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Combined Measurement of Event-Related Potentials (ERPs) and fMRI

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Technical communication

Abstract. The study investigates the possibility of combined recording event-related potentials (ERPs) and functional MRI (fMRI). Visual evoked potentials (VEPs) were elicited by an alternating black and white checkerboard, which was presented blockwise outside the static 1.5 T magnetic field and during an echo planar imaging (EPI). An fMRI sequence with a time window for interleaved EEG-measurement and a measurement protocol which reduces pulse artifacts and vibrations was used. Thus, during an EPI sequence, it was possible to detect VEPs which had the same structure and latencies as VEPs outside the magnetic field and which corresponded well with the observed activated areas of the visual cortex.

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In neuroscience, EEG and fMRI are two well-established techniques to investigate basic mechanisms of cortical activity. Both techniques have different advantages and disadvantages. EEG represents the electrical activity of neurons and makes mapping of cognitive processes on their millisecond timescale possible. However, EEG recordings are affected by the complex interactions of the electric field of the surrounding conductive tissue, particularly the skull and the scalp. Thus the spatial localization of neuronal activity by EEG source analysis is difficult. FMRI, as the measurable correlate of the hemodynamic response, offers a very high spatial resolution. However, the hemodynamic response is only indirectly linked to the energy consumption of the neuronal population. Although recent developments have shown that the hemodynamic responses are modulated by experimental conditions (Rosen et al. 1998), the temporal resolution is limited by the hemodynamic response of the cerebral vasculature (Buckner 1998, Frahm et al. 1993). Therefore, a combined measurement of EEG and fMRI is desirable and could be helpful for a better understanding of cortical mechanisms.

So far a combination of EEG and fMRI has been implemented by performing two separate measurements (e.g. Opitz et al. 1999). There are some disadvantages to this method: a) it cannot be guaranteed that the subjects apply the same cognitive strategies in both experiments, b) the environmental factors (e.g., tightness, volume) are different, c) a training effect might be produced and, d) more time is needed to perform the measurements.

Previous studies have demonstrated the possibility to obtain spontaneous EEG data within a static magnetic field (Allen et al. 1998, Ives et al. 1993, Müri et al. 1998) and during fMRI (Hill et al. 1995, Huang-Hellinger et al. 1995), but only view studies have investigated the relationship between fMRI and event-related potentials (ERPs) (Bonmasser et al. 1999, Kruggel et al. 2000). Bonmasser et al. (1999) and Kruggel et al. (2000) recorded visual evoked potentials during fMRI. Their results emphasize the possibility of recording ERPs during fMRI scanning at 3 Tesla field strength. Because of the strong magnetic field strength they developed different filtering methods. Until now little is known about artifacts in a 1.5 Tesla field strength. However, for a better understanding of information processing the measurement of ERPs is essential because their waveform and timing are determined by the particular cognitive processes activated by the stimulus. The detection of ERPs during MR-scanning poses a lot of methodological problems which are related to the signal-noise distance: a) the amplitude of the signal (~1 – 12 μV) in relation to the induced voltages during echo planar measurement is very small, b) artifacts due to cable movements (e.g., head movements induced by heart action lead to movements of the cables and electrodes, which induce a voltage in the wires), c) possible destructive effects of the EEG-setup on the fMRI signal.

The aim of the present study was to investigate the possibility to measure ERPs during an fMRI session in a 1.5 T magnetic field. We used a standard checkerboard design to elicite visual evoked potentials (VEPs), which have the advantage of a well-defined component structure (Shigeto et al. 1998).

Five healthy right-handed volunteers aged 22-32 (mean age 25.2, SD 4.1, range 22-32; four females and one male) with normal or corrected-to-normal vision took part in the study. Written informed consent was obtained from subjects after the nature and the consequences of the experiment had been explained.

VEPs were elicited by using a reversing black and white checkerboard pattern of 8 x 8 patches (4 Hz frequency) with a central fixation point. During the experiment, subjects watched (*via* a mirror) a small screen placed above their head (attached to the scanner headcoil, width 11.0 cm, height 11.8 cm). Onto this screen the checkerboard was projected with a Toshiba TLP 710 LCD projector, which was placed 4 m from the isocentre of the MR scanner.

The experiment was designed as an fMRI compatible block-design with 16 repetitions. Every block consisted of a 45 s display of a black screen with a fixation point in the center, followed by a 45 s checkerboard stimulation. At the beginning of every session four blocks were presented outside the magnetic field to collect artifact-free EEG data.

For continuous EEG recording a commercially available MR-compatible system with a battery powered amplifier (Schwarzer, Munich, Germany) was used. The amplifier was located approximately 50 cm behind the head coil and was connected *via* a fiber optic link to a standard PC in the MR console room running the Schwarzer acquisition software. The electrodes were plastic-coated Ag/AgCl electrodes with iron free copper leads. They were fixed on the subjects' scalp by a stretchable plastic cap. To reduce artifacts of the EEG by any movements of the electrode cables, the head was fixed in the head coil. The wires were fixed on the electrode caps and were twisted around each other beginning 1-2 cm above the apex of the head and ending 5-6

cm in front of the amplifier. Additionally the cables and the plugs of the amplifier were insulated with aluminium foil. This procedure minimized the area of the head-electrodes-amplifier-loop and reduced ECG-synchronous artifacts. If these were still unacceptably high, they were removed by ECG-triggered subtraction of an averaged artifact as proposed by Allen et all. (2000). To reduce the influence of the vibrations of the MRI scanner on the EEG signals during imaging the amplifier was weighed down by a 5 kg sand bag.

EEG were recorded from eight scalp positions (C3, Cz, C4, P3, Pz, P4, O1, O2) according to the international 10/20 system. To control eye movements and blink artifacts the left VEOG was measured. All electrodes were referenced to right mastoid. Electrode-skin impedance was under 5 kΩ. The digitization rate was 500 Hz. Bandpass filtering was performed from 0.04 Hz to 70 Hz.

Because of the very high voltages generated on the EEG leads during image acquisition we used the 5 s time window between the slice acquisitions for the EEG-data evaluation. We did not evaluate the very first second, because the MRI induced artifact on the EEG tracing lasted longer (about 200-500 ms), so the evaluated EEG time window was 4 s. Although EEG and fMRI recordings were not completely simultaneous, both data windows had equal length, the identical stimulus and the same number of triggers.

First EEG data were band-pass filtered (0.1 Hz, 24 dB / octave attenuation – 30 Hz, 24 dB / octave attenuation) and then segmented (from -20 ms to 200 ms). Baseline correction was made from -20 ms to 0 ms. Artifact rejection was performed in two steps: first, all trials with EOG artifacts were rejected using the Brain Vision Analyzer software (Brain Products), second, every trial in which movement / technical artifacts were detected on only one electrode or in which the amplitudes exceeding 80 μV were rejected. Then a DC detrend was performed. Finally artifact-free EEG segments were averaged.

Functional imaging was performed using a 1.5 T Siemens Vision system (Siemens, Erlangen, Germany). A T_2*-weighted echo planar imaging sequence (TR = 4200 ms, TE = 60 ms, $\alpha = 90°$, field of view 192 mm, in-plane matrix 64 x 64) was applied with a stack of 40 contiguous slices (3 mm thickness each) aligned to the AC-PC-plane. Except for the most inferior cerebellum, this covered the entire brain. The time period for the acquisition of the 40 slices was 4 s. We used a sequence which left a time window of 5 s between the slice acquisitions. A total of 163 images was acquired for each subject, with the first three images being discarded in later data processing. For anatomical correlation, a high-resolution T_1-weighted scan was acquired after the fMRI experiment (TR = 15 ms, TE = 5 ms, $\alpha = 30°$, matrix 256^3, isotropic voxel size 1 mm^3). Analysis of the fMRI data was performed with the SPM99 software on a UNIX workstation. Image series were realigned to the first of the 160 images, then normalized to the standard template, and finally smoothed with a 6 mm FWHM Gaussian kernel. The contrast between the checkerboard stimulation and the black screen was calculated.

Each subject ran through two checkerboard conditions. First, four blocks were presented outside the magnetic field, then the simultaneous fMRI/EEG--measurement followed. The VEP signals collected inside and outside of the scanner have very similar waveforms and latencies, characterized by an initial small negative wave (N60), a major positive wave (P100) and a following negative wave (N145). Fig. 1 shows the grand average for the five subjects. There are no significant differences of the amplitudes between the VEP collected inside and outside the scanner.

As expected, the fMRI data (Fig. 2) show that visual areas of the occipital cortex are activated during the checkerboard stimulation. No artifacts of the electrodes or of the wires were detectable.

The results emphasize the possibility of recording ERPs during fMRI scanning. The VEPs during the fMRI session have the same structure (N60, P100, N45) as the VEP measured outside the magnetic field (Fig. 1). Furthermore, for the fMRI data no artifacts related to the electrodes or wires were detected and, as expected, visual cortical regions were activated during the stimulation (Fig. 2).

One of the main problems in simultaneous measurements of fMRI and EEG are the small pulse-related body movements, whose amplitudes are proportional to the static magnetic field (B_0) and hide the real EEG-signal (Felblinger et al. 1999, Huang-Hellinger et al. 1995, Müri et al. 1998). In contrast to recent studies (Allen et al. 1998, Kruggel et al. 2000), in our experiment these pulse artifacts were of minor importance. Pulse artifacts were detected in only one person and could be eliminated by the artifact subtraction method proposed by Allen et al. (1998). Different reasons might be responsible for this effect: first, we used a complex measurement protocol (the wires were fixed on the electrode caps, twisted around each other and additionally insulated by an aluminium foil), second, we used a small number of

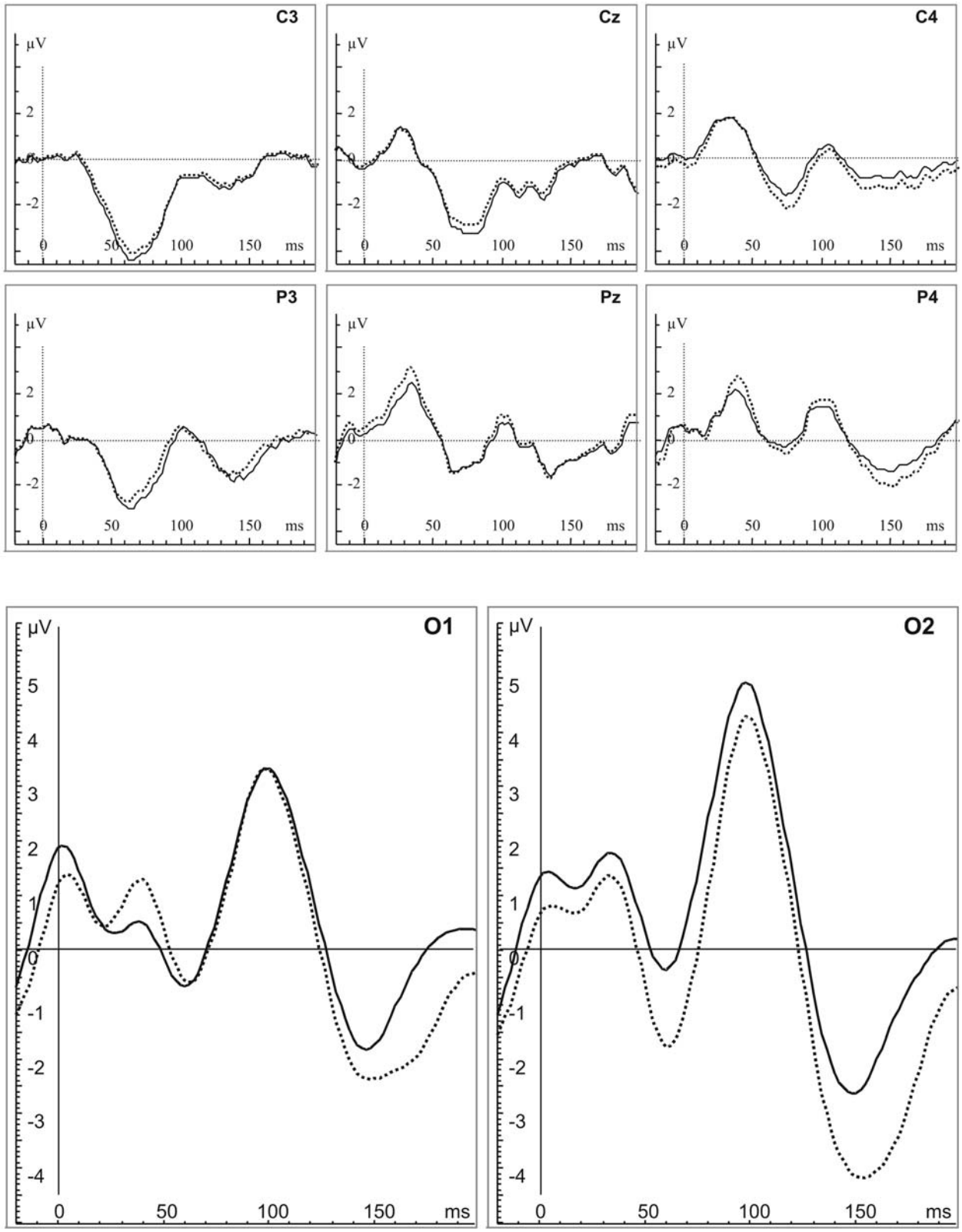

Fig. 1. The grand average VEP of the five subjects in response to the black and white checkerboard stimulation. Data recorded from C3, Cz, C4, P3, Pz, P4,O1 and O2 are shown. The dotted line indicates the measurements outside the magnetic field, the solid line shows the EEG-data during fMRI scanning.

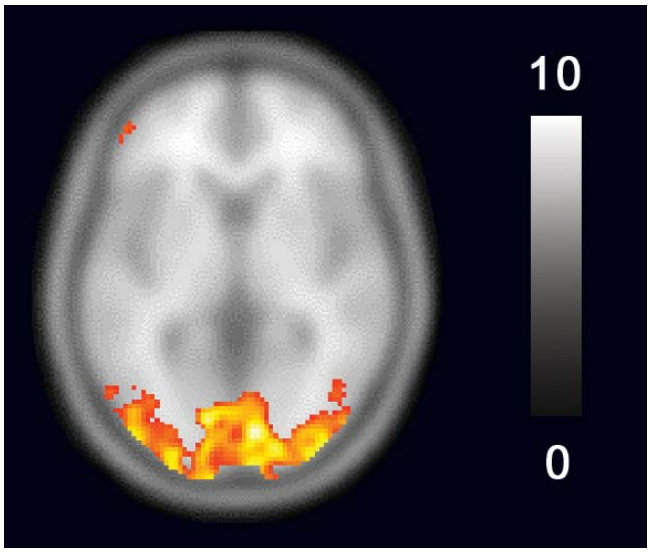

Fig. 2. Contrast between 4 Hz checkerboard stimulation versus black-screen condition rendered to the surface of a single subject template brain (z = 119). Student´s *t*-test functional map demonstrating pronounced activation of the visual areas in occipital regions.

electrodes and, third, the great number of EEG segments allowed a very critical artifact correction.

The results demonstrate the possibility to measure evoked potentials during fMRI scanning. But they can only be a first step toward the aim of using simultaneous measurements in cognitive paradigms. The main problem for cognitive experiments is the low signal-to-noise ratio in combined measurements. In the present study we tackled this problem using a small number of electrodes and a high number of EEG segments for averaging. This is usually not possible in higher-order cognitive tasks, where we are interested in the relationship between different stimulus conditions, the behavioral reactions and the underlying brain processes. However, recent advances in experimental design and data processing may offer solutions (Allen et al. 2000, Burock et al. 1998).

Altogether, a combined measurement of EEG and fMRI can contribute to a better understanding of the relationship between hemodynamic and electrical brain activity and may help to understand the functional organization of the brain.

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