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Neural encoding of food and monetary reward delivery

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ABSTRACT

Different types of rewards such as food and money can similarly drive our behavior owing to shared brain processes encoding their subjective value. However, while the value of money is abstract and needs to be learned, the value of food is rooted in the innate processing of sensory properties and nutritional utilization. Yet, the actual consumption of food and the receipt of money have never been directly contrasted in the same experiment, questioning what unique neural processes differentiate those reward types. To fill this gap, we examined the distinct and common neural responses to the delivery of food and monetary rewards during fMRI.

In a novel experimental approach, we parametrically manipulated the subjective value of food and monetary rewards by modulating the quantities of administered palatable milkshake and monetary gains. The receipt of increasing amounts of milkshake and money recruited the ventral striatum and the ventromedial prefrontal cortex, previously associated with value encoding. Notably, the consumption and the subsequent evaluation of increasing quantities of milkshake relative to money revealed an extended recruitment of brain regions related to taste, somatosensory processing, and salience. Moreover, we detected a decline of reward encoding in the ventral tegmental area, nucleus accumbens, and vmPFC, indicating that these regions may be susceptible to time-dependent effects upon accumulation of food and money rewards.

Relative to monetary gains, the consumption and evaluation of palatable milkshakes engaged complex neural processing over and above value tracking, emphasizing the critical contribution of taste and other sensory properties to the processing of food rewards. Furthermore, our results highlight the need to closely monitor metabolic states and neural responses to the accumulation of rewards to pinpoint the mechanisms underlying time-dependent dynamics of reward-related processing.

1. Introduction

Rewards play a crucial role in guiding our behavior through our daily lives. We define the concept of *reward* as the positive value that someone ascribes to an object or a physiological state (Schultz et al., 1997), that in turn can reinforce associated actions. Some stimuli are innately associated with a positive value, such as palatable food eliciting an unconditioned, pleasant sensation. In contrast to these primary rewards, secondary rewards such as money acquire their value via learning throughout an individual's lifespan (De Houwer and Hughes, 2020; Sescousse et al., 2013). To maximize positive outcomes in everyday life, we need to be able to accurately compute the values of various available options that can include different reward types, while considering our current state and prior experiences. Furthermore, we need to be able to translate this expected value into the motivation to spend effort to obtain the reward. For instance, people work harder to obtain larger amounts of money and food, demonstrating that increasing quantity of desired goods corresponds to greater reward value (Hanssen et al., 2021). These essential skills are carried out by a dedicated system in our brain encompassing the dopaminergic ventral tegmental area (VTA) in the midbrain and its projection targets, the nucleus accumbens (NAc) in the ventral striatum and the ventromedial prefrontal cortex (vmPFC) (Chase et al., 2015; Chib et al., 2009; Lebreton et al., 2009; Lee et al., 2021; Smith et al., 2010).

Even though the different reward types share common processing and can similarly incentivize behavior (Hanssen et al., 2021), they differ in important physical and functional properties. In particular, food possesses distinctive sensory and physiological qualities and short-term

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and long-term consequences for health and well-being (de Araujo et al., 2020; Plassmann et al., 2021). Food consumption acts as a critical nutritional input to energy homeostasis, and as such affects both reward-related neural circuits and metabolic signaling (Meye and Adan, 2014; Thanarajah et al., 2019). Further, disbalances in the complex interplay between food intake, reward-related processing, gustatory processing, and homeostatic regulation have been suggested to underlie metabolic disorders such as obesity — and its severe medical and psychiatric comorbidities (Beutler et al., 2020; Fulton et al., 2021; Pantalone et al., 2017; Plassmann et al., 2021; Rajan and Menon, 2017; Sallam and Borgland, 2021). Unravelling the mechanisms underlying food consumption and valuation would therefore provide essential building blocks for tackling such pathologies.

Surprisingly, despite food's critical role in human behavior, the differences in neural processing of food and monetary reward receipt still remain unclear. While this topic has previously been addressed in the cognitive neuroscience literature using functional magnetic resonance imaging (fMRI), the delivery of the two reward types has not been directly compared within one study. Instead, the focus was either on solely one of the two reward types (Schoenfeld et al., 2004; Small et al., 2003, 2008), or on both but without the actual ingestion of food during fMRI (e.g., Chib et al., 2009; Simon et al., 2015; Verdejo-Roman et al., 2017). The few exceptions that included both food and money delivery did not directly compare the two and were inconclusive with respect to the single main effects (Kim et al., 2011; Stice et al., 2011; Valentin and O'Doherty, 2009). Moreover, the studies focusing on the comparison between food and money used experimental designs including probabilistic learning (Valentin and O'Doherty, 2009), or both an anticipation phase and a subsequent "consumption" phase (Kim et al., 2011; Simon et al., 2015; Stice et al., 2011; Verdejo-Roman et al., 2017). While this procedure allows for insights about prediction error encoding and the temporal course of reward-related processing, it makes it difficult to identify neural responses to reward receipt that are not confounded by the previous announcement of the upcoming reward.

Meta-analytical summaries of the existing literature substantially contributed to identifying the core value-encoding brain system by showing that the ventral striatum and the vmPFC encoded the value of both money and various primary rewards, including food (Arsalidou et al., 2020; Bartra et al., 2013; Chase et al., 2015; Levy and Glimcher, 2011; Sescousse et al., 2013). In addition, they also compared the processing of different reward types, revealing that food relative to other reward types engaged the middle insula and the adjacent frontal operculum associated with gustatory and somatosensory processing, over and above value encoding (Sescousse et al., 2013), in accordance with studies focusing on food consumption only (de Araujo et al., 2012, 2003; Schoenfeld et al., 2004; Small et al., 2003, 2008). However, these meta-analyses partly collapsed various types of primary rewards (e.g., food, positive facial expressions, and erotic pictures), intermixed abstract food cues and actual food ingestion, and relied on experiments that included learning and anticipation in their designs. Therefore, it remains challenging to draw specific conclusions concerning food consumption relative to monetary gains.

To allow for a more specific assessment of common and distinct brain circuits involved in food and money receipt, we delivered both reward types during an fMRI experiment. By this means, we examined the within-subject differences in neural processing of the actual consumption of food — here, palatable milkshake — versus monetary gains. We aimed to identify brain regions that parametrically encode increases in the magnitude of reward delivery, and not simply the processing of reward obtainment relative to reward omission. To this end, we varied the quantity of delivered food and money and recorded participants' liking to assess the resulting change in subjective value. Furthermore, we designed the present study such that any learning or anticipation processes were avoided to specifically target the consumption aspect of reward processing. We hypothesized that the activity in the ventral striatum and the vmPFC would track increases in amounts of received rewards irrespective of reward type, given their central role in general value encoding (Chase et al., 2015; Chib et al., 2009; Lebreton et al., 2009). With respect to differential neural processing, we expected stronger recruitment of the middle insula and the adjacent frontal operculum during milkshake consumption relative to monetary gain due to the involved gustatory and somatosensory processing (Schoenfeld et al., 2004; Small et al., 2008). Provided that we successfully manipulate the subjective value of increasing quantities of rewards equally for food and money, we did not expect a unique neural encoding of monetary gains, over and above the general involvement of value-associated brain regions. In addition to the main focus on the reward delivery itself, we also explored whether the subsequent rating of the received rewards relied on common or different brain regions depending on reward type.

Finally, we tested whether the reward-related processing was stable in the course of the experiment. Particularly when implementing repetitive food consumptions and monetary gains, several factors could modulate the behavioral and neural responses over time, in addition to general phenomena such as habituation or fatigue. The repeated consumption of the same food may increase satiety during the experiment, which can affect the ratings of pleasantness and the associated vmPFC activity (Rolls, 2008). Accumulating monetary gains may also lead to diminishing marginal utility, such that additional gains lead to ever-smaller increases in subjective value (Berkman et al., 2016). And finally, food ingestion in particular may induce not only short-term brain responses related to the current sensory and hedonic experience, but also delayed effects related to nutrient-driven changes in the metabolic state via the gut-brain signaling (de Araujo et al., 2020; Thanarajah et al., 2019). For instance, the ingestion of sugar-rich food elevates endogenous insulin levels, that in turn modulates dopaminergic reward-related brain regions in a time course-dependent manner, including the VTA, the NAc and the vmPFC (Edwin Thanarajah et al., 2019; Liu and Borgland, 2019; Sallam and Borgland, 2021; Thanarajah et al., 2019). Thus, we explored whether reward-related processing changed over time by comparing the behavioral and neural responses in the first relative to the second session of the experiment.

2. Material and methods

2.1. Participants

Twenty-two participants were recruited via the institute's participants database according to the following inclusion criteria: aged 18–55; normal or corrected to normal vision; non-smokers; women: not pregnant or nursing; no history of substance abuse and psychiatric, metabolic, neurological, or eating disorders; no psychopharmacological or metabolically-active medication; fit general prerequisites for MR measurements; like sweets; no food restrictions (i.e. vegan, running diets, lactose intolerance, allergies). One subject with random rating behavior was excluded, resulting in a sample of $N = 21$ (10 females; age in years: $M = 31.25$, $SD = 7.49$, range 22–48; body mass index, BMI: $M = 24.47$, $SD = 3.32$, range 17.28–30.46). All procedures were in accordance with the Declaration of Helsinki and were approved by the local ethics committee of the Medical Faculty of the University of Cologne, Germany (19-1126). All participants signed informed consent and received 10 Euros per hour as compensation for their participation in the study, plus the monetary bonus from the task.

2.2. Power calculations

We estimated the required sample size based on the behavioral data of a pilot study ($N = 7$), using the simulation-based power analysis package for R (simr, version 1.0.5, Green and MacLeod, 2016) along with the same behavioral analysis procedure as described below. The pilot data revealed a strong increase of pleasantness as a function of increasing reward quantity (beta = 0.75, $p < .001$), and no significant main or interaction effects of reward type ($p > .15$). Thus, we considered the

power to detect a quantity-driven increase of pleasantness with an effect size of 0.75, as well as the power to rule out an interaction between reward quantity and type even if the effect size is as small as 0.18. The simulations revealed that a sample size of 21 would have the power of 100% to reject the null hypotheses of no quantity-driven increase of pleasantness, and the power of around 80% to reject the null hypothesis of equal quantity-driven increases across food and money, with a 95% confidence interval, given this particular setup.

2.3. Study procedure

The participants were instructed to arrive after fasting for at least 4 h. Upon arrival, the participants were given a consent form to read and sign and were briefed regarding the experimental procedures. Next, we measured their blood glucose levels by using a BG STAR glucometer and body composition using a medical body composition analyzer (seca mBCA 515, SECA GmbH, Hamburg, Germany). The participants were then asked to report their hunger level on a scale from 1 to 10. Thereafter, they were introduced to five milkshake flavors (chocolate, vanilla, banana, strawberry, and raspberry) and asked to rate the level at which they desired and liked each flavor (on a rating scale from 1 to 10). The milkshakes were created from flavored powder (Kaba, Mondelez Deutschland GmbH GB, Bremen, Germany), whole milk, and cream, according to the following receipt: 170 g whole milk, 30 g cream, and 12 g Kaba powder. The most desired flavor selected by each participant was chosen for that participant's reward task. After reading detailed instructions for the task, the participants entered the scanner and performed the reward task described below. The beginning of the scanning was between 10 am and 4:30 pm (average time 12:40 pm, SD = 1 h 53 min). The overall duration of the entire procedure was approximately 2.5 h.

2.4. Reward task

The reward task was designed to deliver milkshakes and monetary gains to the participants while undergoing fMRI. We used a gustometer, a system of pumps and tubes to deliver small amounts of milkshake into the participant's mouth under a precise control of quantities and timing (Veldhuizen et al., 2007). Each trial started with a fixation cross presented for a mean of 3.5 s (varying durations with an exponential distribution ranging from 1.5 to 7 s), followed by a reward delivery (milkshake or money) for 3.5 s (see Fig. 1a). During reward delivery, a picture of 3 stacked circles appeared on the screen. Inside the circle, an illustration of drops (for milkshake deliveries) or a ten-cent coin (for monetary deliveries) indicated the reward type (see Fig. 1b). Next, a tasteless solution (rinse) was delivered for 1.5 s (0.3 ml). We administered this tasteless rinse after both milkshake and monetary rewards to maintain the trial structure as similar as possible across reward types. Furthermore, by including the rinse immediately after the delivery, we made particularly the comparison of the neural response to the evaluation phase between milkshake and money more comparable. Beside the general effect of rinse on neural processing, rinsing away possible residues of milkshake in the mouth created a similar somatosensory state during the evaluation phase independent of whether it was preceded by a milkshake delivery or not. While the additional delay between delivery and evaluation further improved the statistical dissociation of the two respective BOLD responses, its duration of few seconds was short enough to prevent increased noise in liking ratings. After the rinse, a fixation cross was displayed for a mean of 2 s (varying durations with an exponential distribution ranging from 1 to 5 s). Next, a grayed-out rating scale asking "How did you like this" on German (i.e., "Wie hat es Ihnen gefallen?", ranging from 1 = "gar nicht", not at all, and 10 = "sehr gut", very much) appeared for 1.5 s. The participants were instructed to think about how much they liked the stimulus they had just received without performing button presses. Then, the grayed-out rating scale became colored, and the participants had a maximum of 3 s to rate how much they liked the stimulus they had just received. This pleasantness rating served as a dependent variable for the behavioral analysis. Participants responded by pressing buttons with their index and ring fingers of the right hand to move a marker on the rating scale to the left and right, respectively. They indicated the final marker position by pressing a third button with their middle finger. After this, the marker color turned green for a maximum of 0.5 s to provide a visual feedback for the choice selection. For reaction times > 2.5 s, the duration of this feedback was reduced accordingly to not exceed 3 s maximal response time, and in trials with reaction time < 2.5 s, a fixation cross was shown after the feedback until the 3 s elapsed (thereby additionally lengthening the duration of the fixation cross at the beginning of the next trial).

In order to identify brain regions involved in the tracking of increasing reward value, we varied the quantity of both food and money reward deliveries across four levels. The quantity was indicated by the number of circles colored in yellow vs. grey (control: all grey; low: 1 yellow and 2 grey; medium: 2 yellow and 1 grey; high: all yellow; see Fig. 1b). The control, low, medium, and high quantities for the milkshake rewards were 0.5 ml of rinse, and 0.2 ml, 0.5 ml, and 0.8 ml of milkshake, respectively, whereas the monetary gains were 0 cent, 10 cents, 25 cents, and 40 cents. We have specified these quantities based on two previous pilot studies (n = 15, and n = 7, respectively, for more information see Supplementary Material S1). For both reward types, the increase from control to the low quantity was lower than the increase between low, mid, and high. This was chosen to avoid a large rise in pleasantness between control and low reward quantity, and to obtain a steady increase of subjective value.

A total of 160 trials were divided into 2 sessions, each lasting 20 min and 15 s. During each session, 10 trials were included for each of the 8 different conditions (2 reward types * 4 quantity levels). In total, participants received 30 ml milkshake and 15 Euro. Prior to the beginning of the experiment, the participants were informed that they will be handed out the sum of monetary rewards at the end of the experiment.

2.5. Behavioral analyses

The main aim of the analysis was to test whether the pleasantness of received milkshake and monetary gains increased with increasing reward quantity, and whether this was comparable across the two reward types. Linear mixed effect models were fitted using RStudio (version 1.4.1717; 2009-2021 RStudio, PBC) and the *lme4* package (version 1.1-26, Bates et al., 2015), and significance was tested using analysis of variance as implemented in *lmerTest* (version 3.1-3, Kuznetsova et al., 2017). Before the analysis, we z-scored the pleasantness ratings separately for each participant, so that we report the betas as standardized effect sizes. Following a summary statistics approach, subjects' ratings were then averaged separately for each subject and each of the eight experimental conditions (2 reward types * 4 quantity levels). These mean ratings were specified as the dependent variable, and reward quantity (high, mid, low, control), reward type (milkshake, money), and their interaction as fixed effects, with a random intercept for subject ID. Note that reward quantity was specified as a parametric variable, so that the model tested for the linear increase of pleasantness as a function of reward quantity.

Furthermore, in order to test whether pleasantness changed from the first to the second session, we repeated the above analysis after adding an additional effect of session. Thus, mean ratings (averaged separately for each subject and 16 conditions: 2 reward types * 4 quantity levels * 2 sessions) were specified as the dependent variable, and reward quantity (high, mid, low, control), reward type (milkshake, money), session (1 and 2), and their interactions as fixed effects, with a random intercept for subject ID.

2.6. MRI data acquisition

Imaging data were acquired using a 3T MRI scanner with a 64-channel head coil (MAGNETOM Prisma Fit, Siemens AG, Medical Solu-

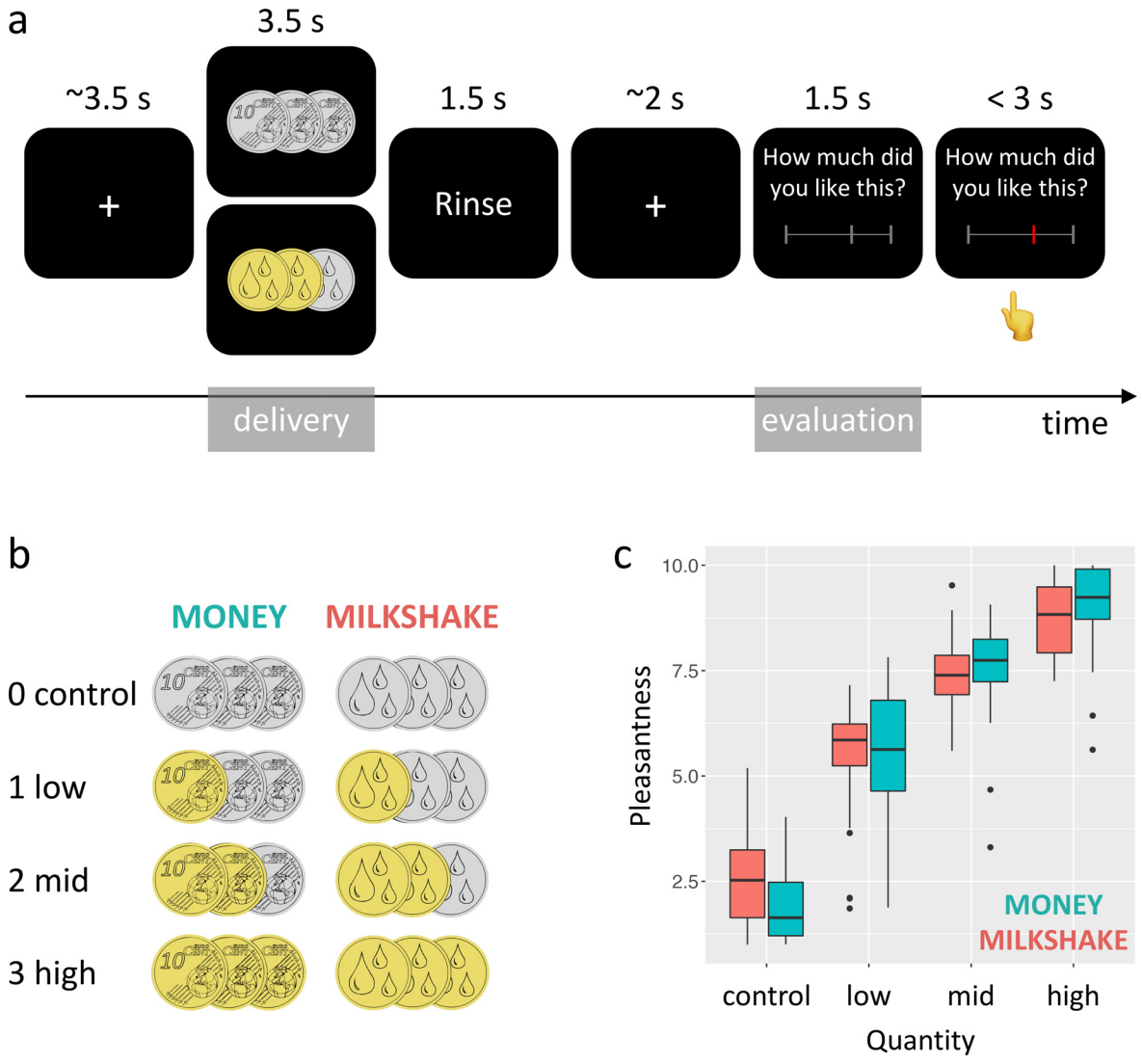

Fig. 1. Experimental procedure and results of pleasantness ratings. (a) Timeline showing the events during a trial of the reward task. In the fMRI analyses, we focused on neural encoding of delivery and evaluation of increasing reward quantities (events marked by gray boxes). Note that motor responses were given only after 1.5 s of reflecting about the evaluation. Durations of the events are shown above the corresponding screenshots. (b) Images displayed parallel to the delivery of different quantities of reward types. All images were composed of three stacked circles, with either drops or cents, to indicate milkshake or money, respectively. The quantity was indicated by the number of yellow circles, with 0, 1, 2 and 3 corresponding to control (0 Euro or 0.5 ml of rinse), low (10 cent or 0.2 ml of milkshake), mid (25 cent or 0.5 ml of milkshake), and high reward quantities (40 cent or 0.8 ml of milkshake), respectively. (c) Subjective pleasantness of milkshake (red) and monetary (blue) rewards strongly correlated with reward quantity. Anchors for pleasantness ratings were 1 = not liked at all, and 10 = liked very much. For interpretation of the references to color in this figure, the reader is referred to the web version of this article.

tions, Erlangen, Germany). Functional data were acquired in two subsequent sessions using multiband echoplanar imaging covering the whole brain (Xu et al., 2013), using the following parameters: multiband acceleration factor of 8; parallel imaging factor (iPAT) of 2; repetition time (TR) = 810 ms; echo time (TE) = 30 ms; flip angle = 53°; field of view (FOV) = 212 × 212 × 144 mm^3; voxel size = 2 × 2 × 2 mm^3; 72 axial slices with no gap between slices. We measured heart rate and respiration during the scan using a finger plethysmograph and a breathing belt, respectively. For each of the two subsequent sessions, we acquired 1500 volumes.

High-resolution T1-weighted images were acquired in a preliminary MRI session using either the modified driven equilibrium Fourier transform (MDEFT), or the magnetization prepared-rapid gradient echo (MP-RAGE) sequence (MDEFT: TR = 1,930 ms, TE = 5.80 ms, FOV = 256 × 256 × 160 mm^3, voxel size = 1 × 1 × 1.25 mm^3, 128 sagittal slices; MPRAGE: TR = 2300 ms, TE = 2.32 ms, field of view = 256 × 256 × 192 mm^3, voxel size = 0.9 × 0.9 × 0.9 mm^3, 213 sagittal slices).

2.7. FMRI data analyses

Preprocessing of the fMRI data was carried out by using the FMRIB Software Library (FSL, version 5.0.10, Oxford UK, Jenkinson et al., 2012) and the SPM software package (SPM12, version 6225, The Wellcome Centre for Human Neuroimaging, implemented in MATLAB R2019b, The MathWorks, Inc.). First, the fMRI time series were corrected for motion and distortion by using FSL tools *mcflirt* (Jenkinson et al., 2002) and *topup* (Andersson et al., 2003). Next, the T1-weighted images were co-registered to the functional images, and then standardized to the Montreal Neurological Institute (MNI) reference space using the unified segmentation approach in SPM12. The resulting deformation parameters were subsequently applied to the func-

tional images (resampled at $2 \times 2 \times 2$ mm^3, according to the voxel size of the raw data) which were then smoothed using an 8 mm full-width-half-maximum Gaussian kernel. Before analysis, the first 10 functional images were removed from the fMRI time series to ensure magnetic saturation.

We analyzed the data using the mass-univariate approach by fitting general linear models (GLMs) in SPM12. At the single-subject level, conditions were modeled using a boxcar reference vector convolved with the canonical hemodynamic response function and its time derivative. The main aim of the analysis was to identify brain regions, that were activated by the *delivery* of rewards of increasing quantity, separately for food and money. To this end, for each scanning session, we modeled the reward delivery events on four regressors (separately for milkshake and money) according to ascending reward quantities (durations set to 3.5 s): (1) control (no reward), (2) low quantity, (3) mid quantity, and (4) high quantity. Additionally, we included the following regressors to specify other trial events and nuisance parameters: rinse (1.5 s duration), evaluation (i.e., rating scale before button presses, separately for milkshake and money, respectively; 1.5 s duration), evaluation response (i.e., rating scale activated for button presses, duration set from the onset to the end of the visual feedback of a choice selection), 24 motion parameters (six motion parameters of the current and preceding volume, respectively, plus each of these values squared (Friston et al., 1996), mean signal extracted from the ventricular cerebrospinal fluid (computed using *fslmeants*), parameters of the physiological tracking (extracted using the TAPAS PhysIO Toolbox Version 2017, Kasper et al., 2017), and a matrix indicating motion outlier volumes (identified using *fsl_motion_outliers*, at the threshold: > 75th percentile + 2.5 interquartile range of the global signal and/or > 1 mm framewise displacement). Low-frequency signal drifts were filtered using a cutoff of 128 s. The contrast images for the different quantities of milkshake and money delivery, respectively, averaged across the two scanning sessions, were then used for the group level analysis.

At the group level, we specified a flexible factorial design with the eight contrast images (corresponding to 2 reward types * 4 quantity levels) and with the factors subject and condition (dependency present in the latter), with all variances set to unequal. This design allowed us to correct for possible departures from sphericity, making the inclusion of random subject blocks unnecessary (Guillaume et al., 2014; McFarquhar, 2019; McFarquhar et al., 2016). Brain regions, in which the activity increased as a function of increasing quantity of reward delivery, were identified by the contrast [-2 -1 1 2] referring to control, low, mid and high quantity, separately for milkshake and money ($milkshake_{quantity}$ and $money_{quantity}$). Note that by including the four different quantities of money and milkshake delivery, respectively, as separate regressors at the 2nd-level of analyses, we were able to visualize the graded increase of BOLD-responses (see plots of contrast estimates in Figs. 2 and 3). This would have not been possible if we had used the parametric modulation option, which tests for a similar effect, but yields only one contrast estimate reflecting the correlation coefficient. We aimed to test for the common encoding of increasing reward quantity, irrespective of reward type. To this end, we analyzed the conjunction between $milkshake_{quantity}$ and $money_{quantity}$ testing for the conjunction null hypothesis ("logical AND", Friston et al., 2005; Nichols et al., 2005). In order to directly compare milkshake and money with respect to the neural encoding of increasing quantity, we computed the contrasts [-2 -1 1 2 2 1 -1 -2] for *milkshake>money*, and [2 1 -1 -2 -2 -1 1 2] for *money>milkshake*. The *milkshake>money* contrast was masked by the effect $milkshake_{quantity}$ to constrain the results to only those brain regions, that indeed increased their activity in response to increasing quantity of milkshake. Similarly, the *money>milkshake* contrast was masked by the effect $money_{quantity}$ (with $p < .001$ for both masks).

In addition, we aimed to explore the neural activity underlying the *evaluation* of increasingly large rewards. To this end, we applied exact the same procedure as described above in a separate analysis, but focused on the *evaluation* instead of delivery of increasing quantities of rewards. At the single-subject level, evaluation events were modeled separately for the four reward quantities, and separately for money and food (referring to the rating scale before button presses, with durations set to 1.5 s, see Fig. 1a). The rest of the first-level GLMs were exactly as described above, except that reward delivery was modeled on two regressors only (one for money, one for milkshake), irrespective of reward quantity. In the group-level flexible factorial design, we used the eight contrast images from these first-level GLMs corresponding to the evaluations of four different quantities of monetary and milkshake rewards, respectively.

Finally, in order to test for the effect of session on the neural encoding of increasing reward delivery, we computed the effects of different quantities of reward delivery separately for the first and the second session and included the resulting sixteen contrast images (corresponding to 2 reward types * 4 quantity levels * 2 sessions) in a supplementary group level analyses (instead of analyzing contrasts averaged across the two sessions, as in the main analysis described above). Moreover, we used a mask including the bilateral VTA (threshold = 0.1, based on Trutti et al. (2021), the bilateral NAc, and the vmPFC (based on the Harvard-Oxford Atlases in FSL, threshold = 10) to be able to constrain the analysis to these regions of interest (ROI).

Whole brain group-level results were thresholded at $p < .05$, FWE-corrected at the cluster level, with an underlying voxel-level threshold of $p < .001$, uncorrected. Due to the over-conservative false positive rate of this test (Friston et al., 2005; Nichols et al., 2005), the significance threshold for conjunction analyses was more lenient: $p < .001$, uncorrected, extent threshold = 45. For the group-level results masked with the ROIs (VTAm NAc, and vmPFC), we first applied a whole brain significance threshold of $p < .001$, uncorrected, and then applied FWE correction for multiple comparisons within the mask, and reported effects with $p_{FWE\text{-}corr} < .05$.

3. Results

The present study aimed to directly compare the neural processing of food and monetary rewards. To this end, we implemented a reward task in which participants repeatedly received varying quantities of palatable milkshakes or monetary gains while undergoing fMRI. Upon arrival, participants reported to be fasted ($M = 10.32$ h, $SD = 4.36$), as confirmed by the measured blood glucose ($M = 96.24$ mg/dl, $SD = 10.79$), and to be moderately hungry ($M = 6.62$, $SD = 2.03$, on a rating scale from 1 to 10). Participants' ratings of different milkshake flavors before the beginning of the reward task revealed that there were no significant differences in average liking of the five flavors (beta = 0.09, $F(1,103) = 2.18$, $p = .143$). Furthermore, all participants had a noticeable desire to consume their favorite milkshake flavor ($M = 9.00$, $SD = 1.30$, on a rating scale from 1 to 10; minimal desirability rating = 5). Inspection of participants' ratings during the reward task revealed that there were very few missing ratings: $M = 0.38$, $SD = 0.67$ (4 subjects with 1 missing response, 2 subjects with 2 missing responses). This was likely due to the response interval of up to 3 s, given that the average reaction time was 1.37 s ($SD = 0.23$). Finally, inspection of participants' head movement during the fMRI revealed that most participants had a maximum framewise displacement (FD) < 3 mm, but 5 sessions had a maximum FD between 3 and 5 mm. As outlier volumes were censored in the 1st-level fMRI analyses, excluding these 5 sessions from the group analyses did not make a difference, so that we included all datasets into analyses.

3.1. Pleasantness of reward delivery

We first tested whether we successfully manipulated the subjective reward value by varying the delivery quantity and whether this effect differed between food and money. To this end, we analyzed whether reward quantity and reward type affected participants' ratings of how

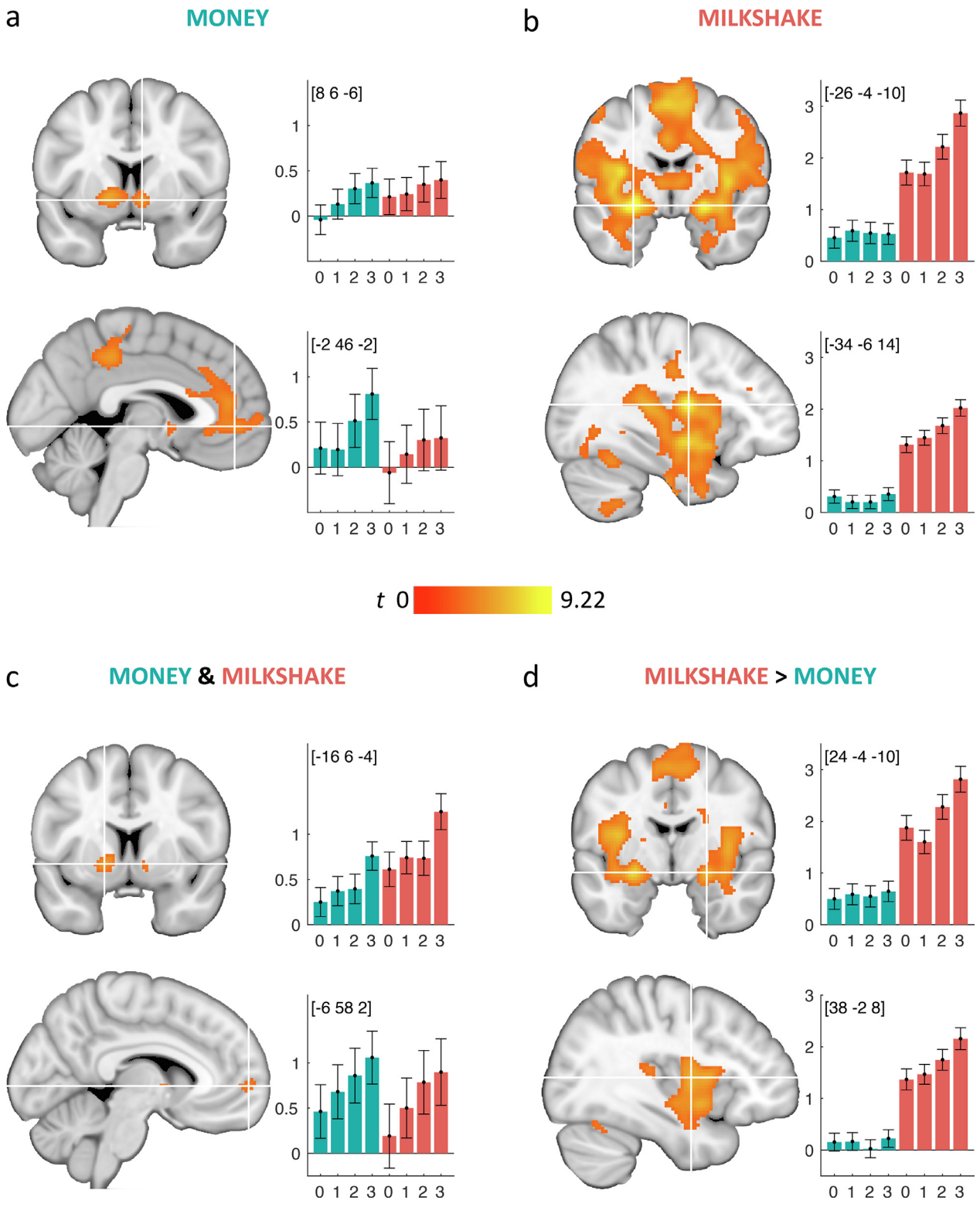

Fig. 2. Neural encoding of reward delivery. Increasing quantity of delivered reward recruited common and distinct brain regions for milkshakes and money. Ventral striatum and ventromedial prefrontal cortex encoded increasing amounts of both money and milkshake delivery (a and c). In contrast, the middle insula, the adjacent frontal operculum, and the amygdala, among others, specifically encoded increasing amounts of milkshake delivery (b and d). (a) Brain regions encoding increasing quantity of money and milkshake (b). (c) Conjunction analysis identified common neural encoding of increasing reward quantity for both money and milkshake. (d) Direct comparison of neural encoding of increasing quantity of milkshake relative to money. Error bars show contrast estimates and standard errors for activation peaks marked with white crosses (with peak MNI coordinates [x y z] in the corresponding plots), separately for four quantities of money (blue) and milkshake (red), respectively: 0, none (control), 1, low, 2, mid, and 3, high. Significance threshold was $p < .05$, FWE-corrected at the cluster level, with a cluster-defining threshold of $p < .001$ (except of c, see Table 1 for more details). SPMs were overlayed on a MNI standard brain. For interpretation of the references to color in this figure, the reader is referred to the web version of this article.

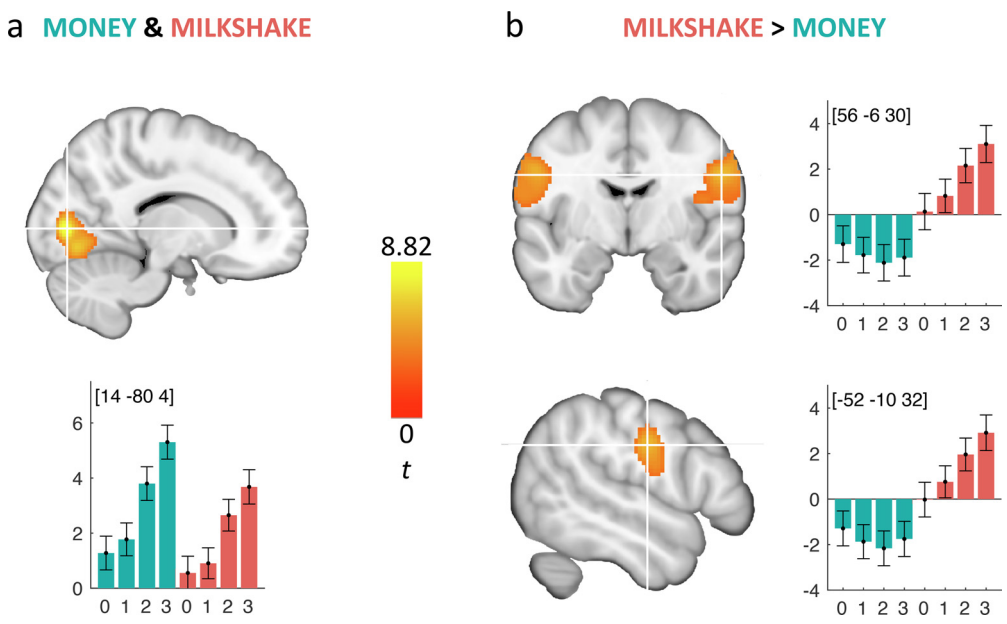

Fig. 3. Neural encoding of reward evaluation. Evaluation of increasingly high quantities of rewards recruited common and distinct brain regions for milkshake and money. (a) The primary visual cortex was commonly involved in the evaluation of increasingly large milkshake and monetary rewards (conjunction analysis). (b) The primary somatosensory cortex was more strongly involved in the evaluation of increasing quantities of milkshake relative to money. Error bars show contrast estimates and standard errors for activation peaks marked with white crosses (with peak MNI coordinates [x y z] in the corresponding plots), separately for four quantities of money (blue) and milkshake (red), respectively: 0, none (control), 1, low, 2, mid, and 3, high. Significance threshold was $p < .05$, FWE-corrected at the cluster level, with a cluster-defining threshold of $p < .001$ (see Table 3 for more details). SPMs were overlayed on a MNI standard brain. For interpretation of the references to color in this figure, the reader is referred to the web version of this article.

much they liked the rewards delivered on each trial of the fMRI experiment. Fig. 1c shows that larger amounts of received milkshake and money induced more favorable ratings. The analysis of the ratings confirmed that pleasantness increased as a function of reward quantity (beta = 0.82, $F(1,164) = 943.15$, $p < .001$). This main effect has a large effect size with a substantial increase of pleasantness from 2.28 in trials with no reward to 8.84 in trials with a maximal reward quantity (averaged across milkshake and money, on a rating scale from 1 to 10, with larger values indicating greater pleasantness). Importantly, there was no significant main effect of reward type (beta = 0.16, $F(1,164) = 2.82$, $p = .095$), or interaction between reward type and reward quantity (beta = -0.10, $F(1, 164) = 3.65$, $p = .058$). Overall, these results indicate that we successfully manipulated subjective values for both stimulus types: Participants reported that they liked the delivered rewards more the larger their quantity was, with no significant difference between milkshakes and money.

Next, we repeated this analysis after excluding all control trials (reward omissions) to test for more subtle differences between quantity levels. Thus, the effect of quantity on milkshake ratings reflects the variance between high, middle, and low quantities of milkshake instead of the variance between varying amounts of milkshake and rinse administration. The same applies to the money condition, where we focused on the difference between different gain amounts instead of focusing on the variance between winning nothing and winning different amounts of money. The results of this model without control trials showed similar results for the main effect of reward quantity (beta = 0.61, $F(1,122) = 274.33$, $p < .001$), with no significant main effect of reward type (beta = -0.05, $F(1,122) = 0.10$, $p = .756$), or interaction (beta = -0.01, $F(1,122) = 0.01$, $p = .924$). These results show that the overall increase of pleasantness was not simply driven by the categorical difference between receiving a reward and receiving no reward at all. Instead, the pleasantness increased due to larger amounts of rewards, and similarly so for both food and money.

3.2. Neural encoding of reward delivery

To investigate the neural encoding of the two different reward types, we analyzed the BOLD response associated with delivering varying quantities of milkshake and money to our participants while they underwent fMRI. We identified brain regions that were activated by increasing quantities reward delivery, separately for milkshake and money.

To provide a descriptive background, we first report the main effects of milkshake and money receipt, respectively. When monetary rewards were delivered, the activity in the bilateral ventral striatum extending into the NAc, and the vmPFC, among other regions, was higher the more money participants received (see Fig. 2a; for a complete list of significant clusters see Table 1a). Upon the delivery of milkshakes, a more extended set of brain regions encoded the increasing quantity, including the bilateral middle insula, the overlying frontal operculum, and the amygdala complex, among others (see Fig. 2b and Table 1b).

Next, using a conjunction test, we identified brain regions that generally encoded an increasing quantity of delivered reward for both milkshake and money. This analysis yielded that the bilateral ventral striatum and the vmPFC, among other areas, showed a significant increase in activity when participants received increasing quantities of reward, irrespective of whether it was money or milkshake (see Fig. 2c and Table 1c). The bar plots in Fig. 2c show that the average activity in these brain regions increased from trials with no reward (0) to those with maximal reward quantity (3) in a similar manner for money (in blue) and milkshake (in red). The subgenual and pregenual parts of the vmPFC recruited by reward delivery are in good accordance with a recent meta-analysis identifying this area to be robustly related to value encoding (Chase et al., 2015). However, we could not demonstrate the involvement of more ventral parts of the vmPFC as shown in some previous fMRI studies on value encoding (e.g., O'Doherty et al., 2001). The very ventral surface of the orbitofrontal cortex was indeed affected by a descending signal-to-noise ratio (SNR), which might have impeded a detection of activations in this circumscribed area (see Supplementary

Table 1
Brain regions encoding the increasing quantity of reward delivery.

	Cluster level		Peak level			
	Size	$p_{FWE\text{-}corr}$	*t*	x	y	z
(a) Money						
Calcarine gyrus (V1)	1161	0.000	6.80	14	-90	0
Pallidum	647	0.000	6.75	-14	2	-4
Ventral striatum (NAc)			4.99	8	6	-6
Ventral striatum (NAc)			4.62	10	14	-4
Ventral striatum (NAc)			4.06	-8	6	-6
Precuneus	483	0.000	5.13	-2	-36	44
Anterior cingulate cortex	1006	0.000	4.79	-4	40	12
Ventromedial prefrontal cortex			4.39	-2	46	-2
Ventromedial prefrontal cortex			4.15	-6	60	2
Dorsolateral prefrontal cortex	307	0.002	4.79	-26	44	46
(b) Milkshake						
Cerebellum	12427	0.000	9.22	-18	-62	-20
Calcarine gyrus (V1)			6.49	12	-90	0
Amygdala (CM)	26952	0.000	9.09	-26	-4	-10
Middle insula			8.49	-34	-6	14
Amygdala (CM)			8.39	22	-2	-12
Postcentral gyrus (SII)			8.14	-58	-18	18
Supplementary motor cortex			7.72	8	0	58
Middle insula			7.65	40	-2	6
Superior temporal gyrus			7.57	58	-28	16
Frontaloperculum (SII)			7.20	62	-16	12
Putamen			6.43	-22	4	0
Putamen			6.40	20	6	2
Midcingulate cortex			6.18	6	10	36
Ventral striatum (vmP)			5.61	16	8	-6
Ventral striatum (vmP)			5.52	-18	6	-4
Cerebellum	1334	0.000	7.30	-16	-64	-48
Dorsal vagal complex			5.48	-6	-40	-44
Postcentral gyrus	524	0.000	4.44	-22	-46	58
(c) Conjunction: Milkshake and Money						
Calcarine gyrus (V1)	879	0.000	6.37	12	-92	0
Pallidum	204	0.076	5.74	-18	2	-4
Ventral striatum (vmP)			5.18	-16	6	-4
Pallidum	86	0.494	4.33	12	2	-12
Ventral striatum (NAc)			3.84	12	10	-6
Hippocampus	85	0.501	4.33	-36	-14	-20
Amygdala			4.04	-32	-4	-26
Dorsolateral prefrontal cortex	107	0.357	4.20	-20	36	40
Ventromedial prefrontal cortex	48	0.809	3.74	-6	58	2
(d) Milkshake > Money						
Amygdala (CM)	4391	0.000	7.15	-26	-4	-10
Middle insula			6.79	-34	-6	16
Postcentral gyrus (SII)			6.42	-58	-18	16
Putamen			4.70	20	6	0
Supramarginal gyrus			4.27	-48	-32	26
Putamen			3.95	-26	6	0
Cerebellum	1559	0.000	6.64	-16	-64	-18
Lingual gyrus (V1)			4.38	-10	-68	4
Amygdala (CM)	4752	0.000	6.10	24	-4	-10
Frontal operculum (SII)			6.07	62	-16	14
Middle insula			5.78	38	-2	8
Superior temporal gyrus			5.59	58	-32	16
Postcentral gyrus			5.06	56	-16	32
Supplementary motor cortex	1598	0.000	5.28	6	-2	58
Midcingulate cortex			5.20	6	10	36
Cerebellum	388	0.004	4.96	-20	-66	-50
Cerebellum	1186	0.000	4.74	18	-60	-16
Lingual gyrus (V1)			4.60	22	-60	-2
(e) Money > Milkshake						
No suprathreshold clusters						

Note. Significance threshold was $p < .05$, FWE-corrected at the cluster level, with a cluster-defining threshold of $p < .001$. Due to the over-conservative false positive rate of the test for the conjunction null (Friston et al., 2005; Nichols et al., 2005), the significance threshold for this test was more lenient: $p < .001$, uncorrected, extent threshold = 45. V1, primary visual cortex; NAc, nucleus accumbens; CM, centromedial nucleus of the amygdala; SII, secondary somatosensory cortex; vmP, ventromedial part of the anterior putamen.

Material S2 for the temporal SNR map). However, in the remaining parts of the brain, the SNR did not indicate major irregularities in data quality.

Finally, we directly compared the neural encoding of the delivery of the two reward types. This contrast revealed that a large set of brain regions, including middle insula, the overlying frontal operculum, and the amygdala complex, among others, was significantly more involved in the encoding of the delivery of increasing amounts of milkshake relative to money (see Fig. 2d and Table 1d). The red bars in Fig. 2b and d show that the average activity in these brain regions was greater the more milkshake was delivered, while no such activity pattern was present for monetary rewards (blue bars). In contrast, no brain regions were significantly more strongly involved in encoding money relative to milkshake delivery.

Note that the above-mentioned findings hold even when controlling for age and BMI (see Supplementary Material S3). In addition, we repeated this analysis after excluding the contrast images relating to control trials (reward omissions) to test for more subtle neural encoding of increasing reward quantity. Thus, the effect of neural tracking of increasing amounts of milkshake will reflect the increase of activity from low to high quantities of milkshake, instead of increasing activity from rinse to varying amounts of milkshake delivery. The same applies to the money condition, where we focused on the neural encoding of different gain amounts instead of focusing on the increase of activity from winning nothing to winning different amounts of money. Furthermore, we also tested for neural encoding of increasing quantities of reward, each contrasted against the respective control (rinse or no money). These models revealed similar results as the model including control trials reported above (see Supplementary Material S4). However, this analysis also revealed that the neural encoding of increasing amounts of rewards partly relied on the stark contrast between reward omission and varying amounts of reward delivery. Whereas the ventral striatal tracking of monetary gain extended into the NAc in the main model, this was not the case in the supplementary model without control trials. Similarly, whereas the activity in the vmPFC increased from rinse delivery to large amounts of milkshake, this increase was not significant when considering only the different amounts of milkshake without the rinse control.

Finally, we repeated the main analysis using pleasantness ratings instead of reward quantity. That is, we modeled the trials separately for the four categories of ratings (lowest, low, high, and highest). As expected due to the strong correlation between reward quantity and pleasantness ratings, these results replicated the results based on reward quantity (see Supplementary Material S5). However, due to the greater noise when relying on participants trial-wise ratings on an analogue visual scale, the effects were weaker than those based on the experimentally manipulated reward quantity.

3.3. Neural encoding of reward evaluation

After the delivery of different amounts of milkshake or money on each trial of the fMRI experiment, participants were presented with a rating scale and asked to think about how much they liked the received reward, and to subsequently indicate their rating by button presses. We analyzed this interval before the button presses (see also the evaluation event in Fig. 1a) to identify brain regions involved in the post hoc evaluation of increasing quantities of reward, separately for milkshake and money.

The primary visual cortex was similarly involved in the evaluation of both reward types. The activity in this area during the evaluation was greater the larger the previously delivered reward, see Fig. 3a and Table 2c. In contrast, the bilateral postcentral gyrus extending into the primary somatosensory cortex was significantly more involved in evaluating increasing quantities of milkshake relative to money (see Fig. 3b and Table 2d). While this area was more activated the more milkshake was previously delivered (see red bars in Fig. 3b, and therefore the more

Table 2
Brain regions encoding the evaluation of increasingly large rewards.

	Cluster level		Peak level			
	Size	$p_{FWE\text{-}corr}$	*t*	x	y	z
(a) Money						
Calcarine gyrus (V1)	1649	0.000	12.23	14	-80	4
(b) Milkshake						
Calcarine gyrus (V1)	791	0.000	8.82	14	-80	4
Postcentral gyrus (SI)	895	0.000	6.24	-52	-10	32
Postcentral gyrus (SI)	830	0.000	6.13	54	-8	30
(c) Conjunction: Milkshake and Money						
Calcarine gyrus (V1)	768	0.000	8.82	14	-80	4
(d) Milkshake > Money						
Postcentral gyrus (SI)	946	0.000	6.02	56	-6	30
Postcentral gyrus (SI)	889	0.000	5.94	-52	-10	32
(e) Money > Milkshake						
No suprathreshold clusters						

Note. Significance threshold was $p < .05$, FWE-corrected at the cluster level, with a cluster-defining threshold of $p < .001$. Due to the over-conservative false positive rate of the test for the conjunction null (Friston et al., 2005; Nichols et al., 2005), the significance threshold for this test was more lenient: $p < .001$, uncorrected, extent threshold = 45. V1, primary visual cortex; SI, primary somatosensory cortex.

the milkshake was liked), it was generally deactivated during the evaluation of monetary rewards (see blue bars in Fig. 3b).

3.4. Effect of session on responses to reward delivery

Accumulating amounts of received milkshake and monetary gains could potentially affect the subjective perception in a time course-dependent manner due to a general decline in marginal value and post-prandial gut-brain signaling. We therefore explored whether the pleasantness of increasingly large rewards changed over time, i.e., from the first to the second session of the fMRI experiment. To this end, we repeated the analyses (including control trials), however, after taking into account the effect of session.

First, at the behavioral level, this analysis did not reveal any significant effect of session on the ratings of pleasantness, as neither the main effect nor any of the possible interactions with reward type or reward quantity were significant, all *p*s > 0.5 (see Supplementary Material S6 for complete statistics and plots).

Next, we tested whether the neural responses to the delivery of increasing quantities of rewards changed from the first to the second session of the experiment. Accumulating amounts of received milkshake and monetary gains could potentially affect the value-encoding activity in the vmPFC as previously documented for feeding to satiety (Rolls, 2008). Furthermore, postprandial gut-brain signaling could modify the response to reward delivery in additional brain regions. For instance, milkshake ingestion is expected to elevate insulin levels in the course of the experiment, which in turn could down-regulate dopaminergic reward-related circuits, including the VTA and the NAc (Liu and Borgland, 2019; Sallam and Borgland, 2021). Our data indeed revealed that the response of these regions to the receipt of increasingly large money gains differed significantly between the first and the second session (see Table 3 and Fig. 4a). A similar trend was observed for milkshake consumption, however the effects were not significant (vmPFC, [-6 58 -6], $t = 3.18$, $p_{FWE\text{-}corr} = .234$; NAc, [-14 10 -10], $t = 2.09$, $p_{FWE\text{-}corr} = .939$; VTA, 2 -14 -16], $t = 1.99$, $p_{FWE\text{-}corr} = .961$; whole brain uncorrected significance threshold set to $p < .05$, with a subsequent FWE correction for multiple comparisons within the ROI mask). The neural encoding of increasing amounts of monetary gains was stronger in the first than in the last 20 min of the experiment in the vmPFC, the NAc, and the VTA (the latter at a non-corrected significance threshold, see Table 3a). In contrast, the neural encoding of increasing amounts of milkshake did not significantly change across sessions (neither in the whole brain nor within the ROIs, i.e., VTA, NAc, and vmPFC). Instead, the conjunction analysis across the two sessions revealed a stable neural encoding of increasing milkshake delivery across the entire experiment length (see Table 3 and Fig. 4b), which overlapped with the overall milkshake effect (see Table 1b and Fig. 3b).

4. Discussion

In the present study, we compared the neural encoding of two types of rewards, palatable milkshakes and monetary gains. Using fMRI, we identified brain regions in which the activity scaled with the increasing quantity of received rewards, the lowest being in response to reward omissions and the highest upon maximal reward quantity. In contrast to previous studies, we examined the neural responses to the actual receipt of food and money, unaffected by any additional cognitive processing such as anticipation or learning. During the experiment, participants consumed varying amounts of milkshake and received different amounts of monetary gains. Subsequent pleasantness ratings of these reward deliveries revealed that the subjective value strongly increased with quantity, similarly for milkshakes and money. Participants liked the larger quantities of food and money significantly more than the lower ones and the omissions. This result demonstrates that we successfully devised a method for manipulating the subjective value of food and monetary receipt in a parametric manner, indicating that these events indeed represent increasingly large rewards. Previous studies used different methods to manipulate food reward value, such as satiety (Kringelbach et al., 2003; Small et al., 2001), or pleasant vs aversive tastes (Grabenhorst et al., 2010; Small et al., 2003), which are not well suited for modulation of value across food and monetary rewards. In the brain, the delivery of increasing amounts of both food and money rewards was encoded by the bilateral ventral striatum and the vmPFC, among other regions. The neural computation of value in a common currency across primary and secondary reward types has been previously substantiated by meta-analyses (Bartra et al., 2013; Chase et al., 2015; Levy and Glimcher, 2012; Sescousse et al., 2013) and studies comparing reward type combinations other than monetary gains and food consumption (Chib et al., 2009; Lebreton et al., 2009; Levy and Glimcher, 2011; Rademacher et al., 2010; Sescousse et al., 2015, 2010; Smith et al., 2010). However, this is the first direct evidence by a within-

Table 3
The effects of session on neural encoding of increasing quantity of reward delivery.

	Cluster level		Peak level				
	Size	$p_{FWE\text{-}corr}$	$p_{FWE\text{-}corr}$	*t*	x	y	z
(a) Session 1 > Session 2							
Money							
Postcentral gyrus (SI/SII)	2024	0.000		5.49	56	-12	30
Precentral gyrus				5.23	50	-2	28
Postcentral gyrus (SI/SII)	1158	0.000		5.35	-60	-14	22
Precentral gyrus				5.33	-56	-6	30
Ventromedial prefrontal cortex*	92		0.013	4.13	-12	44	-12
Ventromedial prefrontal cortex*			0.015	4.10	-6	28	-16
Ventromedial prefrontal cortex*	69		0.015	4.10	8	44	-16
Ventral striatum (NAc)*	16		0.033	3.87	-10	12	-12
Ventromedial prefrontal cortex*	3		0.046	3.77	-12	28	-18
Ventral tegmental area*	2		0.203	3.24	4	-12	-14
Milkshake							
No suprathreshold clusters							
(b) Session 2 > Session 1							
No suprathreshold clusters							
(c) Conjunction: Session 1 and Session 2							
Money							
Calcarine gyrus (V1)	442	0.001		5.81	14	-90	0
Milkshake							
Cerebellum	901	0.000		7.68	-18	-64	-18
Amygdala (CM)	4880	0.000		7.56	-24	-2	-10
Supramarginal gyrus (SII)				6.42	-60	-24	14
Postcentral gyrus (SII)				6.30	-58	-20	16
Frontal operculum (SII)				6.24	-36	-6	14
Middle insula				6.23	-38	-2	6
Putamen				4.63	-24	4	-2
Ventral striatum (vmP)				4.26	-20	6	-10
Ventral tegmental area				4.05	-10	-20	-10
Amygdala (CM)	5303	0.000		7.54	22	-2	-12
Superior temporal gyrus (SII)				6.36	56	-26	16
Frontal operculum (SII)				5.97	40	-4	10
Putamen				5.51	32	8	6
Middle insula				5.47	34	12	6
Putamen				5.35	26	2	0
Frontal operculum				5.08	58	8	12
Ventral striatum (vmP)				4.34	16	6	-8
Supplementary motor cortex	1549	0.000		6.31	6	-4	60
Midcingulate cortex				4.63	-4	-2	36
Cerebellum	634	0.000		5.39	22	-60	-18
Cuneus	735	0.000		4.84	10	-84	34
Calcarine gyrus (V1)				3.63	-4	-80	12
Cerebellum	197	0.056		4.67	-18	-66	-50
Superior frontal gyrus	68	0.590		4.09	-18	30	34
Cuneus	50	0.768		3.92	20	-92	14
Parahippocampal gyrus	67	0.600		3.90	26	-44	-4
Cerebellum	81	0.474		3.89	14	-72	-50
Lingual gyrus	56	0.708		3.75	14	-86	-8

Note. Significance threshold was $p < .05$, FWE-corrected at the cluster level, with a cluster-defining threshold of $p < .001$. Due to the over-conservative false positive rate of the test for the conjunction null (Friston et al., 2005; Nichols et al., 2005), the significance threshold for this test was more lenient: $p < .001$, uncorrected, extent threshold = 45. * Analysis masked for the following regions of interest (ROI): ventromedial prefrontal cortex, nucleus accumbens, and ventral tegmental area, see Fig. 4a; significance threshold used for this ROI analysis was $p < .05$, FWE-corrected at the voxel level within the mask. Note that the ventral tegmental area does not survive this threshold, but is listed due to the a priori hypothesis. V1, primary visual cortex; NAc, nucleus accumbens; CM, centromedial nucleus of the amygdala; SI, primary somatosensory cortex SII; secondary somatosensory cortex; vmP, ventromedial part of the anterior putamen.

subject study that food and monetary reward receipts indeed share a common neural encoding.

However, much less is known about the neural representation of increasingly large food rewards over and above value tracking. Seminal studies did investigate the neural processing of different taste intensities and valences (de Araujo et al., 2003; Small et al., 2003, 2008, 2001; Veldhuizen et al., 2007), however not in direct comparison to monetary rewards. We show that the same brain regions that encode taste in general were also involved in tracking the delivery of increasing amounts of food rewards, associated with increasing subjective value. Being considered as the primary gustatory cortex (de Araujo et al., 2012; Ogawa, 1994; Schoenfeld et al., 2004; Veldhuizen et al., 2011), the middle insula and the overlying operculum were previously shown to be recruited during taste detection and evaluation (Bender et al., 2009; de Araujo et al., 2003; Small et al., 2003, 2008 , 2001; Veldhuizen et al., 2007). In the present study, the same region was selectively activated by milkshake consumption, and this activation was greater the more milkshake was delivered. Given that larger quantities of milkshake were also more liked, this finding is in line with previously demonstrated role of the insula in tracking changes in flavor liking (de Araujo et al., 2013).

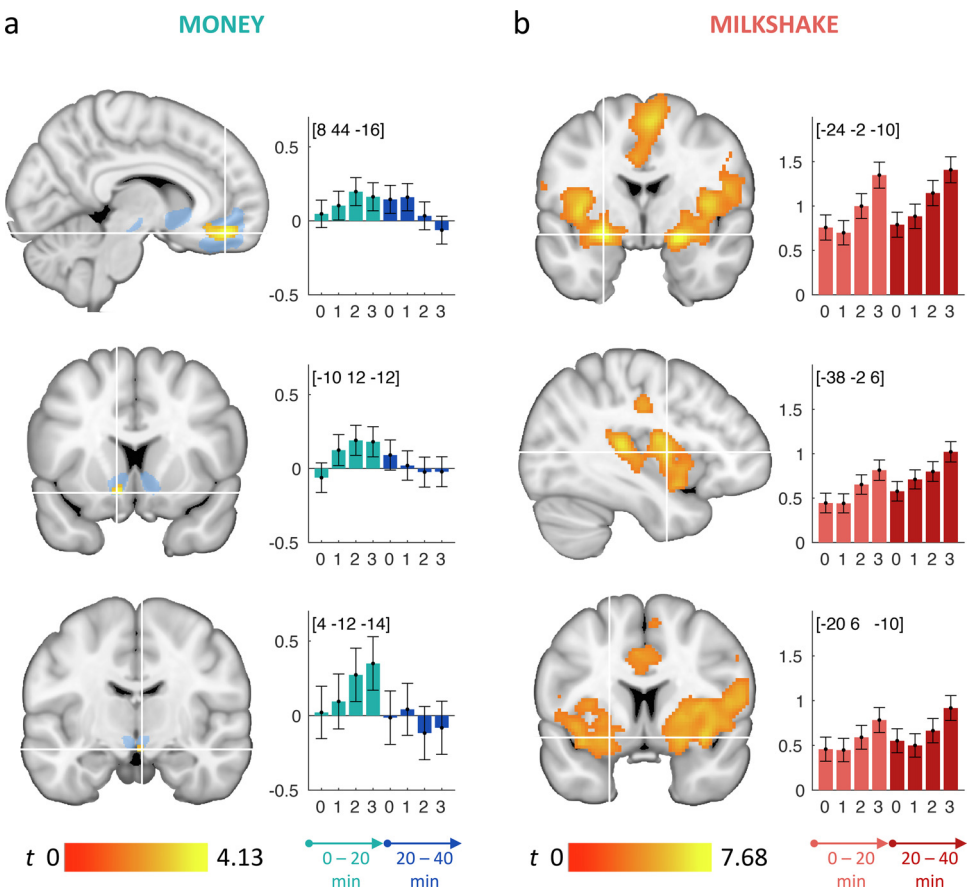

Fig. 4. Effects of session on the neural encoding of reward delivery. (a) The neural encoding of increasing monetary rewards differed across the two sessions of the experiment within the regions of interest: ventromedial prefrontal cortex, nucleus accumbens, and ventral tegmental area (mask overlaid in blue). The direct comparison of the two sessions revealed that the activity in these regions increased with increasing money rewards only in the first session (light blue bars), but not in the second session (dark blue bars). Significance threshold was $p < .05$, FWE-corrected at the voxel level within the mask, see Table 2a for more details. (b) The neural encoding of increasing quantity of milkshake was similar across the first (light red bars) and the second session (dark red bars). Conjunction analysis showed that the activity in the amygdala, middle insula and ventromedial putamen, among other regions, increased with increasing milkshake amounts in both sessions. The significance threshold for the test for the conjunction null was $p < .001$, uncorrected, extent threshold = 45. Error bars show contrast estimates and standard errors for activation peaks marked with white crosses (with peak MNI coordinates [x y z] in the corresponding plots), separately for four quantities of money (blue) and milkshake (red), respectively: 0, none (control), 1, low, 2, mid, and 3, high, with light colors corresponding to session 1 (i.e., the first 20 min of fMRI), and dark colors corresponding to session 2 (i.e., the last 20 min of fMRI). SPMs were overlaid on a MNI standard brain. For interpretation of the references to color in this figure, the reader is referred to the web version of this article.

Furthermore, we also showed that the central nucleus of the amygdala was tracking the increasing quantities of the milkshake delivery. The amygdala is generally highly responsive to motivational salience in different contexts (Cunningham and Brosch, 2012), including food tasting (de Araujo et al., 2003; Rolls, 2008; Small et al., 2003). In particular, the recruited central nucleus of the amygdala was demonstrated to control the craniofacial musculature needed for biting in mice, and was suggested to translate food-related sensory information into goal-directed action (Han et al., 2017). Thus, in our study, its involvement during the consumption of increasing amounts of palatable milkshake may capture the rising salience and coordinate appropriate oral reactions.

Taken together, the neural encoding of increasing amounts of food rewards recruits an extended network over and above value computation. Thus, similar to other primary rewards such as positive facial expressions and erotic pictures, food consumption triggers the integration of multiple cortical and subcortical inputs. However, food consumption also stands out by requiring the encoding of taste and other sensory properties and by inducing complex post-prandial metabolic processing (de Araujo et al., 2020; Plassmann et al., 2021). Importantly, obesogenic diets have been shown to impair different components of neural processing of food consumption, including the reward-related, gustatory, and homeostatic processing (May and Dus, 2021; Mazzone et al., 2020; Sallam and Borgland, 2021). Thus, being able to precisely assess the neural encoding of food rewards plays an important role in investigating the critical mechanisms underlying metabolic pathologies.

The complex multi-modal processing of milkshake consumption extended even into the subsequent evaluation phase. In contrast to monetary gains, the evaluation of increasing amounts of milkshakes recruited the primary sensory cortex adjacent to the central sulcus. This activity may indicate a sustained effect of the sensory processing of the previous food ingestion on the subsequent evaluation. Because the participants received a rinse with a neutral fluid after both milkshake and money delivery on each trial, it seems unlikely that this activity can be merely explained by the presence of fluid in the mouth before the evaluation phase, or by residues of milkshake in the mouth.

In contrast, when we compared the encoding of money relative to food delivery, we did not detect any brain regions that were significantly more responsive to increasing monetary gains. In addition to the pleasantness ratings, this further indicates that we managed to manipulate the subjective value of the reward delivery in a similar manner for money and food. Given that monetary gains recruit brain regions associated with value representation and that the value was similar for the

two types of rewards, it appears plausible that no money-specific neural encoding could be identified. However, meta-analyses comparing brain responses to money versus primary rewards reported that monetary gains elicited a stronger activation of the ventral striatum and the vmPFC (Bartra et al., 2013; Sescousse et al., 2013). Indeed, we observed a non-significant trend for a similar pattern. While the ventral striatum and the vmPFC were recruited by monetary gains as well as milkshakes, their differential activation in response to monetary gains was marginally stronger and extended bilaterally into the nucleus accumbens. Thus, the fact that the accumulated amount of money was handed out only after the experiment does not seem to have weakened the neural responses to single monetary gains. This is not surprising given that the rewarding quality of money in an experimental setting constitutes an abstract representation of being able to acquire goods after participation in the study. Thus, the difference in immediate vs. postponed delivery may represent inherent ecological characteristics of the two different reward types. Moreover, as participants were not able to spend the money before the end of the experiment, the postponed delivery of money did not in fact make a difference.

Over the course of the experiment, the accumulative milkshake consumptions and monetary gains could have gradually induced psychological and physiological effects such as diminishing marginal utility, satiety, and postprandial metabolic signaling affecting the reward-related behavioral and neural responses (Berkman et al., 2016; de Araujo et al., 2020; Sallam and Borgland, 2021; Xu et al., 2015). Thus, we explored whether pleasantness ratings and neural reward-related processing changed from the first to the second experimental session, each lasting 20 min. We could not detect any significant differences concerning the pleasantness ratings, irrespective of reward type, nor the neural encoding of increasing amounts of milkshake delivery. The stability of liking and neural response to milkshake indicates that subjects did not consume to satiety, in accordance with the small total amount of milkshake of 30 ml administered throughout the experiment. Furthermore, more general time-dependent changes in brain responses such as habituation or fatigue are rather unlikely as they would have also affected the neural encoding of milkshake consumption.

By contrast, the neural encoding of increasingly large monetary rewards in the vmPFC, the NAc, and the VTA was stronger in the first than in the second experimental session. A similar decline in these dopaminergic regions of interest was observed for the milkshake consumption as well, however, not to a significant extent. The better propensity of monetary gains to reveal time-dependent declines in the activity of the VTA and its projection targets may be driven by the trend of a generally stronger recruitment of these regions by monetary then food rewards. The observed decline of neural encoding of increasing monetary rewards may relate to the law of diminishing marginal utility, predicting that as gains accumulate, the marginal utility derived from each additional gain declines (Berkman et al., 2016). However, this cannot explain why only the neural encoding of increasing monetary rewards, but not the respective pleasantness ratings, decreased in the second relative to the first task session. It is possible that the neural encoding of increasingly large rewards can reveal modulations in dopaminergic activity even in the absence of changes of overt conscious evaluation (Winkielman et al., 2005). Alternatively, assessing incentive salience like willingness to work for the reward or ratings of wanting instead of liking would have been more sensitive measures (Hanssen et al., 2021; Thanarajah et al., 2019).

The decline of neural encoding of increasing monetary rewards might also be related to metabolic changes in the body that occur in response to food intake. One of the critical postprandial reactions after the ingestion of sugar-rich food is the increase of endogenous insulin, which plays a major role in stabilizing blood glucose levels. Importantly, animal and human research has shown that insulin also acts in the brain in a regional- and time-dependent manner (Edwin Thanarajah et al., 2019; Liu and Borgland, 2019; Sallam and Borgland, 2021; Thanarajah et al., 2019; Tiedemann et al., 2017). More specifically, it increases the dopaminergic signaling in the NAc at the beginning of the ingestion phase, but after around 30 min, higher insulin concentrations decrease the dopaminergic signaling in both the VTA and its projection targets (Liu and Borgland, 2019; Sallam and Borgland, 2021). Such down-regulation of dopaminergic midbrain circuitry is able to generally affect reward-related behaviors, even those unrelated to food intake (Hanssen et al., 2021; Labouebe et al., 2013; Naef et al., 2019; Skrynka and Vincent, 2019; Xu et al., 2015). Hence, we speculate that delayed insulinergic modulations of brain function could explain the weaker neural encoding of monetary rewards by mesoaccumbal regions in the second session of an experiment with repetitive ingestion of sugar-rich food. The existence of systematic post-prandial influences on general reward-related signaling would have far-reaching theoretical implications for research on judgment and decision making. Future studies should therefore further corroborate this notion by closely monitoring fasting durations and blood levels of glucose and insulin and relating these measures to changes in reward-related behavior and neural processing.

Taken together, increasing quantities of food and monetary reward delivery were associated with comparable increases in liking and revealed both common and unique neural representations. Over and above the common value encoding, food rewards engaged an extended and multi-modular neural processing integrating sensory properties of food and the representation of value. Thus, the present study provides new methodological impulses for implementing research on different reward types to better understand the regulation of food intake and its dysfunctions. Moreover, our results reveal a dynamic nature of reward encoding, in line with the idea that food ingestion modulates metabolic and neural function to enable finely tuned homeostatic and motivational regulation over time. This highlights the importance of the consideration of basal metabolic states and the need for well-tailored monitoring of neural and behavioral fluctuations in response to accumulating reward delivery.

Data and code availability statement

The data of the present study will be made available in the data portal (https://www.datalad.org/) with a persistent data identifier (DOI). The data will be stored non-publicly, and access will be granted upon request conditioned by

- a formal data sharing agreement;
- approval from the requesting researcher's local ethics committee;
- a formal project outline;
- a clear reference to the data source in resulting publications.

The code used for the execution of the study and analyses will be made available on GitHub via a request to the authors.

Declaration of Competing Interest

The authors declare no competing financial interests. S.O. was supported by Sagol School of Neuroscience and the Adams Super Center for Brain Studies travel grant, Minerva Short-Term Research Grant, Manna Center Program for Food Safety & Security, and the Israel Science Foundation grant awarded to T.S. (grant number 1798/15). M.T. was supported by funding from Deutsches Zentrum für Diabetesforschung (DZD, German Center for Diabetes Research) – Project-ID 82DZD00502 & 82DZD03C2G, Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – Project-ID 431549029 – SFB 1451, and Germany's Excellence Strategy – EXC 2030 – 390661388.

Credit authorship contribution statement

Shiran Oren: Conceptualization, Methodology, Funding acquisition, Formal analysis, Writing – original draft. **Marc Tittgemeyer:** Supervision, Funding acquisition, Writing – review & editing. **Lionel Rigoux:**

Conceptualization, Writing – review & editing. **Tom Schonberg:** Supervision, Funding acquisition. **Bojana Kuzmanovic:** Conceptualization, Formal analysis, Visualization, Writing – review & editing.

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Supplementary materials

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