

EEG-based functional connectivity and physiological correlates of emotion in fragrance exposure

Ferreira, Hugo Alexandre^{1,*}; Silva, Vasco Marques¹; Fernandes, Sofia Rita¹; Pinto, Pedro Contreiras^{2,3}

¹Instituto de Biofísica e Engenharia Biomédica, Departamento de Física, Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal

¹PhD Trials, Lisboa, Portugal

¹Faculdade de Farmácia da Universidade de Lisboa, Lisboa, Portugal

*Hugo Alexandre Ferreira; Instituto de Biofísica e Engenharia Biomédica, Departamento de Física, Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal; phone: +351217500177; email: hferreira@fc.ul.pt

Abstract (Max 250 words)

Background: Sensorial evaluation of a cosmetic product is a major aspect in product release to the public. Nonetheless, self-reporting of the panels' sensorial experience, as is conventionally done, rarely captures the emotional content with fidelity. This results in a limited translation of the consumer's preferences.

Methods: Twelve women (20-45 years), were enrolled in this study and blindly exposed to a panel of 7 different fragrances presented in randomized order and using a block design. Self-reporting feedback was done with the 3-dimensional Self-Assessment-Manikin (SAM). Neurophysiological correlates were assessed by a 64-channel electroencephalography (EEG) system and functional connectivity metrics were derived. Data analysis was done using the iMotions platform and the MNE tools for EEG functional connectivity data. Group statistical analysis was done using SPSS.

Results: Exposure to fragrances elicited higher connectivity in brain regions related with the olfactory network such as the entorhinal cortex, which receives direct olfactory bulbar input, and the insula as an associative region related to salience and arousal. Limbic structures involved in memory and emotional processes, such as the cingulate, also presented higher connectivity. Pleasant fragrances elicited higher connectivity in the left hemicortex in contrast with unpleasant fragrances, with higher connectivity at the right hemicortex. Pleasant fragrances were associated with higher alpha connectivity in the left lateral-orbitofrontal cortex, a region involved in emotion response.

Conclusion: EEG-based functional connectivity and subjective emotional correlates may be able to provide a means to define objective gold-standards of emotional response for global marketing efforts in cosmetic products.

Keywords: emotions; fragrances; electroencephalography; functional connectivity

1. Introduction

Natural aroma components have always played a significant role in many aspects of our daily lives. Hence, fragrances are a topic of great interest to the scientific community, from playing a significant role in the cosmetic industry to possibly having some relevance to mental, spiritual, or physical healing [1, 2]. A fragrance can be characterized by having a strong-smelling organic compound with a characteristic odor [3]. The sensory information extracted from the interaction of the fragrance molecules with olfactory receptors is processed in well-defined areas in the brain [4]. During this olfactory process, the fragrant molecules attach to the cilia of olfactory receptors in the olfactory epithelium leading to the activation of protein receptors that will generate electrical signals in the brain. These signals are transmitted via the olfactory bulb and higher olfactory cortex, which is mainly found in the inferior part of the temporal lobe. After being recognized in the olfactory cortex, the electrical signal path can be complex and lead to different brain regions associated with memory, cognition or emotions. Since there is such a complex response and multiple optional pathways, it can be fruitful to have a deeper understanding regarding communication between brain regions during inhalation of different types of fragrances.

Electroencephalography (EEG) offers a high temporal resolution and a poor spatial resolution, enabling the evaluation of spatiotemporal brain dynamics. A study based on EEG data showed that odor information was localized in and around the primary and secondary olfactory areas at 100 to 350 ms after odor onset [5]. These areas then expanded to larger regions associated with emotional, semantic and memory processing [5]. When comparing pleasant, unpleasant and neutral odors, a study showed how alpha asymmetry could be used to distinguish the pleasant from the remaining odors [6]. In this case, there was a predominance of alpha left frontal activation during the scent of a vanilla fragrance considered as being a pleasant odor. The use of EEG and electrocardiography data demonstrated the possibility of evaluating the pleasantness of different odors, despite an increasing difficulty in distinguishing neutral and pleasant odors [7]. More robust methods regarding functional connectivity were used in order to obtain cortico-cortical interactions and, by using dynamic causal modeling, it was shown that both unpleasant and pleasant odors actually inhibited connections from the entorhinal cortex to the piriform cortex [8]. Moreover, the odors with a positive valence had a stronger global influence on connectivity dynamics when compared to negative valence odors. A combined functional magnetic resonance imaging EEG study [9] used source reconstruction algorithms that demonstrated activations towards the orbitofrontal cortex, validating the olfactory cascade process described in the literature [10]. Finally, an event-related potential study investigated the olfactory pathway and demonstrated a first ipsilateral activation regarding the stimulated nostril which then extended into both hemicortexes ending at the frontal structures [11].

The aim of the present study was then to evaluate emotional neural responses regarding brain functional communication and its correlation with a set of different pleasant, unpleasant and neutral odors, with the ultimate goal of better understanding addressing consumer's preferences of cosmetic products. A novel approach to analyze EEG signals was used by obtaining source space dipole strength and orientation and then by comparing each labeled time series regarding their oscillation synchronization. Based on previous literature, we hypothesized that pleasant odors should induce different connectivity patterns when compared to unpleasant and neutral odors.

2. Materials and Methods

2.1 Participants. Twelve healthy women participants (mean±standard deviation age of 28.6±7.6 years) with no known neurological or psychiatric disease or sensory impairments were enrolled. All participants signed informed consent prior to the start of the study, as approved by the local ethics committee.

2.2 Fragrances and Study Protocol. In this study, participants were blindly exposed to seven different fragrances in a randomized order, according to a block design protocol (Figure 1). Fragrances from the Aromaster Master Wine 88 aroma kit (Vinofil, Hong Kong) included: lavender, lemon, and vanilla scents, considered “pleasant” scents; kerosene and “horse sweat”, considered “unpleasant” scents; and cedar and vinegar considered “neutral” scents. Following the presentation of the fragrance, participants were asked to complete a self-reporting feedback assessment using the 3-dimensional Self-Assessment-Manikin (SAM) [12]. This questionnaire reports, on a 9-point scale, emotions related to valence (pleasant/unpleasant), arousal (exciting/calming), and dominance (overwhelming/subtle), whilst having a non-verbal design, which enhances the readability of this type of assessment regardless of the age, educational level, or other social factor. The instructions were presented visually using the iMotions platform (iMotions A/S, Denmark), whilst simultaneously collecting electrophysiological signals (see below), following this sequence: (1) 10-second exposure to a fragrance, hovering it 5 cm below the participant’s nose; (2) 20 seconds for assessing the emotional response; (3) 30 seconds for providing SAM feedback using a computer application; and (4) 30 seconds for scent wash-off, in which the participants were asked to smell their own hands before the next fragrance.

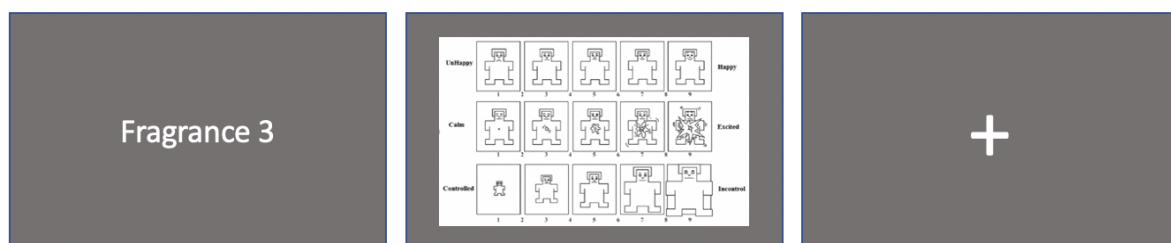


Figure 1. The experimental protocol comprised a bloc design in which participants were exposed to a fragrance for 10 seconds followed by 20 seconds of emotional assessment (left panel), 30 seconds of feedback through the Self-Assessment-Manikin questionnaire (middle panel); and 30 seconds for scent wash-off (right panel) before repeating the cycle with another of the seven fragrances in study.

2.3 Electroencephalography recording. EEG signals were recorded using a 64-channel recording system (actiCHamp Plus, Brain Vision Inc., Morrisville, NC, USA), whilst connected to the iMotions platform. Recordings were acquired in a sitting position with the participants eyes-open facing a computer display at 60-65 cm distance. The signals were obtained by using active electrodes placed in the scalp of the participants according to the international 10-20 system. The FCz electrode was chosen as reference with the ground placed at the Fpz position. The electrophysiological data was digitized with a sampling frequency of 500 Hz and filtered with a band-pass filter with cutoff frequencies of 1 and 40 Hz.

2.4 Signal Processing and the Inverse Problem. EEG data analysis was conducted offline using custom libraries in Python (Python Software Foundation, <https://www.python.org/>) incorporating functions of MNE-Python [13]. Artifact rejection was executed by using Independent Component Analysis (ICA) to obtain independent source signals that explain most of the variance obtained in the covariance matrix between channels. The algorithm used in this domain was Picard Algorithm and the components excluded were based on ocular artifacts or channel artifacts. A Boundary Element Model (BEM) method was used in order to obtain a forward solution to the ill-posed problem related to the unknown source signal space. The head model used was a template (subject sample) provided by MNE-Python and FreeSurfer [14]. The source localization was executed by using dynamic statistical mapping (dSPM) based on a nonlinear post hoc normalization that assures better performance regarding source localization. After reaching a series of dipoles with a certain orientation and strength, these were converted into several time courses each for every brain region determined by the FreeSurfer's parcellation "aparc" used in the "subject sample" brain.

2.5 Functional Connectivity Analysis. Functional connectivity analysis was based upon two different statistical dependency metrics: imaginary coherency (imCoh) [15] and weighted phase lag index (wPLI) [16]. The former evaluates two time series as a correlation metric in the frequency domain, being sensitive to both changes in power and phase relationships, whilst the latter is based specifically on phase synchronization.

These metrics depend on estimates of power and cross spectral density of EEG time series, as given by

$$\text{imCoh} = \text{Im}(E[S_{xy}]) / \sqrt{E[S_{xx}] * E[S_{yy}]} \quad (\text{equation 1})$$

and

$$\text{wPLI} = |E[\text{Im}(S_{xy})]| / E[|\text{Im}(S_{xy})|] \quad (\text{equation 2})$$

in which $E[]$ represents the estimate, $\text{Im} ()$ is the imaginary component, $\sqrt{ } ()$ is the square root of the argument, S_{xx} is the power spectral density of EEG time series x , S_{yy} is the power spectral density of EEG time series y , and S_{xy} is the cross spectral density between EEG time series x and y . For both metrics values of zero (or close to zero) and one represent lack of and complete or full connectivity, respectively.

Herein, these metrics were used to evaluate the coupling strength between 68 parcellated cortical brain regions by considering the oscillation synchronization for each pair of time series. This evaluation was done for a set of different brainwave frequency bands: theta (4-8 Hz); alpha (8-12 Hz); and gamma (30-35 Hz).

2.6 Group analysis. Descriptive statistics for each SAM dimension was done per fragrance using custom-made and publicly available scripts (MATLAB v2015b, www.mathworks.com) [17]. A One-way repeated-measures ANOVA was applied to observe if there were effects in each SAM dimension dependent on fragrance (a significance level of 5% was chosen). The Greenhouse-Geisser correction was applied whenever Mauchly's condition of sphericity was rejected. Pairwise comparisons were applied using paired t-tests with a Bonferroni correction

($p < 0.05/7$). To account for non-normality and ordinal type of SAM dimensions, results were checked with non-parametric Friedman and Wilcoxon-signed rank tests. All statistical tests were performed with IBM SPSS, version 27.

Regarding EEG data, ImCoh and wPLI connectivity strenghts were averaged across participants for each fragrance. The number of moderate to strong connections was then identified for each fragrance and also for left and right hemicortices. The more highly connected (average number of connections above the percentile 90) brain cortical regions were then considered for further analysis, considering the distribution of connections according to the three frequency bands. Trends were analyzed accordingly.

3. Results

3.1 SAM classification per fragrance. Figure 2 below shows the distribution of participants' responses to the SAM questionnaire according to the 3 dimensions of valence, arousal and dominance for the 7 fragrances in study: lavender (F1); "horse sweat" (F2); lemon (F3); kerosene (F4); vanilla (F5); cedar (F6); and vinegar (F7).

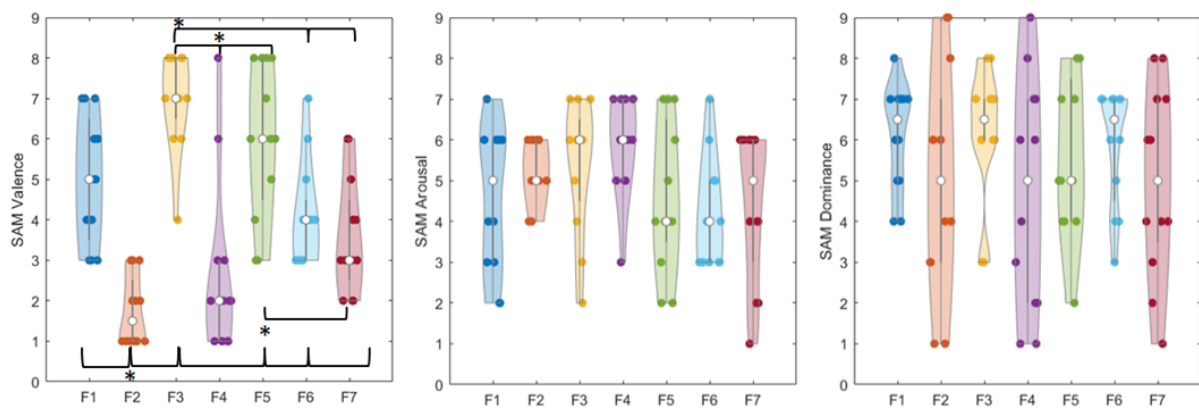


Figure 2. Violin plots with the distribution of SAM classification for each fragrance (N=12). Statistical significant differences after pairwise comparisons (Wilcoxon sign-rank test) are marked by * (Bonferroni corrected, $\alpha = 0.05/7$). F1 = Lavender; F2 = "Horse Sweat"; F3 = Lemon; F4 = Kerosene; F5 = Vanilla; F6 = Cedar; F7 = Vinegar.

The repeated-measures ANOVA test was used to compare SAM's responses regarding fragrance (F1 to F7). Statistical significant differences were found between fragrances only for Valence ($p < 0.001$), considering a significance level of 5%. From pairwise comparisons, fragrances can be grouped according to Valence (figure 2, left panel) into: a) pleasant – F1, F3, F5, with the highest ranking values (median \pm interquartile range (IQR) of 5.0 ± 3.0 , 7.0 ± 1.5 , and 6.0 ± 3.5 points, respectively); neutral – F6, F7, with intermediary valence values (median \pm IQR of 4.0 ± 1.5 , and 3.0 ± 2.0 , respectively); and unpleasant – F2, F4, with the lowest ranking values (median \pm IQR of 1.5 ± 1.5 , and 2.0 ± 2.0 , respectively).

Participants' responses did not attain statistical significant differences according to Dominance ($p = 0.322$) or Arousal ($p = 0.121$), although fragrances could potentially be grouped based on trend values.

Arousal was observed to have lower values for F5, and F6 (median±IQR of 4.0±3.0, and 4.0±2.0); whilst F1, F2, and F7 having intermediate values (median±IQR of 5.0±3.0, 5.0±1.0, and 5.0±3.0, respectively), and F3, and F4 with high arousal values (median±IQR of 6.0±2.0, and 6.0±2.0, respectively).

The dominance dimension could be potentially used to group fragrances on magnitude and dispersion: F1, F3 and F6 have higher dominance and smaller dispersion of values (median±IQR of 6.5±2.0, 6.5±1.0, and 6.5±2.5, respectively); whilst F2, F4, F5 and F7 have lower dominance and larger dispersion of values (median±IQR of 5.0±4.0, 5.0±5.0, 5.0±3.5, and 5.0±3.5, respectively).

Table 1 below shows a summary of the participants' SAM response and grouping, highlighting potential unique emotional response spectra for each fragrance.

Table 1. In-group relative emotional responses to fragrance exposure according to SAM's dimensions of valence, arousal and dominance. Responses should be considered as relative between fragrances. Only the dimension of valence showed significant overall differences in response.

Fragrance	Valence	Arousal	Dominance
F1 = lavender	Pleasant	Neutral	Subtle and consensual
F2 = "horse sweat"	Unpleasant	Neutral	Overwhelming and inconsistent
F3 = lemon	Pleasant	Exciting	Subtle and consensual
F4 = kerosene	Unpleasant	Exciting	Overwhelming and inconsistent
F5 = vanilla	Pleasant	Calming	Overwhelming and inconsistent
F6 = cedar	Neutral	Calming	Subtle and consensual
F7 = vinegar	Neutral	Neutral	Overwhelming and inconsistent

Herein, for example, lemon is interpreted to be pleasant and exciting but not overwhelming one's senses, consistently among participants. On the other hand, kerosene is interpreted to be unpleasant, also exciting but overwhelming one's senses in an inconsistent manner among participants.

3.2. EEG-based Functional Connectivity per Fragrance. Functional connectivity was determined in the three frequency bands: theta, alpha, theta, and gamma, using imCoh and wPLI. Whilst imCoh did not reach values higher than 0.25 (very weak connectivity), wPLI metrics reached values above 0.5 (moderately strong connectivity) in the three frequency bands for all fragrances, and were considered hereafter.

Larger number of connections between brain regions, averaged across participants, were accounted for in the gamma frequency band, with a prevalence of the left hemicortex over the right, except for the alpha band (table 2). The largest number of connections were observed for fragrances F3, and F6 in the alpha frequency band and for F1, F3, and F6 in the gamma frequency band. In the theta frequency band, the number of observed connections is similar across fragrances except for F1, which is considerably lower (table 2). Gamma band presents the highest numbers of intra and inter hemispheric connections.

While theta and gamma bands have higher connections in the left hemicortex, the opposite occurs in the alpha band.

Table 2. Number of moderate to strong connections (wPLI > 0.5) in the theta, alpha, and gamma frequency bands averaged across all participants, in left and right hemicortices and interhemicortexs. In bold are highlighted the largest number of connections observed for each frequency band.

Fragrance	F1	F2	F3	F4	F5	F6	F7	lh	rh	lh-rh	Total
Theta	6	20	29	25	23	27	23	69	24	60	153
Alpha	31	9	76	30	7	69	18	57	68	115	240
Gamma	111	24	74	26	25	64	30	115	93	146	354

lh = left hemicortex; rh = right hemicortex. F1 = Lavender; F2 = "Horse Sweat"; F3 = Lemon; F4 = Kerosene; F5 = Vanilla; F6 = Cedar; F7 = Vinegar.

Table 3 shows a summary of cortical regions with the highest average number of connections (above the percentile 90), according to the frequency band. Overall, higher connectivity was observed in anatomically close cortical regions namely: the frontal pole, the rostral middle frontal and the medial and rostral orbitofrontal cortices; the superior, transverse and inferior temporal along with the supramarginal gyrus and superior parietal; and the isthmus and posterior cingulate, the precuneus, the cuneus and the pericalcarine cortex. We also identified the insula and the entorhinal cortex as regions with higher number of connections, and close to other temporal lobe regions.

A number of brain regions seems to have high connectivity for almost every fragrance. In particular, the isthmus cingulate showed strong connectivity for all fragrances except for F5 (vanilla) in both hemicortices in the alpha frequency band; and the medial and lateral orbitofrontal cortices, the rostral middle frontal and the entorhinal cortex in the gamma frequency band.

Additionally, in the alpha frequency band, F1, F3, and F6 showed the highest connectivity with more regions.

In the theta frequency band, F1 (lavender) was the fragrance showing the lowest connectivity associated with the indicated regions. The same was observed in the gamma frequency band for F2 ("horse sweat"). F1, F3 and F6 showed connectivity for almost all the indicated regions in the gamma frequency band.

Table 3. Regions contributing to > 90% of moderate to strong connections. Fragrances which show connectivity in those regions indicated are marked by 'x'.

Frequency Band	lh Region (number of connections)	1	2	3	4	5	6	7	rh Region (number of connections)	1	2	3	4	5	6	7
Theta	frontal pole (11)		x	x	x		x		posterior cingulate (13)							
	inferior temporal (10)				x		x	x			x	x		x	x	x
	insula (10)			x	x	x	x			x	x	x	x			x
	supramarginal (10)		x	x		x		x								
Alpha	cuneus (30)	x	x	x		x			precuneus (35)	x	x	x	x		x	
	isthmus cingulate (20)	x	x	x	x		x	x	isthmus cingulate (17)	x	x	x	x		x	x
	pericalcarine (17)	x		x			x		pericalcarine (16)	x		x			x	
									superior parietal (22)	x	x	x			x	
Gamma	lateral orbitofrontal (34)	x	x	x	x	x	x		rostral middle frontal (28)							
	medial orbitofrontal (24)	x	x	x	x	x	x			x		x	x	x	x	x
	entorhinal (21)	x		x	x	x	x	x		x		x				x
	superior temporal (21)	x		x	x		x	x								
	supramarginal (20)	x		x			x									

lh = left hemicortex; rh = right hemicortex. F1 = Lavender; F2 = "Horse Sweat"; F3 = Lemon; F4 = Kerosene; F5 = Vanilla; F6 = Cedar; F7 = Vinegar.

In Figure 4, similarities between functional connectivity patterns of F1, F3, and F6 in the alpha and gamma frequency bands can be observed. In the alpha band, a higher connectivity of posterior and occipital regions was observed, as characteristic of the EEG signals in this frequency band. However, for F1, F3, and F6, the connectivity was stronger than for the other fragrances. Regarding the gamma frequency band, higher connectivity was observed more particularly in the left hemicortex and in frontal regions, showing larger similarities between F3 and F6.

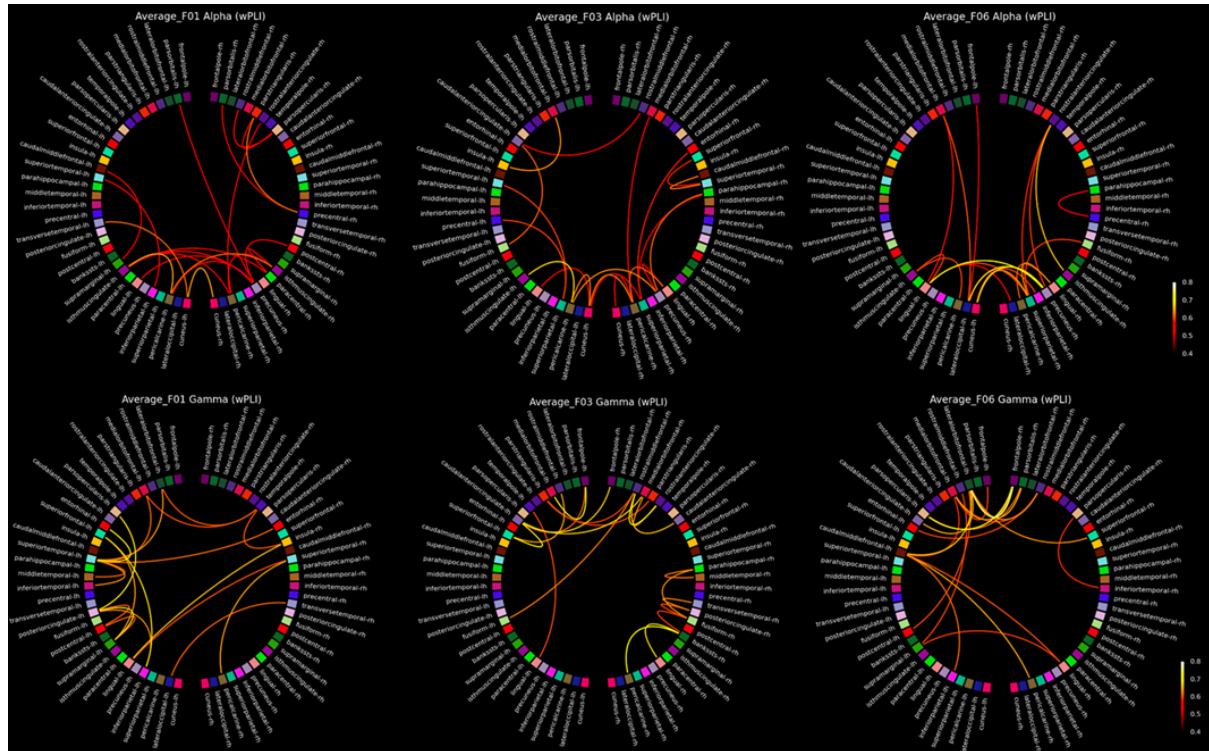


Figure 4. wPLI-based functional connectivity diagrams for F1, F3, and F6 in alpha (top row) and gamma frequency bands (bottom row). F1 = Lavender; F3 = Lemon; and F6 = Cedar.

Table 4 shows a summary of every pair of interhemispheric regions that have a strong connection for more than one fragrance. It can be observed that there are more connected regions for the alpha frequency band than for the theta and gamma frequency bands. Fragrances F3 and F6 seem also to be the most highly connected interhemispherically, in particular in the alpha frequency band.

Additionally, the left hemispheric cuneus and the right hemispheric precuneus seem to be the most highly connected regions, in particular in the alpha frequency band, followed by the left hemispheric pericalcarine gyrus, the left supramarginal and the left lateral and medial orbitofrontal cortices and also the right hemispheric rostral middle frontal gyrus.

Table 4. Interhemispheric functional connectivity across theta, alpha, and gamma frequency bands. Regions in bold represent repeated connected regions for the theta and gamma frequency bands. Underlined regions represent repeated connected regions for alpha and gamma frequency bands.

Theta		F1	F2	F3	F4	F5	F6	F7
medial orbitofrontal-lh	cuneus-rh				x		x	
Alpha								
cuneus-lh	<u>inferior parietal-rh</u>		x				x	
cuneus-lh	lateral occipital-rh					x	x	
cuneus-lh	<u>pars orbitalis-rh</u>						x	x
cuneus-lh	precuneus-rh	x	x				x	
cuneus-lh	rostral anterior cingulate-rh			x			x	
cuneus-lh	superior parietal-rh			x			x	
inferior parietal-lh	precuneus-rh			x	x		x	
inferior parietal-lh	temporal pole-rh			x			x	
isthmus cingulate-lh	pericalcarine-rh	x		x				
isthmus cingulate-lh	precuneus-rh	x		x				
lingual-lh	precuneus-rh	x					x	
lingual-lh	superior parietal-rh			x			x	
pericalcarine-lh	isthmus cingulate-rh	x					x	
pericalcarine-lh	precuneus-rh	x		x			x	
pericalcarine-lh	superior parietal-rh			x			x	
precuneus-lh	<u>inferior parietal-rh</u>		x				x	
precuneus-lh	precuneus-rh		x				x	
<u>supramarginal-lh</u>	entorhinal-rh			x			x	
Gamma								
lateral occipital-lh	inferior temporal-rh			x		x		
lateral orbitofrontal-lh	lateral orbitofrontal-rh	x	x					
lateral orbitofrontal-lh	pars opercularis-rh	x				x		
lateral orbitofrontal-lh	rostral middle frontal-rh				x	x	x	
medial orbitofrontal-lh	frontal pole-rh			x			x	
medial orbitofrontal-lh	rostral middle frontal-rh				x	x	x	
pars opercularis-lh	<u>pars orbitalis-rh</u>						x	x
pars triangularis-lh	<u>pars orbitalis-rh</u>			x				x
pars triangularis-lh	rostral middle frontal-rh	x		x				
supramarginal-lh	<u>inferior parietal-rh</u>	x					x	
supramarginal-lh	precentral-rh	x		x				

lh = left hemicortex; rh = right hemicortex. F1 = Lavender; F2 = "Horse Sweat"; F3 = Lemon; F4 = Kerosene; F5 = Vanilla; F6 = Cedar; F7 = Vinegar.

4. Discussion

The usage of the SAM questionnaire has enabled the distinction between the different fragrances and their clustering according to dimensions of valence, arousal, and dominance (Figure 1). In this sense, the study presented here is in line with previous studies regarding emotional attributes associated with odors. Lavender (F1), lemon (F3), and vanilla (F5) are usually considered by most subjects as pleasant to smell, whereas “horse sweat” (F2) and kerosene (F4) are considered unpleasant, and cedar (F6) and vinegar (F7) with a more neutral valence [18], although other authors refer to lavender and vinegar with a more neutral or negative valence, respectively [19].

Of notice is the observation that odors considered to be more dominant or overwhelming (“horse sweat”, kerosene, vanilla, and vinegar) have also shown to have higher variability of responses, whilst those less dominant (lavender, lemon, and cedar) had the smaller variability in responses, which again may depend on the familiarity of the odors and eventual related emotional content, not herein assessed, but which effects have been described elsewhere [19].

Regarding arousal and dominance, a study considering 25 female and 15 male participants (mean±standard deviation age of 24.6±3.9 years), observed both lavender and lemon with neutral arousal and slight lower dominance [19], whilst in our study lavender was considered as having neutral arousal and slightly higher dominance and lemon was considered as more exciting and with also a higher dominance, showing that there is large variability among studies (Table 1). On the other hand, vinegar was considered to have slightly higher arousal contrary to our findings, which considered neutral arousal and lower dominance (overwhelming). Finally, sweat was considered by both studies to have high dominance (more overwhelming odor).

Herein, different sources of odors were used as well as different odor delivery protocols (manually for 10 seconds vs nasal mask for 4 seconds), and different participant samples, which may justify some of the changes [19]. Moreover, odor interpretation was also shown to vary according to gender, culture, and olfactory knowledge [20]. In particular, women identified more odors as more intense and were able to better categorize them than man. Also, higher interpretation variability was observed for more pleasant odors, as more negative odors seem to be more resilient to cognitive differences.

Regarding EEG functional connectivity, our results show an overall larger number of connections in the left hemicortex compared to the right hemicortex (Table 2): in fact, lateralization of nostril and brain preference for particular tasks have been described but evidence is still scarce [21]. In particular, higher activation was observed in the right orbitofrontal cortex rather than the left counterpart using positron electron tomography brain imaging and also functional magnetic resonance imaging. Nonetheless, pleasant odors were observed to elicit higher responses in the left hemicortex, and conversely unpleasant odors on the right hemicortex.

Fragrances F1, F3, and F6 were associated with the highest reported dominance values (participants in control of the stimuli) and also with the highest number of of connections in comparison with the remainder fragrances in the gamma band (111, 74, and 64 connections

for fragrances F1, F3, and F6 versus 24, 26, 25, and 30 connections for fragrances F2, F4, F5, and F7, respectively; Table 2), which also showed the lowest dominance values (participants overwhelmed by the stimuli). Given that the gamma brainwaves have been associated with cognitive functions such as attention and working-memory, as well as in emotion integration and in the cognitive control of the emotional response [2, 22], it could be reasonable to suppose that the cognitive control over the emotional response to olfactory stimuli, would be translated into higher gamma activity and connectivity, as observed herein. Nonetheless, insofar others have reported instead correlation of dominance with the asymmetry in the alpha frequency band, but in a video gaming context [23].

Regarding valence and arousal, no particular pattern of association with the number of connections observed for each fragrance seems to be evident for theta, alpha, or gamma frequency bands. Nonetheless, frontal alpha asymmetry and power increase have been associated with emotional valence and arousal, respectively [23].

Regarding communication between hemispheres, a predominant set of interhemispheric connections was observed in the alpha frequency band. Further inspection in that frequency range shows a group of paired regions repeated for F1, F3, and F6 fragrances. These fragrances correspond to higher values of dominance and their interpretation can be understood as being part of the secondary pathway of the olfactory process. The gamma frequency band shows repeated pairs of connected brain regions that belong to the primary olfactory cortex (e.g. lateral orbitofrontal cortex and inferior parietal cortex) consistent with initial cognitive identification and processing of olfactory information [24].

Furthermore, theta waves are considered to play a major role in some functions regarding short-term memory or the process of building new memories [25]. In this sense, it can be assumed that all of the fragrances that were considered impactful in any way could enable a considerable number of connections between brain regions related to the recall and/or formation of memories. Herein, connections with the inferior temporal lobe, associated with memory processes and connected to other memory processing regions such as the hippocampus and the amygdala, are observed here. Also, the insula, a secondary associative region related to salience and arousal, is observed with a large number of connections and may be related to attention processes related to exposure to fragrances. Finally, additional regions were observed to be highly connected such as the medial orbitofrontal cortex and the posterior cingulate, respectively related to subjective pleasantness [26] and also to emotional salience [27].

The alpha frequency band is associated with idle but still alert cognitive states. It has also been associated with an enhanced perception of calmness. Despite observing some left frontal activation towards pleasant and neutral fragrances (namely F3 and F6), evidence was not found for that regarding the vanilla scent, as others depicted [6]. Moreover, an elevated number of brain connections for fragrances F1, F3 and F6 were found not only in the right hemisphere, but also between interhemispheric regions. This was true specially for regions communicating with the right hemispheric precuneus region, which is mainly present in the default mode network, also in line with the representation of awareness states characteristically found in the alpha band. This predominance corroborates the fact that positive valence odors could have a stronger global role in connectivity dynamics.

Globally, there is evidence for some connection regarding the description of cognitive states in the literature for each frequency band and the most involved brain regions in this functional connectivity study [28, 29]. Beyond that, it was possible to distribute the fragrances in valence, arousal, and dominance groups while only having statistical significance for the valence group.

Also, connectivity with the primary olfactory cortex was found in all EEG frequency bands studied it was possible to better distinguish the fragrances regarding their valence groups in the alpha band. In this frequency range, it was corroborated the stronger global role in connectivity dynamics for the positive valence group. The gamma band was associated with higher connectivity for higher dominance fragrances (F1, F3 and F6). Dominance possibly relies on cognitive control over emotions due to olfactory stimuli, thus triggering higher gamma activity and connectivity.

This study did not find functional connectivity that could be associated with arousal. The large variability of arousal values across fragrances may have concealed neural correlates for the arousal categories, making these difficult to identify (Table 1). Further studies with a larger sample size could contribute to decreasing the dispersion of values and provide more clarification on the grouping of fragrances. Comparative studies between genders can also help to identify how male and female brains are differently wired concerning emotional responses to olfactory stimuli.

5. Conclusion

This study presented different connectivity patterns associated with pleasant, unpleasant, and neutral scents regarding the EEG frequency band, intensity (number of connections), and cortical regions involved. Not only the emotional valence elicited by the different scents was studied, but also the dimensions of arousal and dominance, as assessed subjectively by the SAM questionnaire and hinted quantitatively by neural correlates.

In spite of the small participant sample size, and lack of standardization and consistency regarding the olfactory stimuli delivery and interpretation, as observed in the literature, interesting insights could be derived from this study, including the involved brain regions in response to the different fragrances and the role of the gamma frequency band connectivity as a putative biomarker of emotional dominance. Nonetheless, larger sample sizes and reproducibility studies are warranted to confirm the obtained results. Also, in order to further expand the reach of this work, fragrance identification or discrimination using neural correlates could be of interest using machine-learning methods given the high number of such correlates and the complexity of the problem.

Finally, this study hinted that the combination of EEG-based functional connectivity and subjective classification tools such as SAM could be a powerful strategy to identify neural correlates for emotional responses to odors. Such EEG-emotional correlates could be a further means to set objective gold standards for studying emotional responses to cosmetic products with a potentially strong impact on marketing strategies and diversification of products available in the market.

Acknowledgments

The authors would like to thank all the participants. This work was partially funded by Fundação para a Ciência e Tecnologia through the grant UIDB/00645/2020.

Conflict of Interest Statement

The author Pedro Contreiras Pinto is a managing partner at PhD Trials.

References

1. Kim J, Sin C, Park JO, Lee H, Kim D, Kim S (2021) Physiological and psychological effects of forest healing focused on plant fragrance therapy for maladjusted soldiers. *Journal of People, Plants, and Environment* 24:429-439. <https://doi.org/10.11628/ksppe.2021.24.4.429>
2. Sowndhararajan K, Kim S (2016) Influence of fragrances on human psychophysiological activity: With special reference to human electroencephalographic response. *Scientia Pharmaceutica* 84:724-752. <https://doi.org/10.3390/scipharm84040724>
3. Panten J, Surburg H (2015) Flavors and fragrances, 1. General aspects. In: Ullmann's Encyclopedia of Industrial Chemistry (Ed.) Wiley-VCH. https://doi.org/10.1002/14356007.a11_141.pub2
4. Shipley MT, Ennis M, Puche AC (2003) The Olfactory System. In: Conn, P.M. (eds) *Neuroscience in Medicine*. Humana Press. https://doi.org/10.1007/978-1-59259-371-2_27
5. Kato M, Okumura T, Tsubo Y, Honda J, Sugiyama M, Touhara K, Okamoto M (2022) Spatiotemporal dynamics of odor representations in the human brain revealed by EEG decoding. *Proceedings of the National Academy of Sciences of the United States of America* 119: e2114966119. <https://doi.org/10.1073/pnas.2114966119>
6. Kline JP, Blackhart GC, Woodward KM, Williams SR, Schwartz GE (2000) Anterior electroencephalographic asymmetry changes in elderly women in response to a pleasant and an unpleasant odor. *Biological Psychology* 52: 241-250. [https://doi.org/10.1016/S0301-0511\(99\)00046-0](https://doi.org/10.1016/S0301-0511(99)00046-0)
7. Kroupi E, Vesin JM, Ebrahimi T (2015) Subject-independent odor pleasantness classification using brain and peripheral signals. *IEEE Transactions on Affective Computing* 7:422-434. <https://doi.org/10.1109/TAFFC.2015.2496310>
8. Rho G, Callara AL, Vanello N, Gentili C, Greco A, Scilingo EP (2021) Odor valence modulates cortico-cortical interactions: a preliminary study using DCM for EEG. 2021 43rd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), 604-607. <https://doi.org/10.1109/EMBC46164.2021.9629910>
9. Masaoka Y, Harding IH, Koiwa N, Yoshida M, Harrison BJ, Lorenzetti V, Homma I (2014) The neural cascade of olfactory processing: A combined fMRI–EEG study. *Respiratory Physiology & Neurobiology* 204:71-77. <https://doi.org/10.1016/j.resp.2014.06.008>

10. Royet JP, Plailly J, Delon-Martin C, Kareken DA, Segebarth C (2003) fMRI of emotional responses to odors: influence of hedonic valence and judgment, handedness, and gender. *Neuroimage* 20:713-728. [https://doi.org/10.1016/S1053-8119\(03\)00388-4](https://doi.org/10.1016/S1053-8119(03)00388-4)
11. Lascano AM, Hummel T, Lacroix JS, Landis BN, Michel CM (2010) Spatio-temporal dynamics of olfactory processing in the human brain: an event-related source imaging study. *Neuroscience* 167:700-708. <https://doi.org/10.1016/j.neuroscience.2010.02.013>
12. Bradley M, Lang PJ (1994) Measuring emotion: The Self-Assessment Manikin and the semantic differential. *Journal of Behavior Therapy and Experimental Psychiatry* 25: 49-59. [https://doi.org/10.1016/0005-7916\(94\)90063-9](https://doi.org/10.1016/0005-7916(94)90063-9)
13. Gramfort A, Luessi M, Larson E, Engemann DA, Strohmeier D, Brodbeck C, Goj R, Jas M, Brooks T, Parkkonen L, Hämäläinen MS (2013) MEG and EEG data analysis with MNE-Python. *Frontiers in Neuroscience* 7:1–13. <https://doi.org/10.3389/fnins.2013.00267>
14. Fischl B (2012) FreeSurfer. *Neuroimage* 62: 774-781. <https://doi.org/10.1016/j.neuroimage.2012.01.021>
15. Nolte G, Bai O, Wheaton L, Mari Z, Vorbach S, Hallett M (2004) Identifying true brain interaction from EEG data using the imaginary part of coherency. *Clinical neurophysiology*, 115:2292-2307. <https://doi.org/10.1016/j.clinph.2004.04.029>
16. Vinck M, Oostenveld R, Van Wingerden M, Battaglia F, Pennartz CM (2011) An improved index of phase-synchronization for electrophysiological data in the presence of volume-conduction, noise and sample-size bias. *Neuroimage* 55: 1548-1565. <https://doi.org/10.1016/j.neuroimage.2011.01.055>
17. Bechtold B, Fletcher P, Holden S, Gorur-Shandilya S (2021). bastibe/Violinplot-Matlab: A Good Starting Point (v0.1). Zenodo. <https://doi.org/10.5281/zenodo.4559847>
18. Doty RL, Shaman P, Dann M (1984) Development of the University of Pennsylvania Smell Identification Test: a standardized microencapsulated test of olfactory function. *Physiology & Behavior*, 32:489-502. [https://doi.org/10.1016/0031-9384\(84\)90269-5](https://doi.org/10.1016/0031-9384(84)90269-5)
19. Bestgen AK, Schulze P, Kuchinke L (2015) Odor emotional quality predicts odor identification. *Chemical Senses* 40: 517-523. <https://doi.org/10.1109/JERM.2019.2948767>
20. Ferdenzi C, Roberts SC, Schirmer A, Delplanque S, Cekic S, Porcherot C, Cayeux I, Sander D, Grandjean D (2013). Variability of Affective Responses to Odors: Culture, Gender, and Olfactory Knowledge. *Chemical Senses* 38:175–186. <https://doi.org/10.1093/chemse/bjs083>
21. Cavelius, M., Brunel, T., & Didier, A. (2021). Lessons from behavioral lateralization in olfaction. *Brain Structure and Function* 227:685-696. <https://doi.org/10.1007/s00429-021-02390-w>

22. Yang K, Tong L, Shu J, Zhuang N, Yan B, Zeng Y. (2020). High gamma band EEG closely related to emotion: evidence from functional network. *Frontiers in Human Neuroscience* 14:89. <https://doi.org/10.3389/fnhum.2020.00089>
23. Reuderink B, Mühl C, Poel M (2013). Valence, arousal and dominance in the EEG during game play. *International Journal of Autonomous and Adaptive Communications Systems* 6:45-62. <https://doi.org/10.1504/IJAACS.2013.050691>
24. Skinner JE, Molnar M, Kowalik ZJ (2000) The role of the thalamic reticular neurons in alpha- and gamma-oscillations in neocortex: a mechanism for selective perception and stimulus binding. *Acta Neurobiologiae Experimentalis* 60:123-142. [PMID: 10769935](https://pubmed.ncbi.nlm.nih.gov/10769935/)
25. Lisman JE, Idiart MA (1995) Storage of 7 ± 2 short-term memories in oscillatory subcycles. *Science* 267:1512-1515. <https://doi.org/10.1126/science.7878473>
26. Kringelbach M (2005) The human orbitofrontal cortex: linking reward to hedonic experience. *Nature Reviews in Neurosciences* 6:691–702. <https://doi.org/10.1038/nrn1747>
27. Maddock RJ, Garrett AS, Buonocore MH (2003) Posterior cingulate cortex activation by emotional words: fMRI evidence from a valence decision task. *Human Brain Mapping* 18:30–41. <https://doi.org/10.1002/hbm.10075>
28. Zhou G, Lane G, Cooper SL, Kahnt T, Zelano C (2019) Characterizing functional pathways of the human olfactory system. *Elife* 8:e47177. <https://doi.org/10.7554/eLife.47177>
29. Arnold TC, You Y, Ding M, Zuo XN, de Araujo I, Li W (2020) Functional connectome analyses reveal the human olfactory network organization. *Eneuro* 7 <https://doi.org/10.1523/ENEURO.0551-19.2020>