



Research Report

Sustained effects of pleasant and unpleasant smells on resting state brain activity



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ABSTRACT

Research suggests that transient emotional episodes produces sustained effects on psychological functions and brain activity during subsequent resting state. In this fMRI study we investigated whether transient emotions induced by smells could impact brain connectivity at rest in a valence-specific manner. The results suggest a sustained reconfiguration of parts of the default mode network which become more connected with areas implicated in olfactory processing, emotional learning, and action control. We found lingering effects of odorants on subsequent resting state that predominantly involved connections of the precuneus with a network comprising the insula, amygdala, medial orbital gyrus. Unpleasant smells in particular predicted greater coupling between insula, hippocampal structures, and prefrontal cortex, possible reflecting enhanced aversive learning and avoidance motivation. More broadly, our study illustrates a novel approach to characterize the impact of smells on brain function and differentiate the neural signatures of their valence, during task-free rest conditions.

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1. Introduction

Despite popular belief, human beings are astoundingly good at processing smells (Jönsson & Olsson, 2003). Most

particularly, we are able to rapidly assign an emotional value to a smell. When people are asked to describe odorants, valence-related words consistently come up, highlighting affect as a major dimension of smells (Khan et al., 2007; Zarzo, 2008). What's more, the valence of smells have extensive

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influences on behavioural and cognitive processes, from learning through to attention and motivation (Villemure, Slotnick, & Bushnell, 2003). For example, participants who dislike an odor show a worsened mood and increased perception of pain unpleasantness after smelling it (Villemure, Slotnick, & Bushnell 2003). Unpleasant smells have also been linked to altered memory recall, and quicker reaction times (Bensafi, 2002; Ehrlichman & Halpern, 1988). Smells that participants rate as being pleasant have been demonstrated to improve mood and decrease anxiety (Lehrner, Eckersberger, Walla, Pötsch, & Deecke, 2000; Rétiveau, Chambers IV, & Milliken, 2004), in addition to making them feel more alert and attentive (Heuberger, Hongratanaworakit, & Buchbauer, 2006). The reason why smells have strong effects on memory retrieval and emotion is thought to be in part due to the physiology of olfactory processing (Gottfried, Deichmann, Winston, & Dolan, 2002). Odorants bind to receptors of olfactory sensory neurons, which project to the olfactory bulb and from there directly connect to a range of areas in the medial temporal and basal frontal lobe (often referred to as the primary olfactory cortex). These include the piriform cortex and amygdala (Gottfried, 2010), both intimately linked to emotion and memory functions. From the primary olfactory cortex, there are further connections to the insula, hypothalamus, orbitofrontal cortex, hippocampus, striatum, and perirhinal cortex (Gottfried, 2010). Thus, there is an exceptionally close overlap between olfactory processing areas and circuits implicated in emotion, motivation, and memory. In particular, the orbitofrontal cortex is critically involved in the processing of olfactory valence (Anderson et al., 2003; Chikazoe, Lee, Kriegeskorte, & Anderson, 2014). The amygdala also plays a central role in processing the valence of smells, though its recruitment may differ depending on both the subjective pleasantness and intensity of odorants (Anderson et al., 2003; Winston, Gottfried, Kilner, & Dolan, 2005). While some areas have been found to show distinct activation patterns for positive vs negative valence (e.g., amygdala, Anderson et al. (2003); Winston, Gottfried, Kilner, & Dolan (2005); Jin, Zelano, Gottfried and Mohanty (2015); Fournel, Ferdenzi, Sezille, Rouby and Bensafi (2016); Sela et al., 2009), overall there is substantial anatomical overlap of limbic responses regardless of this affective dimension (Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012). However, as described above, smells can produce differential effects on behavior, cognitive function, and mood, according to their valence. These effects may occur through the modulation of neural circuits responding to the affective value of smells via connections from limbic to other brain networks. Further, these valence-related effects may arise in a sustained manner in order to differentially influence cognitive and motivational processes following exposure to pleasant or unpleasant odors. Here we specifically set out to determine whether, and how, odor valence might modify brain activity patterns in a way that outlast the olfactory input itself and persist even during resting conditions. Recent observations in neuroscience have suggested that transient emotional events can produce sustained neural changes with valence-dependent effects, which may affect spontaneous brain activity and connectivity at rest. Abundant neuroimaging work has shown that when

people lie quietly and rest, distinct brain areas spontaneously become active, forming what has been called a “default mode network” (DMN; Greicius, Krasnow, Reiss and Menon (2003)). Conversely, these areas often become deactivated during goal-directed tasks. Such activation at rest is thought to correspond with task-independent introspection such as daydreaming and self-related focus, gouging other peoples’ perspectives and contextual information, as well as retrieving personal memories (Buckner & Carroll, 2007). However, activation in the DMN may vary according to the difficulty or nature of a preceding cognitive activity (Buckner et al., 2008). Particular states of mood can also impact on resting state activity and associated ruminative thinking (Piguet et al., 2014). Further, transient emotions induced through watching joyful, fearful, or neutral movies produce lasting changes in the DMN and other emotion-related networks active at rest, most particularly connections between the insula, thalamus, anterior and posterior cingulate cortices, and the precuneus (Eryilmaz, Van De Ville, Schwartz, & Vuilleumier, 2011). Similar results have been found using music (Harrison et al., 2008) and games (Eryilmaz et al., 2014) as a way to induce various emotions. Moreover, transient emotional episodes have been demonstrated to affect how people subsequently process sensory stimuli and behave, with various cognitive, affective, or mnemonic biases arising after emotion elicitation. For example, after viewing negative movie clips, participants are more likely to rate a neutral face as being fearful, while after viewing positive faces, they are more likely to rate an ambiguous face as being happy (Qiao-Tasserit et al., 2017). Pain experienced by oneself or viewed in others is also modulated by transient emotional episodes (Qiao-Tasserit, Corradi-Dell’Acqua, & Vuilleumier, 2018). Given the strong anatomical and functional links between smells and emotions, and their putative role in inducing behavioural changes, we tested whether smells could also evoke powerful lingering effects on brain activity subsequent to odorant exposure, persisting even during resting state when participants have no task to perform. Measuring how pleasant vs unpleasant smells alter network connectivity during rest may give us a valuable indication as to how they differently affect our motivations and moods, as well as subsequent cognitive processes and behavioural performances. The current study therefore used fMRI during both olfactory processing and subsequent resting in order to pinpoint any lasting effects of smells on affect and brain connectivity, and any differential impact according to the valence of these smells.

2. Methods and materials

We report how we determined our sample size, all data exclusions, all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, and all manipulations in the study. Note that we do not report all measures. In particular, we obtained measures of the familiarity participants have with the smell, their state and trait anxiety scores, and an SWI anatomical image of each participant. These measures are not reported because they were not variables of interest in the current study.

2.1. Participants

Twenty students (10 female) of the University of Geneva between the ages of 18–35 ($M = 23.70$, $SD = 3.52$) were recruited on a voluntary basis using flyers and word of mouth. Participants were right-handed, self-reported a normal sense of smell, and free of any psychiatric or neurological history. Participants were instructed not to eat or drink anything 2 h before the study. Participants were compensated 50 chf for their time. The study was approved by the local ethics committee (*Commission central d'éthique de la recherche sur l'être humain des HUG [Central commission of ethics in research on human beings of the University Hospital of Geneva]*) and conducted according to the declaration of Helsinki. Sample size was selected based off of previous studies using wavelet analyses, (Eryilmaz et al., 2014, Eryilmaz, Van De Ville, Schwartz, & Vuilleumier, 2011) and standard guidelines in the field (Friston et al., 1999).

2.2. Procedure

Participants came on two separate days, with one day consisting of only pleasant and no odor conditions, and the other day the unpleasant and no odor conditions. The order in which participants received this was pseudo-randomized across participants. The experiment comprised of 8 experimental runs, 4 on each day (see Fig. 1 for a visualization of the timeline). The procedure for each day, regardless of smell content, was otherwise identical. The 4 runs occurred in the order of No Odor–Smell–Smell–No Odor. One run consisted of 5 repetitions, with each repetition using one specific smell (see Stimuli). The order of the smells was pseudo-randomized for each participant. One smell was presented for a total of 45 s in a trial, where every 15 s a short break would occur, allowing participants to rate the perceived concentration of the smell on a three point scale with answers being 'low' 'medium' or 'high'. After the smell, participants were asked to rate on sliding scales from 0 to 100 how pleasant and then how

intense the smell was, 0 being not at all, to 100 being extremely. Following these questions, participants were instructed to close their eyes and let their thoughts wander for a 90 s resting state period. The screen would briefly flash at the end of the resting state to signal participants to open their eyes again. For 50% of the trials, participants were asked to state what they had been thinking about during the resting state, with answers either being: 1–thoughts provoked by the smell; 2–personal life; 3–the actual environment, like the noise or the MRI; 4–struggle against sleep. Each repetition took between 3 and 4 min to complete. Onset times, responses, and response times were collected using Matlab. Before and after the experiment on each day, participants were asked to complete the PANAS-X. At the beginning of the experiment, participants were asked to sign a consent form and undergo an MRI compatibility check.

2.3. Stimuli

A total of 15 different odors were used initially, each one provided by Firmenich S.A. and selected for having a similar rated intensity. These odors were then validated in a preliminary study in which ten volunteers rated the pleasantness and intensity elicited from each smell on a scale from 1 to 10 (see appendix, table 2 for a list of the smells used, and their intensity and pleasantness values). In order to ensure consistent ratings across participants, the 5 most pleasant and 5 most unpleasant stimuli were selected to be used in the study. In addition, air flow from the olfactometer was used in place of a neutral stimulus (no odor condition). This was motivated by the high personal idiosyncrasies between participant preferences that make it almost impossible to define a smell as being 'neutral' across different people, as well as the general scarcity of low emotion (i.e., neutral) ratings for odors in general. Therefore, to avoid unwanted variability in the control condition, we opted for a 'true' neutral experience with odorless air and confirmed this yielded consistent 'neutral' ratings by participants (see results). The

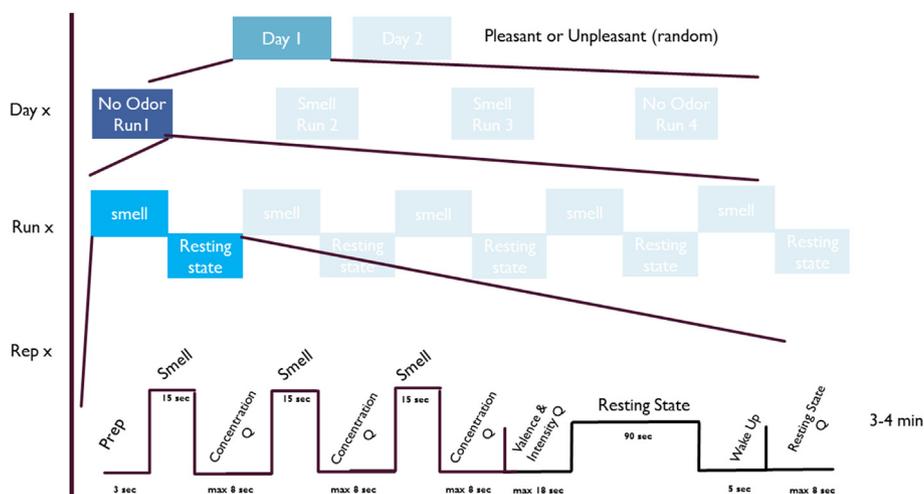


Fig. 1 – Visualization of the study procedure. Each smell run began with a 3 s countdown, followed by the smell. There were small breaks between the smell to test participants' habituation. Participants indicated the intensity and valence of the smell, and then had a 90 s resting period, followed by a flashing screen designed to reorient their attention, and a forced choice question where they had to indicate the content of their thoughts.

Table 1 – Smells used in the preliminary study. Mean and standard deviations for Intensity and Pleasantness are shown for each smell. These smells were rated by 10 volunteers not involved in the study using a continuous scale from 1 to 10, 10 indicating ‘very’ and 1 ‘not at all’.

Smell and Concentration	Pleasantness		Intensity	
	Run1	Run2	Run1	Run2
Unpleasant				
Dimethyl Trisulphate (DMTS) 100 ppm	29.94 ± 18.72	27.40 ± 19.24	68.05 ± 16.65	62.35 ± 20.53
Butyric acid 1%	35.66 ± 19.75	38.04 ± 13.88	54.84 ± 20.07	50.44 ± 23.24
Isovaleric acid 1%	34.40 ± 20.29	32.04 ± 15.12	60.78 ± 19.03	58.64 ± 17.06
Fecal 50 ppm	42.43 ± 15.23	34.03 ± 19.39	44.80 ± 25.11	7.3 ± 20.53
Ghee 5%	35.76 ± 17.54	59.30 ± 19.09	39.25 ± 17.51	57.51 ± 22.45
Pleasant				
Menthone 5%	60.28 ± 20.73	65.85 ± 19.28	69.50 ± 14.57	68.89 ± 19.45
Ariana (Classic shampoo fragrance) 1%	71.05 ± 18.15	74.88 ± 17.51	58.88 ± 16.25	54.19 ± 21.84
Lavender 10%	64.87 ± 19.23	66.97 ± 19.87	60.56 ± 12.54	60.87 ± 12.76
Strawberry 20%	66.57 ± 17.71	62.85 ± 17.71	61.96 ± 17.13	59.35 ± 15.17
Caramel 20%	59.67 ± 16.37	62.27 ± 16.17	56.75 ± 19.67	57.10 ± 15.88

Table 2 – Mean and standard error mean of intensity and pleasantness scores are shown for each smell type. There were 5 different smells used each for pleasant and unpleasant odors. Each smell was rated twice.

Valence	Pleasantness	Intensity
Unpleasant	35.13 ± 7.23	55.33 ± 21.87
Pleasant	65.53 ± 18.60	60.81 ± 17.06
No Odor (Unpleasant day)	49.76 ± 6.49	14.43 ± 20.94
No Odor (Pleasant day)	49.15 ± 7.23	12.17 ± 18.80

mean rating values for all odors used in the study (their intensity and pleasantness) are presented in [Table 2](#).

2.4. Stimuli presentation

2.4.1. Olfactometer

Odors were delivered by an MRI-compatible olfactometer ([Ischer et al., 2014](#)). Odor-containing glass tubes were placed on a plastic support in the MRI acquisition room close to the participant. Odors were connected to a tube which was attached to an intranasal cannula. Each glass vial was pressure fed by a computer controlled air valve, which was switched on and off to send different odorant stimuli. During the neutral, no-odor, condition extra inter-stimulus air vales sent clear air to the nose. The system was connected to a separate air supply of the building and enabled a constant clean delivery of air, with no detectable flow variation when an odor was sent.

2.5. Data acquisition

2.5.1. Physiological recordings

Respiratory activity and heart rate was recorded (1000 Hz sampling frequency) using the Biopac Systems Inc. data acquisition system (MP150). Heart rate was measured using a TSD200-MRI plethysmograph (BIOPAC Systems Inc, CA, USA) attached on the distal phalanx of the ring finger of the left

hand and connected to a PPG100C-MRI amplifier (BIOPAC Systems Inc, CA, USA; gain: 100, low-pass filter: 10Hz, high-pass filter: 0.5Hz). The respiratory activity was recorded through a 2.5 mm tube (interior diameter), taped on the metal nasal tip used to deliver nasal stimulation and connected to a differential pressure transducer (Biopac TSD160A) to continuously record variations in nostril airflow ([Johnson, Russell, Khan, & Sobel, 2006](#)).

2.5.2. fMRI

Structural images were acquired with a T1-weighted 3D sequence (TR/TI/TE: 1900/900/2.27 ms, flip angle = 9°, field of view = 256 mm, PAT factor = 2, voxel dimensions: 1 mm, isotropic 256 × 256 × 192 voxel). Functional images were acquired by using a standard echo planar imaging sequence (TR/TE: 2000/20 ms, flip angle = 80°, voxel size: 3.0 × 3.0 × 2.5 mm³, 0.8 mm slice spacing, 40 slices, 64 × 64 base resolution, field of view = 192 mm). For each participant, we acquired a mean of 2011.78 volumes per session (around 500 volumes per run, amounting to around 4000 in total for each participant). Scans were oriented to the anterior and posterior commissure, and then rotated twenty degrees to ensure proper coverage of the frontal areas of the brain.

3. Analysis

3.1. Behavioural data analysis

The responses to pleasantness and intensity were entered in separate 4 × 2 repeated measures ANOVA for smell type (pleasant, unpleasant, air (no odor) on the pleasant day, no odor on the unpleasant day), and run (one, two). The percentage of responses for each of post-resting state thought content options were calculated and a repeated measures ANOVA was performed on the number of responses for each option with smell type (4 levels) and thought content (4 levels) as the main factors of interest. The PANAS-X responses were used to calculate a positive affect and negative affect score for before and after the study, and the differences between these scores before and after were calculated.

3.2. MRI data preprocessing

fMRI data pre-processing was done according to standard procedures using SPM (version 12; <http://www.fil.ion.ucl.ac.uk/spm/>). All functional images were realigned to the first image, then corrected for slice timing, normalized to the MNI template ($3 \times 3 \times 3$ mm voxel size) and smoothed using an 8 mm (FWHM) kernel. All anatomical images were also normalized to MNI template with a voxel size of $1 \times 1 \times 1$ mm.

3.3. Physiology preprocessing

Respiration and cardiac measures were down sampled to 120Hz and then pre-processed using a comb pass filter (40 slices/2000 ms), and a bandpass FIR filter between .05Hz and 1 Hz. The heart and respiration rates were calculated and the measures were then analyzed according to the RETROICOR method (Glover, Li, & Ress, 2000). A 2nd order Fourier expansion was used to estimate the phase for both cardiac and respiration responses. Respiration volume per time (RVT) and heart rate (HRT) time courses were calculated (RVT: Birn, Smith, Jones and Bandettini (2008); HRT: Chang, Cunningham and Glover (2009)). These were used as nuisance regressors to filter out respiration and cardiac induced noise (see General Linear Model).

3.4. General linear model

Pre-processed fMRI data were first analyzed using the General Linear Model provided in SPM 12 software (<http://www.fil.ion.ucl.ac.uk/spm/>). For each individual participant a design matrix was constructed, containing regressors for the first 2 s participants received the smell, and a different regressor for the next 13 s for every single smell block (neural habituation to odors occurs very quickly in humans, Pellegrino, Sinding, De Wijk and Hummel (2017)). Regressors were added for resting state, periods corresponding to questions, and to variables of non interest (the flashing light of the resting state wake up, the countdown to receiving a smell, and pauses between question periods). The realignment parameters as well as their derivatives were added to account for movement confounds. Due to the extended length of the stimuli presentation, data were low-pass filtered using a cut-off of 1/256 Hz. Because the lower cut-off is less stringent in filtering out physiological nuisance effects, RETROICOR regressors as well as RVT and HRT were included as nuisance regressors (see physiology pre-processing).

For each participant, condition specific effects were estimated according to the general linear model by creating contrast images of each condition (pleasant, unpleasant, their respective no odor counterparts, and resting state periods). In addition, we created contrast images for each of the following statistical comparisons. Main effects of smell were identified by comparing valenced (pleasant + unpleasant) with no odor conditions. Finally, to identify regions generally involved in processing smells, we compared valenced smell conditions with the resting state period. To allow for random effects analyses and inferences at the population level, these contrast images were entered in second-level one-sample t-tests.

Unless stated otherwise, we report activations at the cluster level, using a height threshold of $p < .001$ and reporting cluster $p < .05$ corrected for multiple comparisons (family-wise error rate) based on Gaussian Random Field theory within the entire brain.

3.5. Connectivity analyses

The peak cluster activation in the different comparisons were used to determine the regions of interest (ROIs) for the resting state connectivity analyses (note that we did not use activation comparing resting state conditions against each other to determine the ROIs to avoid double-dipping issues). In total, 27 ROIs were extracted, using spheres of 8 mm (see Table 3).

We computed normalized correlations between regions of interest (ROIs) by extracting the time courses corresponding to conditions of interest for all ROIs. The conditions of interest were the resting state conditions following either the pleasant, unpleasant, or no odor conditions. There were six conditions of interest in total: the resting state post pleasant odor contrasted with its no-odor counterpart, the resting state post unpleasant odor contrasted with its no-odor counterpart, and the resting state post pleasant and unpleasant odors directly compared against each other.

Following related studies, we used an orthogonal cubic B-spline wavelet transform in the temporal domain Eryilmaz et al. (2014), Eryilmaz, Van De Ville, Schwartz, & Vuilleumier (2011), Richiardi et al. (2011) to decompose regional brain activity into different frequency bands. It is argued that this method is a more useful way of examining quick, transient changes in brain states than other methods because of its ability to preserve signal shape Wiltschko, Gage and Berke (2008). The wavelet transform separated the extracted signal in to 4 bands: i) .125–.25 ii) .0625–.125 iii) .03125–.0625 iv) .015625–.03125, with bands 3–4 being of interest as frequencies much higher than .1 Hz tend to pertain to respiration and other types of noise Eryilmaz et al. (2014).

We then computed the correlations between the wavelet coefficients of a particular sub-band with the ROIs, creating a set of correlation matrices for each condition of interest, for each wavelet band, for each subject. In order to test for differences between two resting conditions (e.g.; post pleasant > post no odor), we subtracted one of the matrices from the other and a t-test was done. The correlation matrices were then compared by non-parametric permutation testing Nichols and Holmes (2003). We re-sampled 5000 times to get a reliable estimate of the distribution in order to reject the null hypothesis. The resulting t values were then converted to z scores and compared to the initial t value. All p values less than .005 were considered significant and reported Benjamin et al. (2018).

3.6. Random forest

In order to evaluate to what extent the connectivity results were accurate reflections of the differences in connectivity between pleasant and unpleasant smells, we performed a Random Forest on the different connectivity matrices. The Random Forest used the different connectivity values to predict whether the condition was Pleasant > No Odor, or

Table 3 – ROIs selected as being of interest due to being an area of peak voxel activation on the SPM GLM. Presented are the area names, side of brain and coordinates, contrast selected from, and their corresponding Z score.

Contrast	Region Label	Coordinates			Z-Score	
		x	y	Z		
Smell > Resting	Angular Gyrus	–38	–52	38	7.82	
	Angular Gyrus	38	–56	44	6.96	
	Supplementary motor cortex	6	22	50	8.08	
	Dorsolateral Prefrontal Cortex	48	44	14	9.24	
	Insula	–40	–2	0	5.66	
	Insula	38	6	–8	5.47	
	Precuneus	–10	–70	42	6.96	
	Precuneus	14	–62	38	6.96	
	Posterior Cingulate Cortex	8	–29	22	6.96	
	Posterior Cingulate Cortex	–8	–34	13	6.96	
	Resting > Smell	Medial Prefrontal Cortex	8	50	14	4.41
Dorsolateral Prefrontal Cortex		–22	26	40	4.5	
Hippocampus		28	–20	–18	3.78	
Parahippocampal Gyrus		32	–34	–14	9.41	
Parahippocampal Gyrus		–30	–40	–16	8.34	
Hippocampus		–28	–30	–21	3.52	
Anterior Cingulate Cortex		–9	31	9	3.36	
Anterior Cingulate Cortex		4	22	–18	5.40	
Medial Prefrontal Cortex		–14	62	16	3.49	
Smell > No Odor		Medial Orbital Gyrus	–24	32	–16	6.59
		Medial Orbital Gyrus	22	28	–16	5.94
	Piriform Cortex	–28	8	–20	3.42	
	Piriform Cortex	28	2	–20	4.06	
Pleasant Smell > No Odor	Thalamus	–4	–6	8	3.47	
	Thalamus	4	–8	8	5.75	
Unpleasant Smell > No Odor	Amygdala	–20	–2	–20	4.44	
	Amygdala	16	–4	–16	6.05	

Unpleasant > No Odor. The R Random Forests package was used to classify the data [Liaw and Wiener \(2002\)](#). In this classification, the square root of the number of features (the number of connections) was split at each node, and 5000 trees were grown by bootstrapping the features with replacement. The out of bag estimate of error rate and area under the curve were calculated to determine the accuracy of the prediction (for an explanation of Random Forests and their implementation, see [Liaw and Wiener \(2002\)](#) or [Breiman \(2001\)](#)). The Random Forest is an ensemble of decision tree classifiers that has multiple levels of randomization; each tree is grown using a random subset of the data—each tree is independent from the other ([Breiman, 2001](#)). What’s more, each node in the tree is constructed using a random subset of features. Random Forests give a score for each feature, known as Gini Importance, which summarizes the discriminative power of the feature. The randomization over subjects improves the generalization accuracy, while the randomization over features increases the likelihood of identifying all the functional connections useful for group discrimination (hard to do with features that are highly correlated).

4. Results

In order to observe the lingering effects of smells on resting state, participants were presented with ten different smells (5 unpleasant, 5 pleasant, and a no odor/air only condition). They would smell one of these smells for three 15 s periods,

with small breaks in between during which they were asked to rate certain properties of the smell. Following this, participants were asked to let their thoughts wander for a resting state, after upon which the experiment would repeat with a different smell. Each smell was presented twice, with unpleasant and pleasant smells being given to participants on two separate days.

4.1. Behavioural

After each smell, participants were asked to rate the pleasantness and intensity of the perceived odor using a scale from 0 to 100 for valence (very unpleasant/very pleasant) and intensity (not perceptible/very intense). Participants received each odor twice over two different runs. Subjective pleasantness and intensity ratings of ten different odors were analysed separately using 4×2 repeated measures ANOVA for smell type (pleasant, unpleasant, air-only (no odor) on in the pleasant session, air-only on the unpleasant session), and run within in each session (one, two). Results are shown in [Fig. 1](#), means and standard error of the mean in [Table 1](#).

4.1.1. Pleasantness

Mauchly’s test indicated that the assumption of sphericity had been violated [$\chi^2(5) = .066, p < .001$], therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\epsilon = .53$). There was a significant main effect of smell type for pleasantness rating, [$F(3,19) = 48.772, p < .001, \eta_p^2 = .72$], but no significant effect of runs

[$F(1,57) = .002, p = .97, \eta_p^2 .001$], so the pleasantness ratings of smells stayed consistent. Post hoc pairwise comparisons using Bonferroni correction also suggested that pleasantness ratings were not different between the two no-odor conditions [$t(18) = 1.21, p = .99$]. Importantly, as expected, ratings were significantly higher for pleasant smells than for unpleasant smells [$t(18) = 8.07, p < .001$], the pleasant smells were significantly higher than their no odor condition ratings, and the unpleasant smells were significantly lower than their respective no odor condition ($t(18) = 6.46, p < .001$). These ratings are consistent with the predefined valence categories based on the pilot results from a different group of volunteers.

4.1.2. Intensity

Mauchly's test indicated that the assumption of sphericity had been violated [$\chi^2(5) = 28.90, p < .001$], therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\epsilon = .52$). An ANOVA found a significant main effect of smell type [$F(3,19) = 78.45, p < .001, \eta_p^2 = .805$], but not of runs [$F(1,57) = 1.72, p = .20, \eta_p^2 = .08$]. Post-hoc pairwise comparisons using Bonferroni correction showed that the unpleasant and pleasant intensity ratings were not significantly different from each other [$t(18) = 1.99, p = .37$], nor were the two no odor intensity ratings [$t(18) = 1.19, p = .99$]. Pleasant and unpleasant smells were rated as being higher in intensity than no odor conditions ($t(18) = 10.24, p < .001$ and $t(18) = 8.18, p < .001$, respectively). See Fig 2 for a visualization of the mean pleasantness and intensity results.

4.1.3. Resting state period

On half of the odor stimulation blocks, after the resting period, the participants were asked to classify their predominant mental activity during the immediately preceding 90 s of rest by choosing from four options: i) thoughts

related to the smell, ii) personal issues, iii) experiment environment, such as the noise of the MRI, and iv) struggle against sleep. A repeated measures ANOVA was performed on the number of responses for each option with smell type (4 levels) and thought content (4 levels) as the main factors of interest. Mauchly's test indicated that the assumption of sphericity had been violated [$\chi^2(5) = 18.89, p = .002$], therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\epsilon = .60$). There was a main effect of thought content, [$F(3,57) = 6.05, p = .007, \eta_p^2 = .24$], but no main effect of smell, [$F(3,57) = .39, p = .75, \eta_p^2 = .20$], nor an interaction between the two [$F(9,171) = .81, p = .61, \eta_p^2 = .04$]. Post hoc pairwise comparisons showed that participants answered 'smell content' and 'personal problems' significantly higher than 'scanner noise' and 'sleepiness' [smell content: $t = 1.71, p = .56$; personal problems: $t = 1.79, p = .56$; sleepiness: $t = 2.75, p = .068$] (Fig. 3). The data shows similar occurrences of these broad thought categories regardless of smells, greatly reducing the chances that any changes in brain activity patterns at rest could merely result from focusing on different mental contents across conditions.

4.1.4. PANAS-X questionnaire results

To evaluate changes in affective state, participants were asked to complete the PANAS-X questionnaire before and after each fMRI session. Differences between the pre- and post-experiment scores were calculated for the negative and positive affect questionnaires. Overall, participants rated themselves as feeling less positive after the negative smells ($M = -5.6; SEM = .24$) than after the positive ones ($M = -3.1; SEM = .33$, one tailed $t(19) = -1.88; p = .038$; cohen's $d = .44$, 90% CI [.03, .85]). No statistically significant results were found in the negative affect scores.

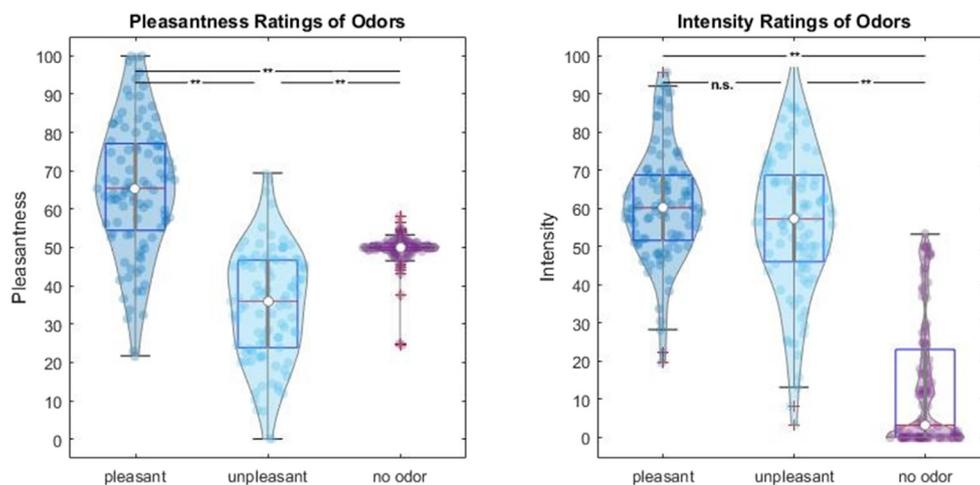


Fig. 2 – Distribution of participants' odor ratings for pleasantness (left panel) and intensity (right panel). The dots represent single data points, with the box plot representing the interquartile range of each distribution. The red line in the center represents the median. Each box-plot is surrounded by a violin plot representing the smoothed distribution of data. Significant differences ($p < .001$) are indicated with two stars. As there were no significant differences between runs, data was subsequently pooled across runs for all stimuli. For the no-odor condition, data for both days are presented together as they did not differ.

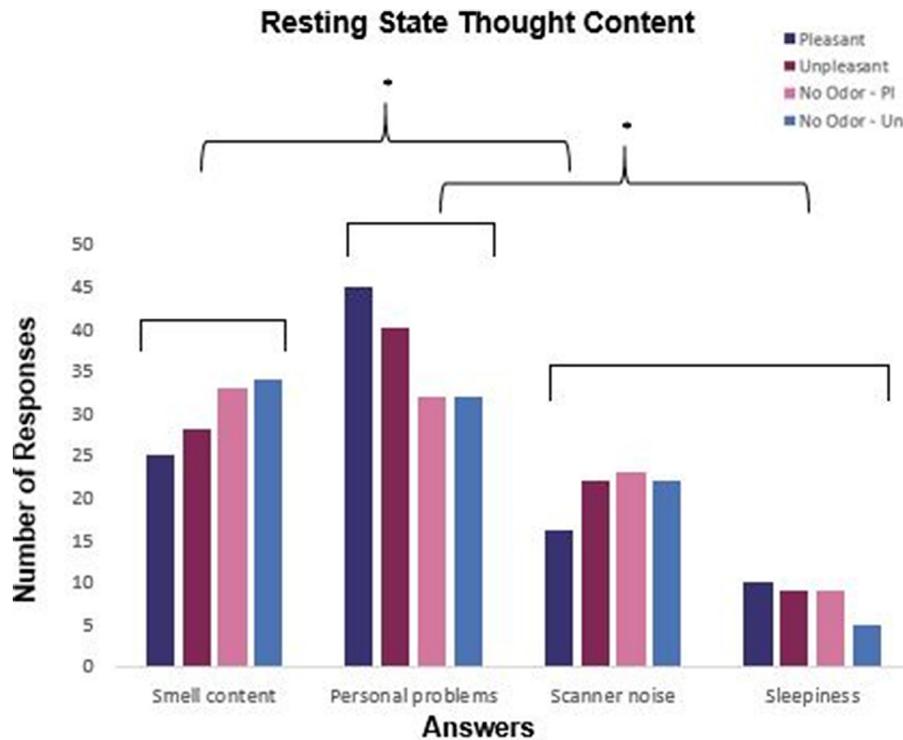


Fig. 3 – Content of predominant mental activity reported during fMRI after resting periods following pleasant, unpleasant, or no odor conditions. Thoughts about ‘personal problems’ were increased in all conditions, followed by thoughts related to the smells (‘smell content’). Significant differences ($p < .01$) are indicated with a star.

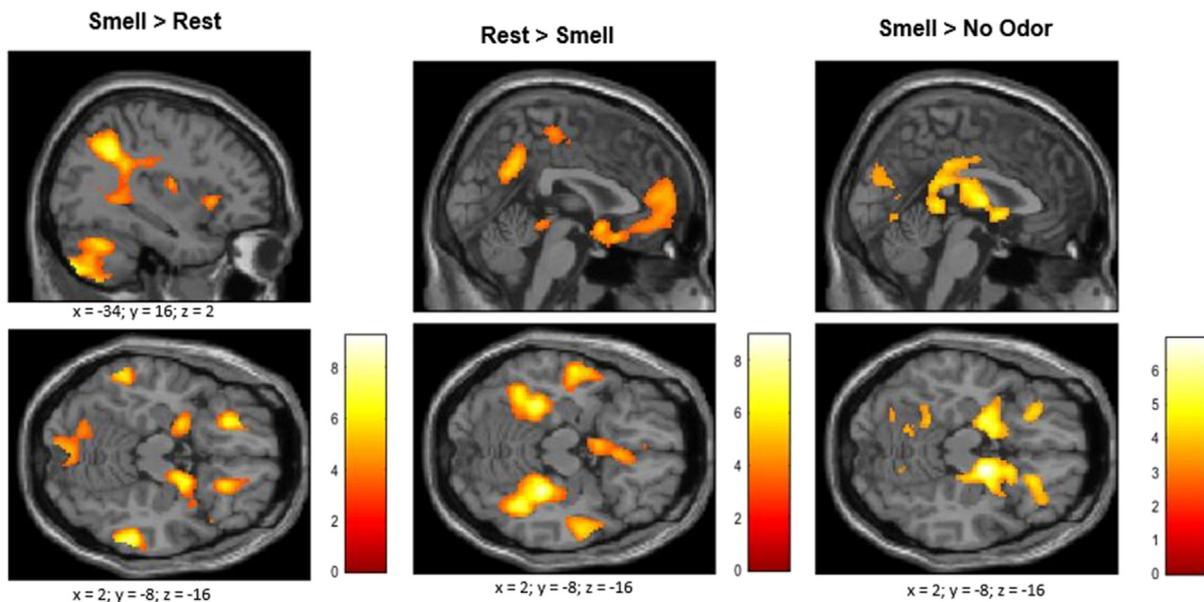


Fig. 4 – Significant main effects of smell and resting state conditions. Activations pertaining to the comparison between smell conditions and resting state periods are displayed on sagittal, axial, and coronal slices of a mean image created by averaging our subjects’ normalized structural images. Effects are displayed at $p < .05$ FWE at the cluster level using an auxiliary height threshold of $p = .001$ uncorrected. Colour bars represent the t-value range depicted in the images.

4.2. GLM results

4.2.1. Identification of brain areas involved in smell processing

To identify regions generally involved in smell processing, we compared smell stimulation blocks with resting state periods. This showed significant increases in activity in areas related to olfaction including clusters around the insula and the bilateral medial orbital gyri, the amygdala extending to the entorhinal cortex, but also cingulate cortex, premotor cortex, as well as somatosensory and visual areas (Fig. 4, left panels). The opposite comparison showed increased activity in brain regions typically reported as part of the default mode network (DMN), such as the precuneus, medial prefrontal cortex, parahippocampal gyrus, and inferior parietal areas (Fig. 4, right panels). Taken together, these large activation patterns across different areas demonstrate the engagement of widespread brain networks during and after odor perception (see Appendix 1, Table 3 for the locations and T values of major clusters).

4.2.2. Effect of valence

To identify regions responding to the valence of smells, we separately compared each valence condition (pleasant and unpleasant) against the no odor condition. This revealed differential activity mainly within the amygdala, hippocampus, striatum, and medial orbital gyrus (Fig. 5, left panel). Pleasant smells (Fig. 5, centre panel) showed activation spreading from the amygdala and medial orbital gyrus up to the ventral striatum, as well as pCC and thalamus. Unpleasant smells (Fig. 5, right panel) activated more restricted clusters around the amygdala spreading to the orbital gyrus and entorhinal cortex. Clusters and their T and p values are in Appendix 1,

Table 4. A direct comparison between pleasant against unpleasant smells (see Appendix 1, Fig. 1) had no significant activation, while the reverse comparison revealed a large cluster around the supplementary motor area.

4.3. Functional connectivity

To evaluate the lingering effects of smell valence on resting state connectivity at the network level, we selected 27 functional ROIs defined from the statistical comparisons obtained in our GLM analyses above. Relevant contrasts to delineate these ROIs are presented in Table 2. For each ROI, we extracted the time courses of activity during rest periods of the post-unpleasant, post-pleasant and post-no odor conditions (separately for each session). For each condition, we decomposed the time courses into different frequency bands using wavelet transforms and built correlation matrices by computing the Pearson correlation coefficient between the wavelet coefficients of different ROIs for two frequency range of interest (.03125–.0625 Hz and .015625–.03125 Hz sub-bands) corresponding to spontaneous fluctuations in resting state Eryilmaz et al. (2014). To identify changes in functional connectivity specific of each valence condition, we then directly compared the connectivity matrix of post-unpleasant and post-pleasant resting state periods with their post no odor counterparts, by subtracting the matrices from each other and running non-parametric statistical analyses on these subtracted matrices. Likewise, to identify differences in connectivity between the two valenced conditions, we compared post-unpleasant with post-pleasant connectivity patterns with corresponding subtractions. Because connectivity matrices are symmetrical, for illustrational purposes we collapsed in a single matrix the significant connection differences found for post-(un)pleasant > post-no odor and post-(un)pleasant ; post-no odor, as

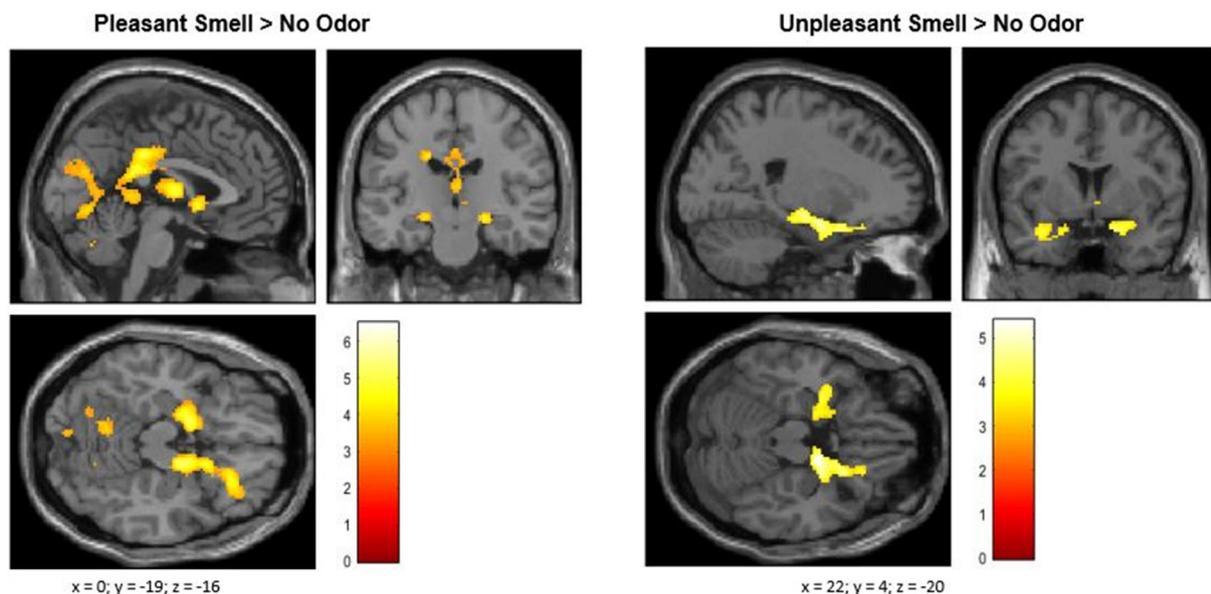


Fig. 5 – SPM group level t-tests examining the effect of smell valence. Both brains show significant activation in the left and right amygdala, as well as some of the orbital gyrus. Note that smells were only compared to neutral conditions which occurred on the same day.

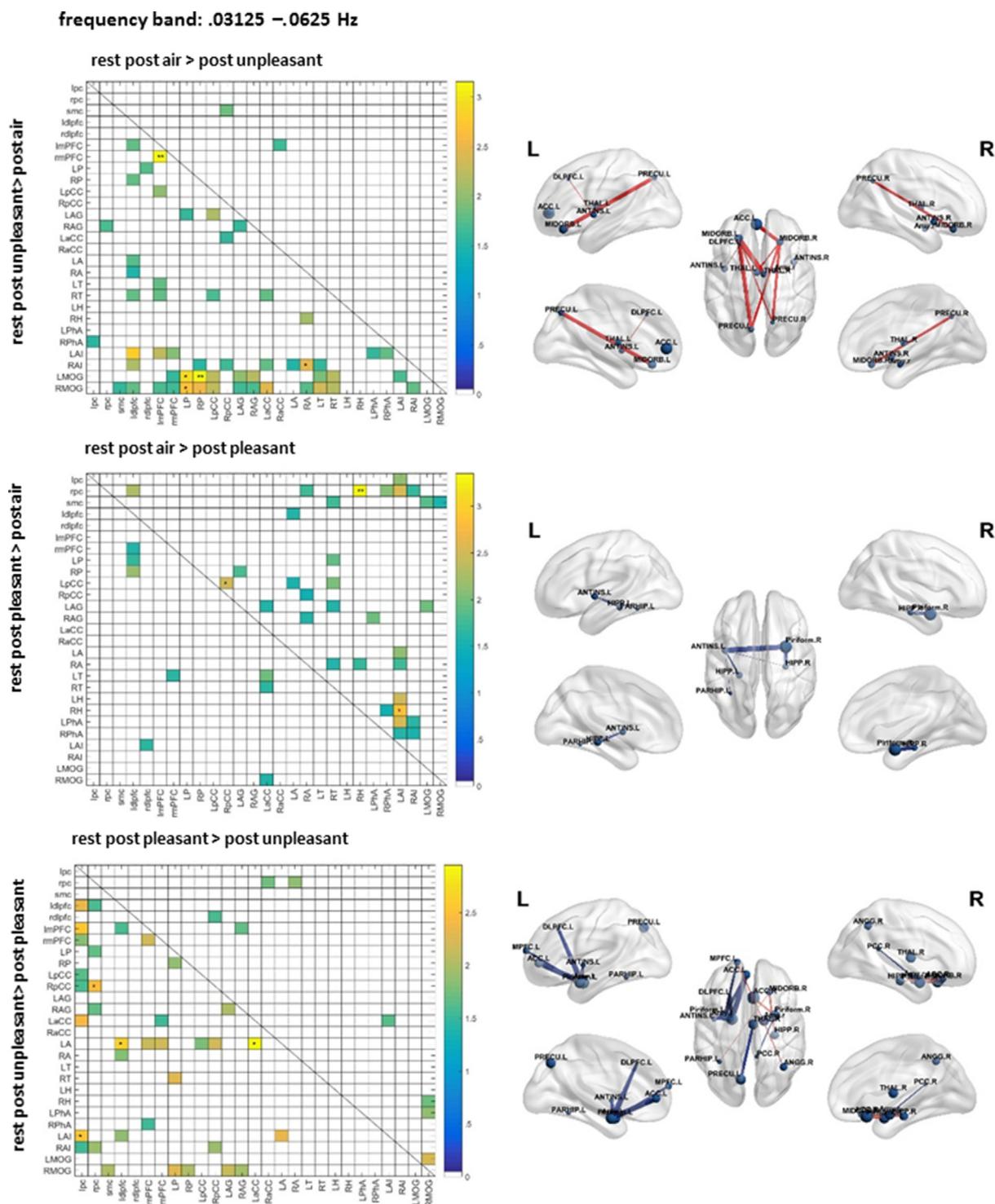


Fig. 6 – Correlation matrices between ROIs for different resting state conditions. * denotes $p < .05$ and ** $p < .001$. The top and bottom triangles of the matrices correspond to the reverse contrast (e.g.,: unpleasant > neutral and neutral > unpleasant). The colourbar corresponds to the z score—only values above a z score of 1 are shown. $z > 2$ is $p < .01$ one-tailed uncorrected, $z > 2.30$ is $p < .0005$ one-tailed uncorrected. See the appendix for a list of the abbreviations (Appendix, Table 1).

well as those for post-unpleasant ; post-pleasant and post-unpleasant > post-pleasant conditions (Figs. 6 and 7). The two frequencies sub-bands of interest showed partly different results and are presented separately below.

4.3.1. Correlation matrices

4.3.1.1. FASTER (.03125–.0625 Hz) SUB-BAND. The comparison of post-unpleasant and its post-air control condition in the first, faster sub-band showed significant increases in

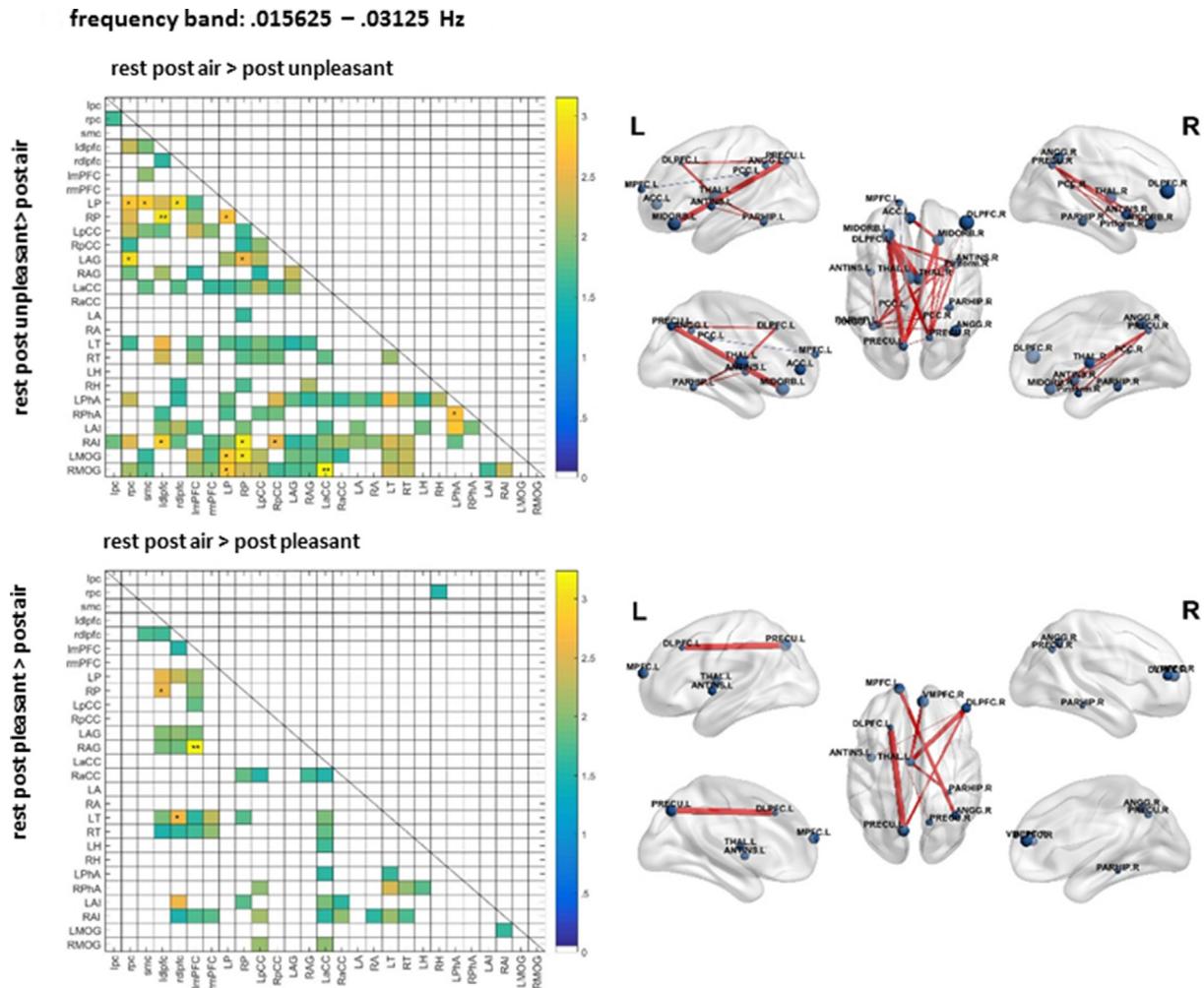


Fig. 7 – Correlation matrices between ROIs for different resting state conditions. * denotes $p < .01$ and ** $p < .001$. The top and bottom triangles of the matrices correspond to the reverse contrast (e.g.,: unpleasant > neutral and neutral > unpleasant). The colourbar corresponds to the z score—only values above a z score of 1 are shown. $z > 2$ is $p < .01$ one-tailed uncorrected, $z > 2.30$ is $p < .0005$ one-tailed uncorrected. See the appendix for a list of the abbreviations (Appendix, Table 1).

functional connectivity of both the left and right precuneus with the medial orbital gyrus following unpleasant odors (Fig. 6 upper panel), i.e., areas associated with the DMN and affective/motivational functions. There were also increases in connectivity between the left and right medial prefrontal cortex, left and right parahippocampal cortex, and between the right amygdala and insula (Fig. 5A upper panel). In contrast, following the pleasant odors, there was a decrease in connectivity between the right hippocampus and insula, the right hippocampus and right piriform cortex, and between the right and left PCC (Fig. 6 middle panel).

When directly comparing connectivity patterns from the post-unpleasant and post-pleasant resting state, significantly higher connectivity was also found between the left amygdala and both the left dlPFC and left aCC, between the right piriform cortex and right pCC, and between the left piriform cortex and left insula for the post-unpleasant condition (Fig. 6 lower panel). No significant results were found

in the inverse comparison (post-pleasant vs post-unpleasant).

4.3.1.2. SLOWER (.015625–.03125 Hz) SUB-BAND. In the second, slower sub-band of interest, for the unpleasant > no odor comparison, the precuneus again became a hub of higher connectivity with other brain areas. There were significant increases between the left precuneus and the right piriform cortex, bilateral medial orbital gyrus, right dlPFC, and supplementary motor area; while the right precuneus was more connected with the left medial orbital gyrus, right insula, left dlPFC, as well as the left precuneus. The left precuneus and right piriform cortex both were also more connected to the left angular gyrus, while the right insula was more connected with the right pCC and left dlPFC, in addition to right precuneus. Finally, the left ACC showed increased connectivity with medial orbital gyrus (Fig. 7 upper panel).

In this sub-band, the pleasant > no odor comparison exhibited higher connectivity between the precuneus and left

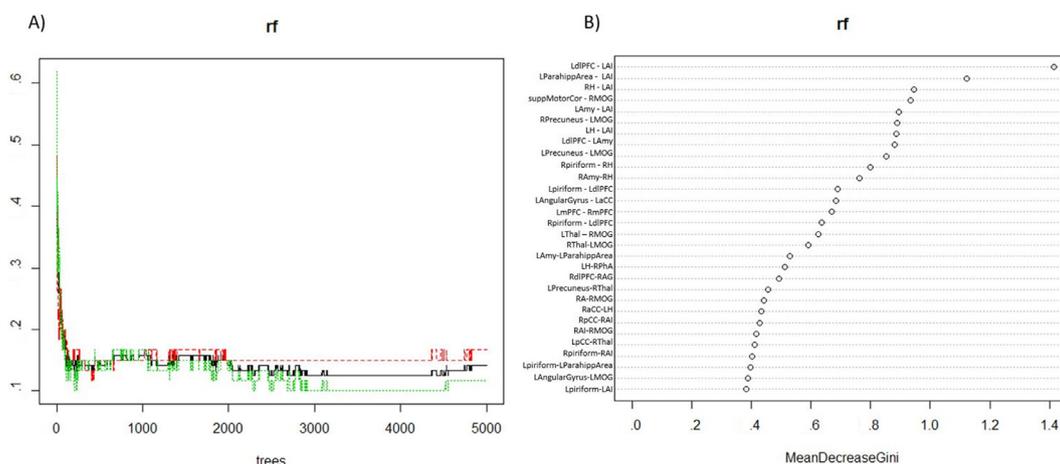


Fig. 8 – A) The percentage error for different numbers of trees. The black line represents out of bag error, the green line the error rate for Unpleasant classification, and the red line the error rate for Pleasant classification. B) The variable importance plot of the random forest. The mean decrease Gini index is determined using the out of bag error, where the more the accuracy of the random forest decreases due to the exclusion of the single variable, the more important that variable is rated. The most important variables are at the top of the graph.

dIPFC, the left thalamus and right dIPFC, and the right angular gyrus and left mPFC (Fig. 5B middle panel). Directly comparing the pleasant and unpleasant resting state conditions showed no significant changes meeting our corrected *p* value threshold (Fig. 7 lower panel).

4.4. Random forest results

To identify connections with the highest ability to distinguish the two valence conditions, we performed a classification analysis with Random Forest on connectivity matrices from all participants and the two sub-bands of interest, using the Pleasant > No Odor and the Unpleasant > No Odor comparisons as predictors. The out-of-bag estimate of error rate was 14.17%, the area under the curve was .9058, and Cohen's Kappa was .7167. The plotted error rate and the Gini scores of the most important variables are presented in Figure 8 (A and B, respectively; see the methods section for a more in-depth explanation of random forests). Within the top five most important connections, four of them were centered on the left insula and showed distinctive connectivity increases following unpleasant smells (Fig. 8 B). These included connections between the left insula and the left dIPFC, left parahippocampal area, right hippocampus, and left amygdala. The last most important connection in the top five was between the supplementary motor area and the left medial orbital gyrus.

5. Discussion

Because smells have been reported to produce strong effects on affect, behaviour, and memory, the current study asked whether and how the pleasantness or unpleasantness of smells could modulate brain activity patterns in a sustained manner during subsequent ninety seconds of rest. We found that the valence of smells significantly changed resting state

connectivity between several brain regions associated not only with the DMN but also with emotion, motivation, and action control. These longer-term neural effects add support to previous behavioural and physiological evidence for changes in mood and cognition after exposure to odors (e.g., (Bensafi, 2002; Herz & Inzlicht, 2002; Sarid & Zaccai, 2016)), and provide novel insight on the neurobiological substrates of such effects. Our findings also add to past research indicating that transient emotions caused by visually or auditory presented valenced stimuli (e.g., movies or music) can produce sustained effects on brain activity patterns (e.g., (Eryilmaz, Van De Ville, Schwartz, & Vuilleumier, 2011; Harrison et al., 2008)) showing these changes may arise through various sensory modalities (with some shared, and some distinct neural substrates). Furthermore, our Random Forest results revealed that the modulation of only a few relevant connections centred on the insula provided sufficient predictive information to distinguish between the two affective resting state conditions elicited by pleasant or unpleasant smells.

5.1. Differential effects of valence

Both positive and negative smells evoked changes in resting state networks when compared to the no-odor condition, but the patterns of activity were quite different. In general, functional connectivity in the faster frequency sub-band showed greater connectivity within the DMN and limbic circuits associated with affect and odor processing, including between the precuneus and the medial orbital gyrus, between the right insula and amygdala, and between the right and left mPFC. Further increases in connectivity during emotional conditions occurred in the slower sub-band linking the precuneus with areas implicated in odor perception and emotion, including piriform cortex as well as medial orbital gyrus and insula, and with areas implicated in action control and decision making such as SMA, aCC, dIPFC, amygdala, and insula. Thus, after

unpleasant smells, the precuneus, medial OFC, and insula became the most important hubs of connectivity and exhibited enhanced functional coupling with other distributed cortical areas. Increased connectivity was also observed between bilateral parahippocampal areas, a brain region associated with memory that is often active at rest (Buckner et al., 2008). The Random Forest classification analysis further highlighted that connectivity changes between the insula and several memory-related structures in medial temporal lobe (hippocampus and amygdala) as well as between medial orbital gyrus and SMA were the strongest predictors of smell valence. Taken together, the data appears to be consistent with the notion that negative smells may promote the formation of perceptual or mnemonic traces impacting on subsequent brain states which could mediate aversive learning and promote adaptive behaviors and action tendencies in terms of avoidance. However, the lack of behavioural data concerning participants' mood and thought content does not allow us to directly link these neural effects to specific behavioral or mental changes, and further work should be done to investigate these aspects. Previous studies have implicated the orbitofrontal cortex, insula, and amygdala in avoidance anticipation behaviour (e.g., (Bolstad et al., 2013; Liu et al., 2011; Ousdal, Reckless, Server, Andreassen, & Jensen, 2012)). The OFC and amygdala are reciprocally connected and crucially involved during emotional association learning (Bolstad et al., 2013). Activity in both the insula and ACC is thought to tag salient events for further processing (Menon & Uddin, 2010) and contribute to aversive learning and negative affect (Kuhnen & Knutson, 2005). The connectivity that we found between these regions at rest indicates a lingering effect of negative smells on brain activity that may hold or consolidate the sensory or memory trace of negative smells to subserve future avoidance. Detecting olfactory signals that indicate unpleasantness (and possible inedibility and danger to health) is crucial for survival in animals – and consistent with humans' ability to detect minute quantities of odors which signal the presence of potential hazards and capture attention (Stevenson, 2010).

Resting state after pleasant odors when compared to no-odor showed mainly decreases in connectivity between sensory and limbic areas in the faster frequency sub-band, most notably in areas implicated in smell processing (piriform cortex, insula) and memory (hippocampus). In the slower frequency band, the pleasant odors condition also increased functional connectivity between several areas within fronto-parietal cortices – including the precuneus, angular gyrus, mPFC, and dlPFC that were more connected with each other and with the thalamus. This network partly overlapped with the DMN but also comprised parts of cortical executive control networks and subcortical nodes in thalamus. The thalamus is a direct relay for information from primary sensory cortices for all senses except olfaction; however it does receive and send sensory information processed in primary and secondary olfactory areas through indirect connections with the orbitofrontal cortex and piriform cortex (Illig, 2005). The role of the thalamus in olfaction is still being debated, but it has been argued to be involved in coding the hedonic valence of smells (Zald & Pardo, 1997), attention capture by smells (Tham, Stevenson, & Miller, 2011), as well as odor-guided

behaviour (Alcaraz et al., 2016; Courtiol & Wilson, 2016). The increased connectivity of the thalamus with areas active during resting state would accord a role in behavioural and cognitive functions engaged by the processing of smells, possibly influencing action selection and attention control in dlPFC, but further studies are needed to better understand its role in olfaction. Speculatively, the connectivity pattern observed here with concomitant decreases in areas associated with memory and avoidance might suggest that positively valenced odors could balance inward and outward directed processing with reduced processing and learning of sensory information from recent olfactory stimuli but enhanced flexibility in attention orienting processes subserved by thalamo-fronto-parietal circuits.

5.2. Sub-band frequency

The current results also support previous literature suggesting that distinct patterns of connectivity can be seen in different frequency bands of spontaneous BOLD fluctuations at rest (e.g., (Eryilmaz, Van De Ville, Schwartz, & Vuilleumier, 2011)). Overall, the slower bands might reveal functional coupling between brain areas more specifically involved in rest, while faster bands reflect connectivity between areas related to more transient and stimulus-driven processing. Alternatively, this temporal dynamics might result from intrinsic functional differences of areas implicated in cognitive and emotional processing, or between different valence-specific states. In our study, the slower bands showed the strongest connections centered on the medial prefrontal areas and precuneus, both prominent parts of the default mode network. Conversely, faster bands involved connectivity to subcortical structures such as the amygdala and hippocampal region, as well as regions with more sensory-driven activity such as medial orbital gyrus and insula. It is also interesting to note that a similar frequency distinction was observed with stronger impact of positive (vs negative) affect on slower (vs faster) connectivity sub-bands in a previous fMRI study on modulation of resting state following transient emotional episodes induced by movie (Eryilmaz, Van De Ville, Schwartz, & Vuilleumier, 2011). However, the reliability and functional significance of such connectivity differences in relatively lower and faster sub-bands of resting activity remains to be determined.

5.2.1. Conclusions

Our study reveals a significant impact of smells in producing sustained changes in brain activity and connectivity patterns at rest, as well as distinctive effects due to their affective valence. Negative (vs no-odor) smells in particular had strong persistent influences on both the DMN and its interaction with brain circuits associated with emotion processing, avoidance motivation, and olfactory learning; whereas positive (vs no-odor) smells produced weaker and more restricted changes in fronto-parietal and thalamic areas putatively associated with attention. Remarkably, classification analysis using Random Forests allowed us to identify features of brain connectivity that reliably signalled odor valence. In particular, connectivity of the insula with the prefrontal cortex, amygdala, and hippocampal structures could discriminate the

impact of unpleasant from pleasant smells, in addition to changes in connection between DMN areas (most notably the precuneus) and regions implicated in emotional and olfactory processing, such as the orbitofrontal cortex, piriform cortex, and amygdala. More generally, our results accord with a defining characteristic of how humans perceive smells – that is, through their affective valence; as well as with a remarkable power of smells on behaviour – that is, their prolonged impact on mood and cognitive functions. However, there are other aspects of olfaction that may affect brain states and potentially the emotions and motivational states that they induce. The arousal response to smells is another key dimension that is typically processed separately from valence (Kaeppeler & Mueller, 2013) and also engages several limbic regions in the brain (Anders et al., 2004). Here arousal was equated between pleasant and unpleasant smells but it is possible that it could have a distinct impact on resting state connectivity by itself (Winston, Gottfried, Kilner, & Dolan, 2005). In addition, familiarity to smell is another important part of odor appraisal. It has been suggested that the processing of novelty and pleasantness of smells may occur sequentially (Delplanque et al., 2009), and novelty can affect how pleasant and intense the smell is perceived (Chrea et al., 2009). However, valence is a major feature of odor perception and our smells were selected to represent very strong instances of pleasant and unpleasant smells across participants, while familiarity may show greater variability across individuals, making it most likely that changes in brain activity and connectivity observed here were primarily driven by differences in valence, regardless of minor differences in familiarity. Nonetheless, even though our study employed smells with very consistent predefined valence, allowing us to compare positive and negative emotional effects across participants, the (un)pleasantness of some odors often may also show important inter-individual variability that would be interesting to explore as well in future studies. Having a wider spectrum of smells would not only allow for the examination of individual differences in valence processing, but also perhaps allow for the inclusion of an odor which could be used as a neutral smell in analyses.

Future research using a greater number and variety of smells will be necessary to tease apart these different dimensions of smell appraisal and better understand the mechanisms by which they affect brain activity and behaviour in both the immediate and long term. While we experience immediate effects of smells, their processing also produces longer-term changes, opening a new avenue of research on the sustained impact of smells on physiology, mental state, and behaviour, as well as the range and duration of such impacts.

Author contributions

Study conception and design: David Sander, Heather Carlson, Isabelle Cayeux, Sylvain Delplanque, Patrik Vuilleumier.

Acquisition of data: Heather Carlson, Joana Leitão, Sylvain Delplanque.

Analysis and interpretation of data: Heather Carlson, Joana Leitão, Patrik Vuilleumier.

Drafting of manuscript: Heather Carlson, Joana Leitão, Patrik Vuilleumier, Sylvain Delplanque.

Critical revision: David Sander, Isabelle Cayeux, Joana Leitão, Patrik Vuilleumier, Sylvain Delplanque.

Open practices

The study in this article earned an Open Materials badge for transparent practices. Materials for the study are available at <https://doi.org/10.26037/yareta:j7grynsytvhs5jrtghx6dtkk5jy>.

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Appendix

Abbreviations Used

Table 1 – Abbreviations used in the paper.

Abbreviation	Area Name
l	Left
r	Right
pc	Piriform cortex
smc	supplementary motor area
dlpfc	dorsolateral prefrontal cortex
mPFC	medial prefrontal cortex
P	precuneus
pCC	posterior cingulate cortex
AG	Angular gyrus
A/Amy	Amygdala
T/Thal	Thalamus
H/Hipp	hippocampus
Pha/Parahip	parahippocampal area
AI/Ant Ins	Insula
MOG	medial orbital gyrus

Initial Odor Ratings

Table 2 – Smells used in the preliminary study. Mean and standard deviations for Intensity and Pleasantness are shown for each smell. These smells were rated by 10 volunteers not involved in the study using a continuous scale from 1 to 10, 10 indicating ‘very’ and 1 ‘not at all’.

Smell and Concentration	Pleasantness	Intensity
Unpleasant		
OMTS 100 ppm	1.5 ± 1.08	7.3 ± 1.25
Butyric acid 1%	1.7 ± .95	5.3 ± 2.11
Isovalyric acid 1%	1.7 ± .67	6.8 ± 1.87
Fecal 50 ppm	1.8 ± .92	5.9 ± 2.23
Ghee 5%	1.6 ± .88	6.4 ± 1.56
Paracresol 1%	3.7 ± .95	4.4 ± 2.07
Sclarymol 2.5%	3.9 ± 2.23	4.0 ± 2.26
Indol 5%	4.0 ± 2.505	4.3 ± 2.06
Mean ± SD	2.11 ± .96	6.10 ± 1.92
Pleasant		
Menthone 5%	7.1 ± .88	6.9 ± 2.02
Ariana (Shampoo) 1%	7.9 ± 1.45	7.0 ± 1.41
Lavender 10%	7.1 ± 2.14	5.4 ± 1.51
Strawberry 20%	7.6 ± 1.89	6.0 ± 1.61
Caramel 20%	8.0 ± .96	7.0 ± 1.82
Caramel 10%	8.0 ± 1.00	7.0 ± 1.82
Lemon 5%	8.0 ± 1.45	7.0 ± 1.70
Zeskover (Mown Grass) 1%	8.0 ± 2.54	7.0 ± 2.04
Violets 3%	8.0 ± 1.49	7.0 ± 1.42
Mean ± SD	7.54 ± .43	6.46 ± .72

SPM GLM Results

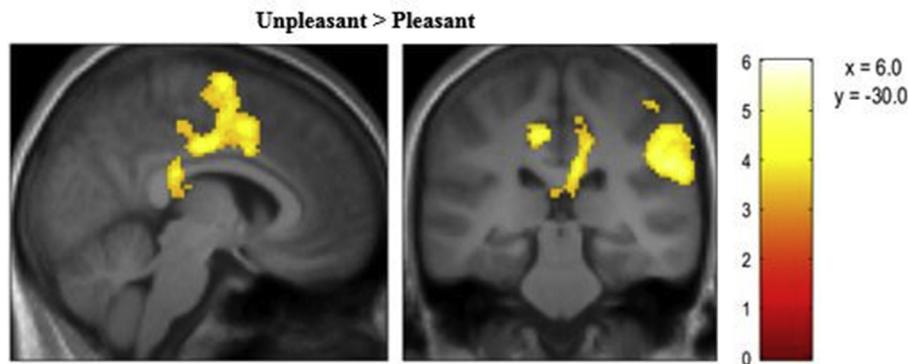


Fig. 1 – SPM group level t-tests examining the effects of the unpleasant > pleasant contrast. Activations pertaining to the comparison are displayed on sagittal and coronal slices of a mean image created by averaging the subjects’ normalized structural image. Effects are displayed at $p < .05$ FWE at the cluster level using an auxiliary height threshold of $p = .001$ uncorrected. Colour bars represent the t-value range depicted in the images. There were no significant results in the pleasant > unpleasant comparison.

Table 3 – Whole brain p-values for the main effects of interest.

Condition	Cluster-level		Peak-level		Mm			
	equiv-k	p(unc)	FWE-corr	T	x	Y	z	
Smell > Rest	10748	5.71E-34	.000	9.242945	48	44	14	
			.000	9.149807	48	48	6	
			7.14E-10	8.366229	40	36	18	
	17578	7.15E-47	.000	9.149455	40	-48	42	
			.000	9.096899	-4	-24	26	
			1.24E-09	8.273524	6	-24	26	
	637	8.84E-06	1.76E-09	8.214787	62	-40	-10	
			780	1.65E-06	1.44E-07	7.45225	-48	46
	1558	6.71E-10	.174566	4.446784	-48	32	28	
			1.09E-05	6.650489	-60	0	12	
			.000329	5.963323	-60	-10	12	
	317	.000671	.001369	5.655869	-40	-2	0	
			1.45E-05	6.594915	-24	32	-16	
			337	.000495	.000197	6.07058	-58	-42
	264	.001552	.002001	5.571615	-22	-2	-16	
			.867759	3.730085	-28	-22	-6	
	Rest > Smell	3989	6.79E-18	.942396	3.611344	-18	-16	-10
1.84E-11				8.964405	42	-60	-10	
2.85E-10				8.518395	32	-34	-14	
3581		1.06E-16	4.38E-08	7.663392	48	-66	-2	
			3.46E-08	7.70437	-30	-40	-14	
			1.08E-07	7.503654	-40	-62	-4	
865		6.36E-07	2.55E-07	7.349815	-34	-80	28	
			8.38E-06	6.700474	-56	-10	-12	
			.000715	5.797657	-56	0	-12	
747		2.4E-06	.000228	6.039792	58	-10	-12	
			.147362	4.497838	54	6	-20	
			.994978	3.384825	48	-18	-2	
1223		1.56E-08	.000257	6.015021	-2	-50	38	
			.005634	5.335674	-10	-52	10	
			.005662	5.334542	-12	-56	18	
385		.000244	.000362	5.943098	-26	30	44	
			733	2.82E-06	.003921	5.419408	-34	-28
	.004699		5.377736	-40	-24	52		
2323	1.07E-12	.085319	4.654254	-50	-24	50		
		.004929	5.366689	0	8	-12		
		.009292	5.217957	-4	52	2		
391	.000224	.02408	4.985769	4	20	-18		
		.005867	5.32623	48	-24	42		
		.170079	4.454729	44	-26	50		

Table 4 – Whole brain p-values for the valence-specific effects of interest.

Condition	Cluster-level		Peak-level		mm		
	equiv-k	p(unc)	FWE-corr	T	x	y	z
Smell > No Odor	8747	1.05E-29	2.47E-06	6.932285	16	-4	-16
			.000341	5.955808	22	-16	-10
			.000539	5.85841	24	14	-22
	788	1.5E-06	.080807	4.669253	50	44	12
			.125433	4.545139	44	12	24
Pleasant > No Odor	9057	2.34E-05	.13314	4.527764	38	6	22
			6.500404	8	-44	18	
			6.11E-05	6.309697	-6	-34	26
	771	1.82E-06	.000888	5.750778	4	-8	8
			.116978	4.565292	-18	-80	-28
			.161876	4.46971	-6	-84	-34
			.328982	4.238491	-20	-86	-38

(continued on next page)

Table 4 – (continued)

Condition	Cluster-level		Peak-level		mm		
	equiv-k	p(unc)	FWE-corr	T	x	y	z
Unpleasant > No Odor	740	2.6E-06	.004186	5.404393	16	−4	−20
			.058908	4.754908	24	14	−20
			.062213	4.740294	22	−14	−10
	327	.000576	.32619	4.241545	−32	0	−22
			.515995	4.059626	−30	0	−30
			.57739	4.006733	−20	−4	−20

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