CHAPTER

Flavor pleasantness processing in the ventral emotion system

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Submitted
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WHAT THIS CHAPTER IS ABOUT

The ventral emotion network – encompassing the amygdala, insula, ventral striatum, and ventral regions of the prefrontal cortex – has been associated with the emotional significance of perceived external stimuli and the production of affective states. Functional magnetic resonance imaging (fMRI) studies investigating chemosensory stimuli have associated parts of this network with pleasantness coding. In the current study we analyzed two datasets in which we examined affective brain responses to flavor stimuli in young adult men. In the first dataset participants judged eight regular off-the-shelf drinking products while participants judged six oral nutritional supplements (ONS) in the second dataset. Using independent component analysis, we successfully isolated the ventral emotion networks for both datasets. In the first dataset, we found that engagement of this network was significantly associated with flavor pleasantness ratings which were given 20 seconds after flavor administration. This relation was not obvious for the ONS dataset. Nevertheless, the spatial similarity was remarkably high and mainly encompassing the right hemisphere. Our results indicate that the ventral emotion network processes the pleasantness of flavors.
6.1 INTRODUCTION

Flavor liking differs widely between individuals. Despite this wide variety, liking expression for a flavor stimulus is very similar across individuals. This is reflected in characteristic positive facial expressions (e.g., lip licking and tongue protrusions) and negative facial expressions (e.g., gaping or making a facial grimace) for liking and disliking, respectively (Berridge, 1996; Berridge et al., 2009).

Based on previous emotion studies, Phillips et al. (2003) theorized a neuronal ventral emotion network encompassing the amygdala, insula, ventral striatum, and ventral regions of the prefrontal cortex. These authors related this network to “identification of emotional significance of environmental stimuli and the production of affective states”. Interestingly, a growing body of neuroimaging studies associated (parts of) this system with pleasantness coding of chemosensory stimuli: tastes, flavors, and odors (e.g., chapter 5, Berridge, 2009; Cerf-Ducastel et al., 2012; Crouzet et al., 2013; de Araujo et al., 2003; Hayes et al., 2014; McCutcheon et al., 2012; Nitschke et al., 2006; Small et al., 2003; Winston et al., 2005). This similarity indicates that the ventral emotion system might also process the pleasantness of chemosensory stimuli.

In the current study, we aimed to capture the ventral emotion network using data-driven analysis and associate engagement of this network with flavor pleasantness coding using fMRI. Several factors complicate investigating pleasantness coding of flavor stimuli using functional magnetic resonance imaging (fMRI). First, flavor is a combination of taste and odor. Because odor-components are mainly processed retro-nasally, flavor processing requires swallowing. Therefore, flavor processing is associated with MRI movement artifacts. Second, brain activation may be evoked by somatosensory stimulation instead of flavor or in addition to flavor. To overcome this, several researchers contrasted the taste stimulus with a baseline stimulus such as water or a solution containing artificial saliva. However, both water and tasteless artificial saliva still activate gustatory areas (de Araujo et al., 2003; Veldhuizen et al., 2007) and elicit affective responses (Bender et al., 2009). Therefore, contrasting with such baseline stimuli reduces sensitivity. Third, to investigate pleasantness coding in the brain, previous studies induced liking responses with a limited set of taste or flavor stimuli. Consequently, brain responses associated with affective responses may have been confounded with taste or flavor quality. We (chapter 5) and Rudenga & Small, (2013) addressed this issue by investigating the difference between subjects that either liked or disliked the same stimulus. Both studies associated the difference between likers and dislikers with an area in the ventromedial PFC/medial OFC.

In the current study, we hypothesized that flavor pleasantness is processed in the ventral emotion system. To relate the ventral emotion system to flavor pleasantness, we analyzed two data sets in which affective brain responses to flavor stimuli were examined in young adult men. These men were exposed to regular off-the-shelf drinking products and Oral Nutritional Supplements (ONS) in the first and second data set, respectively. To isolate functional networks as well as to address the above-mentioned limitations, we applied a data-driven analysis. Subsequently, we related functional networks to perceived pleasantness scores. Furthermore, we regarded flavor quality as a random factor in our analysis to address possible confounding effects of stimulus quality in investigating flavor pleasantness.
6.2 MATERIALS AND METHODS

6.2.1 General Procedure
In the current study, we used fMRI data from a larger flavor experiment, which was divided into a screening session, an fMRI session, six daily repeated-exposure sessions, and a second fMRI session. In the screening session, inclusion and exclusion criteria were checked, and participants were familiarized with the experimental procedure. For the current study, we only used data from the first fMRI session. Participants were instructed not to eat or drink during a two-hour period prior to the fMRI session, which was scheduled between 8:00 am and 12:00 pm or between 4:00 pm and 7:00 pm. Results from the remainder of the study have been reported elsewhere (see e.g., chapter 2).

6.2.2 Participants
A total of 45 male Caucasian university students were recruited for the experiment. Participation was on the basis of written informed consent and the study was in accordance with the requirements of the medical ethical committee at the University Medical Center Groningen. Participants were randomly assigned to two experimental groups. The first group (n=23, mean age = 23.43, SD=2.33, range: 21–28) was recruited to taste commercially available drinks (referred to as regular products) during a morning session. The second group (n=22, mean age = 24.67, SD=3.37, range: 21–33) was recruited to taste ONS products in the afternoon. Participants were included when they reported no history of taste, smell, neurological, or psychological disorders. They were right handed, non-smoker for at least three months, and had normal or corrected to normal vision with MR-compatible lenses. Participants who had any psychiatric disorder, a history of drug abuse, non-removable metal inside their body or who used any form of medication that possibly affected taste perception (i.e. gastrointestinal complaints, dry mouth, nausea, and taste disturbance) were excluded from the study. Participants received a monetary compensation for their participation.

6.2.3 Taste stimuli and delivery
The drinks were divided into two groups. The first group of drinks consisted of eight products that were commercially available in Dutch supermarkets at the time when the experiment was conducted. The drinks can be subdivided into two subgroups: four water-based drinks (flavors: apple-blueberry 27 Kcal / 100 ml, apple-peach 28 Kcal / 100 ml, orange-tangerine 27 Kcal / 100 ml and pineapple-mango 28 Kcal / 100 ml) and four yogurt drinks (flavors: raspberry 33 Kcal / 100 ml, coconut 32 Kcal / 100 ml, lemon 33 Kcal / 100 ml and orange-cinnamon 30 Kcal / 100 ml). The second group contained six ONS products. All six ONS products were milk based (flavors: apricot, vanilla and neutral, peach-ginger, cappuccino and orange-lemon, 160 Kcal / 100 ml). All liquids were administered at room temperature using a custom-made gustometer. This apparatus contained separate sterile syringes for each liquid, which were connected to a central mouthpiece by separate tubing for each liquid. Stimuli were administered manually. Timely stimulus administration was guaranteed by auditory countdown. See chapter 4, for more details on the gustometer.
6.2.4 Experimental design

A schematic overview of the fRMI paradigm is given in Figure 1. Participants engaged in a tasting task containing 48 or 36 trials for the regular products and ONS group, respectively. During the course of the experiment, participants received visual cues and instructions in Dutch via a paradigm constructed in E-prime (Psychology Software Tools Inc., Pittsburgh). Every flavor stimulus was delivered 6 times balanced over all imaging runs and counterbalanced between participants. The paradigm was presented during four and three imaging runs, for the regular products and ONS group, respectively. Each imaging run lasted for approximately 15 minutes (depending on reaction times) and contained a series of 12 trials. During each trial, participants were warned for an upcoming taste delivery by an asterisk appearing centered on the screen (duration: 2s.). Subsequently, 2 ml of a taste stimulus was delivered in the mouth and participants were instructed to taste this stimulus with the cue “Taste” (in Dutch: “Proeven”, duration: 3.5s.). After tasting, participants were instructed to swallow the solution, cued as “Swallow” (in Dutch: “Slikken”, duration: 4s.), followed by a period in which they needed to passively “Judge” the taste (in Dutch: “Beoordelen”, duration: 22.5s.). Finally, a 7-point Likert scale appeared on the screen, ranging from “very unpleasant” to “very pleasant”. Participants were instructed to express perceived pleasantness of the taste on the scale by using a button box held in their right hand. Every trial ended with a rinsing procedure, in which participants received a 2 ml bolus of a 5% artificial saliva solution (Saliva Orthana, TM) twice. The entire paradigm lasted for approximately 90 minutes, in which either 288 ml or 216 ml of liquid was consumed, for the regular products and ONS group, respectively.

As baseline, we included four 15-second periods in each imaging run within both data sets, during which the participant was looking at a black screen with a red cross centered in the middle.

6.2.5 Data acquisition

MRI scans were performed using a 3-Tesla MR scanner (Philips Intera, Best, the Netherlands) equipped with a 32-channel head coil.

A T1-weighted 3D fast field echo (FFE) whole brain image was obtained in transverse

<table>
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<tr>
<th>Condition</th>
<th>Cue</th>
<th>Taste</th>
<th>Swallow</th>
<th>Judge</th>
<th>Rate</th>
<th>Rinsing</th>
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<tr>
<td>Paradigm screen</td>
<td>8</td>
<td>Taste</td>
<td>Swallow</td>
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<td>Duration</td>
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Figure 1. The figure shows the trial structure of the fMRI taste paradigm. Every taste stimulus was delivered 6 times distributed over the entire paradigm. Every trial started with a visual cue, followed by the taste. The participant was subsequently instructed to swallow, judge and provide a pleasantness rating for the stimulus. Finally, the participant was instructed to rinse the mouth twice.
orientation for anatomical reference. Acquisition parameters: field of view (FOV) 256 × 232 × 170 mm³ (rl, ap, fh); voxel size 1 mm isotropic; TR = 9 ms; TE = 3.5 ms; flip angle 8°; SENSE factors: 2.5, 1 (ap, fh); 170 slices, scan duration = 246.3s.

Functional brain images were acquired in sagittal orientation using the Principles of Echo-Shifting with a Train of Observations (PRESTO) sequence. Acquisition parameters: FOV 153 × 230 × 230 mm³ (rl, ap, fh); voxel size 2.87 × 2.87 × 3 mm³; TR = 20 ms; TE = 30 ms; flip angle 7°; SENSE factors: 1.9, 1.9 (rl, ap); scan time per volume 1.532s.

6.2.6 Data analysis
Data was analyzed in R (http://www.r-project.org, version 3.1.2, 2014-10-31), and in SPM12 (Wellcome Trust Centre for Neuroimaging, (http://www.fil.ion.ucl.ac.uk/spm) and the GIFT Toolbox v3.0a (http://mialab.mrn.org) running in Matlab 2012b (The MathWorks Inc., Natick, MA). Functional images were registered to the mean functional image, co-registered to the T1 image and normalized to the MNI template. Finally, the images were smoothed with an 8 mm full-width at half-maximum (FWHM) Gaussian kernel and resliced to a voxel size of 2x2x2 mm.

Due to technical difficulties with the gustometer or scanner, data was missing for several trails. We removed participants missing more than 25% of their data (3 in the regular drinks group, 1 in the ONS group). Therefore, fMRI analysis was performed on data from 19 and 21 participants for the regular drinks and ONS groups, respectively.

6.2.6.1 Pleasantness scores analysis
To provide insight in differences in scoring behavior between both datasets, we analyzed pleasantness-scoring behavior using linear mixed models (LMMs). LMMs are provided in R by the lmer-function from package lme4 (version 1.1-5, http://cran.r-project.org/package=lme4) (Bates et al., 2014; Pinheiro and Bates, 2000). Subsequent statistical tests on the LMMs were performed using the Satterthwaite’s approximation for the degrees of freedom, provided in the package lmerTest (version 2.0-11, http://cran.r-project.org/package=lmerTest) (Kuznetsova et al., 2014). We tested both the difference in mean pleasantness-score as well as the difference in pleasantness-scoring behavior as a function of time during the experiment between both data sets. Within the model, pleasantness scores were entered as dependent variable while dataset, trial number, and their interaction were entered as independent variables. Finally, the variable participant constituted a random variable.

6.2.6.2 Independent component analysis
Independent component analysis (ICA) is a technique that extracts signal sources from a mixture of signals. McKeown and Sejnowski (1998) introduced ICA in the spatial domain for fMRI analysis. Spatial ICA (sICA) assumes that each voxel contains a mixture of source signals. By grouping all voxels that elicit co-occurring signals, the measured signal mixtures are separated into spatially independent voxel patterns, termed independent components (ICs). Each IC represents a functional brain network (Calhoun et al., 2001; McKeown and Sejnowski, 1998; Xu et al., 2013). Since its introduction, spatial ICA has been widely used as a technique for extracting functional networks from fMRI data (Xu et al., 2013). An additional
advantage of spatial ICA is its ability to isolate signal sources originating from MRI artifacts. These artifactual signal sources such as head motion, MR scanner noise and cardiac and respiratory pulsations show spatially independent characteristics. (McKeown and Sejnowski, 1998; Xu et al., 2013). In the current study, we made use of both strengths of spatial ICA by applying it for artifact removal prior to first-level analysis and for task-specific functional network extraction at second-level (Calhoun and Allen, 2013).

6.2.6.3 ICA artifact removal
We applied an ICA artifact removal (ICA-AR) method analogously to implementations by Kim et al. (2008) and Stevens et al. (2007) before first-level analysis. First, we reduced data dimensionality using two principal component analysis (PCA) data reduction stages; on subject-level, data was reduced to 45 principal components (PCs), after which data from all subjects were concatenated in time and reduced from 45 to 30 PCs at group-level. Note that the optimal number of ICs is often determined by the minimum description length (MDL) algorithm while using the GIFT Toolbox (Li et al., 2007). As the number of scans in our scanning paradigms approximately ranged from 1750 to 2350 scans per participant, such an algorithm produces high component estimations (~90). Running ICA using a high number of components produces components that reflect relatively small brain areas, which poorly correlate with full brain white matter and CSF probability maps. Therefore, we chose to estimate 30 ICs, which approximates the number of components extracted by Kim et al. (2008).

Spatial ICs were estimated using the Infomax algorithm (Bell and Sejnowski, 1995). ICs were subsequently spatially correlated with prior probabilistic maps of white matter and cerebral spinal fluid (CSF) within the standardized MNI brain space, provided in SPM12. We thresholded spatial correlation values at $r^2 = 0.025$ and $r^2 = 0.005$ for white matter and CSF, respectively. These threshold values were based on visual inspection of the components. Components showing high correlations ($r^2$) with these maps were considered artifacts and removed from the data. Finally, ‘cleaned’ fMRI datasets were reconstructed from the remaining ICs using the GIFT Toolbox. These data sets were used for first-level statistical analysis.

6.2.6.4 First-level statistical analysis
For the first-level statistical analysis, we constructed mass-univariate general linear regression models for each participant. The regressors included: 1) conditions ‘Taste & Swallow’, ‘Judge’, and ‘Rate’ for each taste trial separately, allowing subsequent modeling of repetition effects on second level, and 2) a global condition ‘Rinse’. These task-related regressors were convolved with the canonical hemodynamic response function (HRF) and a high-pass filter of 128 seconds was applied.

Due to technical difficulties, several PRESTO images were missing at random time intervals for 10 participants (on average 0.54% per data set). To minimize the effect of missing volumes, we replaced these volumes with the first PRESTO volume of the imaging run, and included a separate regressor for each missing volume in the first-level statistical analysis such that it does not affect effect size estimates.
6.2.6.5 Second-level ICA

In the current study, we aimed to extract functional networks associated with flavor pleasantness processing. Therefore, we applied ICA for extracting task-specific functional networks on second-level (see Calhoun and Allen (2013) for a validation of second-level ICA). Compared to classical mass-univariate analysis of fMRI data, this approach provides several major advantages: first, it avoids the multiple-comparisons problem within mass-univariate analysis; second, by using blind source separation, the response dynamics to flavor pleasantness need not be exactly specified beforehand; and third, several studies suggest that spatial ICA is more sensitive in detecting task-related changes in fMRI signal than traditional mass univariate approaches (see e.g., Kim et al., 2011; Xu et al., 2013).

Second-level ICA was run separately on both data sets using the 48 (regular products group) or 36 (ONS group) beta maps of the ‘Taste & Swallow’ (flavor) condition from the first-level statistical analysis as input data. First, these beta maps were demeaned in the spatial domain. Subsequently, the number of ICs was estimated using the MDL algorithm (Li et al., 2007), which resulted in 15 and 13 ICs, for the regular products group and ONS group, respectively. For the regular products group data was reduced to 23 PCs on an individual level and to 15 PCs on a group level, while for the ONS group data was reduced to 14 PCs on individual level and subsequently to 13 PCs on group level. These differences arise due to differences in available data points (beta maps) for both data sets.

Note that ICA results in ICs containing information in a spatial domain (functional brain networks) and a time domain (a time-course per network) when ICA is performed on first-level. However, on second (group) level, the time domain is equivalent to a flavor condition domain representing a profile that indicates how strong each IC is represented in each condition per participant. We will refer to profiles in this domain as flavor condition profiles.

6.2.6.6 Relating independent component maps to flavor pleasantness

In order to relate the resulting ICs of each data set to flavor pleasantness, we applied additional LMMs. For all constructed models, flavor condition profiles were entered as dependent variables, while flavor pleasantness scores constituted independent variable. Finally, the participants and flavor quality constituted as random variables in the LMMs. These random variables corrected for possible systematic differences between participants and stimulus type (see e.g., Judd et al., 2012).

6.3 RESULTS

6.3.1 Behavioral results

To give an overview of the pleasantness scores, frequencies of scores are given in Figure 2. The LMM on the pleasantness data indicated that the drinks in the ONS dataset were perceived as less pleasant than in the regular products dataset (β = -0.75, T(37.58) = -3.61, p < 0.001). Furthermore, pleasantness scores significantly decreased per trial in the ONS dataset (β = -0.02, P < 0.001), whereas scores did not significantly change in the regular products dataset (β = -0.003, P = 0.40). The difference between these trial-effects in both datasets was significant (β = 0.02, P > 0.05).
6.3.2  Functional MRI results

6.3.2.1  ICA artifact removal

ICA was applied on both datasets, separately, and 30 ICs were estimated. Figure 3 indicates the spatial correlation of all components with WM and CSF probability maps. For both data sets, we identified 10 components having considerable spatial overlap with WM and CSF. The 20 retained components were used for “cleaned” fMRI signal reconstruction. Resulting fMRI time courses were used in the first-level statistical analysis. Two subsets of the removed components are given in Figure 4 showing an example of the various artifactual signals that have been removed from the data.
A. Regular Products Group

B. ONS Group

Figure 4. The figure illustrates an overlay of 4 (regular products group) and 5 (ONS group) out of 10 independent components (ICs) representing various types of artifactual influences on fMRI signal. For visualization purposes, only a subset of ICs is shown. Colors refer to specific ICs. Component maps are thresholded at $z > 2$.

Figure 5. Independent components encompassing the ventral emotional system in (A) the regular products group and (B) ONS group. Images are thresholded at $|z| > 1$. Both components showed high similarity (spatial correlation: $r^2 = 0.55$). Several key areas have been highlighted: the amygdala (A), parahippocampal gyrus (PhG), right ventral prefrontal cortex (rPFC), insula (I), ventral striatum (vS), and caudate nucleus (C).
6.3.2.2 Second-level ICA result

In both datasets, the second-level ICA result contained one component showing large spatial overlap with the ventral emotional system. The components encompassed the left parahippocampal gyrus, right amygdala, insula, ventral striatum and ventral prefrontal cortex. Spatial maps of these components are given in Figure 5 while Figure 6 indicates the relation between the condition loadings of these components and pleasantness scores. The components were highly similar in both data sets (spatial correlation: \( r^2 = 0.55 \)). In the regular products group, flavor condition profiles highly correlated with pleasantness scores (\( T(906.6) = -2.93, \ P < 0.005 \)). However, in the ONS dataset, we found no relation between condition loadings and pleasantness scores (\( T(89.6) = 1.0, \ P = 0.32 \)).

6.4 Discussion

To the best of our knowledge, the current fMRI study is the first to investigate flavor pleasantness processing using a network-based analysis. In two separate datasets we isolated a functional network showing great overlap with the ventral emotional network, theorized by Phillips et al. (2003). Whereas activity of this ventral emotion network was associated with flavor pleasantness of off-the-shelf drinks, we found no association between this emotion network and pleasantness ratings of oral nutritional supplements.

Phillips et al. (2003) associated the ventral emotion network with the amygdala, insula, ventral striatum, and ventral regions of the prefrontal cortex. Although lateralized to the right hemisphere, our analysis included all of these regions within one functional network. Additionally, the network we isolated in the current study, encompassed the left parahippocampal gyrus as well. Interestingly, between pleasant and unpleasant flavor processing a spatial segregation existed in the right amygdala, right insula, right ventral prefrontal cortex and the left parahippocampal gyrus (see figure 5).

6.4.1 Amygdala

Although early neurobiological chemosensory studies associated the amygdala with processing of aversive stimuli only (Small et al., 1997; Zald et al., 2002, 1998), other studies
indicated that this structure showed activity for pleasant as well as unpleasant chemosensory stimuli (Baxter et al., 2002; O’Doherty et al., 2001b; Small et al., 2003). Moreover, multiple studies have found no correlation between amygdala responses and taste or flavor pleasantness ratings (Cerf-Ducastel et al., 2012; de Araujo et al., 2003b; Small et al., 2001). Instead, the amygdala was found to be responsive to taste intensity (Cerf-Ducastel et al., 2012; Small et al., 2003; Spetter et al., 2010). Interestingly, these intensity effects in the amygdala were found to interact with stimulus pleasantness. Winston et al. (2005) found that intense odors evoked greater amygdala responses compared to weak odors for an unpleasant and a pleasant stimulus, while there was no difference in amygdala response between intensities of a neutrally pleasant odor. These results indicate that the amygdala is involved in processing the emotional salience of pleasant and unpleasant chemosensory stimuli but not of neutral stimuli. In correspondence with these findings, our study also indicates that the amygdala is associated with both pleasant and unpleasant flavors. Furthermore, co-activation of the amygdala, nucleus accumbens and ventral prefrontal regions is in line with connectivity studies of the amygdala indicating (reciprocal) connections between these areas (Baxter et al., 2002; Davis and Whalen, 2001; Roy et al., 2009).

6.4.2 Insular cortex

Crouzet et al. (2015) showed that the insular cortex is involved in early taste quality processing. Furthermore, neuroimaging studies indicate that the insular cortex is not only involved in taste or flavor quality processing, but also in processing its associated intensity and pleasantness (Bender et al., 2009; Small, 2012; Small et al., 2003, 2001; Smeets et al., 2006; Spetter et al., 2010). In previous work, we showed that insular processing of these taste characteristics is lateralized; taste quality and taste pleasantness processing is dominated in the left insula, while taste intensity processing is dominated in the right insula (chapter 4). Furthermore, Nitschke et al. (2006) showed that cognitive manipulations altering perceived taste pleasantness (e.g., providing false intensity information on the upcoming taste stimulus), are reflected in insular taste stimulus processing.

In a previous study we found that right anterior insula activity was predominantly associated with taste intensity (chapter 4). Although, we associated the exact same insular area with flavor pleasantness in the current study, these results do not necessarily contradict. Pleasantness and intensity highly correlate. In the current study, we did not manipulate nor measure perceived intensity and, therefore, are unable to disentangle these flavor characteristics in the current study.

6.4.3 Ventral striatum

The ventral striatum, and in particular the nucleus accumbens (NAc), has been associated with processing pleasantness (Berridge, 2009, 2003). Gottfried et al. (2002) showed the ventral striatum also associates with odor pleasantness learning. These authors paired odor presentations with facial expressions and found that NAc activity increased over time during pleasant olfactory learning. Additionally, ventral striatal activity has been associated with cognitive manipulations in affective value of taste and flavor (Grabenhorst et al., 2008). Fi-
nally, a more recent study suggests that the ventral striatum may also be associated with processing aversion (McCutcheon et al., 2012). In line with these studies we found that the right ventral striatum positively correlated with the full flavor pleasantness range. Furthermore, ventral striatum activity clustered together with ventral medial prefrontal cortex activity. This is in correspondence with a study by Di Martino et al. (2008) who showed strong functional connectivity between these areas.

6.4.4 Orbitofrontal Cortex / Ventral Prefrontal Cortex
A growing body of neuroimaging studies associated the orbitofrontal cortex (OFC), (also termed ventral prefrontal cortex in many studies), with pleasantness coding (de Araujo et al., 2003b; Kringelbach and Radcliffe, 2005; Kringelbach and Rolls, 2004; Small et al., 2007, 2003, 2001). The posterior part of the OFC is thought to process multimodal integration of sensory information, while the anterior part processes reward value (Kringelbach and Radcliffe, 2005). Furthermore, an important distinction can be made between the medial (m) and lateral (l) OFC. Whereas the mOFC is associated with reward value processing, the lOFC is associated with the evaluation of punishment, which may lead to behavioral change (Kringelbach and Radcliffe, 2005; Kringelbach and Rolls, 2004; O’Doherty et al., 2001a). Hayes et al. (2014) performed a meta-study on processing pleasant and unpleasant chemosensory stimuli. The authors found great overlap within OFC areas in response to pleasant and unpleasant stimuli. Differences between pleasant and unpleasant stimuli were found in the mOFC and left lOFC, showing increased activation for pleasant stimuli, whereas unpleasant stimuli were associated with the right caudolateral OFC activity.

In line with the studies mentioned above, we found a clear distinction between the right medial and lateral OFC (or vPFC). We found that the right mOFC was associated with increasing pleasantness, whereas the right lOFC was associating with decreasing pleasantness.

6.4.5 Parahippocampal gyrus
Interestingly, our network-analysis also indicated involvement of the left parahippocampal gyrus. Involvement of the hippocampus/parahippocampal gyrus in chemosensory studies has been reported in multiple studies (see e.g., Bragulat et al., 2010; Gautier et al., 2001; Haase et al., 2011). Reviews have indicated that the parahippocampal gyrus may be involved in energy regulation (Davidson et al., 2007; Tracy et al., 2001). Furthermore, this area has been associated with emotional memory coding and especially when modulated by arousal (Kensinger and Corkin, 2004; Kilpatrick and Cahill, 2003; LaBar and Cabeza, 2006). Future research should elucidate the role of this area in the emotional response to chemosensory perception.

6.4.6 Limitations
For the ONS stimuli we were unable to find a relation between flavor pleasantness and the ventral emotion network. This may be caused by multiple limiting factors within this study. First, the experiment was not optimized to reliably evoke pleasantness as well as disgust within each participant. Consequently, the current study suffers from measurement sensitivity with respect to whole pleasantness range. Second, we showed that pleasantness ratings
decreased during the course of the experiment in the ONS group, whereas we found no such effect in the regular products group. This result indicates that participants in the ONS group were different in their scoring behavior, which might be caused by the unfamiliarity of these products.

6.5 CONCLUSION

Using data-driven analysis we isolated the ventral emotion network in two datasets and examined its relation with flavor pleasantness. This network encompassed the amygdala, insula, ventral striatum and orbitofrontal cortex in the right hemisphere and the parahippocampal gyrus in the left hemisphere. The engagement of the ventral emotion network was associated with flavor pleasantness scores, which were rated 20 seconds after flavor administration. Most areas within the network showed a spatial segregation between pleasant and unpleasant flavor processing.