



SIMULTANEOUS EEG-fMRI RECORDINGS TO LOCALIZE NEURAL SOURCE MODELLING OF ENDOGENOUS POTENTIALS (ERPs), ELICITED BY OMITTED TARGETS.

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Introduction and Aims: ERPs occurring independently of any specific sensory event are purely *endogenous (emitted potentials)*: and their neural generators univocally linked with cognitive components.

The P3 (also known as P300 or P3b or late positive component LPC; see fig. 1 top panel) is the most studied ERP component, defined as supramodal, positive component peaking from 300 to 800 ms. However despite the numerous investigations, the neural sources of the P3 remain somehow elusive. Aim of the study was to localize and compare the cortical and subcortical neural sources of the scalp-recorded ERPs from two similar visual tasks: a standard two-stimulus oddball and an omitted-target oddball task, combining the high temporal resolution of electrophysiology with the fine spatial information provided by fMRI (EEG-fMRI simultaneous recordings).

Materials and Methods: Thirteen healthy right-handed volunteers (5 females; mean age 26 years, range 22-29), were enrolled. The high temporal resolution of electrophysiology was combined with the fine spatial information provided by functional MRI. In addition, the source modelling (dipole analysis) of ERPs was seeded to the clusters of fMRI activations. The simultaneous recording of EEG and fMRI guaranteed that the cognitive states of the subjects were the same during the experimental session.

Results:

Post-stimulus ERP waveforms for the two tasks (fig. 2)

- The P1 component peaked at 115 ms on medial occipital sites
- Two prefrontal components (pN1 and pP1) peaked at 120 and 190 ms
- The negative N1 peaked at 210 ms with bilateral parieto-occipital distribution
- The posterior P2 peaked at 295 ms at the occipital sites

These components were present and comparable in all experimental conditions, except in the omitted target task. As expected, no sensory - related components emerged when the stimulus was missing

Two longer-latency component clearly detectable following all target stimuli positive peak over the frontal derivations (the pP2, peak 300 ms), larger and earlier in the oddball task than in the omitted (peak 350ms). A centro-parietal P3 for target stimuli (peak 450 ms in the oddball task and 520 ms in the omitted target task) was evident.

The results of both the omitted-target oddball and the standard oddball task were unanimous in depicting an antero-to-posterior neural circuitry for the detection of rare, task-relevant events. P300 (P3b) was generated in the frontal, temporo-parietal and parietal areas (these latter only in the standard oddball), namely the temporo-parietal junction (TPj), the premotor and motor area (M1) and the anterior intraparietal sulcus (aiPs). Anterior Insula contributed to the pP2, a recently described prefrontal component (different from the well known P3a) associated with the stimulus-response mapping. The anticipatory (i.e., pre-stimulus) prefrontal negativity (pN) and Bereitschaftspotential (BP), also endogenous in their nature, were produced by anterior areas, namely the inferior and middle frontal gyrus over the lateral brain surface and the SMA-CMA areas over the medial cortex.

Neural Sources Reconstructions

ERP - fMRI combination (fig.3)

Oddball task

- ✓ The earliest slow rising negativity (pN) in the iFg
- ✓ The BP-like activity activity equally represented by the adjacent SMA and CMA (single source)

After stimulus onset:

- ✓ N1 and P2 components best represented in the medial extrastriate visual area
- ✓ The pP2 component with activation in the bilateral anterior Insula (alns)
- ✓ P3 by activation in the aiPs, TPj and lateral premotor and motor cortex

Omitted target task

- ✓ Earliest ERPs in the mFg
- ✓ pN component in iFg
- ✓ BP-like shift by adjacent SMA and CMA
- After stimulus onset:
- ✓ pP2 bilateral anterior insula (alns)
- ✓ P3 in the TPj and lateral premotor and motor areas

Discussion: recording *emitted* ERPs from omission of target stimuli in a simultaneous EEG-fMRI event-related paradigm allows a detailed spatio-temporal modeling of the neural generators of purely endogenous late potentials and provide useful insight to the interpretation of emitted/endogenous ERPs.

Results: data depicted an antero-to-posterior neural circuitry for the rare, task-relevant events. P300 (P3b) was generated in frontal, temporo-parietal and parietal areas (these latter only in the standard oddball), namely the temporo-parietal junction (TPj), the premotor and motor area (M1) and the anterior intraparietal sulcus (aiPs).

Anterior Insula contributed to the pP2, a recently described prefrontal component (different from the P3a) associated with the stimulus-response mapping. The anticipatory prefrontal negativity (pN) and Bereitschaftspotential (BP) were produced by anterior areas, namely the inferior and middle frontal gyrus over the lateral brain surface and the SMA - CMA areas over the medial cortex.

Conclusions: recording emitted ERPs from omission of target stimuli in a simultaneous EEG-fMRI event-related paradigm allows a detailed spatio-temporal modeling of the neural generators of purely endogenous late potentials and provide useful insight to the interpretation of emitted/endogenous ERPs.

Bibliography: Ragazzoni A, Di Russo F, Fabbri S, Pesaresi I, Di Rollo A, Perri RL, Barloscio D, Bocci T, Cosottini M, Sartucci F.: ["Hit the missing stimulus". A simultaneous EEG-fMRI study to localize the generators of endogenous ERPs in an omitted target paradigm.](#) *Sci Rep.* 2019 6; 9(1): 3684 – 99.

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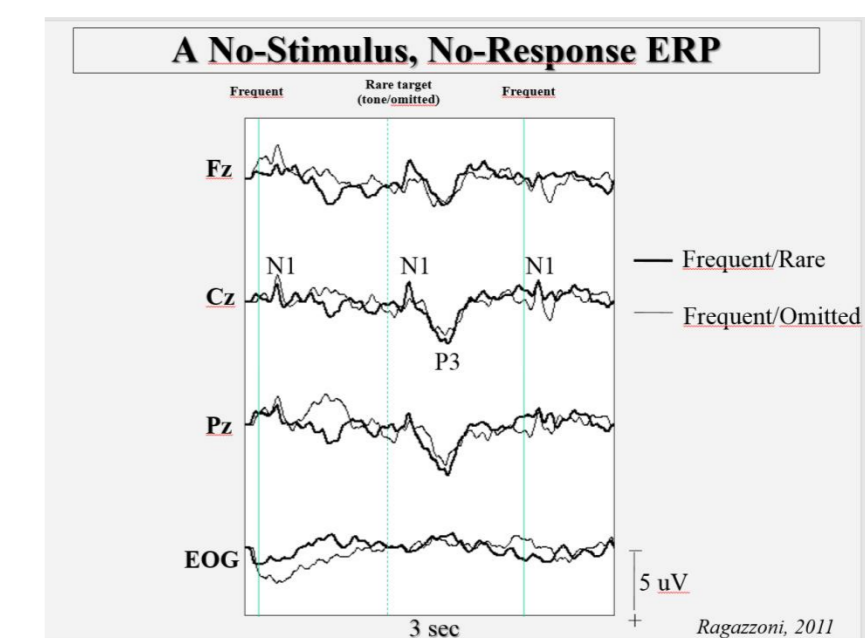


Fig. 1: Schematic representation of P3 (also known as P300 or P3b or late positive component LPC, upper panel) and of the two experimental tasks: a) Standard visual Oddball; b) Omitted-Target Oddball. s: standard-frequent stimuli. T: target-rare stimuli (Visual stimulation managed by VisuoStim-Resonance Technologies, Northridge, CA, U.S.A and delivered with compatible fiber-optic goggles).

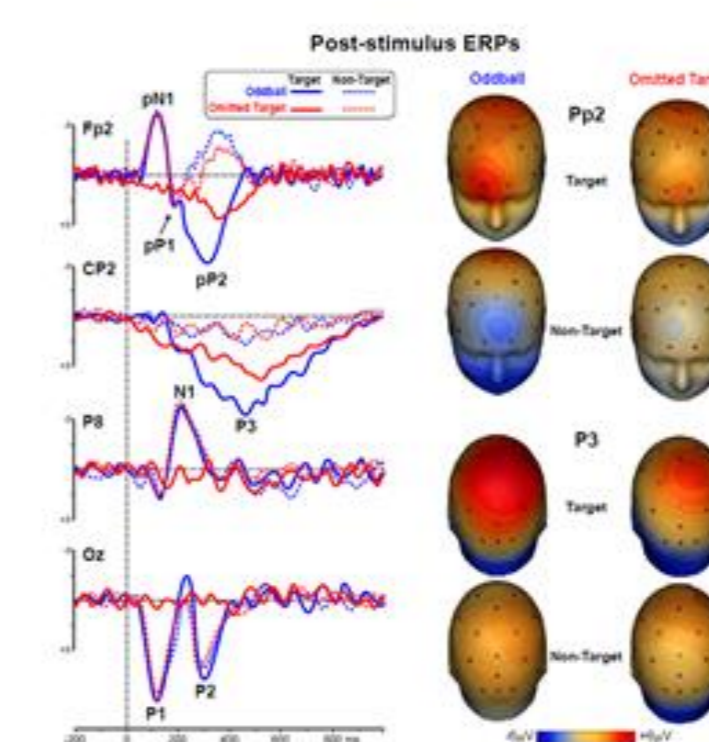


Fig. 2: Left: ERP waveforms of the post-stimulus responses to non-target and target stimuli in the two tasks. Right: scalp topography of the pP2 and P3 components.

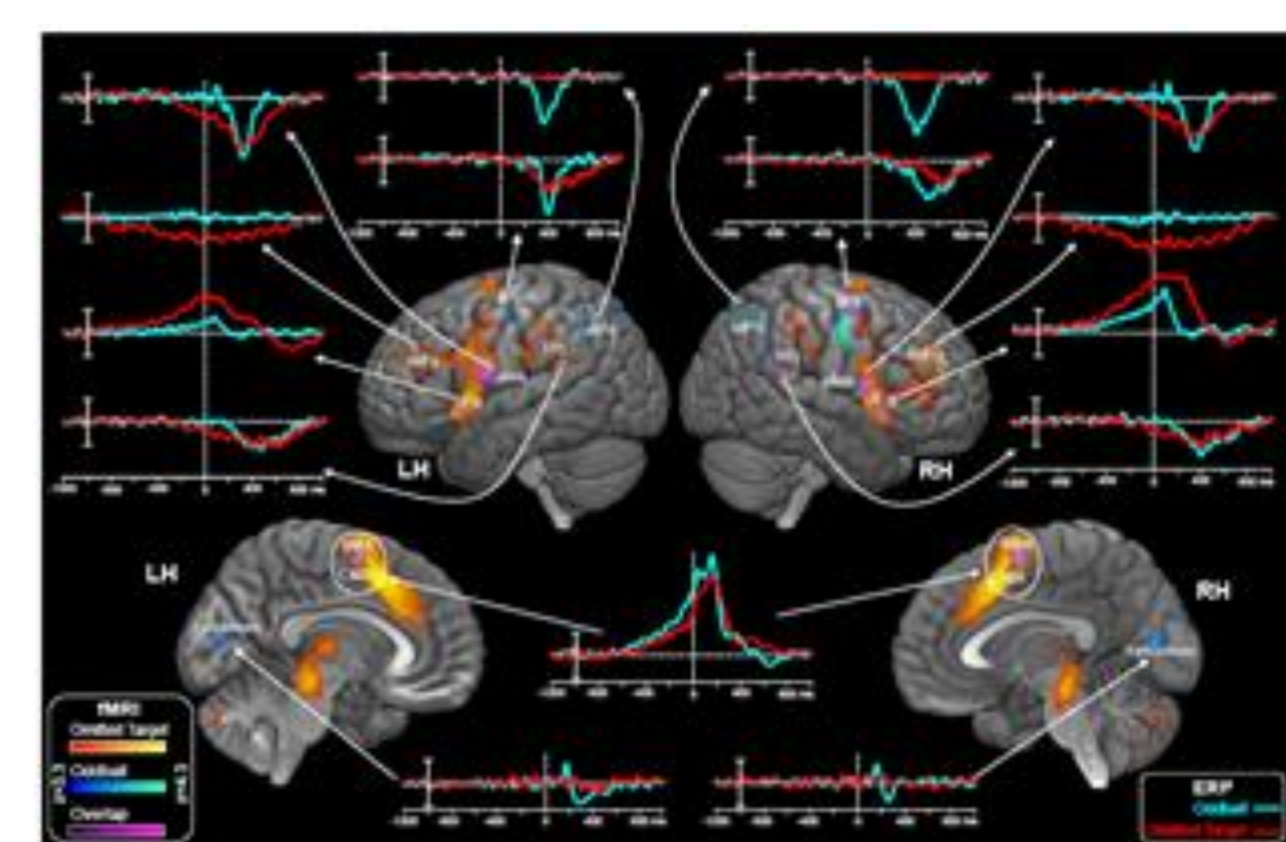


Fig. 3: Spatiotemporal mapping obtained by the combination of ERP and fMRI data. fMRI activations resulting in the active-passive contrast for target stimuli for both tasks and their overlap from mesial and lateral views. LH, left hemisphere; RH, right hemisphere. Waveforms correspond to the ERP-based time-courses of the neural sources obtained from the fMRI-seeded dipoles. LH: left hemisphere. RH: right hemisphere. alns: anterior Insula. aiPs: anterior Intra-Parietal sulcus. CMA: Cingulate Motor Area. iFg: inferior Frontal gyrus. mFg: middle Frontal gyrus. M1: motor cortex. SMA: Supplementary Motor Area. TPj: Temporo-Parietal junction.