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# Colouring perception: package colour cues affect neural responses to sweet dairy drinks in reward and inhibition related regions

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## Abstract

Extrinsic product cues such as package colour may change product perception and perceived reward value during product evaluation. Healthier foods (*i.e.,* 'light', sugar- or fat-reduced) often have different packages than regular products, e.g., they may be less vibrantly coloured. People vary in their degree of health-interest and self-control ability and may be affected differently by package colour. This study assesses the extent to which package colour and participant characteristics interact and influence product perception and brain responses.

Thirty-four healthy females performed a functional MRI task in which they viewed four differently coloured packages (regular vs. healthier; differing in brightness and saturation levels) with or without simultaneously tasting a either a regular or a healthier calorie-reduced drink.

Results indicate main effects of package and taste and a package*taste interaction effect. Compared to healthier packages viewing regular packages enhanced activation in region implicated in inhibitory control (inferior frontal gyrus) and a reward-related region (striatum), the latter even more so as participants' health interest increased ($r = 0.43$, $p = 0.01$). Incongruent package-taste combinations decreased activation in the orbitofrontal cortex (OFC, a region implicated in reward representation) compared to congruent combinations. Tasting the healthier compared to regular product enhanced activation in the middle and superior frontal gyrus, which are implicated in inhibitory control, as well as the striatum and OFC, suggesting a cognitively driven preference for the healthier product.

In conclusion, this paper provides evidence for the conditions under which package colour and taste properties modulate neural correlates related to reward and inhibition. Individual differences in health-interest and impulsivity influence package- and taste-related neural

correlates and thus underscore the importance of taking participant characteristics into account in food research.

47 **Keywords**

48 Product perception; Package colour; BOLD fMRI; Health interest; Impulsivity

## 1. Introduction

At the basis of food preference lies the attractiveness of intrinsic food properties such as the taste and flavour of a product (Clark 1998). However, at the point of purchase, extrinsic food properties such as packaging or labelling are leading determinants of food choice since intrinsic food properties cannot be evaluated properly at this stage (Schifferstein, Fenko et al. 2013). There is accumulating behavioural evidence that extrinsic food properties can influence taste perception (Ng, Chaya et al. 2013, Gutjar, de Graaf et al. 2014, Piqueras-Fiszman and Spence 2015, Tijssen, Zandstra et al. 2017).

We recently demonstrated that package colour properties not only influence product expectations but also actual flavour perception of a product after tasting. Certain combinations of hue, brightness and saturation corresponding with more vibrant package colouring (*i.e.* high saturation, low brightness) were perceived as most attractive and least healthy which influenced both sensory expectations and flavour perception (Tijssen, Zandstra et al. 2017). Effects seen in behavioural studies may be driven by reward and inhibitory control processes in the brain, which is the focus of the present study.

The orbitofrontal cortex (OFC), anterior cingulate cortex (ACC) and amygdala encode reward value of foods and the striatum (putamen, caudate nucleus, nucleus accumbens) and ventral and dorsolateral prefrontal (dlPFC) areas are involved in reward anticipation, inhibitory control and reinforcement learning (Berridge 1996, O'Doherty, Deichmann et al. 2002, Aron 2007, Rolls 2011, Rolls 2015). The frontal operculum and anterior insula, which contain the primary taste cortex have been shown to differentiate between objective qualities of taste, *i.e.* taste identity and intensity (Rolls 2011).

Intrinsic properties such as nutritional value and flavour of foods can affect preference and reward value (Birch 1999, Sørensen, Møller et al. 2003). For example, different brain responses to solutions of sugars and non-caloric sweeteners in water have been found (Smeets, de Graaf et al. 2005, Frank, Oberndorfer et al. 2008, Smeets, Weijzen et al. 2011, Griffioen-Roose, Smeets et al. 2013, van Rijn, de Graaf et al. 2015). Frank et al., (2008) showed that tasting a caloric (sucrose) solution versus a non-caloric (sucralose) solution, which were matched in pleasantness, gave rise to stronger neural activations in taste areas and reward areas. Smeets et al., (2011) showed that caloric versus non-caloric soft drinks (matched on sensory properties) gave rise to stronger amygdala activation. Although Van Rijn et al., (2015) did not find differences in taste areas when tasting a caloric or non-caloric solution, they did find differences in reward areas. They also demonstrated differences in activation in frontal regions as a result of sweet versus non-sweet versions of a similar drink indicating that sweetness affects neural activation irrespective of caloric content.

Extrinsic properties, such as packaging, can influence expectations but also affect food preference, taste perception and reward value (for a review see Okamoto and Dan (2013, Piqueras-Fiszman and Spence (2015)). Studies that investigate expectation-based effects of (in)congruent verbal labels on taste perception and reward processing using functional magnetic resonance imaging (fMRI) indicate expectancy driven modulation of verbal sensory (taste) descriptors (*e.g.,* "very sweet" and "less sweet") on activation in taste related areas such as the anterior insula and frontal operculum (Nitschke, Dixon et al. 2006, Veldhuizen, Douglas et al. 2011, Woods, Lloyd et al. 2011). Expectancy driven modulation of hedonic and health descriptors (*e.g.,* "treat" and "healthy") on taste related activation is less conclusive (Grabenhorst, Rolls et al. 2008, Veldhuizen, Nachtigal et al. 2013). Evidence for expectancy driven modulatory effects of verbal hedonic and health descriptors as well as brand and price

cues in reward and attention related areas is growing (*e.g.*, OFC, striatum, ACC, inferior frontal gyrus, amygdala, ventromedial prefrontal cortex (vmPFC)) (McClure, Li et al. 2004, de Araujo, Rolls et al. 2005, Plassmann, O'Doherty et al. 2008, Veldhuizen, Douglas et al. 2011, Grabenhorst, Schulte et al. 2013, Kuhn and Gallinat 2013, Okamoto and Dan 2013).

As demonstrated by the abovementioned literature, research on expectancy driven neural modulations of product perception mostly uses clear, rather obvious, verbal, visual descriptors emphasizing taste or hedonic properties. Yet in reality, expectancy driven modulations likely follow less obvious, subconscious and non-verbal cues. It remains to be seen to what extent the abovementioned research findings translate to less explicit, less obvious non-verbal cues such as package "impression" that is associated with certain degrees of healthiness or attractiveness. Investigating more realistic and subtle expectancy driven modulations can give better insights into the effects of these subtle everyday cues on perception and neural correlates.

The present study primarily aims to explore the neural correlates of subtle extrinsic cues (*i.e.*, healthiness and attractiveness related features signalled through package colour) combined with intrinsic properties (*i.e.*, the flavour of a dairy drink) to determine the neural mechanisms behind expectation influencing taste perception and food hedonics. The study aims to shed light on the interaction of top-down cortico-cortical influences (*e.g.*, valuation, pleasantness) and more primary sensory-related processes (*e.g.*, taste intensity) that underlie the effects of package colour cues on sensory taste perception and hedonic evaluations. These separate representations of psycho-physical attributes (e.g. intensity) and psycho-hedonic attributes (e.g. pleasantness, healthiness) of taste, engages differential brain systems/pathways. We wanted to explore whether the effect of package colour induced influences on taste would be reflected in neurocognitive functions more oriented towards affective, evaluative processing versus more

primary sensory-related processing. A priori regions of interest included taste related brain regions, *i.e.,* primary and secondary taste cortex (anterior insula/frontal operculum, OFC)(Iannilli, Noennig et al. 2014), as well as reward, salience and inhibition related regions, including the amygdala, (pre)frontal cortex (including OFC, vmPFC, dlPFC), striatum and anterior cingulate cortex (ACC)(Rogers, Owen et al. 1999, Pochon, Levy et al. 2002).

In addition, behavioural and neuroimaging research has shown that health-related product cues affect consumers differently depending on personal characteristics. Neural susceptibility to hedonic or health cues in reward regions (OFC, ACC, striatum) can depend on BMI, inhibitory control, trait impulsiveness and health interest (Zandstra, de Graaf et al. 2001, Guerrieri, Nederkoorn et al. 2007, Veldhuizen, Nachtigal et al. 2013, van Rijn, Wegman et al. 2017). Maintaining a healthy lifestyle may involve a goal of healthy eating. This requires a certain degree of inhibitory-control, *i.e.,* exerting effort to withhold from unwanted behaviour. Both trait impulsivity as well as inhibitory control deficits have been associated with unhealthy eating (Jasinka et al., 2012). Having a goal to eat healthy may induce a cognitively driven preference for healthy options as opposed to a stimulus driven preference for unhealthy options (van Rijn, Wegman et al. 2017).

Our secondary aim was to investigate whether neural activation in response to processing of packaging cues is modulated by trait impulsivity (Patton and Stanford 1995) and attitudes towards health and taste (Roininen, Lahteenmaki et al. 1999).

Based on the findings described above, we predicted that package colour cues will influence product expectations and taste perception. It was hypothesized that the effects of package colour cues will be mainly reflected in psycho-hedonic properties such as taste attractiveness, with altered brain activity in cognition - and reward related regions such as the OFC, ACC, striatum

and amygdala, which feed backwards to primary sensory regions (top-down). It was expected that more vibrantly coloured packages (*i.e.*, low brightness, high saturation) will enhance activation in these regions compared to less vibrantly coloured packages. Furthermore, it was expected that top-down effects will be different depending on personality characteristics. In particular, health interest may induce a cognitively driven preference for the healthier option, reflected in brain regions where integration of cognitive and stimulus driven cues takes place such as the striatum, amygdala, OFC and ACC. The degree of trait impulsiveness may play a role in brain activation, with ('hard to resist') vibrantly coloured packages decreasing activation in inhibition related regions (PFC, *i.e.* inferior frontal gyrus) compared to less vibrantly coloured packages.

## 2. Materials and methods

### 2.1 Participants, screening and training

39 Dutch female participants (considered as healthy as measured in a self-report questionnaire) were recruited to participate in the study. Five participants were excluded because of data loss as result of technical difficulties concerning the MRI. Data of 34 participants (aged 18-35 years, mean=21.7, ±SD=2.4, all right handed, BMI mean=21.9, ±SD=1.3) were analysed. 31 out of 34 participants completed high school prior to the experiment. All participants were familiar with the used product category and not colour blind (tested using Ishihara's colour test (Ishihara 1951)). Participants did not have stomach or bowel diseases, did not have any psychiatric, neurological disorders or other relevant medical history that would affect the results of the study (*e.g.* chronic diseases such as diabetes, thyroid- or kidney disease, taste or smell disorders, allergies/intolerances for products under study, were not pregnant or lactating), did not use daily medication other than oral contraceptives, paracetamol or H1-antihistaminergic drugs, did not smoke more than one cigarette/cigar a day, did not have a history or current alcohol consumption of more than 21 units per week, did not change in body weight (more than 5 kg) or follow an energy restricted diet during the past two months and had no contra-indications for MRI scanning (*e.g.* pacemaker). Before enrolment participants were screened on inclusion and exclusion criteria via a questionnaire, gave written informed consent and received monetary reimbursement for their participation (€65,-). The study was conducted in accordance with the Declaration of Helsinki (amendment of Fortaleza) (World Medical 2013), approved by the Medical Ethical Committee of Wageningen University and registered in the Dutch Trial Registry (NTR5899).

### 2.2 Stimuli

Four package stimuli, adopted from Tijssen et al., (2017) were used. Stimuli were based on a previously commercially available dairy drink 'Optimel Puur Rode Vruchten' (Royal

184 FrieslandCampina, Amersfoort, The Netherlands) and differed in hue (blue and red), brightness
185 (high vs. low) and saturation (high vs. low) levels signalling more/less healthy product
186 properties. Based on package colour, two package stimuli were chosen to represent healthier
187 packages (*e.g.* 'light', sugar- or fat-reduced) and two to represent regular packages (Figure 1).
188 Except for package colour, all information on the packages was kept the same. The packages
189 state that they contains 0% fat, no sweeteners and no added sugar.
190
191 [INSERT FIGURE 1 HERE]
192
193 Two tasted product stimuli were used: 1) the regular product taste stimulus was a commercially
194 available sweet (white coloured) dairy drink 'Vifit Rode Vruchten' (Royal FrieslandCampina,
195 Amersfoort, The Netherlands) and 2) the healthier product taste stimulus was a mix of this dairy
196 drink and tap water (ratio of 4:1 g dairy drink to tap water). Due to the decrease in caloric, and
197 sugar content, we perceive this stimulus as healthier. The original dairy drink 'Optimel Puur
198 Rode Vruchten' was taken of the shelves prior to the experiment. For this reason, we needed to
199 determine and include an alternative sweet dairy drink that matched the original. The healthier
200 taste stimulus was selected on the basis of the results from a pilot experiment ($n$=15). This sweet
201 dairy drink ('Vifit Rode Vruchten') and this specific dilution ratio gave rise to a comparable
202 sensory profile compared to the sensory profile obtained in Tijssen et al., (2017), where we
203 included 'Optimel Puur Rode Vruchten'. The pilot experiment included a multitude of sweet
204 dairy drinks ($n$=5) as well as several dilution ratios of sweet dairy drinks relative to tap water
205 (2:1; 3:1; 4:1; 5:1). The aim was to find a comparable match in sensory profile (on taste, flavour
206 and texture) with respect to the original sweet dairy drink 'Optimel Puur Rode Vruchten'.
207 Matching was determined by means of Analysis of variance (ANOVA) tests comparing sensory
208 scores per attribute of the piloted stimuli to the original 'Optimel Puur Rode Vruchten'. A match

consisted of no significant differences between the piloted and original product samples at $p<0.05$ for any of the sensory attributes questioned.

Tap water was used to rinse between taste stimuli, all stimuli were administered at room temperature. The usage of package and taste stimuli was permitted by, and cleared with, Royal FrieslandCampina.

### 2.3 Participant characteristics and attitudes

The Health and Taste Attitude Scale (HTAS) was employed to measure the importance of health and taste aspects of food in the choice and consumption processes (Roininen, Lahteenmaki et al. 1999). HTAS contains 44 statements (*e.g.* "*I reward myself by buying something really tasty*") divided among 3 taste related subscales and 3 health related subscales. Participants responded using a 7-point scale ranging from "strongly disagree" to "strongly agree" and responses were averaged per subscale.

The Barratt Impulsiveness Scale, version 11, (BIS-11) (Patton and Stanford 1995) was also employed and contains 30 statements (*e.g.* "*I say things without thinking*") divided into three subscales measuring sub traits of attentional-, motor- and non-planning impulsivity. Attentional impulsiveness represents an inability to focus attention or to concentrate. Motor impulsivity represents acting without thinking and non-planning impulsiveness represents lack of forethought (Barratt 1985). Participants respond using a 4-point scale ranging from "seldom/never" to "almost always". On average, our participant group scored medium on impulsiveness.

### 2.4 Procedure

After the initial screening session (study day 1) participants completed a training session (study day 2) to practice the fMRI procedure and collect data regarding behavioural characteristics (*e.g.*, HTAS, BIS-11). During the fMRI session (study day 3), participants arrived between

08.30 and 12.30 h at the test location (Hospital Gelderse Vallei, Ede, The Netherlands) after a fast of at least 2 h (no food, only water). First they reported their hunger level on a 100-unit Visual Analogue Scale (VAS) presented online using an online questionnaire (Logic8 EyeQuestion software, version 4.2.11). After this, participants received verbal instructions and were placed into the MRI scanner where they performed two fMRI tasks; a choice task (data reported elsewhere) and the taste task described below.

During the latter task participants were asked to pay attention to a package image (*i.e.* package trial) presented using a back-projection screen, which could be viewed by the participants via a mirror positioned on the head coil, or a package image simultaneously accompanied by small sips (2 ml) of the product taste stimulus (*i.e.*, package-taste trial), administered through programmable syringe pumps (New Era Pump System Inc., Wantagh NY) at 50 ml/min.

All package images were presented 20 times (without taste stimuli) resulting in 20 x 4 = 80 package trials, and presented 10 times in combination with each taste stimulus (4 x 2 = 8 unique combinations, of which ½ congruent and ½ incongruent package-taste combinations) resulting in 10 x 8 = 80 package-taste trials. An example of a congruent package-taste trial consisted of a healthier product package stimulus (BHL package) simultaneously presented with the healthier product taste stimulus delivery (dairy drink 'Vifit Rode Vruchten' and tap water). An example of an incongruent package-taste trial consisted of a healthier product package stimulus (BHL package) simultaneously presented with the regular product taste stimulus delivery (dairy drink 'Vifit Rode Vruchten'). All trials were randomized and divided into three runs. Runs were presented to participants in one of three randomly generated orders. Each stimulus was presented on a light grey background. An intra-trial interval (4 - 6 s) started with a white crosshair (3.5 - 5.5 s – 'rest') followed by a 0.5 s timeframe where the crosshair either turned

blue (cueing a package trial) or red (cueing a package-taste trial) for anticipation purposes. Subsequently a package image was presented for 3 s (package trial) or 7 s (package-taste trial). Following package-taste trials a 2 s 'swallow' cue was presented on the screen, followed by a 3.5 s 'rinse' cue accompanied by a 2 ml tap water stimulus, again followed by a 2 s 'swallow' cue. To ensure that proper attention was paid to the package images in the package-taste trials, participants were asked once per congruent combination (*i.e.,* healthier package + healthier taste stimulus or regular package + regular taste stimulus) to rate healthiness and attractiveness using a 7-point scale anchored 'not at all' to 'very', presented directly after swallowing the tasted stimulus (data not reported). See Figure 2 for an schematic overview of a package, and package-taste trial. Responses were collected via a MRI-compatible button box.

[INSERT FIGURE 2 HERE]

Following the fMRI task, after a 15 minute break, participants evaluated all eight package-taste combinations outside the scanner, one by one, in random order, on hedonic (liking, healthiness, attractiveness) and sensory (sweetness, creaminess, fruitiness, flavour intensity) attributes using a 100-unit VAS (anchored 'not at all' to 'extremely') in an online questionnaire presented via EyeQuestion. Hedonic attributes were followed by sensory attributes and attributes were randomized within the attribute domain. Package images were presented above the questions on the computer screen and taste stimuli were presented at room temperature in white opaque plastic cups (100 ml) containing 40 ml of the taste stimulus, distinguishable by (randomly generated) 3-digit-codes. Participants were instructed to pay attention to the package, take a sip and pay attention to both package and taste when answering the questions. Between each sample, during at least a 10 s break, participants were asked to clean their palate using water and/or crackers to avoid sensory fatigue and carry over effects.

## 2.5 MRI data acquisition

Each fMRI scan session (study day 3) consisted of 3 functional runs in which 1029 functional volumes were acquired using a $T_2^*$-weighted echoplanar imaging sequence (TR=2140 ms, TE=25 ms, 90° flip angle, FOV=192×192 mm, 43 axial slices acquired in descending order, voxel size=3×3×3 mm) on a 3 T Siemens Magnetom Verio (Siemens, Erlangen, Germany). In addition to this, a $T_1$-weighted anatomical scan was acquired (MPRAGE, TR=2300 ms, TE=2.98 ms, 9° flip angle, FOV=256×256 mm, 192 sagittal slices, voxel size=1×1×1 mm).

## 2.6 Data analysis

### 2.6.1 Behavioural data analysis

All behavioural (and correlation-) analyses were carried out in SPSS (version 23; SPSS Inc., Chicago, IL, USA). Cronbach's alpha was determined for the BIS-11 and HTAS questionnaires as a measure of scale reliability.

#### 2.6.1.1 Participant characteristics

The HTAS contains 44 statements divided among 3 taste related subscales and 3 health related subscales. Participants responded using a 7-point scale and responses were averaged per subscale and compared to earlier research (Roininen, Tuorila et al. 2001).

The BIS-11 contains 30 statements divided into three subscales. Participants respond using a 4-point scale and responses are summed up per (sub)scale, *e.g.* scores for BIS sum range from 30 to 120. According to (Stanford, Mathias et al. 2009) the following division can be made: low (score <52), medium (score 52-71) or high (score >71) impulsivity.

Pearson correlation coefficients were calculated to determine the associations between HTAS subscales and BIS-11 subscale scores.

#### 2.6.1.2 Sensory and hedonic analysis

To investigate the effects of package colour properties and product properties on perceived hedonic and sensory responses, Linear Mixed Model analyses (LMM) were carried out per hedonic and sensory attribute with package and taste as main factors as well as a package*taste interaction effect. Participant was added as a random factor (including intercept) and the HTAS and BIS-11 subscales were added as covariates. The assumption of normal distribution of dependent variables was checked using QQ plots and Kolmogorov-Smirnov tests, and equal variances were assessed using Levene's tests. The assumption of normality was not violated. Additionally, controlling for BMI and hunger levels at baseline did not change any of the reported results and these variables were therefore not included in the reported analyses. Least Significant Difference (LSD) post-hoc tests were conducted to further assess significant differences within each factor/interaction. Tests were performed two-sided and *p*-values below 0.05 were considered significant. Results will be reported as mean (±SDs) unless otherwise specified.

### 2.6.2 MRI data analysis

fMRI data were pre-processed and analysed using the SPM12 software package (Wellcome Department of Imaging Neuroscience, London, UK) in conjunction with the MarsBar toolbox (http://marsbar.sourceforge.net) run with MATLAB 7.12 (The Mathworks Inc. Natick, MA). Functional images per participant were slice time corrected, realigned to the mean volume of the first run, coregistered to the anatomical image, normalized to Montreal Neurological Institute space (MNI space), and spatially smoothened with a Gaussian kernel of 6 mm full-with at half maximum. The volume artefact tool from ArtRepair (version 4; http://cibsr.stanford.edu/tools/human-brain-project/artrepair-software.html; 27) was used to

detect and repair anomalously noisy volumes. Volumes that moved more than 1mm/TR were repaired and participants with >25% of volumes repaired were excluded from the analyses. On average 3.14% of the volumes were repaired. None of the participants were excluded from the analyses.

For every participant, a statistical parametric map was generated by fitting a boxcar function to each time series, convolved with the canonical hemodynamic response function (HRF). Data were high-pass filtered with a cut-off of 128 s to remove low-frequency noise.

Ten conditions were modelled: viewing healthier package images [P_Healthier], viewing regular package images [P_Regular], tasting healthier taste + viewing healthier package images [PT_HH], tasting healthier taste + viewing regular package images [PT_RH], tasting regular taste + viewing healthier package images [PT_HR], tasting regular taste + viewing regular package images [PT_RR], rest (crosshair), swallowing, rinsing, stimulus rating. Swallowing, rinsing and stimulus rating responses were not included in further analyses. Realignment parameters were added to the model as regressors to account for motion-related variance. Parameters were estimated and T-contrasts were calculated for each participant for every viewing and tasting + viewing condition minus rest (*i.e.,* [P_Healthier-rest], [P_Regular-rest], [PT_HH-rest], [PT_RH-rest], [PT_HR-rest], [PT_RR-rest]).
Note that letters P and T in the modelled conditions stand for Package (P) and Taste (T) combinations. Letters H and R in the T-contrasts stand for Healthier (H) or Regular (R) package or product versions.

For group analyses we started with exploratory whole brain analyses to verify overall activation in response to the cues. Subsequently, we use a region of interest (ROI) approach. A priori

regions of interest were selected from literature (mainly based on the appetitive brain network (Dagher 2012)) and included regions involved in reward (Berridge 1996, Tremblay and Schultz 1999, O'Doherty, Deichmann et al. 2002, Delgado 2007), cognition, salience, inhibition (Corbetta and Shulman 2002, Aron 2007, Zandbelt and Vink 2010, Lenartowicz, Verbruggen et al. 2011) and tasting (Nitschke, Dixon et al. 2006, Rolls 2015): striatum (caudate nucleus, putamen, nucleus accumbens), pallidum, amygdala, OFC, frontal gyri, opercula, hippocampal gyri and the insula. ROIs from the Automated Anatomical Labelling (AAL) atlas were bundled to create one ROI mask using the Wake Forest University Pickatlas toolbox (Tzourio-Mazoyer, Landeau et al. 2002, Maldjian, Laurienti et al. 2003). We combined all ROIs into one mask to avoid multiple testing. A mean grey matter image of all participants was calculated and multiplied with the ROI mask to obtain a grey matter analysis mask.

To test and visualise the effects of package, taste and package*taste interactions on brain activation, a flexible factorial was performed (on all viewing + tasting conditions minus rest) including factors participant, package, taste, package*taste interaction. Average parameter estimates were extracted for significant clusters with the use of the MarsBar toolbox. To correct for multiple testing across brain voxels cluster extent threshold for the minimum cluster size needed for a family-wise error-corrected $p<0.05$ across the analysis mask volume was determined for the analysis with the SPM cluster size threshold tool available at (https://github.com/CyclotronResearchCentre/SPM_ClusterSizeThreshold). This yielded a cluster extent threshold of $k > 44$ voxels. In addition, we report results at a more liberal threshold of $p=0.001$, $k > 19$ contiguous voxels to allow for meta-analysis. Such a threshold inflates the risk of false positives, but it is more stringent than the arbitrary $k=10$ threshold used by many studies (Eklund, Nichols et al. 2016) and much more stringent than recommended by (Lieberman and Cunningham 2009).

### 2.6.3 Correlations behavioural and MRI data

Pearson correlations (significant at $p<0.05$) were assessed between sensory and hedonic scores from the behavioural data and average parameter estimates for significant clusters from package-taste contrast (*i.e.,* [PT_HH-rest], [PT_RH-rest], [PT_HR-rest], [PT_RR-rest]). Next to this, average parameter estimates for healthier product ([PT_HH-rest] & [PT_RH-rest]) and regular ([PT_HR-rest] & [PT_RR-rest]) product were calculated as well as differences between parameter estimates of regular and healthier product ([PT_HR-rest] & [PT_RR-rest] – [PT_HH-rest] & [PT_RH-rest]). Similarly, average sensory and hedonic scores from behavioural data were calculated for both the healthier and regular product. A difference between regular and healthier product was also calculated per sensory and hedonic attribute. Pearson correlations (significant at $p<0.05$) were assessed between average hedonic scores from behavioural data and average parameter estimates for both the regular and healthier product.

## 3. Results

Prior to the MRI scan, participants reported medium hunger levels (mean=60.7, ±SD=11.7).

### 3.1 Behavioural results

#### 3.1.1 Participant characteristics

Regarding the HTAS, compared to earlier research (Roininen, Tuorila et al. 2001) our participant group scored medium/high on the health interest subscales on average (General Health Interest (GHI) mean=4.80, ±SD=0.70, range 3.00-6.00, α=0.67; Light Product Interest (LPI) mean=3.25, ±SD=1.15 range 1.00-6.00, α=0.82; Natural Product Interest (NPI) mean=3.62, ±SD=1.11, range 2.00-6.00, α=0.78) and medium on taste attitude subscales (Food As Reward (FAR) mean=4.25, ±SD=0.84, range 2.00-6.00, α=0.63; Pleasure mean=4.80, ±SD=0.69, range 4.00-7.00, α=0.41; Craving for Sweet (CS) mean=4.01, ±SD=0.77, range 3.00-6.00, α= 0.26).

Regarding the BIS-11 results, for the BIS sum our participant group scored on the high end of the medium scale regarding impulsivity (medium scores range from 52-71; BIS sum mean=67.74, ±SD=4.29, range 58-77, α=0.21; BIS attention mean=16.27, ±SD=1.96, range 14-21, α=0.12; BIS motor mean=21.53, ±SD=2.88, range 15-27, α=0.38; BIS non-planning mean=29.94, ±SD=2.98, range 25-35, α=0.38).

When investigating relationships between HTAS subscales and BIS-11 subscales, Pearson correlations showed significant inverse correlation between HTAS General Health Interest and Craving Sweet subscales ($r$=-0.412, $p$=0.02) as well as HTAS Light Product Interest and Food As Reward subscales ($r$=-0.374, $p$=0.03).

### 3.1.2 Sensory and hedonic results

Linear Mixed Model analysis yielded significant main effects for package and taste. Sensory and hedonic behavioural results are shown in Figures 3 and 4. For package, healthier packages yielded slightly higher scores compared to the regular package versions for perceived healthiness ($F(1,235)=16.17$, $p<0.001$), fruitiness ($F(1,235)=14.31$, $p<0.001$), sweetness ($F(1,235)=5.31$, $p=0.02$) and perceived attractiveness ($F(1,235)=5.52$, $p=0.02$), but there was no significant main effect for liking ($F(1,235)=1.03$, $p=0.31$), creaminess ($F(1,235)=2.59$, $p=0.11$) or flavour intensity ($F(1,235)=0.12$, $p=0.73$). For taste, there were significant main effects for all attributes. Figures 3 and 4 show that the healthier taste yielded slightly higher scores compared to the regular taste for perceived healthiness ($F(1,235)=12.83$, $p<0.001$) as well as slightly lower scores for perceived attractiveness ($F(1,235)=9.83$, $p<0.001$) and lower scores for liking ($F(1,235)=78.52$, $p<0.001$). Healthier taste yielded lower scores on sweetness ($F(1,235)=113.87$, $p<0.001$), creaminess ($F(1,235)=340.83$, $p<0.001$), fruitiness ($F(1,235)=50.78$, $p<0.001$) and flavour intensity ($F(1,235)=109.65$, $p<0.001$). No significant 2-way interactions between package*taste were found (healthiness $F(1,235)=1.06$, $p=0.30$; liking $F(1,235)=0.20$, $p=0.65$; attractiveness $F(1,235)=0.26$, $p=0.63$; sweetness $F(1,235=0.02$, $p=0.90$; creaminess $F(1,235)=0.02$, $p=0.90$; flavour intensity $F(1,235)=0.07$, $p=0.79$; fruitiness $F(1,235)=1.02$, $p=0.31$). This indicates that the taste perception of the regular product versus the healthier product was not influenced significantly different by the type of package shown during tasting (or vice versa). Behavioural covariates (HTAS, BIS-11 subscales) did not significantly affect results, *e.g.*, healthiness perception did not co-vary with health or taste orientation from HTAS, nor with impulsivity measures from BIS-11 (all $p$-values>0.05).

[INSERT FIGURE 3 AND FIGURE 4 HERE]

### 3.2 Neuroimaging results

Table 1 gives an overview of ROI brain regions that were differentially activated by packages, tastes or package*taste interactions.

[INSERT TABLE 1 HERE]

#### 3.2.1 The effect of package type on brain activation

When comparing regular with healthier packages (irrespective of the tasted product), brain areas activated stronger when viewing the regular packages compared to the healthier packages included bilateral inferior frontal regions (including inferior frontal and orbitofrontal parts, *i.e.,* OFC) as well as left sided putamen (see Table 1 and Figure 5). Additionally, putamen activity during viewing regular packages was correlated positively with the General Health Interest (GHI) scores from the HTAS ($r$=0.431, $p$=0.01) (Figure 5) and negatively with BIS attention subscale scores ($r$=-0.461, $p$=0.01). Similarly, differences in putamen activity between regular and healthier packages correlated with BIS attention subscale scores ($r$=-0.349, $p$=0.04), which was driven mainly by greater putamen activation when viewing the regular package in less impulsive participants.

[INSERT FIGURE 5 HERE]

#### 3.2.2 The effect of tasted product on brain activation

When comparing tasting healthier taste with tasting regular taste (irrespective of the package), several brain regions responded significantly stronger to the taste of healthier taste compared to regular taste; left sided middle and inferior frontal region (Figure 6), bilateral putamen, right sided caudate nucleus, and pallidum (see Table 1). Next to this, we found a significant negative

correlation between HTAS General Health Interest scores and superior frontal gyrus (dlPFC) activation when tasting the regular taste ($r$=-0.459, $p$=0.01).

[INSERT FIGURE 6 HERE]

### 3.2.3 The effect of package*taste interaction on brain activation

When looking at *package*taste* interactions, congruent combinations (*i.e.* healthier package + healthier taste or regular package + regular taste) gave rise to more activation in the left lateral OFC (Figure 7) compared to incongruent combinations (*i.e.* healthier package + regular taste or regular package + healthier taste) which resulted in deactivation in the left lateral OFC (see Table 1).

[INSERT FIGURE 7 HERE]

For the effects of package and taste on activation patterns in the remaining clusters from Table 1, we kindly refer to the Supplementary Materials. All the activation patterns in the package condition were in the same direction, as were the activation patterns in the taste condition (albeit opposite from the package condition).

## 3.3 Correlations behavioural and MRI data

We investigated overall Pearson correlations between parameter estimates from significant clusters of contrasts from package-taste combination (*i.e.,* [PT_HH-rest], [PT_RH-rest], [PT_HR-rest], [PT_RR-rest]) and sensory and hedonic behavioural scores. No significant correlations above $r$=0.25 ($p$<0.05) were found for any of the sensory and hedonic attributes across parameter estimates from contrasts of package-taste combinations. Similarly, no

493 significant correlations above $r$=0.25 ($p$<0.05) were found between average parameter
494 estimates from regular or healthier product (*e.g.*, PT_HH-rest & PT_RH-rest) and average
495 hedonic scores from behavioural data. Therefore none of the significant results were
496 documented here.
497

## 4. Discussion

In this study the effects of taste and package colour cues on brain activity patterns in taste, reward and inhibitory control regions were explored to determine whether effects are mediated via bottom-up (sensory related) or top-down (valuation realted) pathways. Modulatory influences of personal characteristics (*i.e.*, impulsiveness, health and taste attitude) were also studied.

Effects of taste and package colour cues were seen on neural activation in regions that are, among other things, related to reward and inhibitory control, but not in primary taste processing regions (insula). In line with expectations, neural activation in striatal and OFC regions was reduced when viewing healthier packages compared to regular packages while tasting. A higher health interest related to lower neural activation in the striatum (regular package). These striatal and OFC regions have been related to reward processing. Viewing healthier packages also resulted in reduced neural activation in the IFG compared to regular packages (while tasting), which was not what we hypothesized. These IFG regions have been related to inhibitory control. The taste of the healthier product, regardless of package, enhanced activation in the striatum, OFC and dlPFC compared to the taste of the regular product. Among other things, the striatum and OFC have been related to reward processing, whereas the dlPFC has been related to inhibitory control. For consumers with a goal of healthy eating this may suggest a cognitively driven preference for the taste of the healthier product as opposed to a stimulus driven preference for the taste of the regular product. Lastly, incongruency (*e.g.* healthier package + regular taste) gave rise to deactivation in the lateral OFC while congruency (*e.g.* healthier package + healthier taste) of package-taste combinations resulted in activation in the lateral OFC. This region is often related to reward processing as well as attentional processing.

These findings suggest that (valuation related) top-down processes modulate brain activity by package and taste properties, rather than (sensory related) bottom-up processes. Furthermore, they illustrate the importance of taking participant characteristics such as health interest into account when investigating the effects of package and taste on neural activation.

Viewing a regular, more 'indulgent', package induced stronger activation in the putamen and OFC compared to the healthier package. Enhanced activation in these regions implies enhanced reward (anticipation) (Schultz, Tremblay et al. 2000, Tremblay and Schultz 2000, Tremblay and Schultz 2000, O'Doherty, Deichmann et al. 2002, Small, Jones-Gotman et al. 2003, Rolls 2015). Enhanced activation in reward related regions is in line with earlier research when using more hedonic, preferred cues ((Grabenhorst, Rolls et al. 2008); OFC, ventral striatum), a stronger brand cue ((Kuhn and Gallinat 2013); OFC) or a higer priced wine ((Plassmann, O'Doherty et al. 2008); ventral stiatum). Furthermore, HTAS General Health Interest scores correlated positively with putamen activation when viewing the regular packages. An explanation, though speculative, may be that participants with stronger health interest hold stronger implicit associations that healthier package colours (more bright, less saturated) are associated with healthiness and the regular package colours (less bright, more saturated) with attractiveness.

Viewing a regular, more 'indulgent' package also induced stronger activation in the IFG compared to the healthier package. Enhanced IFG activation may reflect an enhanced need for inhibitory control to suppress the 'urge to indulge' in our health-interested consumers (Guerrieri, Nederkoorn et al. 2007, van der Laan, Barendse et al. 2016).

Regarding taste effects, the healthier product contained less calories and sugar. This product was perceived as less attractive, liked, sweet, creamy, fruity and flavour intense compared to the regular product. In contrast to our expectations, the healthier calorie-reduced product (compared to the regular product) resulted in greater activation in regions implicated in (among other things) reward representation (OFC), reward anticipation and reward delivery (striatal regions). From an evolutionary perspective, rewarding properties of calories may be essential to survival and innately humans are predisposed to like or dislike basic tastes (*i.e.*, sweet and bitter, respectively) as they provide direct information about the presence of nutrients. For example an innate preference for sweet may indicate the presence of calories (Cabanac 1971, Steiner 1979, Anderson 1995), whereas an innate aversion for bitter may indicate the presence of toxic or poisonous substances.

In line with this notion, examination of a caloric stimulus versus non-caloric stimulus (irrespective of taste pleasantness) has been linked to stronger activation in taste and reward related regions (Frank, Oberndorfer et al. 2008), as well as the amygdala (Smeets, Weijzen et al. 2011). Additionally, examination of taste pleasantness (*e.g.*, liking or attractiveness) for basic tastes and flavour such as sweetness has been linked to activation of the OFC and other reward related regions in response to hedonic experiences (O'Doherty, Kringelbach et al. 2001, Kringelbach and Rolls 2004, Kringelbach 2005, van Rijn, de Graaf et al. 2015). The activation we observed in brain (*e.g.* striatum) regions when tasting does not align with these standpoints and findings. Next to this, we have difficulty explaining the opposite directionality of activation patterns between package- and taste- based effects.

The involvement of other processes related to participants' (health) associations, attitudes and cognitions, which are also reflected in (*e.g.*) the striatum, may have interfered with neural activation (Berridge 1996, Balleine, Delgado et al. 2007, Delgado 2007). Therefore, activation

in (*e.g.*) the striatum may not simply reflect a mere nutritional related reward. Enhanced reward-related activation for the healthier calorie-reduced product may reflect a cognitively driven preference which fits well with participants' healthy eating goal, as reflected in the relatively high HTAS scores of our population. This was also seen in van Rijn et al., (2017). Such a cognitive preference for the healthier calorie-reduced product may also explain the enhanced neural activation in dlPFC (middle and superior frontal gyrus), implicated in inhibitory control, compared to the regular product.

An alternative explanation is related to familiarity and novelty perception. Regions such as the OFC as well as dlPFC have been implicated in attentional processes related to novel or unexpected stimuli. Enhanced brain activation in such regions has been found with respect to novel or unexpected stimuli to aid identification and learning (Berns, McClure et al. 2001, Veldhuizen, Douglas et al. 2011). Here, the regular product was readily available on the market whereas the healthier product (diluted version of the regular product) was not. As our participants were familiar with the product category, they may have been familiar with the actual stimulus used for the regular product. The novelty of, or unfamiliarity with, the healthier product may have resulted in enhanced activation in the OFC and dlPFC in relation to processing of this unfamiliar, novel stimulus. Unfortunately, we did not measure familiarity with the exact stimuli used, which is suggested for a next study.

Next to package- and taste-based effects on neural activation, incongruent combinations of package and taste resulted in deactivation in the lateral OFC compared to congruent combinations which resulted in activation. The OFC is often related to reward processing and value. Lack of predictability and breaches of expectation have been related to enhanced activation in regions related to attention (IFG) and reward (OFC). Attentional brain activation

with respect to breaches of expectation however is often found in opposite direction to aid identification and learning (Berns, McClure et al. 2001, Veldhuizen, Douglas et al. 2011). As predictability or taste expectation may not have been obviously signalled through package colour (*i.e.* no differences in striatal activation, a region involved in signalling reward prediction error, between congruent and incongruent trials), we do not know if this was the case here but lack an alternative explanation. Next to this, we have difficulty explaining the opposite directionality of activation patterns between package- taste- based effects. Deactivation in the lateral OFC for incongruent combinations may simply reflect less rewarding properties of incongruent package-taste combinations compared to congruent package-taste combinations.

No evidence for bottom-up effects of package colour properties on neural activity in taste processing regions such as the anterior insula was found. The lack of findings in the insula could be a result of interactions of bottom-up effects with other (top-down) processes in which the insula is also involved, such as salience and emotional processing (Critchley, Wiens et al. 2004, Kurth, Zilles et al. 2010). Specifically, simultaneous viewing while tasting may have also influenced attentional focus resulting in an apparent lack of taste related activation. Along a similar line, (Grabenhorst and Rolls 2008) demonstrated that focussing on either affective value or physical properties of a stimulus activates different brain areas, with only insula activation when the focus was on taste intensity.

One concern in relation to the interpretation of the neuroimaging results is the lack of significant relations between neural and behavioural data. An explanation for the lack of significant relations may be found in an ill-timed sensory and hedonic testing. In hindsight, placing the sensory evaluation of package-taste stimuli prior to the rather demanding fMRI task instead of following the fMRI task, may have given better comparability with our fMRI results. This may

have also given better comparability with our previous sensory findings (Tijssen, Zandstra et al. 2017) in a similar and much larger population sample. Sensory specific satiety and tiredness may have influenced the behavioural measures.

The diversity of experimental designs and stimuli used in other research makes it hard to generalise and interpret findings of taste, label and price effects across studies. Some studies have shown effects of taste, brand, label and price cues in reward, taste and inhibitory control coding brain regions (de Araujo, Rolls et al. 2005, Grabenhorst, Rolls et al. 2008, Plassmann, O'Doherty et al. 2008, Veldhuizen, Douglas et al. 2011, Grabenhorst, Schulte et al. 2013, Kuhn and Gallinat 2013). Others, however, reported no effects in reward related brain regions (Nitschke, Dixon et al. 2006, Woods, Lloyd et al. 2011, Veldhuizen, Nachtigal et al. 2013). Differences in population characteristics, such as gender (Wang, Volkow et al. 2009), BMI (Stoeckel, Weller et al. 2008), health interest and impulsivity (van der Laan, Barendse et al. 2016, van Rijn, Wegman et al. 2017), provide potential explanations for discrepancies between earlier and current findings.

Furthermore, differences in experimental set-ups may have contributed to the diverse findings reported in literature: (1) different use of stimuli: others used taste solutions, soft drinks, wines or odours whereas in our study we used a rich flavoured and creamy dairy drink, (2) inclusion of ratings after each trial resulting in potential differences in terms of an active cue-stimulus evaluative component compared to our more passive cue-stimulus evaluation due to no compulsory rating after each stimulus presentation, (3) timing and nature of cues: prior studies used verbal cues, often preceding the tasted stimuli, to impose a certain focus on, for example, taste or hedonics, whereas in the present study subtle visual package colour cues were presented simultaneously to tasting (Grabenhorst and Rolls 2008).

There are several strengths and limitations of the present study worthwhile to discuss. A strength is the use of realistic subtle non-verbal package cues. Image colour is seen as a low level content feature, whereas verbal descriptors are seen as higher level content features (Liu, Zhang et al. 2007). Processing of lower level features is more automatic and subconscious, therefore more in line with the automatic, subconscious nature of expectancy driven modulations and food evaluations compared to more cognitively processed verbal descriptors. The novelty of our subtle cues extends prior findings of higher level cognitive influences (McClure, Li et al. 2004, de Araujo, Rolls et al. 2005, Nitschke, Dixon et al. 2006, Grabenhorst, Rolls et al. 2008, Plassmann, O'Doherty et al. 2008, Veldhuizen, Douglas et al. 2011, Woods, Lloyd et al. 2011, Grabenhorst, Schulte et al. 2013, Kuhn and Gallinat 2013, Veldhuizen, Nachtigal et al. 2013).

Related to reliability, the more stringent statistical threshold used compared to other related papers (*e.g.,* around 5 voxels vs. our primary threshold of k=44 voxels and secondary most liberal threshold of k=19 voxels at $p$=0.001 (McClure, Li et al. 2004, Veldhuizen, Douglas et al. 2011, Grabenhorst, Schulte et al. 2013, Veldhuizen, Nachtigal et al. 2013)) decreases the chance of false positives.

There are also several limitations and recommendations worth mentioning. As mentioned above, in hindsight the behavioural measurements may have been ill-timed, resulting in a lower reliability of these measurements. It is therefore recommended to either make sure no tiredness or sensory specific satiety have occurred prior to the behavioural measurements or place the behavioural measurements at a different (here; prior to) timing relative to MRI measurements.

The next recommendation relates to familiarity of the used stimuli. Although we included consumers of the sweet dairy drink product category, we did not measure their familiarity with the actual products used nor did we take into account potential differences in preference for certain types of sweet dairy-based drinks. Some participants may have been familiar with and preferred thick, creamy, very sweet dairy-based drinks whereas others may have been less familiar with these types of drinks and preferred less thick, less creamy, low sweet dairy-based drinks. The differences in familiarity and preference may have influenced the results of our study. Including measurements on familiarity and preference a priori or including a unified participant sample with regards to familiarity and preference would be suggested for future studies.

Next to this, the results found here may be product (taste) or product category specific. Replicating this study using other product packages and tastes, such as savoury products (*e.g.* soups), as well as in different populations (*e.g.* in terms of health consciousness), would give a better idea about boundary conditions and generalisability. Lastly, investigating interactions with other package elements (*e.g.*, material, package shape, text) would be valuable. For example, credence characteristics, referring to (package) characteristics that influence the credibility of the seller in relation to the buyer have been shown to influence liking (Fernqvist and Ekelund 2014).

To conclude, our findings underscore the potential ability of package colour properties to influence perception and neural activation in reward and inhibition related brain activation via more valuation related (top-down) systems. Individual differences in health interest and impulsivity modify package and taste related brain responses which underscore the importance

of taking participant characteristics into account in food research. This paper highlights some of the mechanisms and conditions under which these effects operate.

## Author contributions statement

IT, GJ, EZ and PS all contributed to the exact definition of the research question. IT together with GJ, EZ and PS proposed the methodology and experimental design. IT and RG carried out the experiment and collected data. IT analysed data with the help of PS. Data were interpreted by IT with help of PS, EZ, GJ. The manuscript was written by IT, and revised with help of PS, GJ, EZ, RG and CG.

## Conflict of interest statement

The authors IT, PS, RG, CG and GJ declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

EZ is employee of Unilever R&D Vlaardingen, The Netherlands, which markets food, home and personal care products.

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## References


Anderson, G. H. (1995). "Sugars, sweetness, and food intake." The American Journal of Clinical Nutrition **62**(1): 195S-201S.

Aron, A. R. (2007). "The neural basis of inhibition in cognitive control." Neuroscientist **13**(3): 214-228.

Balleine, B. W., M. R. Delgado and O. Hikosaka (2007). "The role of the dorsal striatum in reward and decision-making." Journal of Neuroscience **27**(31): 8161-8165.

Barratt, E. S. (1985). "Impulsiveness subtraits: Arousal and information processing." Spence JT, Itard CE, editors. Motviation, emotion and personality. Amsterdam: Elsevier: 137-146.

Berns, G. S., S. M. McClure, G. Pagnoni and P. R. Montague (2001). "Predictability modulates human brain response to reward." Journal of neuroscience **21**(8): 2793-2798.

Berridge, K. C. (1996). "Food reward: Brain substrates of wanting and liking." Neuroscience & Biobehavioral Reviews **20**(1): 1-25.

Birch, L. L. (1999). "Development of food preferences." Annual review of nutrition **19**(1): 41-62.

Cabanac, M. (1971). "Physiological Role of Pleasure." Science **173**(4002): 1103-1107.

Clark, J. E. (1998). "Taste and flavour: their importance in food choice and acceptance." Proceedings of the Nutrition Society **57**(4): 639-643.

Corbetta, M. and G. L. Shulman (2002). "Control of goal-directed and stimulus-driven attention in the brain." **3**: 201.

Critchley, H. D., S. Wiens, P. Rotshtein, A. Öhman and R. J. Dolan (2004). "Neural systems supporting interoceptive awareness." Nature Neuroscience **7**(2): 189-195.

Dagher, A. (2012). "Functional brain imaging of appetite." Trends in Endocrinology & Metabolism **23**(5): 250-260.

de Araujo, I. E., E. T. Rolls, M. I. Velazco, C. Margot and I. Cayeux (2005). "Cognitive Modulation of Olfactory Processing." Neuron **46**(4): 671-679.

Delgado, M. R. (2007). "Reward-related responses in the human striatum." Reward and Decision Making in Corticobasal Ganglia Networks **1104**: 70-88.

Eklund, A., T. E. Nichols and H. Knutsson (2016). "Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates." Proceedings of the National Academy of Sciences **113**(28): 7900-7905.

Fernqvist, F. and L. Ekelund (2014). "Credence and the effect on consumer liking of food–A review." Food Quality and Preference **32**: 340-353.

Frank, G. K., T. A. Oberndorfer, A. N. Simmons, M. P. Paulus, J. L. Fudge, T. T. Yang and W. H. Kaye (2008). "Sucrose activates human taste pathways differently from artificial sweetener." Neuroimage **39**(4): 1559-1569.

Grabenhorst, F. and E. T. Rolls (2008). "Selective attention to affective value alters how the brain processes taste stimuli." European Journal of Neuroscience **27**(3): 723-729.

Grabenhorst, F., E. T. Rolls and A. Bilderbeck (2008). "How cognition modulates affective responses to taste and flavor: Top-down influences on the orbitofrontal and pregenual cingulate cortices." Cerebral Cortex **18**(7): 1549-1559.

Grabenhorst, F., F. P. Schulte, S. Maderwald and M. Brand (2013). "Food labels promote healthy choices by a decision bias in the amygdala." Neuroimage **74**: 152-163.

Griffioen-Roose, S., P. A. Smeets, P. L. Weijzen, I. van Rijn, I. van den Bosch and C. de Graaf (2013). "Effect of replacing sugar with non-caloric sweeteners in beverages on the reward value after repeated exposure." PLoS One **8**(11): e81924.

Guerrieri, R., C. Nederkoorn, K. Stankiewicz, H. Alberts, N. Geschwind, C. Martijn and A. Jansen (2007). "The influence of trait and induced state impulsivity on food intake in normal-weight healthy women." Appetite **49**(1): 66-73.

770 Gutjar, S., C. de Graaf, A. Palascha and G. Jager (2014). "Food choice: The battle between
771 package, taste and consumption situation." Appetite **80**: 109-113.
772 Iannilli, E., N. Noennig, T. Hummel and A. Schoenfeld (2014). "Spatio-temporal correlates of
773 taste processing in the human primary gustatory cortex." Neuroscience **273**: 92-99.
774 Ishihara, S. (1951). Tests for colour-blindness. Tokyo?, Nippon Isho Shuppan Co.
775 Jasinska, A. J., Yasuda, M., Burant, C. F., Gregor, N., Khatri, S., Sweet, M., & Falk, E. B.
776 (2012). Impulsivity and inhibitory control deficits are associated with unhealthy eating
777 in young adults. Appetite, 59(3), 738-747.
778 Kringelbach, M. L. (2005). "The human orbitofrontal cortex: linking reward to hedonic
779 experience." Nature Reviews Neuroscience **6**(9): 691.
780 Kringelbach, M. L. and E. T. Rolls (2004). "The functional neuroanatomy of the human
781 orbitofrontal cortex: evidence from neuroimaging and neuropsychology." Progress in
782 neurobiology **72**(5): 341-372.
783 Kuhn, S. and J. Gallinat (2013). "Does Taste Matter? How Anticipation of Cola Brands
784 Influences Gustatory Processing in the Brain." Plos One **8**(4).
785 Kurth, F., K. Zilles, P. T. Fox, A. R. Laird and S. B. Eickhoff (2010). "A link between the
786 systems: functional differentiation and integration within the human insula revealed by
787 meta-analysis." Brain Structure and Function **214**(5): 519-534.
788 Lenartowicz, A., F. Verbruggen, G. D. Logan and R. A. Poldrack (2011). "Inhibition-related
789 Activation in the Right Inferior Frontal Gyrus in the Absence of Inhibitory Cues." Journal
790 of Cognitive Neuroscience **23**(11): 3388-3399.
791 Lieberman, M. D. and W. A. Cunningham (2009). "Type I and Type II error concerns in fMRI
792 research: re-balancing the scale." Social Cognitive and Affective Neuroscience **4**(4): 423-
793 428.

Liu, Y., D. Zhang, G. Lu and W.-Y. Ma (2007). "A survey of content-based image retrieval with high-level semantics." Pattern Recognition **40**(1): 262-282.

Maldjian, J. A., P. J. Laurienti, R. A. Kraft and J. H. Burdette (2003). "An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets." NeuroImage **19**(3): 1233-1239.

McClure, S. M., J. Li, D. Tomlin, K. S. Cypert, L. M. Montague and P. R. Montague (2004). "Neural correlates of behavioral preference for culturally familiar drinks." Neuron **44**(2): 379-387.

Ng, M., C. Chaya and J. Hort (2013). "The influence of sensory and packaging cues on both liking and emotional, abstract and functional conceptualisations." Food Quality and Preference **29**(2): 146-156.

Nitschke, J. B., G. E. Dixon, I. Sarinopoulos, S. J. Short, J. D. Cohen, E. E. Smith, S. M. Kosslyn, R. M. Rose and R. J. Davidson (2006). "Altering expectancy dampens neural response to aversive taste in primary taste cortex." Nature Neuroscience **9**(3): 435-442.

O'Doherty, J., M. L. Kringelbach, E. T. Rolls, J. Hornak and C. Andrews (2001). "Abstract reward and punishment representations in the human orbitofrontal cortex." Nature neuroscience **4**(1): 95.

O'Doherty, J. P., R. Deichmann, H. D. Critchley and R. J. Dolan (2002). "Neural responses during anticipation of a primary taste reward." Neuron **33**(5): 815-826.

Okamoto, M. and I. Dan (2013). "Extrinsic information influences taste and flavor perception: a review from psychological and neuroimaging perspectives." Semin Cell Dev Biol **24**(3): 247-255.

Okamoto, M. and I. Dan (2013). "Extrinsic information influences taste and flavor perception: A review from psychological and neuroimaging perspectives." Seminars in Cell & Developmental Biology **24**(3): 247-255.

819 Patton, J. H. and M. S. Stanford (1995). "Factor structure of the Barratt impulsiveness scale."
820 Journal of clinical psychology **51**(6): 768-774.
821 Piqueras-Fiszman, B. and C. Spence (2015). "Sensory expectations based on product-extrinsic
822 food cues: An interdisciplinary review of the empirical evidence and theoretical accounts."
823 Food Quality and Preference **40**: 165-179.
824 Plassmann, H., J. O'Doherty, B. Shiv and A. Rangel (2008). "Marketing actions can modulate
825 neural representations of experienced pleasantness." Proceedings of the National Academy
826 of Sciences of the United States of America **105**(3): 1050-1054.
827 Pochon, J., R. Levy, P. Fossati, S. Lehericy, J. Poline, B. Pillon, D. Le Bihan and B. Dubois
828 (2002). "The neural system that bridges reward and cognition in humans: an fMRI study."
829 Proceedings of the National Academy of Sciences **99**(8): 5669-5674.
830 Rogers, R. D., A. M. Owen, H. C. Middleton, E. J. Williams, J. D. Pickard, B. J. Sahakian and
831 T. W. Robbins (1999). "Choosing between small, likely rewards and large, unlikely
832 rewards activates inferior and orbital prefrontal cortex." Journal of Neuroscience **19**(20):
833 9029-9038.
834 Roininen, K., L. Lahteenmaki and H. Tuorila (1999). "Quantification of consumer attitudes to
835 health and hedonic characteristics of foods." Appetite **33**(1): 71-88.
836 Roininen, K., H. Tuorila, E. H. Zandstra, C. de Graaf, K. Vehkalahti, K. Stubenitsky and D. J.
837 Mela (2001). "Differences in health and taste attitudes and reported behaviour among
838 Finnish, Dutch and British consumers: a cross-national validation of the Health and Taste
839 Attitude Scales (HTAS)." Appetite **37**(1): 33-45.
840 Rolls, E. T. (2011). "Taste, olfactory and food texture reward processing in the brain and
841 obesity." International Journal of Obesity **35**(4): 550-561.
842 Rolls, E. T. (2015). "Taste, olfactory, and food reward value processing in the brain." Progress
843 in Neurobiology **127-128**(Supplement C): 64-90.

844 Schifferstein, A. Fenko, P. M. Desmet, D. Labbe and N. Martin (2013). "Influence of package
845 design on the dynamics of multisensory and emotional food experience." Food Quality and
846 Preference **27**(1): 18-25.
847 Schultz, W., L. Tremblay and J. R. Hollerman (2000). "Reward Processing in Primate
848 Orbitofrontal Cortex and Basal Ganglia." Cerebral Cortex **10**(3): 272-283.
849 Small, D. M., M. Jones-Gotman and A. Dagher (2003). "Feeding-induced dopamine release in
850 dorsal striatum correlates with meal pleasantness ratings in healthy human volunteers."
851 NeuroImage **19**(4): 1709-1715.
852 Smeets, P. A., C. de Graaf, A. Stafleu, M. J. van Osch and J. van der Grond (2005). "Functional
853 magnetic resonance imaging of human hypothalamic responses to sweet taste and
854 calories–." The American journal of clinical nutrition **82**(5): 1011-1016.
855 Smeets, P. A., P. Weijzen, C. de Graaf and M. A. Viergever (2011). "Consumption of caloric
856 and non-caloric versions of a soft drink differentially affects brain activation during
857 tasting." Neuroimage **54**(2): 1367-1374.
858 Sørensen, L. B., P. Møller, A. Flint, M. Martens and A. Raben (2003). "Effect of sensory
859 perception of foods on appetite and food intake: a review of studies on humans."
860 International journal of obesity **27**(10): 1152.
861 Stanford, M. S., C. W. Mathias, D. M. Dougherty, S. L. Lake, N. E. Anderson and J. H. Patton
862 (2009). "Fifty years of the Barratt Impulsiveness Scale: An update and review." Personality
863 and Individual Differences **47**(5): 385-395.
864 Steiner, J. E. (1979). "Human facial expressions in response to taste and smell stimulation."
865 Advances in child development and behavior **13**(5).
866 Stoeckel, L. E., R. E. Weller, E. W. Cook Iii, D. B. Twieg, R. C. Knowlton and J. E. Cox (2008).
867 "Widespread reward-system activation in obese women in response to pictures of high-
868 calorie foods." NeuroImage **41**(2): 636-647.

Tijssen, I., E. H. Zandstra, C. de Graaf and G. Jager (2017). "Why a 'light' product package should not be light blue: Effects of package colour on perceived healthiness and attractiveness of sugar- and fat-reduced products." Food Quality and Preference **59**: 46-58.

Tremblay, L. and W. Schultz (1999). "Relative reward preference in primate orbitofrontal cortex." **398**: 704.

Tremblay, L. and W. Schultz (2000). "Modifications of reward expectation-related neuronal activity during learning in primate orbitofrontal cortex." Journal of Neurophysiology **83**(4): 1877-1885.

Tremblay, L. and W. Schultz (2000). "Reward-related neuronal activity during go-nogo task performance in primate orbitofrontal cortex." Journal of Neurophysiology **83**(4): 1864-1876.

Tzourio-Mazoyer, N., B. Landeau, D. Papathanassiou, F. Crivello, O. Etard, N. Delcroix, B. Mazoyer and M. Joliot (2002). "Automated Anatomical Labeling of Activations in SPM Using a Macroscopic Anatomical Parcellation of the MNI MRI Single-Subject Brain." NeuroImage **15**(1): 273-289.

van der Laan, L. N., M. E. A. Barendse, M. A. Viergever and P. A. M. Smeets (2016). "Subtypes of trait impulsivity differentially correlate with neural responses to food choices." Behavioural Brain Research **296**: 442-450.

van Rijn, I., C. de Graaf and P. A. Smeets (2015). "Tasting calories differentially affects brain activation during hunger and satiety." Behav Brain Res **279**: 139-147.

van Rijn, I., J. Wegman, E. Aarts, C. de Graaf and P. A. Smeets (2017). "Health interest modulates brain reward responses to a perceived low-caloric beverage in females." Health Psychol **36**(1): 65-72.

892 Veldhuizen, M. G., D. Douglas, K. Aschenbrenner, D. R. Gitelman and D. M. Small (2011).
893 "The anterior insular cortex represents breaches of taste identity expectation." The Journal
894 of neuroscience : the official journal of the Society for Neuroscience **31**(41): 14735-14744.
895 Veldhuizen, M. G., D. J. Nachtigal, L. J. Flammer, I. E. de Araujo and D. M. Small (2013).
896 "Verbal descriptors influence hypothalamic response to low-calorie drinks." Molecular
897 Metabolism **2**(3): 270-280.
898 Wang, G.-J., N. D. Volkow, F. Telang, M. Jayne, Y. Ma, K. Pradhan, W. Zhu, C. T. Wong, P.
899 K. Thanos, A. Geliebter, A. Biegon and J. S. Fowler (2009). "Evidence of gender
900 differences in the ability to inhibit brain activation elicited by food stimulation."
901 Proceedings of the National Academy of Sciences **106**(4): 1249-1254.
902 Woods, A. T., D. M. Lloyd, J. Kuenzel, E. Poliakoff, G. B. Dijksterhuis and A. Thomas (2011).
903 "Expected taste intensity affects response to sweet drinks in primary taste cortex."
904 Neuroreport **22**(8): 365-369.
905 World Medical, A. (2013). "World medical association declaration of helsinki: Ethical
906 principles for medical research involving human subjects." JAMA **310**(20): 2191-2194.
907 Zandbelt, B. B. and M. Vink (2010). "On the Role of the Striatum in Response Inhibition."
908 PLOS ONE **5**(11): e13848.
909 Zandstra, E. H., C. de Graaf and W. A. Van Staveren (2001). "Influence of health and taste
910 attitudes on consumption of low- and high-fat foods." Food Quality and Preference **12**(1):
911 75-82.
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## Tables

**Table 1** ROI clusters with significant different activation when comparing packages, tastes and package-taste combinations using a flexible factorial fMRI analysis.

| Effect | ROI | Side | Cluster size | X | Y | Z | Peak Z-score |
|---|---|---|---|---|---|---|---|
| **Main package effect** | | | | | | | |
| Regular package vs Healthier package | Inferior frontal gyrus (vlPFC) | R | 40 | 51 | 26 | -1 | 4.33 |
| | Putamen (ventral striatum) | L | 19 | -15 | 5 | -7 | 4.74 |
| | Orbital inferior frontal gyrus (OFC) | L | 37 | -48 | 32 | -13 | 3.73 |
| **Main product effect** | | | | | | | |
| Healthier product vs Regular product | Caudate (dorsal striatum)* | R | 56 | 18 | -16 | 23 | 5.02 |
| | Middle frontal gyrus (BA46) (dlPFC)* | L | 204 | -24 | 50 | 17 | 4.06 |
| | Orbital inferior frontal gyrus (OFC) | L | 25 | -21 | 35 | -10 | 4.56 |
| | Pallidum (ventral striatum) | R | 35 | 27 | -7 | -7 | 4.13 |
| | Putamen (dorsal striatum) | R | 30 | 24 | 11 | 5 | 3.92 |
| | Putamen (dorsal striatum) | L | 21 | -24 | 14 | 2 | 3.8 |
| | Superior frontal gyrus (dlPFC) | L | 21 | -15 | 26 | 50 | 3.87 |
| **Package * product interaction effect** | | | | | | | |
| Healthier package + Healthier product & Regular package + Regular product vs Healthier package + Regular product & Regular package + Healthier product | Orbital inferior frontal gyrus (OFC) | L | 19 | -36 | 41 | -10 | 3.75 |

MNI peak coordinates, significant at $p_{uncorrected} < 0.001$, voxel threshold: 19 voxels.

*Significant at $p_{FWE} < 0.05$ ($p_{uncorrected} < 0.001$, k > 44 voxels)

## Figure captions

**Figure 1** Package stimuli, signaling healthy and regular product properties, varying in hue and levels of brightness and saturation. The usage of package stimuli was permitted by, and cleared with, Royal FrieslandCampina, Amersfoort, The Netherlands.

**Figure 2** Overview of a package trial (top) and a package-taste trial (bottom) during the fMRI task. Note that the 'rating' of either healthiness or attractiveness only occurred once per congruent package-taste trial.

**Figure 3** Mean (±SD) of perceived hedonic attributes per package or tasted product, * indicate significant differences between products or packages at $p<0.05$.

**Figure 4** Mean (±SD) of perceived sensory attributes per package or tasted product, * indicate significant differences between products or packages at $p<0.05$.

**Figure 5** Difference between contrasts of viewing healthier packages and regular packages while tasting in the left sided putamen and mean (±SD) parameter estimates for this cluster. F-map overlaid on mean anatomical image, $p<0.001$, F>11.33. Flexible factorial analysis was performed comparing contrasts of healthier and regular package viewing while tasting. Bottom right: Average cluster parameter estimates of left sided putamen when viewing a regular package while tasting plotted against General Health Interest scores from HTAS, $p<0.05$.

**Figure 6** Difference between contrasts of tasting healthier product taste and regular product taste in the left middle frontal gyrus and mean (±SD) parameter estimates for this cluster. F-map overlaid on mean anatomical image, $p<0.001$, F>11.33. Flexible factorial analysis was performed comparing contrasts of healthier and regular product tasting versus rest, irrespective of presented packages.

**Figure 7** Difference between contrasts of congruent and incongruent package-taste combinations in the left lateral OFC and mean (±SD) parameter estimates for this cluster. F-map overlaid on mean anatomical image, $p<0.001$, F>11.33. Flexible factorial analysis was performed comparing contrasts of congruent- and incongruent package-taste combination versus rest, irrespective of presented packages.

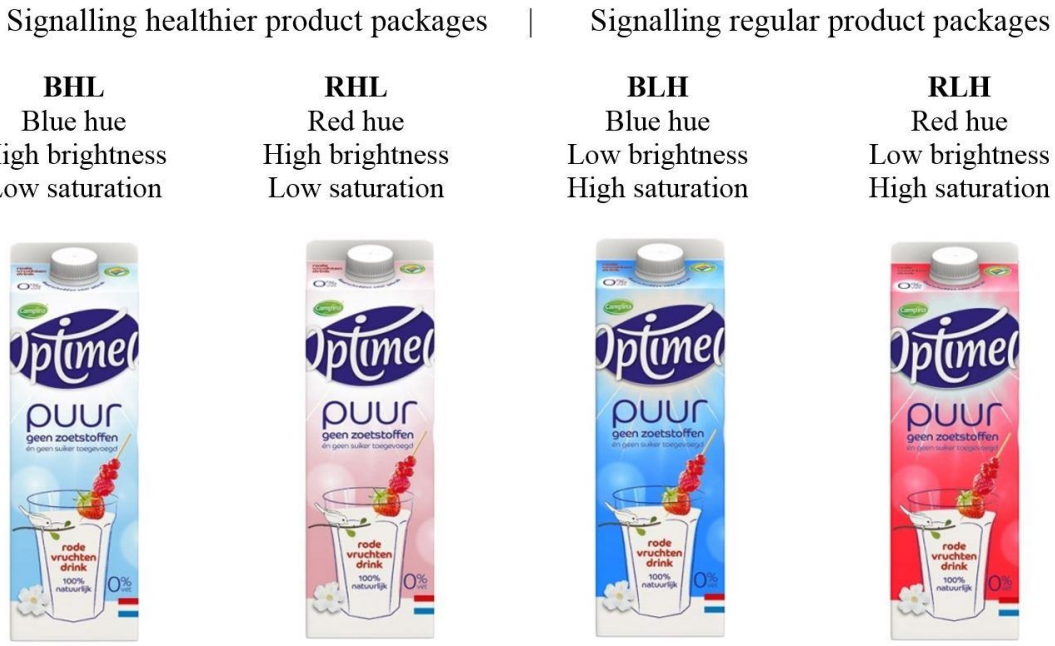
Supplementary materials

**Figure 8** Difference between contrasts of viewing healthier packages and regular packages

**Figure 9** Difference between contrasts of tasting healthier product taste and regular product taste

**Figure 10** Correlations between behavioural indices and BOLD-signal in several ROIs

962 Figure 1

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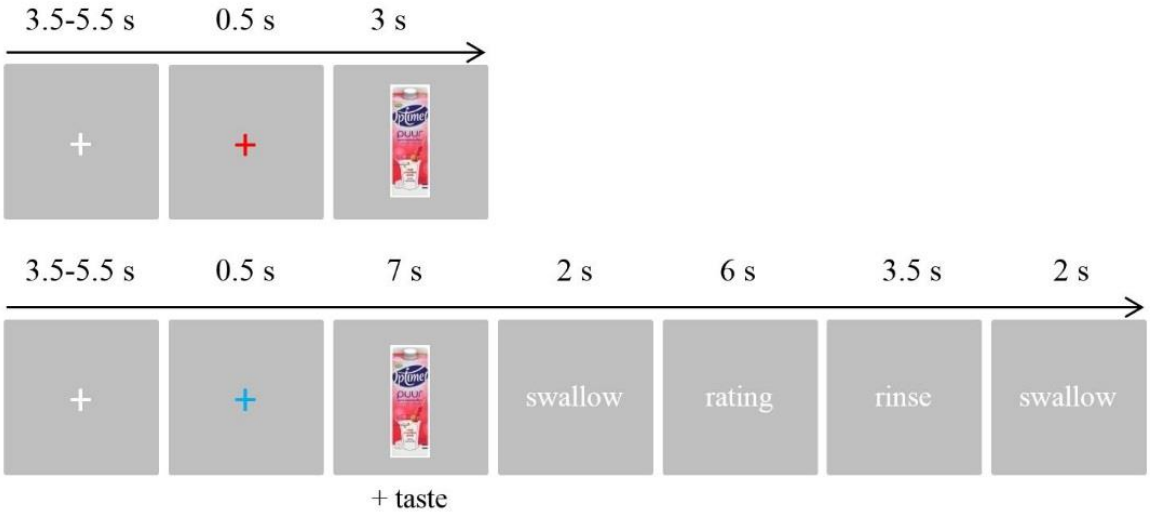
965 Figure 2

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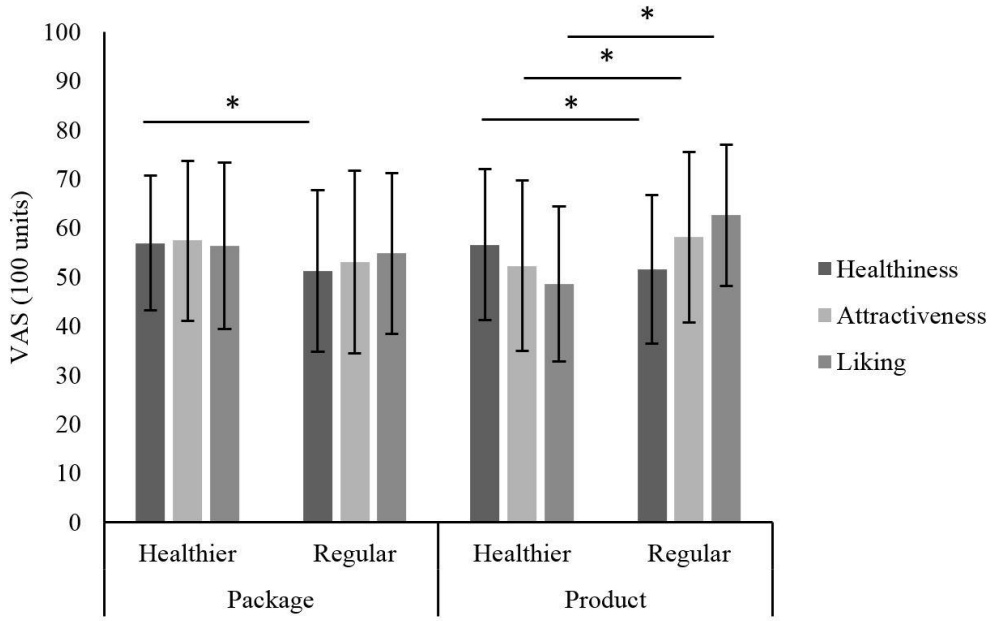


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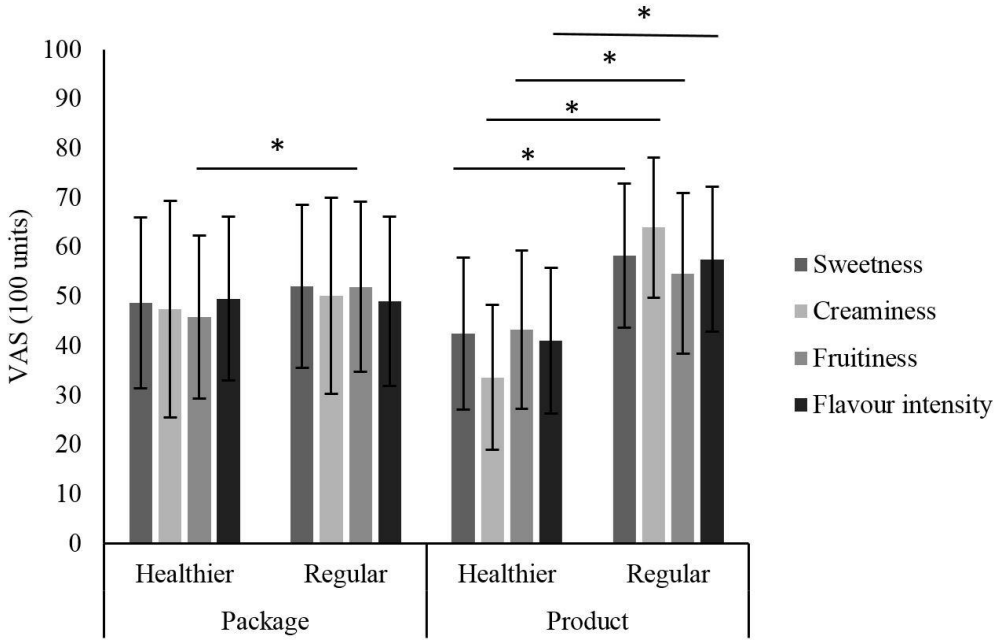
972 Figure 4

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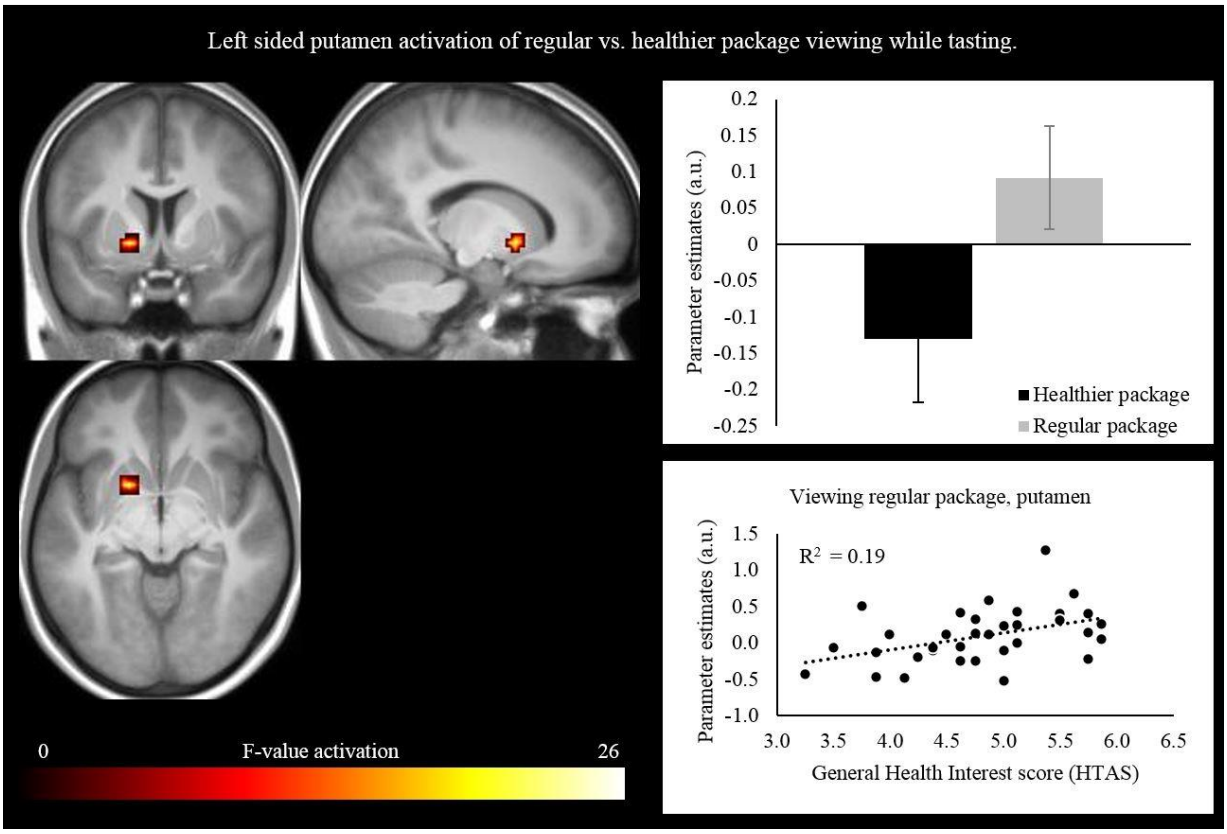
975 Figure 5

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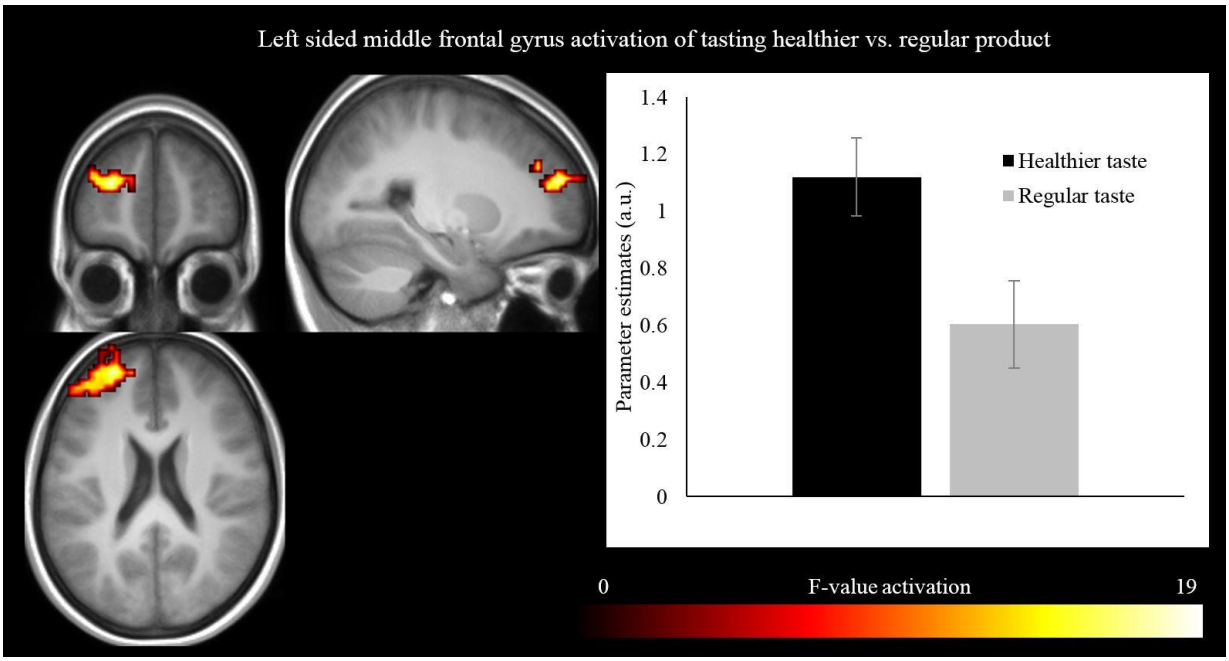
978 Figure 6

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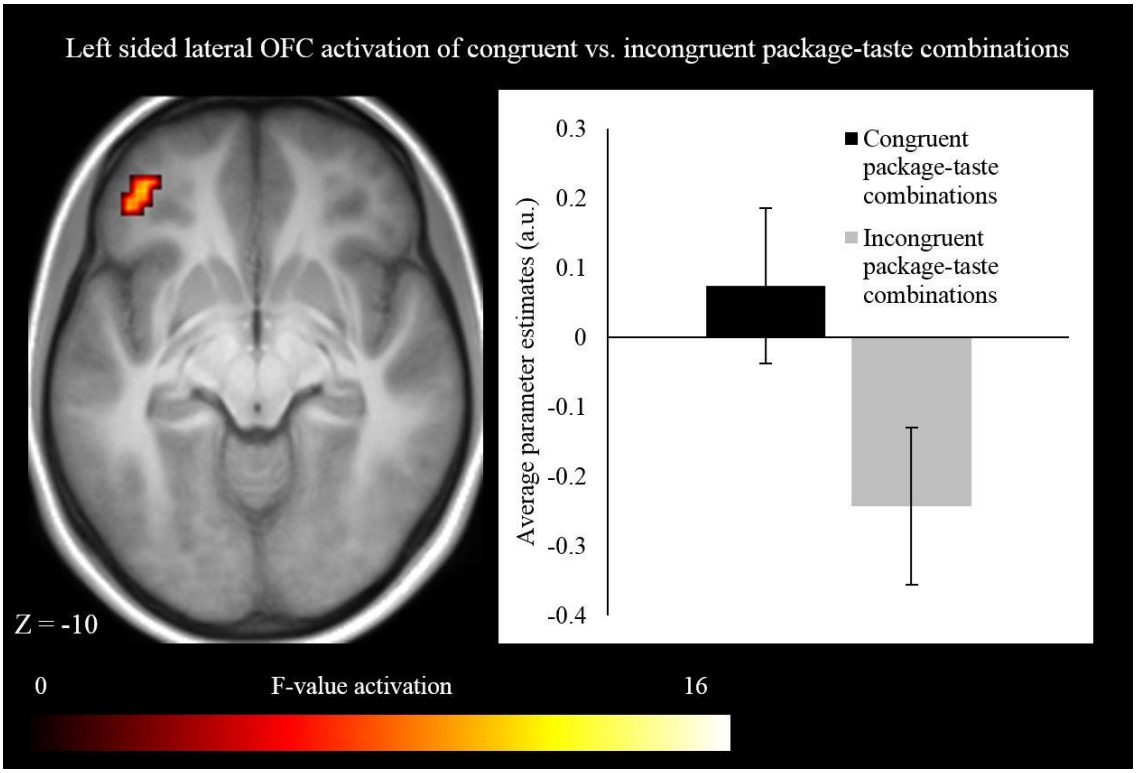


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985 Supplementary Materials

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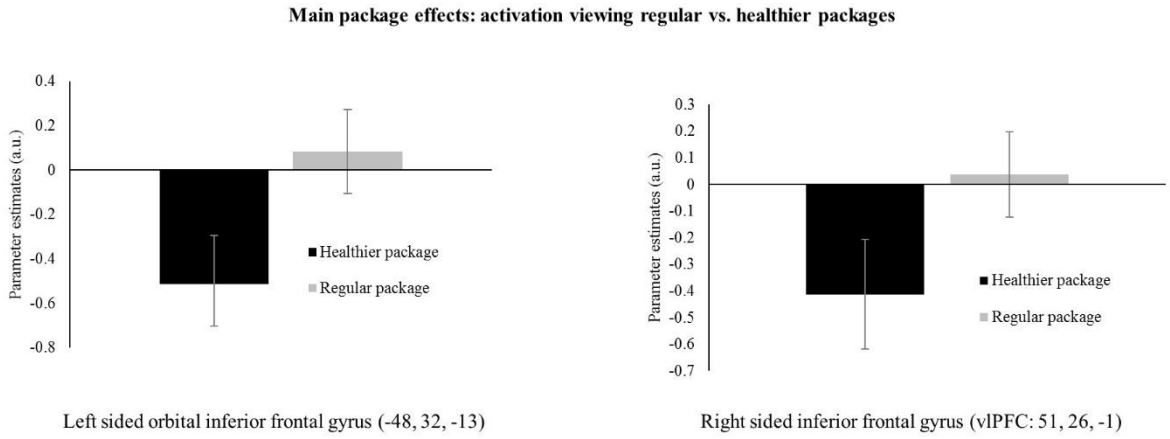


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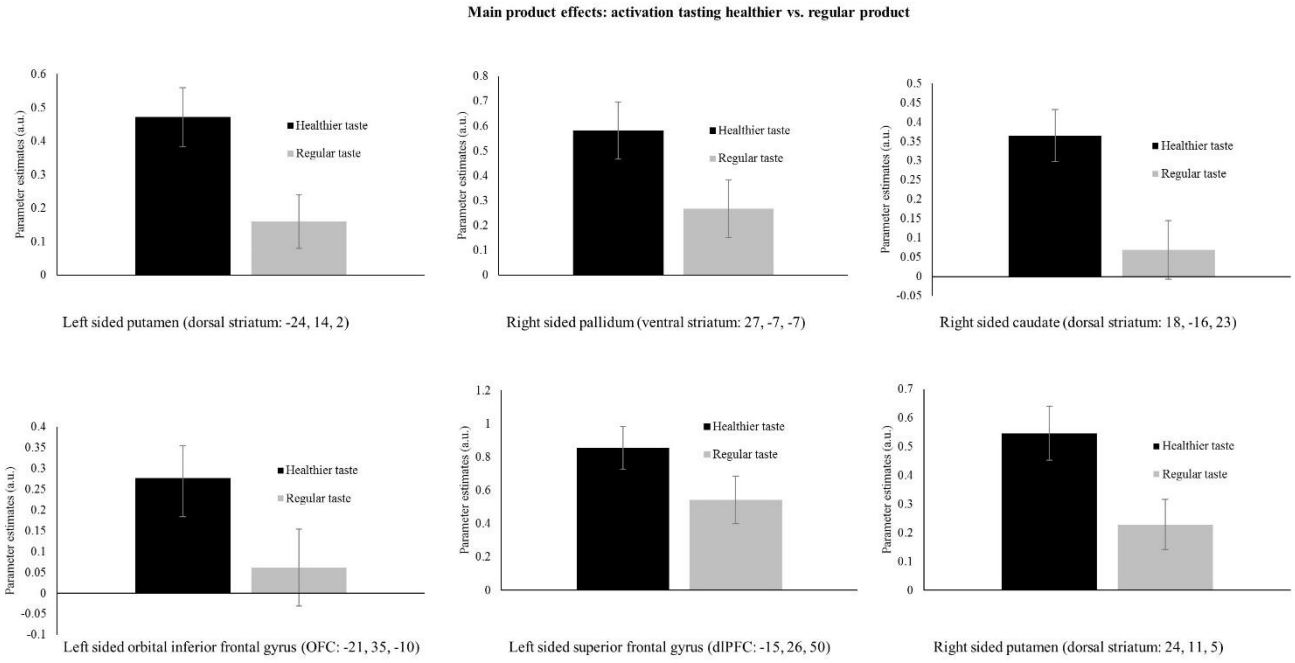


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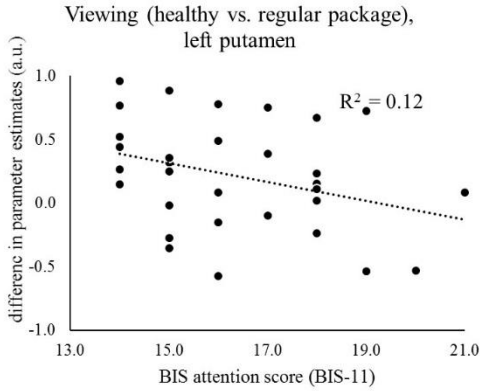


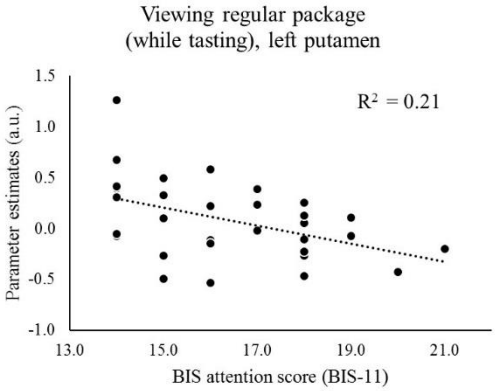


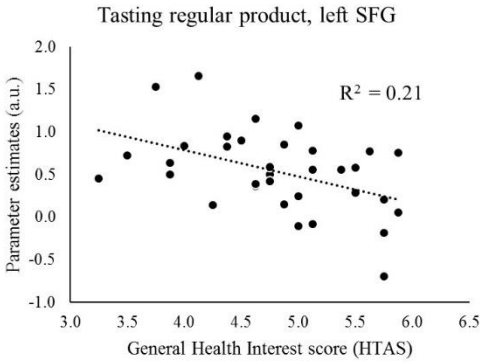


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