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A pilot study of the reading processes combining reading-related potentials (RRPs) and fMRI

S. Casarotto[1], A. M. Bianchi[1], S. Cerutti[1], G. A. Chiarenza[2], E. Maccagnano[3], P. Vitali[4]
[1]Department of Biomedical Engineering, Polytechnic of Milan, Milan, Italy
[2]Department of Child and Adolescent Neuropsychiatry, Az. Osp. "G. Salvini", Rho Hospital, Rho, Italy
[3]Department of Neuroradiology, Istituto Nazionale Neurologico "C. Besta", Milan, Italy
[4]Department of Clinical Neurophysiology, University of Genova, Italy

Abstract—**Aim of this work is to describe temporally and spatially the activation of the cerebral areas involved in reading processes by combining fMRI and reading-related potentials (RRPs). RRPs and fMR images were recorded in separate studies during a specifically designed experimental procedure. The protocol consisted of three visual tasks of increasing complexity. In the first two tasks subjects were asked to passively watch at letters and symbols respectively without making any effort in reading or articulating silently them. In the third task subjects were asked to read aloud letters appearing on a screen at a rate of 0.5 Hz. 7 young healthy subjects participated in the experiment. The analysis of RRPs highlighted the following results. During non-alphabetic symbols presentation the amplitude of the potentials was lower in comparison to presentation of letters. Reading aloud generated RRPs of greater amplitude than implicit reading. The analysis of fMRI scans revealed that the visual presentation of both letters and symbols produced similar activation of primary visual areas. Besides these areas, reading aloud activated the motor and pre-motor cortices and the left anterior temporal lobe. The combined analysis of RRPs and fMRI characterizes both temporally and spatially the development of reading processes.**

Keywords— **EEG, hemodynamic response, left anterior temporal lobe, motor cortex, pre-motor cortex, primary visual areas, visual stimulation.**

I. Introduction

Reading abilities are important for social and working life of each individual. They are influenced by intellectual and sensory functions, environment and received education. Reading processes belong to the higher cognitive functions and involve perceptual processes, both visual and auditory, verbal-motor coordination, attention, phonological skills, memory and feedback mechanisms [1]. Therefore, the study of such processes requires to consider the interaction among different neuronal networks, each working at characteristic spatial and temporal scales.

In this perspective, reading-related potentials (RRPs) describe the variations of the cerebral electrical activity on the scalp with high temporal resolution: furthermore, this approach is simple and low-cost. The application of functional magnetic resonance imaging (fMRI) techniques extracts cortical activation maps corresponding to specific brain responses and conditions: this method is non-invasive and has a good spatial resolution. The combination of these two methods is useful to integrate the data obtained with different modalities, thus benefiting of their specific properties [2,3].

In this study we describe the morphology of RRPs and the topography of fMR maps recorded from healthy subjects during the same stimulation paradigm, consisting of different reading-related tasks.

II. Methodology

A. Subjects

Participants were 7 voluntary right-handed and healthy subjects (2 females, mean age 26.1 yrs., range 25-26 yrs.) They were undergraduate and PhD students of Biomedical Engineering at the Polytechnic of Milan. Two subjects were Spanish native speakers, whereas the others were Italian native speakers.

B. Materials

The stimuli were Italian alphabetic capital and small letters and non-alphabetic symbols visually presented. The stimulation protocol consisted in three different tasks. The first two tasks (*symbol presentation* SPR and *letter presentation* LPR) are considered as *passive* because subjects passively watched at symbols and letters respectively without making any effort in reading or articulating silently them. The third task (*externally-paced letter recognition* LRE) is considered as *active* because subjects read aloud the letters that appeared on the screen every 2 s. We employed simple stimuli, i.e. single letters and symbols, to prevent the subjects resort to high-level functions for reading, such as inferences from the context. The stimulation protocol was developed in a blocked design: 10 sets of 10 sequentially presented stimuli were alternated with 10 resting periods consisting in passively watching a fixation point on the screen. The stimuli presentation rate was 0.5 Hz and the stimuli persistence on the screen was 16 ms. Each set of stimuli and each resting period lasted 20 s. Each task was performed in a separate session. The stimulation was run using Presentation® software (Version 0.76, http://www.neurobs.com). RRPs and fMRI were recorded in separate studies because of the artifacts superimposed to the EEG recordings caused by the variable magnetic fields inside the MR magnet.

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C. EEG recording

EEG was recorded from 19 standard 10-20 scalp sites referred to earlobe. EOG was bipolarly recorded using 2 electrodes placed over and below the right eye. EEG and EOG recordings were bandpass filtered between 0.02-30 Hz. Each trial lasted 2 s, 750 ms pre- and 1250 ms post-stimulus. The sample rate was 256 Hz. Stimuli were presented on a CRT screen.

D. Scanning procedure

Neuroimages were obtained from a 1.5 T whole-body MRI scanner (GE Medical Systems Signa) with a received-only whole-head coil for signal reception. Special constraints were used to limit head movements of the examined subjects. Structural scans were acquired using a high-resolution axial sequence (0.98 mm × 0.98 mm × 1.2 mm voxels). Functional images were collected with a gradient-echo-planar sequence sensitive to blood-oxygenation-level-dependent (BOLD) contrast (TR = 3000 ms, TE = 60 ms, flip angle = 90°). Each functional run consisted in 100 brain volumes of 20 contiguous slices (128 x 128 matrix; 1.88 mm × 1.87 mm × 5 mm voxels). Functional slices were acquired parallel to the anterior-posterior commissure plane. The functional runs lasted about 6.5 min each. Five volumes of each functional run were discarded from statistical analysis. Stimuli were generated by a Windows OS computer and projected onto a screen located near the bottom of the bore. Subjects could see the stimuli by means of a mirror mounted on the head coil. All the procedure lasted about 45 min.

E. Data analysis

Averaged RRPs were computed for each task and subject. Ocular artifacts were reduced applying a PCA method [4]. Remaining artifact-contaminated trials were visually rejected before averaging. Grand averages of RRPs were obtained for each task. The latency and amplitude of the most relevant RRP components were measured by a skilled technician.

Functional MRI data were analyzed with Statistical Parametric Mapping software (SPM2; Wellcome Department of Cognitive Neurology, London, UK) running under the MATLAB® environment (Version 6.5, http://www.mathworks.com). The functional images acquired in the three sessions were realigned and unwarped separately for each subject and successively normalized to the same EPI template obtained from SPM2 website (http://www.fil.ion.ucl.ac.uk/spm/spm2.html). Images were smoothed with a Gaussian filter (5 mm × 5 mm × 7 mm full-width half-maximum). Regression analysis and the theory of Gaussian random fields were used to determine the brain regions showing significantly greater activation during reading tasks in comparison to resting periods. The reference waveform representing the event train was convolved with the canonical hemodynamic response function and its first-order temporal derivative. A significance level of $p < 0.05$ corrected for multiple spatial comparisons and a minimum cluster size of 50 voxels were considered. Activated voxels were color-coded and superposed on the corresponding anatomical images to depict functional/structural images. Grand averages of cortical activation maps were computed to represent the results.

III. Results

A. RRPs

Fig. 1 shows the superimposition of grand averages of RRPs recorded in the letter presentation (LPR thinner lines) and symbol presentation (SPR thicker liner) tasks. Considering the frontal and central cortical regions, the area subtended by N4 is smaller in SPR than in LPR; furthermore, the latency of P2 (Δl = 32 ms) and the amplitude of P4 (Δa = 0.8 μV) are greater in SPR than in LPR. The amplitude of P1 (Δa = 1.4 μV) is decreased in the SPR compared to LPR task.

Fig. 2 shows the superimposition of grand averages of RRPs recorded in the letter presentation (LPR thinner lines) and letter recognition (LRE thicker lines) tasks. The area subtended by N4 is generally much higher in LRE than in LPR.

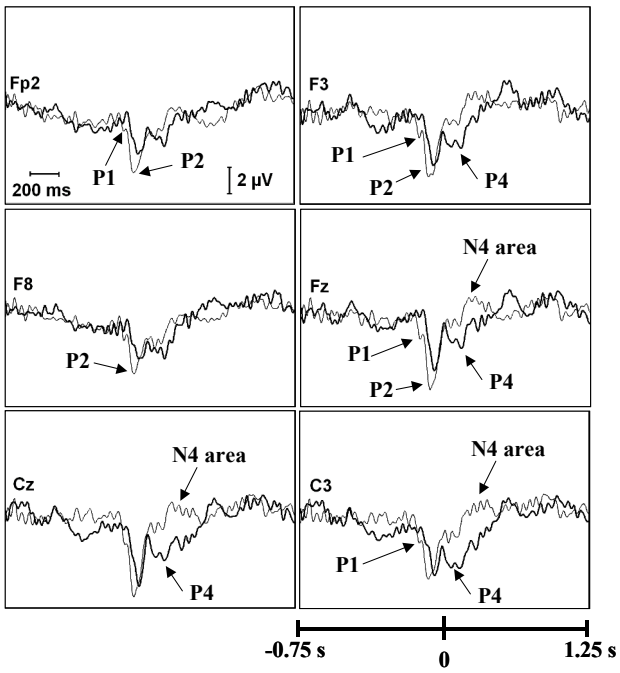

Fig. 1. Superimposition of grand averages of RRPs recorded in LPR (thinner lines) and SPR (thicker lines).

Considering the latency of the RRP components in the occipital-frontal direction, the components N3 and P4 showed a positive gradient in an occipital-frontal direction, while N4 showed a negative gradient.

B. fMRI

All the tasks produced activation of the primary visual cortex, Brodmann's areas (BAs) 17-18. Fig. 3 shows the mean cortical activation maps corresponding to the LPR task. There were not significant differences in the patterns of activation between the LPR and SPR tasks. In the letter recognition (LRE) task, activated voxels were detected in the motor and pre-motor cortices (BAs 4-6), in the posterior parietal cortex (BA 7) and in the left temporal lobe (BAs 20-21-22-38). Fig. 4 shows the mean cortical activation maps corresponding to the LRE task. The differences in the activation patterns of LPR and LRE tasks (LPR vs. LRE) were localized in the motor and pre-motor cortex (BAs 4-6) and in the left temporal lobe (BAs 20-21-38), as shown in fig. 5. These results are summarized in table I.

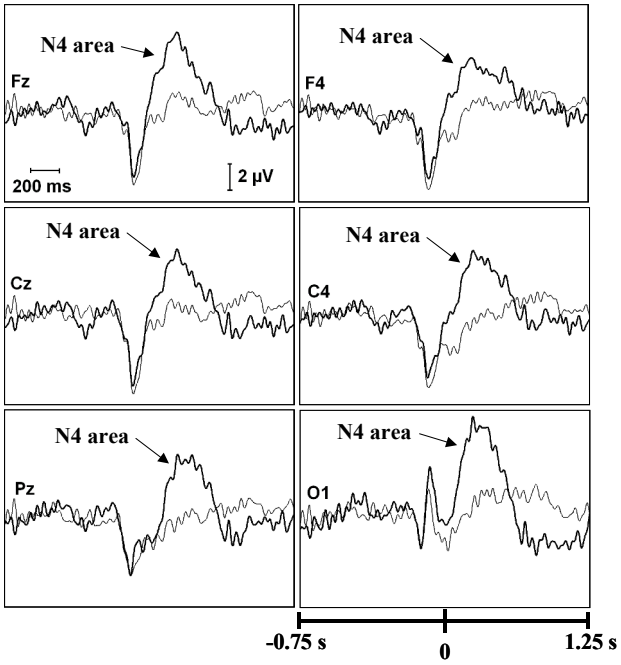

Fig. 2. Superimposition of grand averages of RRPs recorded in LPR (thinner lines) and LRE (thicker lines).

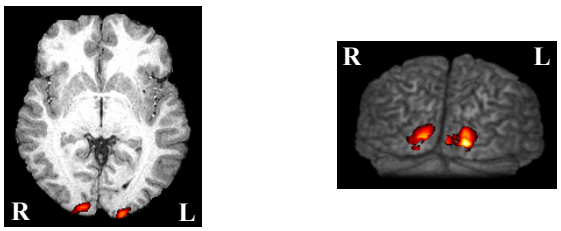

Fig. 3. Activated voxels in the primary visual areas (BAs 17-18) during the LPR task. Axial view on the left and posterior rendered view on the right.

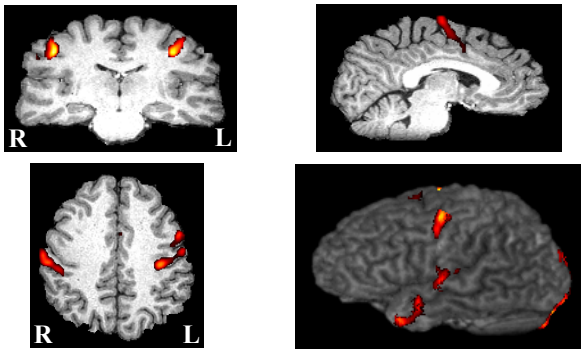

Fig. 4. Activated voxels in the motor and pre-motor cortices and in the left temporal lobe (BAs 4-6-7-20-21-22-38) during the LRE task. Coronal view on the top left, axial view on the bottom left, sagittal view on the top right and lateral rendered view of the left hemisphere on the bottom right.

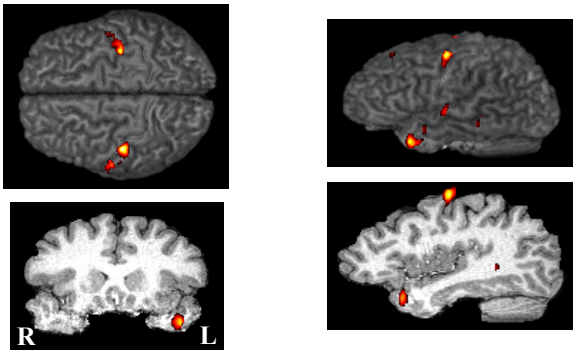

Fig. 5. Differences in activation patterns between the LPR and LRE task are located in the motor and pre-motor cortices (BAs 4-6) and in the left temporal lobe (BAs 20-21-38). Rendered view of both hemispheres on the top left, rendered view of the left hemisphere on the top right, coronal view on the bottom left and sagittal view on the bottom right.

TABLE I
REGIONS DEMONSTRATING SIGNIFICANT ACTIVATION DURING THE TASKS LPR, SPR, LRE AND DIFFERENTIAL RESPONSE DURING LPR IN COMPARISON TO LRE

Region	BAs	Task
Striate area	17	LPR, SPR, LRE
Parastriate area	18	LPR, SPR, LRE
Inferior-temporal gyrus	20	LRE, LPR vs. LRE
Middle- temporal gyrus	21	LRE, LPR vs. LRE
Sperior-temporal gyrus	22	LRE
Pre-central gyrus	4	LRE, LPR vs. LRE
Pre-motor and supplementary motor cortex	6	LRE, LPR vs. LRE
Posterior parietal cortex	7	LRE
Temporal polar cortex	38	LRE, LPR vs. LRE

IV. Discussion and conclusion

Previous studies [5,6] suggest that the components of reading-related potentials can be divided into three periods, according to their temporal occurrence. In the pre-lexical period (0-160 ms) the short-latency components P0, N1, P1 are recorded: they are mainly related to sensory processing of stimuli. The lexical period (160-420 ms) is represented by the middle-latency components N2, P2, N3 that are likely related to stimuli categorization. The post-lexical period (420-800 ms) consists of the long-latency components P4, P600, N4: they are probably concerned with long-term memory and feedback processes.

In the neurophysiological domain, the main morphological differences between the LPR and SPR tasks were noticed in the frontal-central regions. The amplitude differences in the components associated to the pre-lexical period can be explained by observing that processing non-alphabetic symbols requires less effort than processing letters [7]. The finding of morphological differences in the lexical and post-lexical components highlighted the existence of specific cognitive mechanisms for processing alphabetic letters. The potentials recorded during the LRE task were generally characterized by a greater amplitude compared to those of the LPR task. This result agrees with the increasing of attention demand caused by reading aloud [8].

In the functional neuroimaging domain, all three tasks determined a robust activation of the occipital visual cortex, without significant differences. In the letter recognition task, the articulation deriving from reading aloud activated motor and pre-motor regions. Pre-motor cortex receives inputs from the prefrontal, parietal and temporal association areas: it guides motor cortex in executing skilled movements, as facial expression, articulation and phonation. In particular, the supplementary motor area, located on the medial surface of the frontal lobe, is related to the initiation and maintenance of speech. Furthermore, motor planning is influenced by the integration of multiple sensory modalities mediated by the posterior parietal cortex. Significantly activated clusters of voxels were also identified in the left temporal polar areas, that are important for word retrieval and for the identification of objects when discrimination requires the use of colour, orientation, pattern and shape [9, 10]. The explicit reading of letters confidently requires the recognition of graphic signs characterized by specific shape and orientation. Regions of significantly different cortical activation between LPR and LRE tasks were found in the motor and pre-motor cortices, due to the movements during verbal articulation. Furthermore, the differences in the left anterior temporal lobe denote that these areas are much more activated by reading aloud than by implicit reading.

Even if in this study the potentials and the functional images of the brain were not directly integrated in a unified model, some interesting results have emerged. First, the temporal sensitivity of RRPs allowed to put into evidence the subtle differences between the LPR and SPR task. Functional imaging failed to discriminate between letters and symbols presentation, probably because the hemodynamic responses of the nuclei that specifically contribute to these tasks are not well differentiated as the electric responses. Second, most of the morphological differences among the RRPs recorded in the different tasks were quite spread over the cerebral cortex and did not clearly show the topography of activity in the different cerebral areas. fMRI recordings revealed the changes in the brain responses with high spatial resolution. The integration between RRPs and fMRI contributes to describe both "where" and "when" specific phenomena occur in the brain.

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