Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

Combining Near Infrared Spectroscopy and Functional MRI during Continuous Performance Test in Healthy Subjects

Michele Butti, Aurora Pastori, Anna Merzagora, Anna Bianchi, Alessandra Bardoni, Vincenzo Branca, Antonella Costa, Sergio Cerutti, Gianluigi Reni

Abstract—**The study of cognitive functions is a major challenge of the modern functional imaging. Activation of specific cerebral area is obtained from the observation of physic characteristic affected by changes occurring in the blood flow resulting from an increased metabolic consumption. In this work two imaging techniques are used, the functional magnetic resonance (fMRI) and the Near Infrared Spectroscopy (NIRS), in order to assess cerebral performance during the execution of a well known sustained attention task, the Conners' Continuous Performance Test (CPT). With fMRI analysis were found activations in the frontal, parietal and supplementary motor areas, whereas NIRS system showed a region-wise difference in the variations of parameters and different activation trend localized in the middle-right frontal area. The combined analysis of the two techniques allows to obtain more detailed information and places itself as a first step toward a result of multimodal image integration.**

I. Introduction

Functional magnetic resonance imaging (fMRI) is a recent method of neuroimaging that enables to determine which parts of the brain are activated by different types of physical sensation or activity, such as sight, sound or movement of a subject. This technique shows and localizes cerebral activation areas consequently to a suitable task. For this reason it is the main way of *in vivo* studies of cerebral organization. Actually, fMRI method does not measure cerebral electrical activity directly but, through the BOLD effect, it is able to identify the changes in signals in response to changes in cerebral blood flow related to neural activity in the brain [1]. Likewise, functional near-infrared (fNIR) spectroscopy uses specific wavelength of light, injected at the scalp, to allow the measure of changes in the concentrations of oxy- and deoxy-hemoglobin (oxy-Hb and deoxy-Hb) during task-related brain activity [2]. Sustained attention is defined as the ability to maintain an high vigilance level for a long time, allowing the subject to respond against presentation of infrequent and unpredictable events. It is a basic cognitive process that influences other aspects of attention (as selective attention) and all superior function (memory, learning). A sustained attention task which demands an automatic response may be the Continuous Performance Test (CPT). Many studies were made using the CPT test and a world-wide literature attests the scientific importance of this research method [3]-[5]. Pioneering studies [6],[7] about fMRI during a sustained attention task highlight activation regions in the medium frontal circulus and in the right parietal lobe. More recent studies focus significant increase of activation in the medium prefrontal cortex.

Manuscript submitted April 21, 2006.

M. Butti is with the Department of Biomedical Engineering, Polytechnic University of Milan, Italy (e-mail: michele.butti@polimi.it).

A. Pastori is with the Bioengineering Laboratory, IRCCS "E. Medea", Bosisio Parini, Lecco, Italy (e-mail: aurora.pastori@gmail.com).

A. Merzagora is with the School of Biomedical Engineering, Science and Health Systems, Drexel University, Philadelphia, PA 19104 USA (e-mail: am396@drexel.edu).

A. Bianchi is with the Department of Biomedical Engineering, Polytechnic University of Milan, Italy (e-mail: anna.bianchi@polimi.it).

A. Bardoni is with Neurorehabilitation Unit, IRCCS "E. Medea", Bosisio Parini, Lecco, Italy (e-mail: alessandra.bardoni@bp.lnf.it)

V. Branca is with the Department of Diagnostic and Interventional Neuroradiology, Ospedale Maggiore Policlinico, IRCCS "Mangiagalli e Regina Elena", Milan, Italy (e-mail: vincebrait@yahoo.it).

A. Costa is with the Department of Diagnostic and Interventional Neuroradiology, Ospedale Maggiore Policlinico, IRCCS "Mangiagalli e Regina Elena", Milan, Italy (e-mail: lella_costa@yahoo.it).

S. Cerutti is with the Department of Biomedical Engineering, Polytechnic University of Milan, Italy (e-mail: cerutti@biomed.polimi.it).

G. Reni is with the Bioengineering Laboratory, IRCCS "E. Medea", Bosisio Parini, Lecco, Italy (e-mail: gianluigi.reni@bp.lnf.it).

II. Materials and Methods

A. CPT Task

The CPT fMRI-version test was implemented with the software "Presentation version 0.81, build" (Neurobehavioral Systems). The package "Presentation" is able to make the stimulus and to synchronize it with the MR scanner (mripulse function). Moreover it is possible to obtain a logfile with the onset times of stimuli and the response times of the subject. This CPT version consisted of 26 different letters, of the English alphabet, which were presented sequentially in random order on the glasses system used by the subject during the acquisition of MR images. Furthermore, by means of a headphone system it is possible to give instructions about the test. The inter-stimulus interval (ISI) was of 1sec or 2sec and the presentation time of each letter was 250 ms. The experiment involved 450 stimuli, 25 X letters (Target stimuli) and 425 other letters (NoTarget stimuli). Subjects were instructed to press the response button with the index finger of their right hand as fast as possible when occurred any letter other than X, and to inhibit the response when occurred the X. The rest time

(useful for comparison with the activation period) was 2 min of meaningless images (geometric lines with various directions) administered before and after performing the test. The activation time (CPT test) was of 10 min.

B. Scanning Procedure

All neuroimaging was performed with a 1.5 T MRI scanner (Eclipse Marconi - Philips system - Department of Diagnostic and Interventional Neuroradiology, Ospedale Maggiore Policlinico, IRCCS, Milano) using a standard head coil. Anatomical MRI data were collected immediately prior to the fMRI data to identify anatomical landmarks and to obtain high-resolution structural images to coregister with functional images. A sagittal T1 weighted image was obtained. For functional imaging, a T2*-weighted gradient-echo sequence was used: TR (repetition time)=3 s, TE (echo time)=60 ms, FA (flip angle)=90°, FOV (field of view)=24x24 cm^2 , slice thickness=4 mm contiguous. A total of 26 transaxial 64x64 images (parallel to the line linking the anterior and posterior commissures CA and CP) were acquired with a plane resolution of 3.97 mm^2 , providing coverage of the whole brain. During the CPT test 290 image volumes per subject were acquired: the first 10 volumes (30s) were discarded from the following analysis, to allow steady state to be reached. Hence 280 volumes were used: the volumes from 11 to 50 (2 min) are the first rest time, the volumes from 51 to 250 (10 min) are the active time, the volumes from 251 to 290 (2 min) are the second rest time. Duration of test was approximately 14 minutes.

C. fNIR Analysis and Recordings

Functional near-infrared (fNIR) spectroscopy relies on the placement of light sources and detectors on the scalp. Light in the near-infrared range (wavelengths between 700 and 900 nm) is used to optically monitor changes in oxy-hemoglobin and deoxy-hemoglobin (oxy-Hb and deoxy-Hb) associated with brain activity. When light enters the tissue, it undergoes absorption and scattering. According to the Modified Beer-Lambert Law (1), the intensity of the light that exits form the tissue after absorption and scattering is:

$$I = G\, I_0\, e^{-(\alpha Hb\, CHb + \alpha HBO2\, CHbO2)L} \quad (1)$$

Where G is constant attenuation, I_0 is the input light, α_{Hb} and α_{HBO2} are the molar absorption coefficients of oxy-Hb and deoxy-Hb, C_{Hb} and C_{HbO2} are the the concentrations of oxy-Hb and deoxy-Hb, L is the light path which is function of absorption and scattering in the tissue. Using two different wavelengths in the near-infrared range, it is possible to obtain ΔC_{Hb} and ΔC_{HbO2}, i.e. the changes of oxy-Hb and deoxy-Hb concentrations relative to an initial baseline. Also the blood volume (BV) has been computed.

The fNIR device used for this study was provided by Drexel University (Philadelphia, PA) and is comprised of a flexible probe that covers the forehead, a control box for data acquisition and a computer for data analysis. The sensor consists of 4 LED light sources and 10 photodetectors, giving 16 acquisition channels.

D. Subjects

Nine healthy volunteers took part in the present study but NIRS acquisitions were available only for seven of them. All subjects were right handed, with a mean age of 24 years (SD 2.9 years, range 18–28 years). All volunteers were native Italian speakers and were not paid for their participation, 8 of the subjects were male and 1 was female. They all had normal vision and had no history of psychiatric disorders. The participants were screened thoroughly for neurological symptoms: they all did not show neuro-psychological illness; cognitive level and attentive capability were in a normal state; none had first-degree relatives with a psychiatric illness. Written informed consent was obtained from all volunteers after the examination and test procedure had been explained. The study was approved by the ethical review board of the "E. Medea" institute.

E. Data Analysis

Functional fMRI data were analyzed offline using a PC with a software to convert the raw data from DICOM format to Analyze format and with SPM5 software packages (Wellcome Department of Cognitive Neurology, London-UK) to estimate the activation maps. The 280 image volumes were realigned and coregistered to the anatomical images of each subject. Then, they were spatially normalized to the neuroanatomical atlas of Talairach and Tournoux (using a 12 parameter affine approach and a T2* weighted template image) and smoothed, using Gaussian kernels of 10 mm, in order to remove slow drifts in signal intensity. A block design was used in the statistical analysis: one regressor for each of 5 intervals (length 2 min, 40 image volumes) of the CPT test was assigned, the 2 rest times were used as baseline. Afterwards functional maps were generated, one for each block, using simple t test comparing active versus rest periods; the P-value threshold used to determine regions of activation was $P < 0.001$ without correction. The activation maps for the 5 block were obtained initially for each subject distinctly, then the 9 subjects were analyzed together in order to obtain mean activation map. Functional maps were superimposed on the anatomical T1 weighted image normalized to the neuroanatomical atlas of Talairach.

The analysis of fNIR measures was performed after obtaining variations of oxy- and deoxy-Hb through the Modified Beer-Lambert Law. Recorded data were divided in 2 minutes blocks for consistency with fMRI data analyses. A repeated measure ANOVA test was performed to look for possible significant changes between the beginning and the end of the task and for possible differences in activated areas. In order to do that, values for each subject in the two stages (beginning and end of the task) were normalized to the mean in the first stage.

III. Results and Discussion

From observation of obtained fMRI images, it can be seen that the contribution of frontal cerebral areas and superior

motor areas was of primary importance to understand sustained attention task. Involvement of these areas can be attributed to recruitment of AAS (Anterior Attentional System) which has a function to identify and classify stimulus characteristics. An homogenous distribution of cerebral activation regions is observed. In particular the fronto-opercularis area (F3), the superior temporal gyrus (T1) and the supplementary motor (SMA) proved to be activated. During the first two minutes of test (Fig.1 a), all volunteers displayed a significant and stable activation in the T1, F2 (medial frontal gyrus) and F3 areas, without lateralization; in the following two minutes the activations increased in two subjects, while in the others ones they substantially remained unchanged. The following blocks demonstrated a progressive decrease of this activities particularly in F3 e T1 areas, on the contrary in the SMA a progressive increase of activation was observed. Finally, in the last block (Fig.1 b), the activations were further reduced, especially in the SMA. Regarding the previous studies which showed mainly the involvement of the frontal and parietal regions and of the SMA [6]-[7], we found an important activation in the temporal areas too.

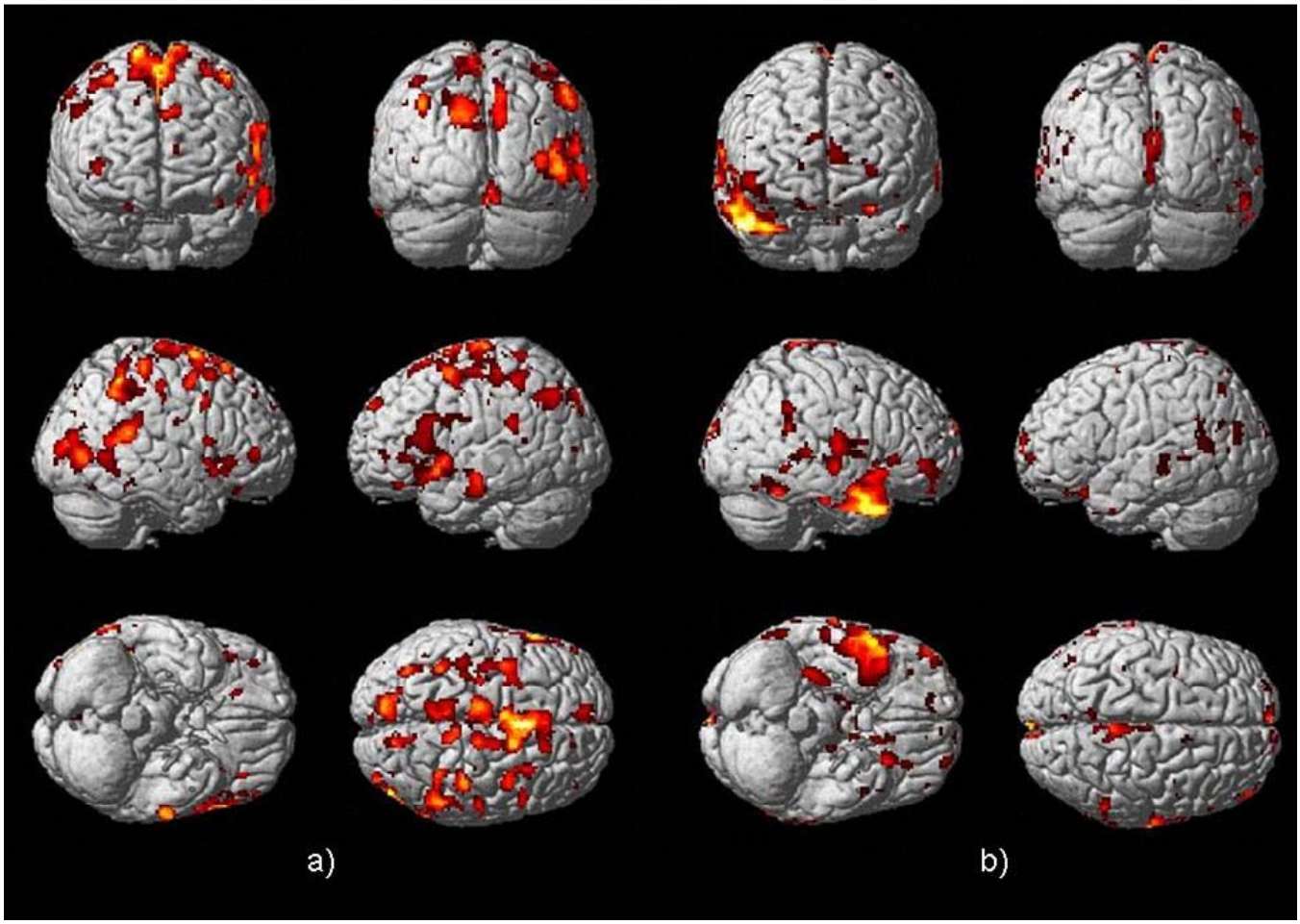

Fig. 1: Continuous Performance Test for one subject. Statistical parametric map of the t-scores. Beginning (a) and end of the task (b)

Results from fNIR measurement uncovered significant variations connected to the stage of the task (beginning or end) and revealed the localization of these most significant changes. Both oxygenation and deoxygenation values showed significant differences ($p<0.05$) between the first block and the last block. An example of the complete temporal evolution for mean oxy-Hb, deoxy-Hb and BV is shown in Fig.2 for one subject. Moreover, when comparing changes between beginning and end of the task region-wise, deoxygenation values do not show any significant difference (as shown in Fig.3). When analyzing oxygenation data, instead, an altered trend is observed in the middle-right region (Fig.4); in particular, significant variations are observed in the middle region ($p<0.05$).

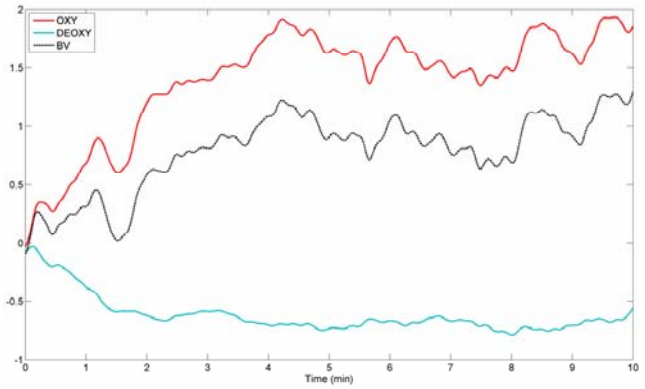

Fig. 2: Complete temporal evolution of oxygenation, deoxygenation and blood volume changes for one subject. The increase in the final stages of the task is apparent.

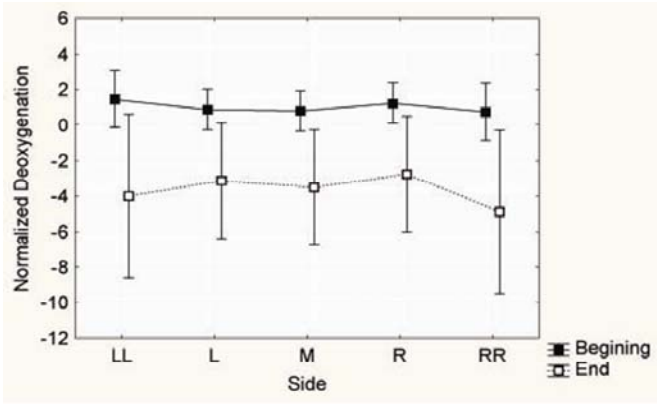

Fig. 3: Deoxygenation values.

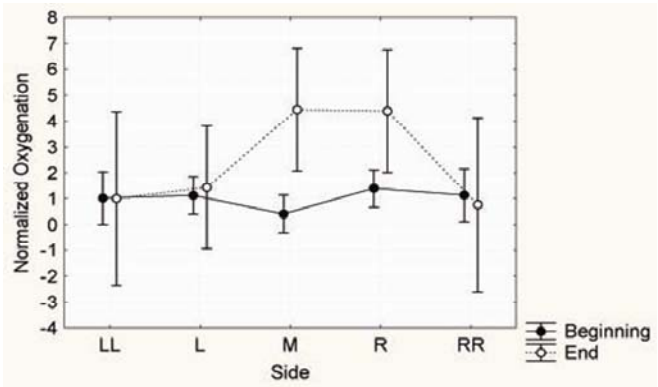

Fig. 4: Oxygenation values.

IV. Conclusion

In this study the cerebral activations patterns was identified during a sustained attention task in a group of healthy subjects. Using the neuroimaging fMRI method it has been demonstrated that activation areas are the same in all subjects for localization and temporal trend. The activations in the frontal, parietal and supplementary motor areas, which were found, confirm results of literature . The activation of temporal areas is not documented in previous studies and it is not yet interpreted. Timing analysis has shown that the group is able to maintain the activity altogether stable with a decrease in the final phase of the test. This trend is confirmed in the frontal region with fNIR data, which complemented fMRI results with oxygenation data. These values are able to show a region-wise difference in the variations between the beginning and the end of the task. Moreover, the different activation trend is localized in the middle-right frontal area, in agreement with other functional neuroimaging studies [8] of sustained attention protocols.

Acknowledgment

We are grateful to the Drexel University (Philadelphia, PA) for making their apparatus available for us. We would like to thank K. Izzetoglu for his training and for helpful comments and suggestions.
This work has been partially supported by the HINT@Lecco project founded by CARIPLO.

References

[1] P.A. Bandettini, E.C. Wong, R.S. Hinks, R.S. Tikofsky and J.S. Hyde, "Time course EPI of human brain function during task activation," *Magn. Reson. Med.* vol. 25, pp. 390-397 (1992).

[2] A. Villringer, B. Chance, "Non-invasive optical spectroscopy and imaging of human brain function," *Trends Neurosci.* vol. 20, pp. 435-442 (1997).

[3] J.W. Campbell, R.C. D'Amato, D.J. Raggio, K.D. Stephens, "Construct validity of the computerized Continuous Performance Test with measures of intelligence, achievement, and behaviour," *Journal of School Psychology* vol. 29, pp. 143-150 (1991).

[4] W.T. Seidel, M. Joschko, "Assessment of attention in children," *Clinical Neuropsychologist* vol. 5, pp. 53-66 (1991).

[5] S.H. Klee, B.D. Garfinkel, "The computerized continuous performance task: A new measure of inattention, "*Journal of Abnormal Child Psychology* vol. 11, pp. 487-498 (1983).

[6] J.S. Lewin, L. Friedman, D. Wu, "Cortical localization of human sustained attention: detection with functional MR using a vigilance paradigm," *J. Comput. Asst. Tomogr.* vol. 20, pp. 695-701 (1996).

[7] J.L. Sunshine, J.S. Lewin, D. Wu, "Functional MR to localize sustained visual attention activation in patients with attention deficit hyperactivity disorder. A pilot study," *Am. J. Neuroradiol.* vol. 18, pp. 633-37 (1997).

[8] R. Cabeza, L. Nyberg, "Imaging cognition II: An empirical review of 275 PET and fMRI studies," *J. Cogn. Neurosci.* vol. 12, pp. 1-47 (2000).