MeMeA 2009 - International Workshop on Medical Measurements and Applications
Cetraro, Italy
May 29-30, 2009

Objetive Assessment of olfactory function using Functional Magnetic Resonance (fMRI)

A device for generating automated olfactory stimuli

S.Borromeo, J.A.Hernández-Tamames, G.Luna, F.Machado, N.Malpica
Electronic Technology Department
Rey Juan Carlos University
Móstoles, Spain
susana.borromeo@urjc.es

A.Toledano
Servicio de Otorrinología
Fundación Hospital de Alcorcón
Alcorcón, Spain
atoledano@fhalcorcon.es

Abstract—. **In this work, a device for generating automated olfactory stimuli in functional magnetic resonance imaging (fMRI) studies is described. The novel issues of our design are: synchronization between the acquisition and the olfactory task, automated control of experimental parameters (odorants sequences, frequency, time and concentration of stimuli). Finally, we present the preliminary results obtained on a General Electric 3 Tesla MRI scanner belong to The Alzheimer Project of the Fundación Reina Sofía.**

Keywords-component; fMRI;olfatometer;feedback

I. MOTIVATION

A few studies about the reactions of the human brain because of the olfactory senses have been done and compared with others like the voluminous studies on visual, auditory, and somatic sensations, until quite recently. Unlike the others, meaning the auditory, visual, or somatic sensory modalities, it is very difficult to do an objective quantified exploration of the olfactory system. This difficulty is due to the lack of the different adequate methods to produce a selective and controlled stimulation of the olfactory system. Recently, the scientific interest on the evaluation of the olfactory function has been increased because of the close connections which have been established between the impairment of the olfaction sensibility and some other neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease [1-8]. Surely it may be that an early detection of the olfactory dysfunction can be used to assess the possible risk for developing Alzheimer's disease or Parkinson's disease in asymptomatic individuals. Nowadays an effective strategy to combat these diseases will have to include an early detection of their pathologic processes and also therapies to retard their advance.

On the other hand, fMRI makes it possible to study the brain activity noninvasively during task performances. For studies of the effects of olfactory stimuli, the functional neuroimaging has gained a wide-spread interest during the last years. You will find a summary of fMRI studies of olfactory function in [9]. Functional neuroimaging techniques enable researchers to observe the brain regions activated by olfactory stimuli in human subjects. Functional magnetic resonance imaging (fMRI) makes it possible to study in a non-invasively way the human brain running, through the detection of blood oxygen level-dependent (BOLD) signal changes. These changes are believed to the result of the neuronal responses induced by recurrent epochs of stimulation (i.e., experimental conditions) versus no-stimulation (i.e., control conditions).

The purpose of this work is to evaluate the feasibility of a device which generates automated olfactory stimuli suitable for fMRI experiments.

II. BACKGROUNG

Several designs for olfactometers or different systems capable of generating odorants have been developed and published [10-15]. All of them consist of three modules: an airflow preparation unit, an odor generation unit and a delivery unit. It's very important to have in mind that to be suitable for fMRI experiments, it is not allowed any ferrous or metal components near the MR scanner.

However, another important aspect, which has not been stressed sufficiently so far, is the role of the synchronization between the image acquisition (by a trigger signal of MR scanner) and the stimuli deliver. On the other hand it is also important to design in a full automated way the different tasks controlling the frequency, time and concentration of olfactory stimuli.

fMRI stimulation paradigms typically use either "Block Designs" or design Event-Related (ER). In a block design, one common paradigm is to alternate between 15 or 30 second blocks of stimulus, and blocks without stimulation. Ten images of the brain can be acquired with EPI (Echo Planar Imaging) sequence.

Experimental design can be complex and the synchronization with acquisition time is vital to an accuracy data analysis.

III. DESIGN

In the following paragraphs we will describe our nine-channel olfactometer. The following image (Fig.1) shows a schematic diagram of the developed device.

978-1-4244-3599-9/09/$25.00 ©2009 IEEE

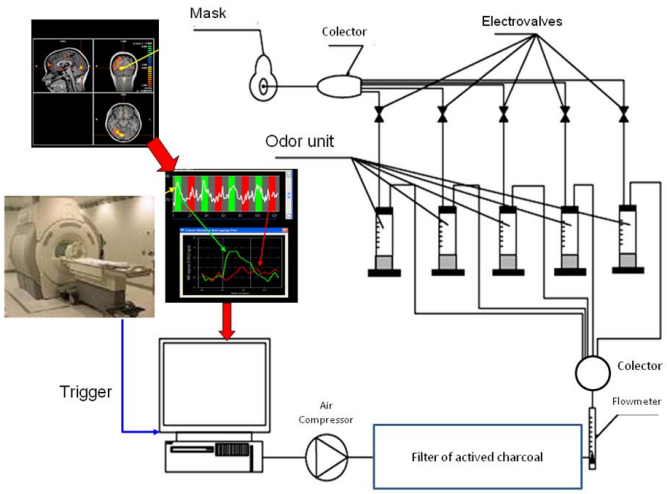

Figure 1. Schematic diagram

Briefly, the olfactometer has been designed to alternate between odorized and non-odorized airflows. Up to eight different odorants can be administered within a given experiment.

The odor generation unit is built with eight canisters with different odor solution (Fig.2), one electrovalve per channel (Fig.3) and a carrier air stream. Compressed air for the olfactometer is supplied by an air compressor and the compressed air is purified by an activated charcoal filter.

With the olfactometer we are able to administrate any of the eight odorants as also clean air. Whole system is controlled by a PC which includes the software and data acquisition board to operate the olfactometer. The system allows the programming of several sequences, choosing experimental parameters such as: the odors, the frequency, time and concentration of olfactory stimuli. Furthermore, the developed system provides the capability to synchronize the onset of odor presentation with the acquisition by a trigger signal of the MR scanner.

Finally, to complete the system to assess the olfactory function, objectively, an odor identification test based on the Connecticut Chemosensory Clinical Research Center (CCCRC) test has been designed [16].

Figure 2. Odor generation unit:canister

Figure 3. Electrovalves

IV. EXPERIMENTAL DESIGN

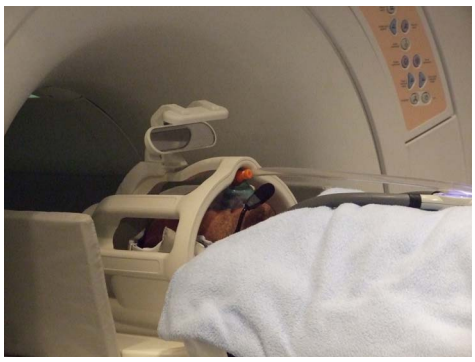

Figure 4. A a volunteer with mask and 8 channel surface coil

Imaging was performed on a General Electic 3 Tesla MRI scanner belong to The Alzheimer Project of Fundación Reina Sofía.

To test the performance of our system the subjects were exposed to two odors: coffee and cacao and clean air during the blocks without stimulation.

Odorant presentation paradigm used during fMRI scannig consists on blocks of 30s. Deliver over a 30s period of clean air, deliver over a 30s period of coffee and deliver over a 30s period of cacao. This sequence has been repeated three times, and we are used a repetition time (TR) of 3000 ms. It is to say that each block consists of 10 acquisition.

Each brain volume consists of 40 slides of 2x2x3 mm. For each one it accumulates a time series in response to stimulation paradigm (Fig.5).

Furthermore, diffusion tensor imaging data have been acquired to reconstruct neural tracts.

An important issue is the delay (24s-30s) which appears between odor administration and the odorant presentation. Having in mind the delay we have, it's therefore that it appears the need to synchronize the acquisition of the image with the patient stimuli recognition. It is also to have in mind that it also appears a delay on the deactivation of the stimuli which takes about the 12s.

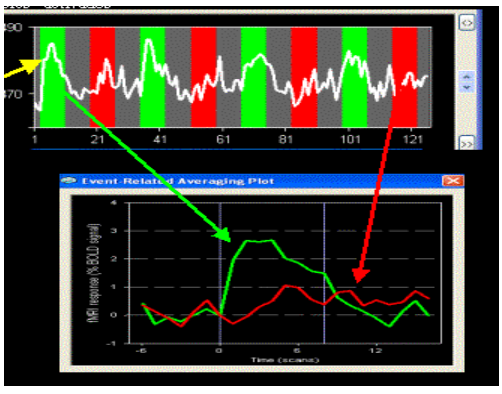

Figure 5. Hemodynamic response in olactory-related brain areas

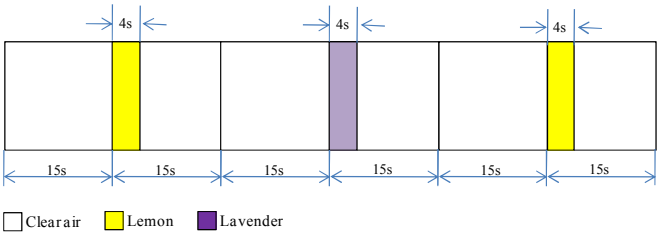

Figure 6. Odorant presentation paradigm using during fMRI scanning

More recent fMRI event-related stimulus paradigms have proven highly effective in visualizing olfactory-related activation and have largely eliminated the effects of POC (primary olfactory cortex) habituation [17]. The delay between odor administration and the odor presentation makes impossible permit the study odor-event-related stimulus paradigms.

Being aware of this limitation, to overcome the same, the air compressor's flow rate has been increased up to 7l/min and essential oils have been used instead of the hot liquid-based odorants which add condensation problems. With these modifications, we achieve a delay not higher than 3s. The achieve value and the control software of the electrovalves make possible to use of event-related design. Here below we describe the tests carried out based on event-related design.

Fig.6 shows the odorant presentation paradigm used during fMRI scanning. Although it consists on blocks of 15s, odorant were presented for 4s. By this way, we try to simulate event-related design. Lemon and lavender were the odorants used.

An EPI gradient echo sequence was used: repetition time (TR) =3000 ms, echo time (TE) =37.6 ms, and flip angle=90°. Spatial resolution was set by a 128×128 matrix and a field of view (FOV) of 22. 1.0 mm-thick slices with 0.2.

V. RESULTS

The fMRI data have been analyzed using two commercial neuroimaging software packages: BRAINWAVE (GE Medical Systems) and BrainVoyager (Brain Innovation B.V). Fiber reconstruction has been accomplished using FuncTool (GE Medical Systems).

The results confirm entorhinal cortex activation. Talairach coordinate are shown on Fig.7 to illustrate activation in primary olfactory cortex.

Fig.8 shows the three-dimensional reconstruction of the activated area within the olfactory bulb as well as the olfactory pathways innerving this area. The fMRI data was obtained after stimulating a volunteer with our proposed experiment.

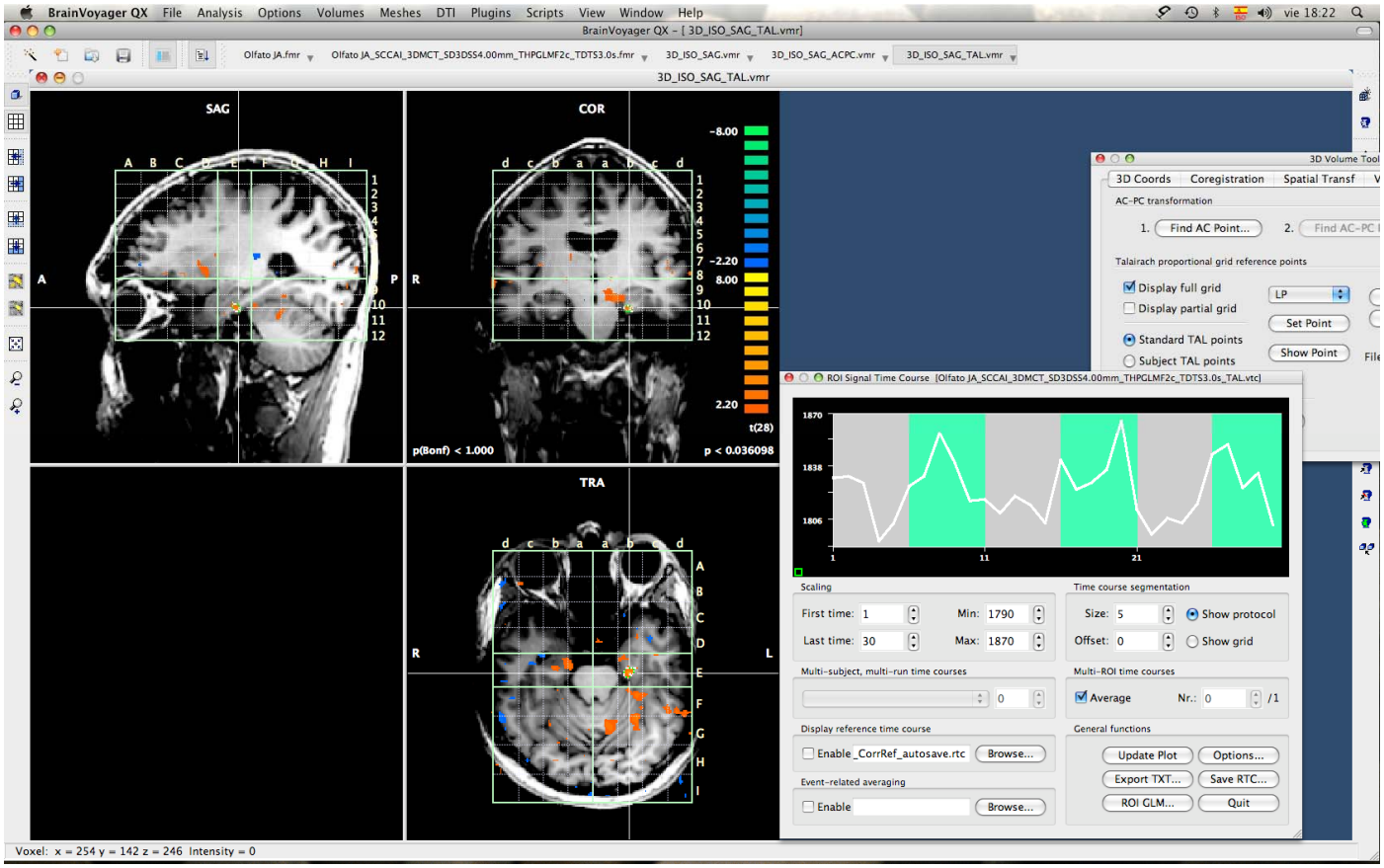

Figure 7. fMRI data analyzed by BrainVoyager .Talairach coordinate match up entorhinal cortex.

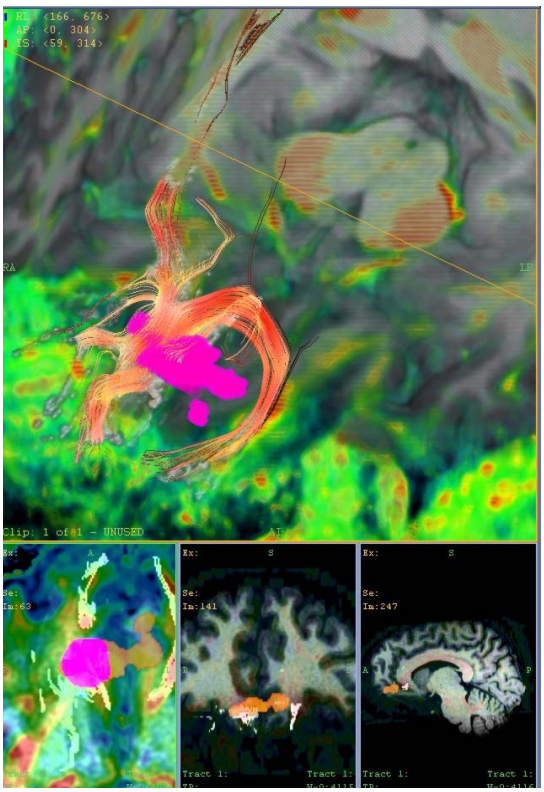

Figure 8. Three-dimensional reconstruction resulting from the cortical and fiber activation in olfactory paths.

In addition to the activity of the olfactory bulb, olfactory activity has also been observed in the temporal area of the parietal lobe.

VI. CONCLUSIONS

The proposed device has demonstrated its effectiveness in stimulating olfactory areas and its capability to adapt to the scanner acquisition times.

Although there still is a long way to make this equipment suitable for clinical assessment in neurodegenerative and neurological prodromes, it led us to open a research of enormous actuality and interest that, for example, could lead us to asses the olfactory capability, the minimum threshold for aromas to become consciously perceived and the relationships between the olfactory areas and other brain areas, such us emotional ones which could be triggered due to memories evoked by different aromas.

There is ongoing work focussed on enhancing the BCI (Brain Computer Interface) technique. This technique selects the different olfactory stimulus, their intensity and frequency depending on the brain activity. Our aim is to add a feedback loop to our proposed device consisting on the brain activity resulting from the olfactory stimulus.

ACKNOWLEDGMENT

The authors would like to thank Eva Alfayate, radiologist of Fundacion Reina Sofia and J. Alvarez-Linera, M.D., of Ruber International Hospital for their collaboration.This work was supported by OLFACTOSENSE Network (CAM-S-SEM-0255-2006) from Comunidad Autónoma de Madrid.

REFERENCES

[1] M.W.Alberts, M.H.Tabert, D.P.Devanand, “Olfactory dysfunction as a predictor of neurodegenerative disease”. Neurology and Neuroscience Reports 2006, 6:379–386. Current Science Inc.

[2] M. M. Ponsen, D. Stoffers, J. Booij, B. L. van Eck-Smith, E. C.Wolters and H. W. Berendse, “Idiopathic hyposmia as a preclinicalsign of Parkinson's disease”. Ann Neurol., vol. 56, pp. 173-81, 2004.

[3] S. Barz S, T.Hummel, E.Pauli, et al. "Chemosensory event-related potentials in response to trigeminal and olfactory stimulation in idiopathic Parkinson´s disease”. Neurology 1997;49(5):1424-1431.

[4] CH. Hawkes. “Assessment of olfaction in multiple sclerosi”s. Chem. Senses 1996;21:486.

[5] K.Sakuma, K.Nakashima, K.Takahashi. “Olfactory evoked potentials in Parkinson´s disease, Alzheimer´s disease and anosmic patients”. Psychiatry Clin Neurosci. 1996;50(1):35-40.

[6] R. McCaffrey, K.Duff, G.Solomon. “Olfactory Dysfunction Discriminates Probable Alzheimer´s Dementia from Major Depression: a Cross-Validation and Extension”. J Neuropsychiatry Clin Neurosci 2000;12(1):29-33.

[7] D.Royall, L.Chiodo, M.Polk, et al. “Severe Dysosmia is Specifically Associated with Alzheimer-Like Memory Deficits in Nondemented Elderlyo Retirees”. Neuroepidemiology 2002;21:68-73.

[8] A.Gray, V.Staples, K.Murren, et al. “Olfactory identification is impaired in clinic-based patients with vascular dementia and senile dementia of Alzheimer type”. Int J Geriatr Psychiatry 2001;16:513-517.

[9] M.H.Tabert, et al. “Validation and optimization of statistical approaches for modelling odorant-induced fMRI signal changes in olfactory-related brain areas”. NeuroImage 34 (2007) 1375–1390

[10] B.N. Johnson, N.Sobel, “Methods for building an olfactometer with known concentration outcomes”. Journal of Neuroscience Methods 160 (2007) 231–245.

[11] L.Marciani, J.C. Pfeiffer, J.Hort, K. Headb, et al. “Improved methods for fMRI studies of combined taste and aroma stimuli”. Journal of Neuroscience Methods 158 (2006) 186–194.

[12] T.S.Lorig, D.G.Elmes, D.H Zald, D, J.V. Pardo. “A computer-controlled olfactometer for fMRI and electrophysiological studies of olfaction”. Behavior Research Methods, Instruments & Computers, 31,370-375.

[13] R.Popp, M.Sommer, J.Müller, G.HajaK, “Olfactometry in fMRI studies: odor presentation using nasal continuous positive airway pressure”. Acta Neurobiol. Exp. 2004,64:171-176.

[14] S.Lowen, S.E.Lukas, “A low-cost, MR-compatible olfactometer”. Behav Res Methods. 2006 May ; 38(2): 307–313.

[15] M.Vigouroux, B.Bertrand, V.Farget, J.Plailly, J.P Royet, “A stimulation method using odors suitable for PET and fMRI studies with recording of physiological and behavioral signals”. Journal of Neuroscience Methods 2005;142:35–44. [PubMed: 15652615]

[16] A.Toledano, E.González, G.Rodríguez, A.N Galindo, “The validity of CCCRC test in patients with nasal polyposis”. *Rhinology*. 2007;45(1):54-8.

[17] C.Zelano, N. Sobel, N. “ Humans as an animal model for systems-level organization of olfaction”. Neuron 48, 431–454.