE = 0.041, 95% CI [-0.220, -0.058], P = 0.0015, BF = 3.91; see Fig. 4B), suggesting that the satiation effect was larger for the milkshake than the control taste stimulus. Moreover we found a significant effects of session (β = 1.866, SE = 0.885, 95% CI [0.131, 3.601], P = 0.040, BF = 0.279) and interaction between taste stimulus and session (β =-1.561, SE = 0.717, 95% CI [-2.968, -0.155], P = 0.034, BF = 0.241), suggesting that the taste stimuli were perceived as being less pleasant during the second session. None of the effects terms involving the factor intervention reached significance. Specifically concerning our hypothesis on the impact of the intervention on the perceived pleasantness of taste: there was no significant interaction between taste stimulus, condition and intervention (β = 0.374, SE = 0.717, 95% CI [-1.031, 1.780], P = 0.604, BF = 0.041), nor between

taste stimulus, condition, satiation and intervention (β = 0.012, SE = 0.018, 95% CI [-0.024, 0.049], P = 0.526, BF = 0.012).

fMRI results

The RM-ANOVA testing the interaction between intervention (placebo or liraglutide) × session (pre- or post-intervention) showed no significant voxel that survived FDR correction. The analysis revealed a main effect of the pleasantness modulator which activated brain regions typically involved in reward processing such as the ventromedial prefrontal cortex (vmPFC) (peak voxel coordinates : x = -7, y = 34, z= -14, *k* = 4; right peak voxel coordinates: x = 3, y = 49, z = -18; *k* = 3), and bilateral amygdala (left peak voxel coordinates : x = -22, y = -6, z = -18, *k* = 50; right peak voxel coordinates x = 24, y = -3, z = -18: see Fig. 5). A summary of the BOLD activations for the sensory pleasure main effect are displayed in Table 1.

Discussion

In this randomized, single-centre, double-blind, placebo-controlled, parallel group, prospective clinical trial, we investigated whether GLP-1 analogue liraglutide affect food-related sensory pleasure in patients with obesity using an fMRI-compatible gustometer. We measured both self-reports of sensory pleasure and neural responses.

As expected and previously documented [29–31], we found a large effect of the medication on weight loss – the liraglutide group significantly lost more weight than the placebo group. Moreover, the weight loss we observed was comparable to previous studies.

Behaviorally, there was no significant interaction involving the intervention factor on the perceived pleasantness of the stimuli. Our data is consequently consistent with the idea that there is no difference in self-reported sensory pleasure between the liraglutide and placebo groups.

Analyses of patients' neural responses to the milkshake and control taste stimuli revealed a main effect of the pleasantness modulator, which activated the vmPFC and the amygdala, brain regions known to be involved in reward processing [32, 33]. Although no conclusion can be inferred from the absence of a significant interaction effect, our data is consistent with the proposal that there is no difference in sensory pleasure between the liraglutide and placebo groups. As in any experiment, we cannot exclude classical limitations, such as methodological or sample size ones. More specifically regarding sample size, we want to point out that the study was not powered to find effects of the intervention on the perceived pleasantness during taste consumption, which limits the conclusions we can drive from the group comparisons tests. With this limitation in mind, our results are consistent with the proposal that there is no effect of liraglutide treatment on sensory pleasure. Additionally, we found that amygdala and vmPFC activations correlated with the perceived pleasantness during taste consumption. Taken together, these results do not provide any evidence that liraglutide alters sensory pleasure while consuming food. This contrasts with what is often reported in the literature about potential gastrointestinal sides of liraglutide in terms of nausea [34, 35].

However, reward processing is not a unitary concept. Decades of research in affective neuroscience have shown that reward processing can be parsed into motivational and hedonic components [36–38]. The motivational component has been defined as the motivation to obtain a reward (i.e., wanting), whereas the hedonic component, that we particularly studied here, encompasses the subjective hedonic experience during the consumption of a reward (i.e. liking) [39].

A prevalent idea of what drives our reward-seeking behavior assumes a hedonic perspective: what we want directly depends on what we like. While these two states usually adhere together, they can also dissociate under particular

circumstances. For instance, persons with addiction disorders frequently report an irrational wanting of the drug despite not liking its effects any more [40]. A key observation of the investigation of the shift from voluntary towards compulsive consumption has been the increasing gap between wanting and liking, which was formally conceptualized in the incentive-sensitization theory of addiction (IST) [41). Here we focused on the liking component of reward. It would be consequently relevant to consider these results in the light of another component of reward: the wanting component.

To conclude, this study suggests that liraglutide leads to weight loss but does not provide evidence that it is by altering food-related sensory pleasure in patients with obesity.

Declarations

Author Contributions: GC, ERP, DS, ZP, DC designed research; GC, LL, AE, LLP, AA, AG, ZP performed research; DMT, ERP, LW, AA analyzed data; GC, ERP, DS, and ZP wrote the paper. All authors approved the final version of the paper.

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Table

Table 1: Summary Results of BOLD Activations for the Sensory Pleasure main effect

Cerebellum	L	1	19.406	-10	-69	-61
Cerebellum	R	1	17.576	12	-60	-54
White Matter	L	13	27.034	-16	-51	-36
Middle Temporal Gyrus	L	11	31.545	-67	-21	-21
Amygdala	L	50	37.946	-22	-6	-18
Subcallosal cortex	L	50	32.184	-10	7	-14
Amygdala	R	4	23.287	15	-6	-18
Amygdala	R	2	18.802	24	-3	-18
Not in Atlas	L	1	17.914	-1	-3	-18
Ventromedial PFC	R	3	19.947	3	49	-18
Ventromedial PFC	L	4	19.991	-7	34	-14
Putamen	R	1	17.609	33	-12	4
Frontal Pole	R	22	25.258	9	67	15
Frontal Pole	L	3	17.674	-7	64	11
Lateral Occipital Cortex	R	2	18.192	39	-75	22
White Matter	R	2	18.308	15	19	26
Lateral Occipital Cortex	R	56	29.572	12	-75	62
	L	2	20.321	-16	-78	62

Note. Thresholding $p < 0.001$ voxel wise FDR corrected. Table shows the peak level statistics and coordinates. Coordinates are expressed in the Montreal Neurological Institute (MNI) space in the left-right, anterior-posterior, and inferior-superior dimensions, respectively.

Figures

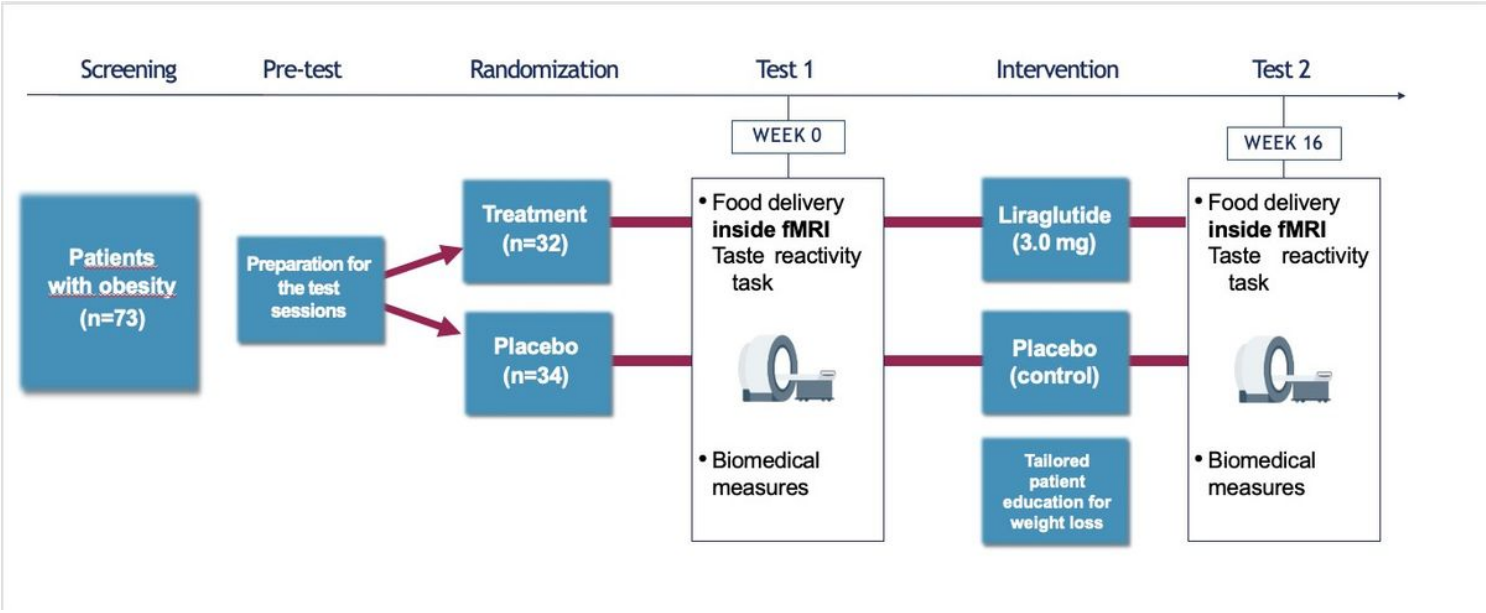

Figure 1

Trial overview. Participants with obesity participated in a pretest before being randomly assigned to the treatment (liraglutide) or placebo (control) group. They underwent a first test session in which they performed a taste reactivity task in the scanner. Biomedical measures were also taken, as well as other experimental tasks not described here. After 16 weeks of treatment, they came back to the laboratory and went through a similar test session.

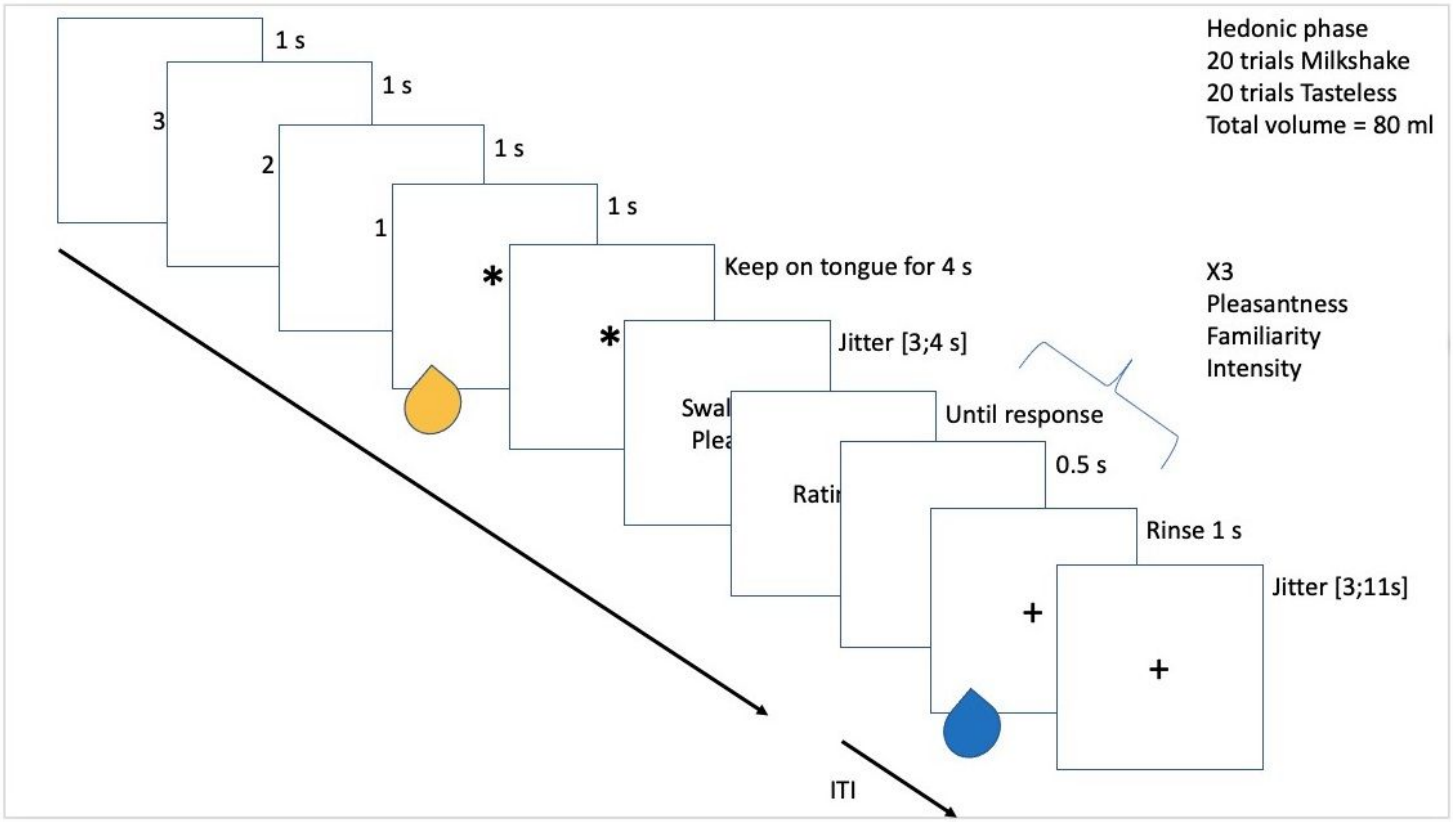

Figure 2

Overview of the taste reactivity task. This task was performed while participants were lying in the scanner and equipped with a 3D-printed pacifier-shape fMRI mouthpiece paired with a gustometer. After a countdown (3 to 1), participants saw a fixation cross followed by the delivery of a tasteless solution or a chocolate milkshake. They were requested to keep the solution of their tongue for 4 seconds before being asked to swallow it. They were asked to rate the pleasantness, familiarity and intensity of the solution. Rinse trials were intertwined with experimental trials so that patients could get their palates cleaned.

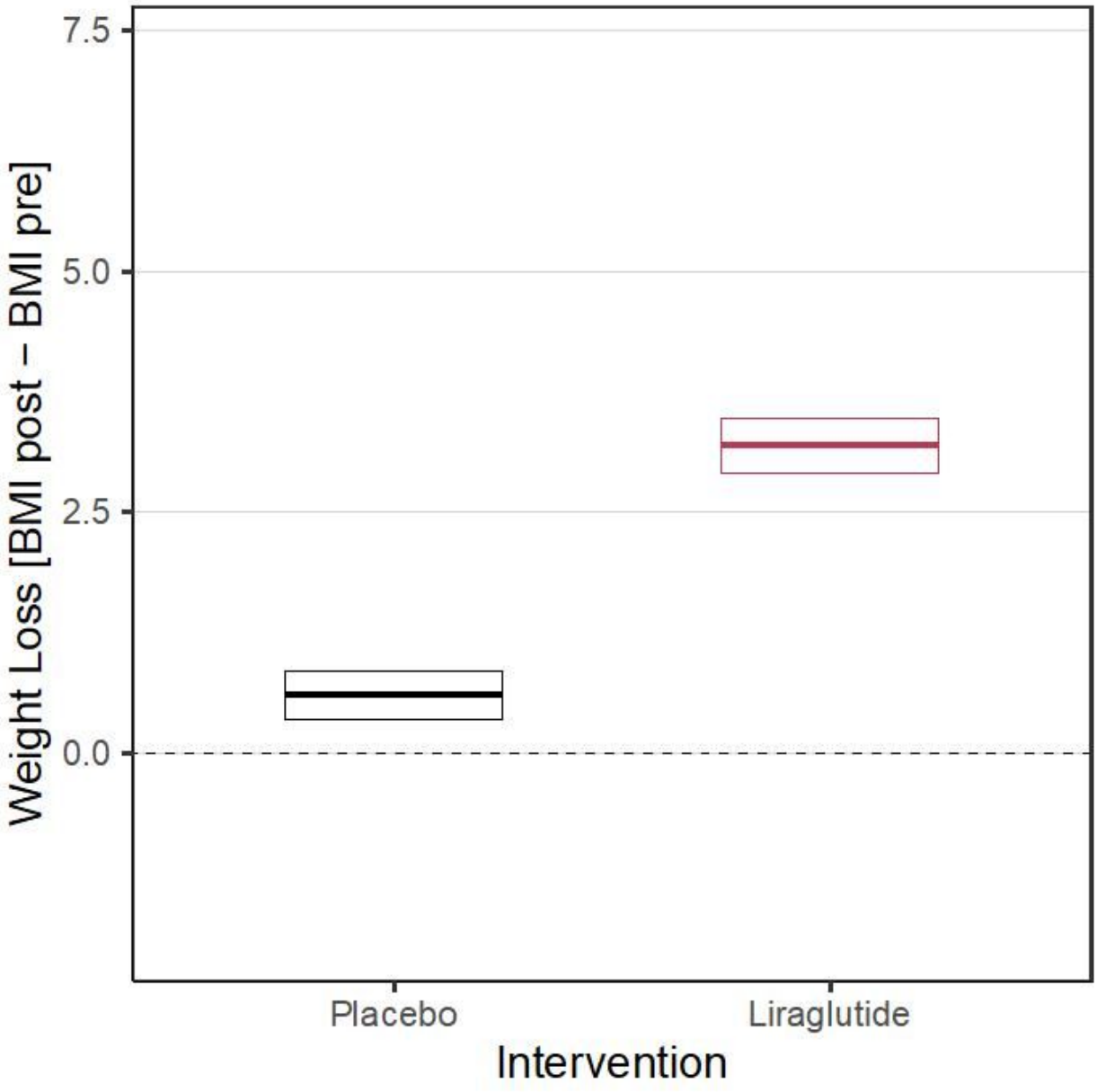

Figure 3

Weight loss results. Individual estimates, densities, and overall mean of the weight loss measured in BMI units (BMI post intervention − BMI pre intervention) of the placebo (N = 24) and liraglutide (N = 20) groups. Error bars represent standard errors to the mean.

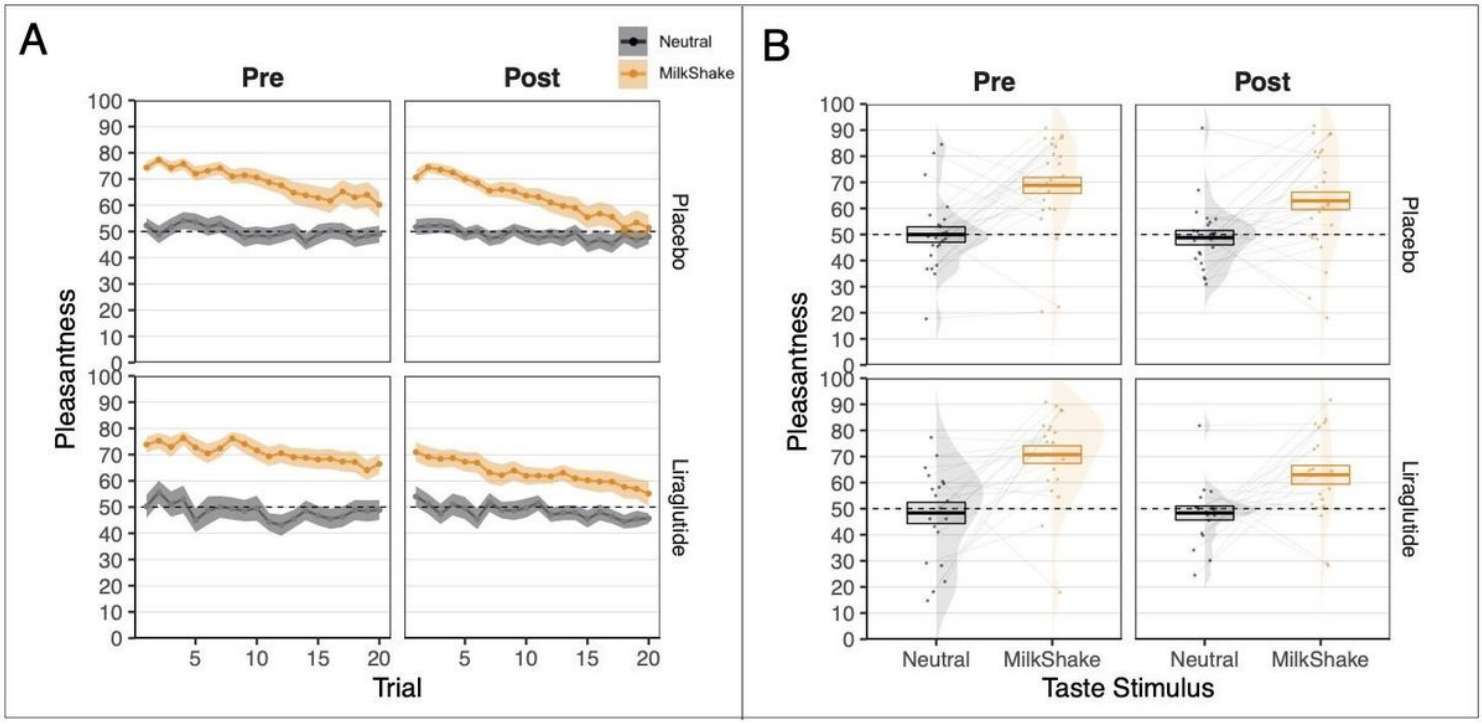

Figure 4

Pleasantness over trial repetition for the rewarding and the neutral taste stimuli in the placebo (N = 20) and the liraglutide (N = 24) groups before (i.e., pre) and after (i.e., post) intervention (A) over trial repetition and (B) individual estimates, densities, and overall mean. Error bars and shaded areas represent standard errors to the mean.

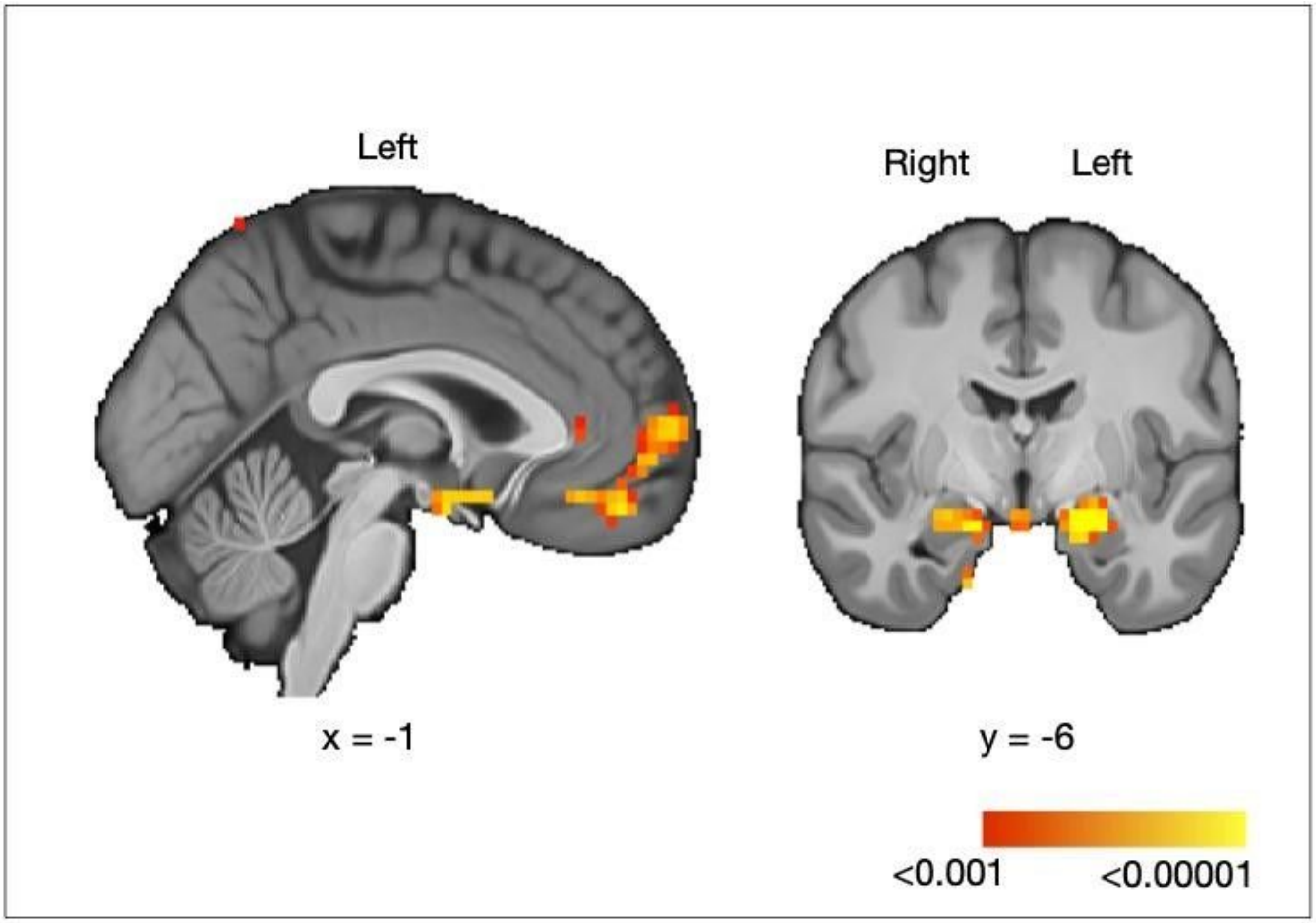

Figure 5

Neuronal correlates of sensory pleasure. Regions in which the BOLD signal positively correlated with the magnitude of the pleasure experienced within participants (*N* = 44). For display purposes statistical maps are shown with a threshold of 0.001 uncorrected. Color scale bar represents p-values. Detailed results are presented in Table 1.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementaryinformation.docx