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ELECTRODYNAMICS OF OLFACTORY INDUCED SIGNALS: AN ELECTRO-ENCEPHALOGRAPHIC STUDY

Sitwat Qureshi[1,2], Muhammad Jahangir[2,3], Rizwan ur Rehman[2,3], Imran Siddiqui[2], Syed Zeeshan Abbas[2] and Che Azurahanim Che Abdullah[4]

[1]*Department of Physics, Federal Urdu University of Arts, Science and Technology, University Road Karachi.*
[2]*Department of Physics, University of Karachi, University Road, Karachi.*
[3]*Government National College, No.1, Karachi.*
[4]*Department of Physics, University Putra, Malaysia.*

ABSTRACT

The goal of our study is to find the spatio-temporal behavior of the olfactory induces oscillation. Independent component analysis algorithm is used for potential of the scalp electrode. Electroencephalographic response to pleasant and unpleasant smell is recorded. Boundary element head model is used to represent the head volume conductor. Artifact rejection is performed by visual and semi-automatic method. After rejection of unwanted signal independent component analysis (ICA) is performed with the Electroencephalography (EEGLAB). Current source localization is done by fitting an equivalent current dipole model. Oscillatory phenomena as; delta, theta, alpha, beta and gamma are responses to an event, are observed. We find that, 0.5-13Hz activity is pronounced for pleasant odor in frontal regions and 13-50Hz is more active for unpleasant smell in occipital and temporal regions. After stimulation, 200 to 400ms is active time window for the signal amplitude and frequency as well for unpleasant smell. Dipole analysis shows higher residual variance (RV) for pleasant odor than unpleasant. These results would be cutting-edge steps in solving inverse problem and digitizing the odor.

Key-words: Electroencephalograph, spatio-temporal, source localization, artifact

INTRODUCTION

There are three major part of brain known as cerebrum, cerebellum and brain stem. The cerebrum has two hemispheres with a complex surface called cortex. Cerebrum has four main lobes the frontal, parietal, temporal and occipital lobe. Voluntary muscles movement is controlled by cerebellum. Rhythmic activities like respiration, heartbeat etc., are the working of brain stem. Posterior part of the brain that connect the spinal cord to the brain is called brain stem, it transfers information from body to brain and vice versa (Ackerman, 1992). Brain imaging studies can be categorized into two: invasive and non-invasive. For invasive studies, electrodes or sensors required surgery for implantation. Intracortical recording and electrocardiogram (ECOG) are types of invasive method. For non-invasive methods, it includes the electroencephalography (EEG), magneto-encephalography (MEG), functional magnetic resonance imaging (fMRI) as well as near infrared spectroscopy (NIRS). These non-invasive techniques offer advantages such as no surgery or even a cut on the skin. Among non-invasive methods, fMRI and NIRS are not considered due to the less temporal resolution. Although invasive technique gives more robust results but due to their risk factors including ethical issue (Rao, 2013), thus the non-invasive technique is more preferred. Among non-invasive techniques, EEG is chosen owing to its benefits such as portable, safe, economical and having good temporal resolution as compared to MEG and fMRI (Graimann, 2010). Previous researcher, Richard Caton in 1875 noticed brain waves when conducted an experiment on exposed brain of rabbits and monkeys. 50 years later, in 1929 German scientist Hans Berger performed an experiment on brain electrical currents and showed that weak signals of brain can be recorded from the scalp without any surgery (Coenen and Zayachkivska, 2013). Berger's experiment first time showed the existence of alpha waves that has frequency range from 8-13Hz (Bronzino, 1995). Following the discovery of alpha rhythm, different oscillatory activities were then discovered. The oscillations can be grouped into several bands of frequencies as delta, theta, alpha, beta and gamma. Some important characteristics of these bands are shown in Fig. 1.

Senses in brain propagate through groups of receptor cells present in the sense organs, these cells respond to any activity or stimuli (Lovinger, 2008). Our sense of smell is a powerful and complex sense. Its journey starts from nose and connect with old memory in the limbic system along sensory neurons. In vertebrates' sensory neurons of smell are present in the olfactory epithelium in the nose. Humans have about 10 cm^2 of olfactory epithelium surface area (Bear *et al.*, 2009). Starting from nose receptors sense the smell and send it to olfactory bulb. Through olfactory tract, these signals go to the olfactory cortex of the brain in the temporal lobe. This lobe is involved in the organization of the sensory inputs. Limbic system is attached with the cortex where emotion processed. Limbic system has amygdala, hippocampus and hypothalamus. Emotional response for the odor comes from Amygdala while odor related memories processed from hippocampus and regulation of response to the odor signal is addressed by hypothalamus. Limbic system processes the signal from sense to emotion (Walinga and Stangor, 2014).

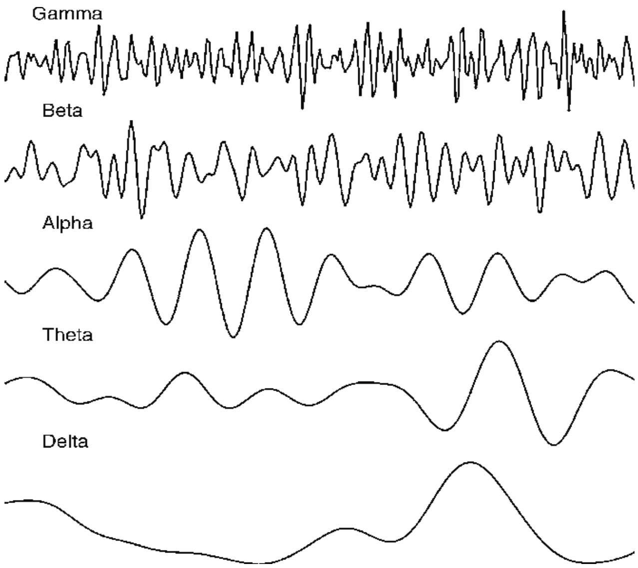

Fig. 1. EEG Rhythms for delta, theta, alpha, beta and gamma (Ahangi, 2012).

- 0.5-4 Hz corresponds to Delta band, arise in sound sleep
- 4-8 Hz oscillation are called Theta, arise in meditation and sleep as well.
- 8-13 Hz waves are alpha wave that was first discovered by Berger, it shows relaxation condition.
- 13-30Hz, Beta waves shows awake and working condition
- >30Hz Gamma band shows cognition and working of brain

Oscillations in brain, due to olfactory network undergo a wide range of frequencies from 1 to 150 Hz that depends on many factors as, type of odor, concentration and latency etc. On experiment on rats, functional involvement of beta and gamma oscillations is observed for odor perception and memory (Martin and Ravel, 2014). In an EEG analysis, with the help of constrained low-resolution electromagnetic brain tomography, cortical region of interest across subjects are analyzed for cognitive tasks (Courellis *et al.,* 2017). During recall of the aural stimulation EEG Brain Signal Source Localization has been studied (Tomohiro *et al.*, 2007).

For identifying signal oscillations, combination of the olfactory bulb slice with MEA (micro electrode array) is a useful technique. Delta, theta, and alpha oscillation were present in all layers of the OB (olfactory bulb) slice (Chen *et al.,* 2013). The inhalation of essential oils results in significant changes in alpha activity (Masago *et al.,* 2000). An fMRI study showed that odors are sensory probes for the processing of food reward within the cortico-striatopallidal circuitry (Jiang *et al.,* 2015). SLORETA analysis on EEG signal showed that cognitive performance can be improved by the odor of mouth rinses like caffeine and maltodextrin (De Pauw *et al.,* 2015). Every neuron receiving synaptic inputs is a dipole with a specific orientation and polarity. Apart from spatio-temporal analysis forward solution also requires information about neuronal current sources for the particular activity. Voltage pulse due to single dipole is very faint and could not be detected with scalp electrode but when a large population of neuron trigger simultaneously a larger voltage pulse arises, and this can be transferred to scalp electrode. Region of these sources are called neural current sources in the brain, produce scalp surface potentials that can be measured (Tripp, 1983; Mosher *et al.,* 1999).

MATERIALS AND METHODS

Independent component Analysis

Blind source separation problem to find independent source was proposed as independent component analysis (Comon, 1994). For two recorded mixture of speech signals at time t, $s_1(t)$ and $s_2(t)$, received by two microphones $m_1(t)$ and $m_2(t)$, the recorded signal can be written as

$m_1(t)= b_{11}s_1(t)+ b_{12}s_2(t)$ (1)

$m_2(t)= b_{21}s_1(t)+ b_{22}s_2(t)$ (2)

Matrix parameters depend on the distance between microphone and speakers, and also depend on the properties of the microphone also. For n independent mixtures (Hyvärinen and Oja, 2000).

$m_i=b_{i1}\, s_1+b_{j2}\, s_2+b_{i3}\, s_3+\ldots\ldots b_{in}\, s_n$ for all i (3)

Then Vector-matrix can be written as;

m=Bs (4)

m= random mixture matrix with elements $x_1, x_2, \ldots. x_n$

B= mixing matrix with elements b_{ik}

s= source elements $s_1, s_2, \ldots. s_n$

The statistical organization of Equation (4) is called independent component analysis with non-Gaussian consideration.

Dipole Analysis

In the majority of the EEG source localization methods, Spherical Head Model or Boundary Element Head Models are used to represent the physical properties of the human head volume conductor (Kavanagk *et al.*, 1978; Oostendorp and Van Oosterom, 1989). Here boundary element model (BEM) is applied as forward model. Dependence of these sources with magnetic and electric field outside the surface can be measured with this method. The BEM model consists of three 3-D surfaces include skin, skull and cortex Two-dimensional Laplace equation (5) is used (Nédélec, 2001)

$$\frac{\partial^2\phi}{\partial^2x^2}+\frac{\partial^2\phi}{\partial^2y^2}=0 \qquad (5)$$

An interior boundary value problem like our head requires to solve Equation (5) in two-dimensional region R (O_{xy}-plane) bounded by a closed curve *C* subject to boundary condition.

$$\phi=f_1(x,y) \quad for\ (x,y)\in C \qquad (6)$$

For general points (ξ,η) the particular solution to Equation (5) will be:

$$\phi(x,y)=\frac{1}{2\pi}\ \ln\sqrt{(x-\xi)^2+(y-\eta)^2} \qquad (7)$$

for $(x,y)\neq(\xi,\eta)$

Hence fundamental solution for two-dimensional Laplace equation is;

$$\phi(x,y;\xi,\eta)=\frac{1}{4\pi}\ \ln[(x-\xi)^2+(y-\eta)^2] \qquad (8)$$

ϕ satisfy equation (5) everywhere except at (ξ,η) where it is not well defined.

Wavelet Analysis

Alfred Haar was the first who used the term "wavelet" in 1909. After then the theory is recommended by Jean Morlet and the methods of wavelet analysis mainly proposed by Y. Meyer (Farge, 1992). In the last decade of 20^{th} century the effort of Ingrid Daubechies, Ronald Coifman, and Victor is worthwhile (Misiti *et al.*, 1996).

For input signal *x*(t) the transformation will be

$$\mathrm{WT(a,b)}=\int x(t)\psi^*_{a,b}(t)dt \qquad (9)$$

Where '*' is the complex conjugate, $a\in R^+$ is scale parameter $b\in R^+$ is translation. $\psi^*_{a,b}(t)$ is calculated from mother wavelet at time a and b:

$$\psi_{a,b}(t)=\frac{1}{\sqrt{a}}\psi\left(\frac{t-b}{a}\right) \qquad (10)$$

In general mother wavelets are orthogonal dyadic functions. Then mother wavelet is:

$$\psi_{j,k}(t)=2^{-\frac{j}{2}}\psi(2^{-j}t-k) \qquad (11)$$

$$\{\psi_{j,k}(t),j,k\ \in Z\}\ \text{for}\ L^2(R) \qquad (12)$$

These sinusoidal wavelets are being used for time-frequency decomposition in EEGLAB (Delorme and Miisiti, 2004). Frequency perturbation related to an event need a specific time span (window) that is a function of frequency and time both. As a result, image pixel colors indicated the related power and its height will show the corresponding frequency. Average for 'n' trials can be stated as

$$ERSP(f,t) = \frac{1}{n}\sum_{k=1}^{n}|F_k(f,t)|^2 \quad (13)$$

In this analysis we have used wavelets for which number of cycles is slowly increased with corresponding frequency (Fig. 4).

Experimental Setup and Analysis

In current study four female subjects have participated with ages from 19-30 years and mean ± S.D = 23.25 ± 4.99 years. All are in good health and have no history of neurological disorder. They were trained for about two weeks before the final observations. Written consent is obtained as per the ethical committee of the university. For two hedonic stimuli rose flower and onion are presented to them. Experiments are performed in Neurophysics Intelligence Modeling (NIM) research laboratory, Department of Physics, University of Karachi using MDX NeuroPro32 EEG recording device. The device is capable of gathering braining signals at 200 samples per second, i.e. the device sampling rate 200 Hz and has a precision of 12 bits with 10 MΩ input impedance. Brain signals are obtained using 19 Ag/AgCl electrodes. Spatial and Spectral analysis is performed to understand the electrodynamics of brain in olfactory domain. Experiment is conducted in sound- and light-insulated room. Subjects are asked to be relaxed, don't take any stress, can ask any concerned question that irritate them. Most of them were asking about not to get hurt by the electrode placing on the scalp. Then they have been told that we are not going to give them any electric shock but instead we are recording the signals that their brain generates during smelling process. To avoid high amplitude alpha activity with closed eyes, participants kept their eyes open (Krbot *et al.,* 2015).

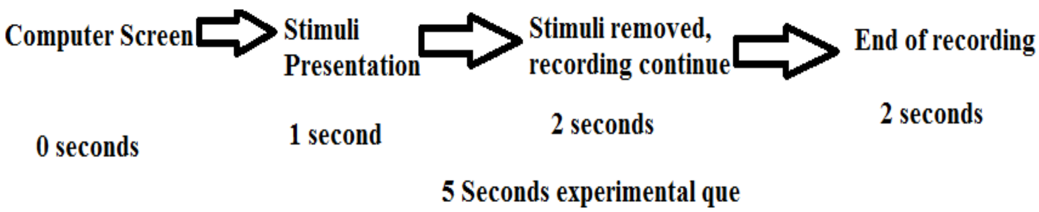

Fig. 2. Experimental Timeline.

Experimental que is arranged as subject is asked to be calm and watch grey cross on screen, after one second, smell command is appeared and odorant is presented 1-2 inch below her nostril, after 2 seconds it is removed but signal recording continue till 2 more seconds (Fig. 2). Triggering time of odor evoked oscillation in brain is not fixed it may vary from few seconds to minutes. In the absence of any particular time interval for odor perception stimulus time is chosen to keep the balance between wipeout the last odors and avoiding the fatigue effect (Wang *et al.,* 2002; Zelano *et al.,* 2007).

After a single run subjects are given a break of 5 minutes, in order to wipe out completely the odors' effect. When this break is over, the procedure is repeated. The length of the trial, including pauses and set-up time, is 45 minutes per subject.

Data is analyzed by EEGLAB v14.1.1 running under MATLAB environment. EEGLAB is an open software (Delorme and Makeig, 2004) for brain data analysis. Preprocessing is performed by removing artifact associated by removing cough, jaw clenching, sneezes effects. This rejection is performed by visual inspection which is based on the presence of high frequency greater than 50Hz and high amplitude signals greater than 300μv. Hence, we have performed visual inspection as well as semi-automatic rejection to our data. ICA is applied to the clean data. After getting independent sources the forward problem is estimated by using the Boundary element model. Now Automatic fitting of multiple dipoles with their bilateral dipoles is performed. Dipoles only within the head volume are considered. For more than one dipole formation only with least variance are taken into consideration. Wavelet analysis begin with 3 cycles and the lowest frequency window is about 0.5 seconds long is performed for the desired components.

RESULTS AND DISCUSSION

In this study, rose and onion are used as pleasant and unpleasant odor respectively. Independent components for pleasant smell are 76 (19 electrodes x number of subjects) and the same number is formed for unpleasant event. Hence a total of 152 (76+76) components were analyzed. For each time latency one with smallest variance is then chosen. As a result, we have selected 4 components for each case. These components with dipole location in cerebral cortex are depicted in Figure 3. Event related spectral perturbation of localized dipole components with power distribution in decibel is presented in Fig. 4, also potential of brain signal due to olfactory stimulation in μV with respect to latency is also shown in the same figure.

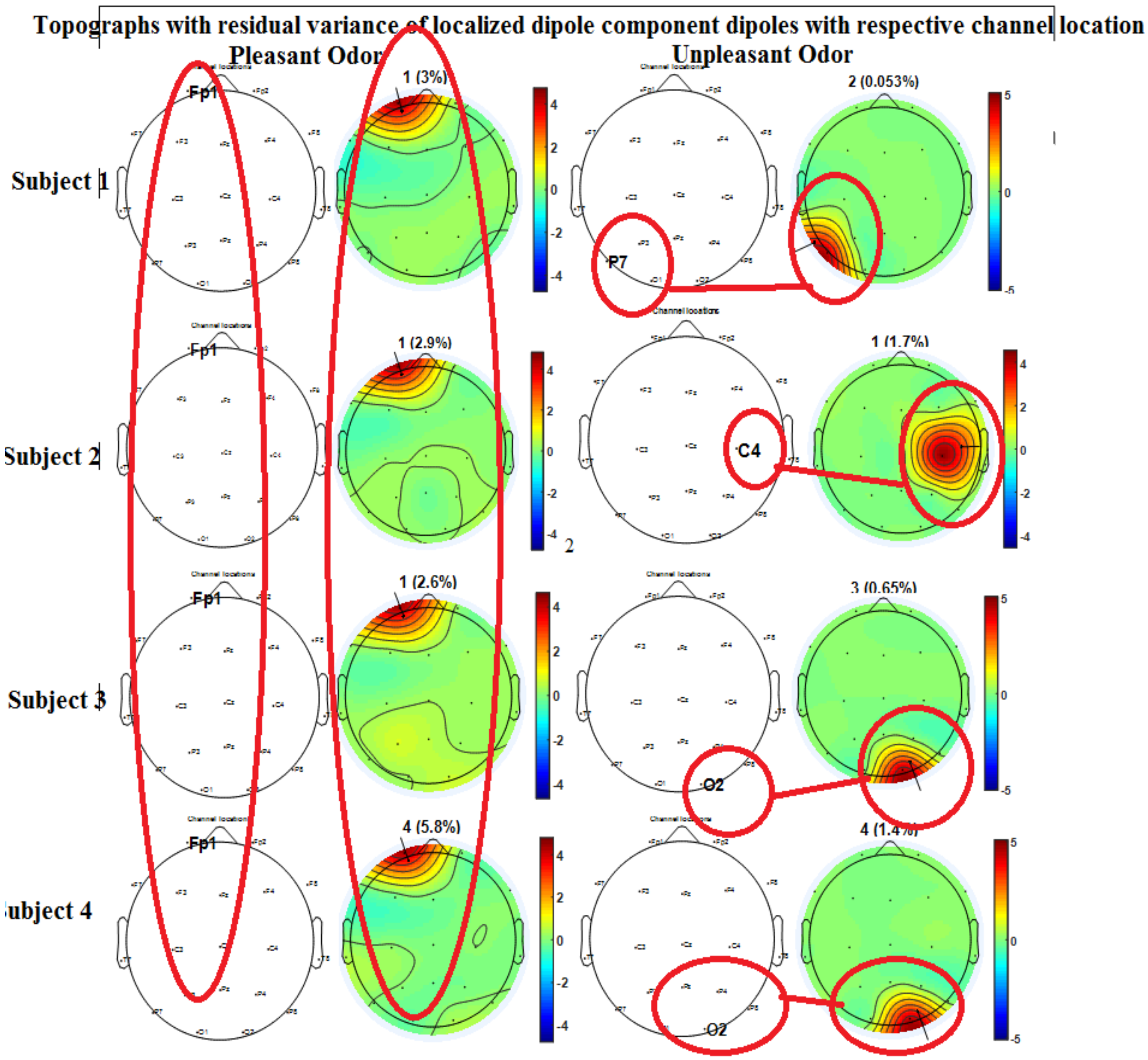

Fig. 3. Spatial distribution of neuronal current generators: Electrodes position for localized dipole within an independent component with decibel power scale.

Scalp topographic plot (Fig. 3) is showing that pleasant oscillation is creating localized dipoles in frontal lobe, while unpleasant oscillation making localized dipoles in temporal and occipital lobes. Our results are consistent with the previous work (Kline *et al.*, 2000; Kim *et al.*, 2003). Power distribution bar on the right-hand side of dipolar plots are showing that unpleasant odor has more dipolar power than pleasant oscillation. Figure 3 shows that residual variance for pleasant odor ranges from 2.5-5.8% while for unpleasant case 0.053-1.7%, this result is showing that localization is in good agreement for unpleasant oscillation. Time-frequency analysis (Fig 4) are showing scattered spectrum for pleasant odor. At the stimulation time β and γ oscillation with low power are present in all four subjects. Then with the time these positive signals reduce till the negative peaks, subsequently frequency decreases to δ, θ and α band with low power (decibels). For unpleasant stimulation, significant potential can be observed in the middle latent time interval from 2500 to 4000ms. Spectral power distribution is also significant. Peak to peak penitential varies ±2μV in case of pleasant and ±10μV unpleasant case.

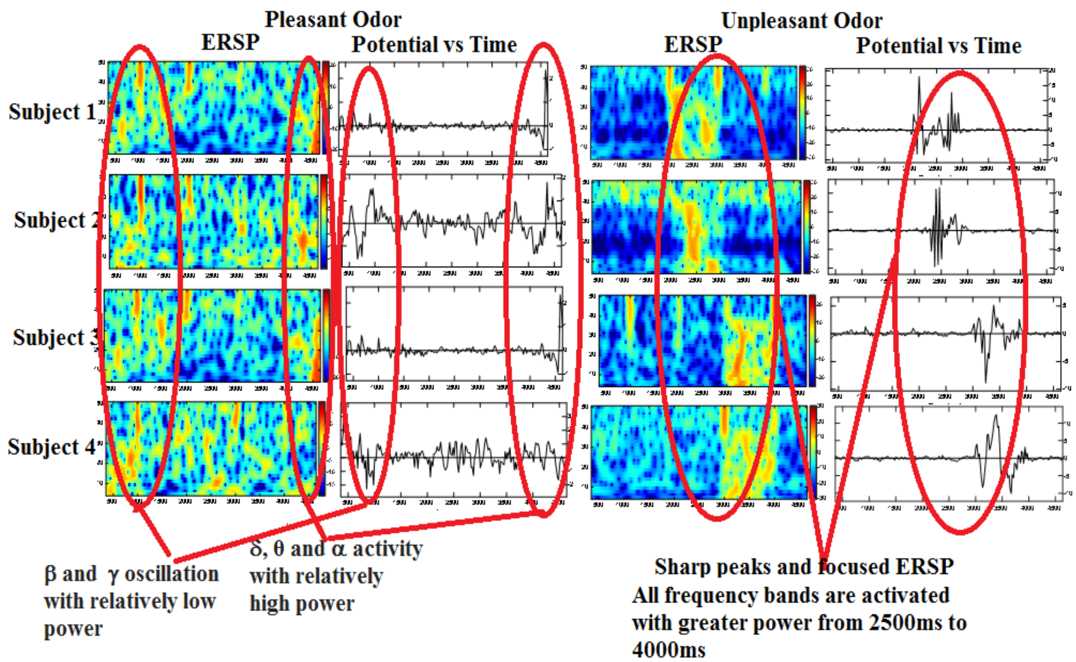

Fig. 4. Time-Frequency analysis for olfactory induced signals. Plots in black and white are showing variation of potential in μV with respect to latency. Color plots are showing frequency (Hz) distribution with the power (decibel) of the signal with time.

Conclusion

Time-frequency analysis is showing that olfactory induced oscillation may trigger a great frequency range from 0.5-50Hz which is consistent with previous literature (Frederick *et al.,* 2016), (Pinto *et al.,* 2014). Smelling signals can activate the whole brain (Fig. 4). We have found that time perceiving the smell is not robust but in case of unpleasant smell it seems that it confines after 200 to 300ms after stimulation. This result is also in good agreement with the literature (Wang *et al.,* 2002; Zelano *et al.,* 2007). Our dipole study on EEG signal is showing that current sources in brain are more confined during unpleasant odor stimulation than in case of pleasant stimulation.

Future work

In this study we have proposed preliminary results about time-frequency and dipole behavior for the odor oscillation. To find accurate information about how to send smell through electronic signals, i.e. a solution of forward problem, this work needs more subjects with different odorants at different latencies.

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