Contents

Introduction
EEG/fMRI – from methodological validation to cutting-edge science

EEG/fMRI Applications
Epilepsy, resting state, cognitive control and other areas of interest: the broad spectrum of simultaneous EEG/fMRI applications

Non-EEG sensors add new dimensions to brain research

EEG/fMRI studies
Examining the benefits of sparse scanning and ICA-based ERP extraction in combined EEG-fMRI
by Aureliu Lavric, Nino Bregadze, Abdelmalek Benattayallah

BOLD Correlates of continuously fluctuating epileptic activity isolated by independent component analysis.
by Kay Jann

Fluctuations in electrodermal activity reveal variations in single trial brain responses to painful laser stimuli - A fMRI/EEG study
by Dr. Jürgen Brinkmeyer

Compatibility tests
Siemens
Philips

Products for EEG & fMRI
Hardware: BrainAmp MR - BrainAmp MR plus - BrainAmp ExG MR - SyncBox
Sensors: GSR MR module
MR Extension: PowerPack
Electrode Cap: BrainCap MR
Software: BrainVision Analyzer - BrainVisio Recorder - BrainVision RecView

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**EEG/fMRI – from methodological validation to cutting-edge science**

The combined, simultaneous EEG/fMRI is coming of age: the focus of research is shifting dramatically from purely methodological studies to actual scientific inquiries. Brain Products is proud to have been a major contributor to this shift. Of the 60 published studies that involved equipment supplied by Brain Products which were carried lately and were added to the PubMed database, only 12 were purely methodological, while the remainder treated EEG/fMRI as an established technique for the investigation of brain function.

The reason for this success lies in the innovative approach that Brain Products brings to EEG/fMRI-related problem-solving. We provide a ready-to-use system that includes an fMRI-usable amplifier, the BrainAmp MR, that can be placed in the scanner bore during EEG/fMRI recordings, plus some sophisticated software solutions - BrainVision Analyzer 2 and BrainVision RecView - for eliminating potential gradient and cardioballistic artifacts. Synchronization of the scanner clock and the EEG clock using our SyncBox can also immensely improve data quality.

Figure 1 shows the growth over the years in the number of EEG/fMRI studies that have made use of the BrainAmp MR amplifier. The complete list of publications can be found on our website at [http://www.brainproducts.com/references.php](http://www.brainproducts.com/references.php). The following two sections will describe the most recent applications of inside-the-scanner recordings involving EEG and non-EEG physiological sensors. We anticipate that the range of such applications will continue to grow.

![Figure 1. Published studies using Brain Products equipment added to the PubMed database](image-url)
Epilepsy, resting state, cognitive control and other areas of interest: the broad spectrum of simultaneous EEG/fMRI applications

More and more researchers are realizing the power of a combined EEG/fMRI approach. But is a simultaneous recording really necessary for combining the temporal resolution of EEG and the spatial resolution of fMRI? Couldn’t the results of separate sessions simply be combined?

The answer naturally depends on what is being sought. With a standard paradigm, it can be assumed that if the same stimulus is presented, the response should be the same. However, there are situations where this assumption is not valid and the EEG and fMRI data must be acquired at exactly the same moment. Figure 2 shows the distribution of major application areas covering simultaneous EEG/fMRI studies and using Brain Products amplifier systems that were added to the PubMed database in 2010 and the first quarter of 2011.

The most straightforward example of when EEG and fMRI data must be acquired at the same moment involves the study of epilepsy. Epileptic patients generate interictal spikes between seizures. These spikes are believed to be generated by the same sources as the seizures themselves. Therefore the ability to localize the source of the spike will help considerably in gaining a better understanding of epilepsy. In order to localize the interictal spike it is necessary to know at what moment it occurs. A patient cannot generate these spikes at will, so they have to be located retrospectively. It is therefore essential to record EEG activity in parallel with fMRI scanning.

The good thing about spikes is that they have a large amplitude and therefore yield a high ratio of signal to noise. The bad thing about them is that their shape is variable, and that they can merge with artifacts such as movement artifacts in the scanner. Brain Products’ support is always ready to help customers inspect their EEG data and distinguish spikes from artifacts. The spectacular results of the group led by Prof. Louis Lemieux (University College, London) demonstrate how much additional information can be acquired in epileptic patients using EEG/fMRI (Vulliémoz, et al. 2010). Recently they went so far as to make simultaneous recordings of intracranial EEG with fMRI (Vulliémoz, et al. 2011).

On the one hand, visual perception illustrates a behaviorist paradigm in which the stimulus predicts the response. Also, unlike auditory stimuli, visual stimuli do not interact with the loud acoustic noise produced by the scanner. On the other hand, visual stimuli do not impinge on a tabula rasa. The brain’s state is changing, and this affects the process of perception. To determine what happens with
a visual stimulus when it coincides with different phases of ongoing brain activity and loci in the brain, simultaneous EEG and fMRI must be recorded. For example, it has recently been shown that the visual cortex’s BOLD response is lower when a stimulus arrives at the peak of an alpha signal rather than at the trough (Scheeringa, et al. 2011).

What is the brain doing when it is not performing a task? This is a crucial question, because only 5% of the brain’s metabolism is responsible for task execution, while the remainder is expended on maintaining the brain in a state of readiness. For a long time, EEG rhythms were the sole window on the resting state of the brain. Recent fMRI studies have demonstrated the presence of networks in the brain that are active during the resting state, most importantly the so-called default-mode network. The connection between EEG rhythms and the resting-state networks can be established with simultaneous EEG/fMRI.

For example, it has been established that ongoing brain activity consists of metastable microstates that can be distinguished by their EEG signatures and are associated with certain default brain networks (Musso, et al. 2010).

An important special case of the resting state is sleep. Spoormaker and colleagues investigated connectivity during different sleep stages (Spoormaker, et al. 2010a).

Picchioni and colleagues correlated the oscillations in the infraslow range (<0.1 Hz) with fMRI and discovered that the correlation is positive in subcortical areas, but negative in cortical areas (Picchioni, et al. 2011). Sämann and colleagues used EEG in the scanner to monitor the different sleep stages and to follow the changes in the default-mode network through successive stages. BrainVision’s RecView software was used for online monitoring of the sleep stages (Sämann, et al. 2011).

Task execution depends on cognitive control. The subjects monitor their performance and adjust it according to feedback. A variety of ERP components, such as N2, P3, ERN and CNV, are known to be cognitive control task performance markers. Using the individual-trial amplitude of those components as regressors in fMRI analysis helps to dissociate the respective roles of different brain networks during particular cognitive control tasks. For example, Karch and colleagues looked at the brain areas that correlated to the single-trial amplitudes of the N2 and P3 components of ERPs during the voluntary selection stage in a modified Go-NoGo task (Karch, et al. 2010). Scheibe and colleagues used the modulation of single-trial CNV variation to reveal the brain areas that were sensitive to prior probability in the stimuli during decision-making (Scheibe, et al. 2011). In a recent dual-task study, Hesselman and colleagues used the single-trial P3 amplitude to study the networks responsible for the so-called psychological refractory period (Hesselmann, et al. 2011).
Other applications of EEG/fMRI in recent years have involved memory, pain, somatosensory perception and ADHD. But the spectrum of possible applications is not restricted to this list. Your ideas can contribute to the field. For our part, we can assure you that the equipment you might need is already available for you to use.

Figure 2. Distribution of major application areas covering simultaneous EEG/fMRI studies and using Brain Products amplifier systems that were added to the PubMed database in 2010 and Jan. - Mar. 2011.
Non-EEG sensors add new dimensions to brain research

The combination of EEG and fMRI opens a window onto the brain. However, established techniques such as electromyography (EMG) and galvanic skin response (GSR, also known as SCR or EDA) ought not to be dismissed. Accordingly, some preliminary studies involving the use of GSR and EMG in the MR environment appeared shortly after the new BrainAmp ExG MR system (for the coregistration of bipolar and peripheral signals) was released.

GSR measurement is an essential tool in studies of classical conditioning. Spoormaker and colleagues measured GSR inside the scanner in a fear-conditioning paradigm (Spoormaker, et al. 2010b). The increase in GSR was used as a marker of successful conditioning. In a further application of the same paradigm, the authors introduced a period of sleep between fear conditioning sessions. GSR in conjunction with the fMRI results confirmed the hypothesis that REM sleep has a positive role in fear extinction (Spoormaker, et al. 2011).

Shitara and colleagues recorded EMG during TMS stimulation inside the scanner. The EMG made it possible to discriminate the sub- and suprathreshold TMS activations. Accordingly, the authors were able to demonstrate differences in the fMRI responses between sub- and suprathreshold fMRI activations (Shitara, et al. 2011).

Besides this example, other novel applications are being tried, e.g. facial EMG for monitoring emotions. This is an encouraging trend. We at Brain Products strongly believe that using auxiliary sensors to monitor non-neuronal physiological responses will add weight to the results of any fMRI or EEG-fMRI study.

References


Examining the benefits of sparse scanning and ICA-based ERP extraction in combined EEG-fMRI

by Aureliu Lavric, Nino Bregadze, Abdelmalek Benattayallah

Though promising, concurrent EEG-fMRI is challenging, because it leads to additional artifacts relative to those seen when the techniques are used separately; these extra artifacts are particularly severe for EEG. One of them, cardioballistic artifact-voltage resulting from peripheral effects of cardiac activity such as pulsation of the scalp with EEG electrodes on it in the scanner magnet-is very difficult or impossible to avoid. In contrast, ‘gradient’ artifact-voltage induced by rapid switching of spatial encoding (gradient) magnetic fields is largely under the experimenter’s control. Indeed, by spacing out the acquisition of fMRI images, one can have EEG stretches that are gradient artifact-free.

There have been three approaches to such ‘sparse’ fMRI scanning in the context of combined EEG-fMRI. If the no-scanning stretches of EEG are sufficiently long (~30 s), it is relatively straightforward to perform pulse artifact correction in these ‘gaps’ without having to correct for gradient artifact at all [1]. The drawback of this approach is that the EEG and fMRI data are not associated with the same stimuli. Another approach has been to reduce the no-fMRI ‘gaps’ to about 10s [2], thus enabling one to examine the ERP and fMRI responses to the same stimuli, by relating the amplitude of ERP components in groups of several trials to cumulative BOLD fMRI signal changes [2]. Nevertheless, because this procedure does not allow EEG/ERP-fMRI correlation over single trials, it restricts the kind of ERP paradigm it can be applied to. Indeed, one of the primary incentives for combining data acquisition in the two modalities is to correlate the measurements over single trials [3]. The third approach to ‘sparse’ scanning in the context of combined EEG-fMRI addresses this issue. It exploits the sluggishness of the BOLD fMRI signal (which spans an interval of ~12-18 s), leaving brief (e.g. 0.5-2 s) fMRI-free intervals. This ‘fast’ sparse imaging procedure suits well the ERP technique (which tends to rely on segments of 1 s or less), ensuring that the statistical analyses of the EEG/ERP and fMRI data reflect the physiological responses to the same stimuli. Indeed, this approach has been adopted in some influential studies in the field [3,4]. However, it too has drawbacks. The number of ERP trials and fMRI images is considerably reduced as a consequence of interleaving the two measurements, thus reducing the signal-to-noise ratio. The BOLD function is systematically undersampled and its sampling is not uniform.

A legitimate question is, therefore, whether the benefits of using sparse fMRI to ensure gradient-free EEG stretches outweigh the costs. Studies which have recently examined this issue by comparing the amplitude and latency of visual components of the ERP (P1
and N1) have reported good correspondence between the ERP components acquired within/outside the gradient artifact [5,6]. However, this validation work has been concerned with the detection of ERP components (peaks), whereas cognitive neuroscientists are typically interested in the modulation of the amplitude, latency and scalp distribution of components. Because such experimentally-induced modulations are much smaller in magnitude and more variable than the peaks themselves, it is important to examine the effects of gradient artifact on these modulations. This was the primary aim of the study, which I briefly outline below [7]. We aimed to facilitate generalisation by employing: a well-characterised cognitive paradigm (the ‘go-nogo’ task), widely used gradient and cardioballistic artifact correction procedures, conventional ERP analysis (along with other analyses) and a standard fMRI protocol.

Another aim of our study was to assess the benefit of signal decomposition by means of ICA for the extraction of ERP components [cf. 3]. ICA-based decomposition has the potential to improve the detection of experimental effects in ERP components for at least three reasons: (1) it is likely to separate ERP components from artifacts; (2) it may disentangle (un-mix) temporally overlapping ERP components with different topographies, (3) it makes more data available for analysis (improving the SNR), by largely obviating the need to discard stretches containing artifact (e.g. ocular artifact). Here, we examined these expectations by performing all analyses with and without ICA-based decomposition.

The study employed a ‘go-nogo’ task that required a right-hand button-press in response to the presentation of two letters (‘go’ stimuli, probability 0.75) and withholding the response to two other letters (‘nogo’ stimuli, probability 0.25). To ensure an adequate number of (rare) ‘nogo’ trials, each participant was tested in two separate sessions (whose order was alternated over participants) about 1-3 days apart: in one (hereafter: ‘gradient’) session stimulus presentation was restricted to the 2 s fMRI volume acquisition, while in the other (hereafter: ‘no-gradient’) session stimuli were restricted to the 2 s gaps between fMRI volumes. To orthogonalise the timing of the ERP components relative to the timing of the gradient artifact (thus enabling average-based artifact cancellation), the onset of the 700-ms ERP segment was systematically jittered from trial to trial within the 2 s window (see above) in 10 steps of 100 ms.

The EEG (and ECG) was acquired using a 32-channel BrainCap MR cap and BrainAmp MR amplifier (both from Brain Products) at the full bandwidth of the amplifier (0.016-500 Hz) and its maximum sampling rate (5000 Hz). First we performed gradient artifact correction, as implemented in BrainVision Analyzer 1.05. The onset of individual gradient artifact stretches was marked by triggers received from the scanner during acquisition and the duration of these stretches was set to the temporal
interval between the triggers (4 s). The template for gradient correction was based on the average of all gradient artifacts in all but three datasets (for which the artifact was stable) and on a sliding average of 50 epochs in the remaining datasets (for which the artifact was more variable). The same gradient correction procedure was used for the two EEG-fMRI sessions (with stimuli in/outside the gradients). Following low-pass filtering (50 Hz) and downsampling to 250 Hz, the EEG was then subjected to template-based cardioballistic artifact correction in BrainVision Analyzer in semiautomatic mode (template and ECG episodes identified automatically, but subsequently inspected and confirmed) using the amplitude and cross-correlation criteria. The time-delay between the ECG episodes and cardioballistic artifact (in EEG channels) was determined using global field power employing the Analyzer Solution CBC Parameters. Correction was based on a sliding average of 21 artifacts.

For the no-ICA analysis, eye-blinks were identified in frontal channels and markers set using the blink detection function in the regression-based ocular correction module in Analyzer. Trials containing blinks were discarded during the ERP segmentation in the no-ICA analysis, but not in the ICA-based analysis. In the ICA-based analysis, ICA was run in Analyser on the continuous EEG data, and only ICA components that had central midline topography and showed N2 and P3 deflections following segmentation were back-transformed into the EEG channel space (mean number of components selected=1.8, SD=1).

Our statistical analysis of the amplitude changes in the ‘go-nogo’ task (the amplification of the N2 and central P3 components) comprised: (1) a conventional ERP analysis based on averaging segments, (2) an analysis in which the independent t statistic was computed for every participant on the basis of single-trial N2 and central P3 amplitudes, (3) correspondence analyses over the two (‘gradient’ and ‘no-gradient’) sessions; two kinds of correspondence were examined: first we assessed the stability of the ‘go-nogo’ modulations of N2/P3 amplitude.
across sessions by computing relative (Pearson’s r) and absolute (Cronbach’s alpha) measures of reliability; second, we assessed measurement error by computing the split-half reliability (again by means of Pearson’s r and Cronbach’s alpha) and compared those for the two sessions.

**Figure 2.** The scalp distribution of the go-nogo difference. Note the influence of P3b differences (see Fig. 1) on the topography of N2 effect in the no-ICA (but not in the ICA-based) analysis.

Because all the above analyses were done with and without ICA-based decomposition, its presence/absence was entered as a factor in all the ANOVAs.

We found little/no evidence of the benefit of sparse fMRI scanning for the detection of experimental differences in ERP components. Indeed, our analyses, whose results are illustrated in Figures 1 and 2, identified the N2 and central P3 effects in both sessions, and the differences between sessions in their detectability did not approach statistical significance. Furthermore, the correspondence between the ‘go-nogo’ effects in the gradient and no-gradient sessions, as assessed by cross-session reliability, was good, particularly if one takes into account the relatively small sample size (9 participants). Even without ICA decomposition, three out of four Pearson coefficients were above 0.5 and three out of four Cronbach coefficients above 0.7.

Our results revealed marked benefits of ICA-decomposition for examining ERP effects of a known topography. First, ICA improved the validity of our ERP measures. By separating the N2 and P3 effects with midline-central distribution from a delay in the posterior P300 (P3b) (see reduced P3b amplitude in the ICA-based analyses in Figure 1), ICA helped recover the typical midline-central topography of the N2 effect (see Figure 2, top panels). Second, ICA improved the stability of the measurement (session to session reliability) and substantially reduced the measurement error (split-half reliability).

While similar considerations apply to ERP acquired outside the scanner, ICA may be particularly useful for ERP component extraction in combined EEG-fMRI
References


BOLD Correlates of continuously fluctuating epileptic activity isolated by independent component analysis.


by Kay Jann, University of Bern, University Hospital of Psychiatry, Department of Psychiatric Neurophysiology

In epilepsy the correct diagnosis of the syndrome and the identification of the irritative zone are of great interest since it is necessary for correct treatment and eventually surgical intervention. This irritative zone is not only involved in the epileptic crises, but also produces fluctuating interictal activity. Interictal activity fluctuates spontaneously, has typical EEG signatures, and is assumed to mostly result from activity in sharply delimited regions.

Therefore, a method that detects random events with high temporal and spatial resolution is needed. This is provided by simultaneous EEG/fMRI recordings. Combined EEG/fMRI has indeed been demonstrated to be a valuable tool to delineate the irritative zone defined as the area with altered BOLD during epileptiform activity (Krakow et al., 1999 or Salek-Haddadi et al., 2006). The identification of epileptiform activity has so far been based on subjective selection of ‘suspicious’ events, simplifying the epileptiform activity to an on/off phenomenon. While this has been successful in a reasonable amount of cases, this approach is certainly loosing sensitivity because it subjective, does not take into account the variance in the length and amplitude of the single interictal epileptic discharges (IED) and cannot account for intermittent rhythmic discharges. Moreover, subthreshold IEDs are not accounted for.

Our study has therefore used an Independent Component Analysis (ICA) to identify epileptiform activity continuously. The decomposition of the EEG into ICA components separates normal physiological EEG activity from components representing artifacts (e.g. eyeblinks, scanner noise, cardioballistogram, etc.) and, most important for our purpose, it isolates factors representing epileptiform activity (Iriarte et al., 2006; Jung et al., 2000). The temporal evolution of these epileptiform ICA factors can then again be correlated with the fMRI BOLD signal. This has the advantage that the epileptiform ICA factors include also subthreshold epileptiform activity and account for the length and the amplitude of separate IEDs. Moreover, the ICA based identification eliminates the need to manually select single events, which is cumbersome and errorprone. We expected that this should increase the sensitivity of the method as compared to the conventional approach using a binary (on-off) predictor for the BOLD signal.
Twenty patients with different types of focal and generalized epilepsy syndromes were investigated in a 3T Siemens Magnetom Trio MR scanner. Simultaneously a 92 channel EEG was recorded with 3 MR usable BrainAmp amplifiers. To avoid aliasing of the scan pulse artifact, the EEG sampling was locked to the clock of the MR scanner using the Brain Products SyncBox (Mandelkow et al., 2006). Additionally, a second EEG dataset was recorded outside the MR environment. MR scan pulse artifact correction was performed according to the average artifact subtraction (AAS) method described by Allen et al. (2000).

Afterwards the EEG recorded outside the scanner and the MR scan pulse corrected EEG were combined and decomposed using an extended infomax ICA algorithm (Delorme and Makeig, 2004). Thereby the outside recorded EEG provides a baseline for the ICA algorithm to learn the uncontaminated EEG. This improved the separation of factors and yielded a small set of ICA factors with little spectral amplitude outside the scanner and markedly increased amplitude inside the scanner. This is the behavior that we expected for factors related to scanner and cardioballistic artifacts.

Two experienced neurophysiologists selected the factors coding for epileptiform activity based on their temporal dynamics (activity at the same timepoint as IEDs present in the original EEG) and their load on the electrodes (e.g. scalp distribution).

The factor rated as most accurately meeting the criteria was considered for further analysis. The absolute amplitude of the selected ICA factor was convolved with a double gamma hemodynamic response function (HRF) to account for neurovascular coupling. This convolved signal used to compute voxelwise correlations with the BOLD signal. As covariates motion in six directions (translation and rotation along the X, Y, and Z-axis) were used. To validate our hypothesis that our more physiological predictor may increase the sensitivity, we also analyzed each patient with the conventional approach.

The ICA separated artifacts from physiological and pathological activity in each patient. In seventeen of twenty patients, the BOLD correlates of epileptic activity were in accordance with the suspected EEG sources, the clinical semiology and, if present, the structural lesions. In those cases that were clinically equivocal, the BOLD correlates helped to establish the proper diagnosis of the underlying type of epilepsy. In one patient who suffered from temporal lobe epilepsy, the affected hippocampus could be identified by the BOLD correlates of rhythmic delta activity. This is a case where the conventional approach typically fails.

Overall, we could demonstrate that the ICA based approach increased the sensitivity for proper lateralization in our very heterogeneous group of patients with diverse types of epilepsies form 50% (conventional approach) to 80% (ICA approach).
The ICA EEG/fMRI approach is a safe, non-invasive and easily applicable technique, which can be used to identify regions with altered hemodynamic effects related to IEDs as well as intermittent rhythmic discharges in different types of epilepsy.

Graphical overview of analysis procedure and an example of results for one patient with temporal lobe epilepsy.

References


Fluctuations in electrodermal activity reveal variations in single trial brain responses to painful laser stimuli - A fMRI/EEG study

by Dr. Jürgen Brinkmeyer

In a recent psychophysiological study using simultaneous electroencephalography/functional magnetic resonance imaging (EEG/fMRI) to investigate pain processing in the human brain we also sought to evaluate the usefulness of recording galvanic skin response (GSR)/electrodermal activity (EDA) during the course of the experiment. Our questions/objectives were a) is it possible to obtain single-trial EDA data in response to experimental pain during echoplanar functional magnetic resonance imaging? b) what is the cortical representation of electrodermal activity in response to experimental pain? c) can the psychophysiologicaly measured EDA further inform fMRI (and EEG) analysis? d) analysis of the changes in GSR as an intraindividual single-trial valid pain indicator for the simultaneous EEG/fMRI recording.

The galvanic skin response (GSR) measures sweat gland function and can be used to capture the response of the autonomous/sympathetic nervous system to a wide range of external stimuli. In essence, an increase in EDA represents a decrease in the skin’s impedance that is mainly caused by the filling with sweat of the sweat ducts in the dermis and epidermis (Fowles, 1986). EDA is associated with arousal in response to various types of stimuli such as novelty, intensity, emotional content and significance (Critchley, 2002). In the context of experimental pain, it has been shown that markers of sympathetic arousal, including EDA, correlate with subjective ratings of pain (Chapman et al., 2001, 2002).

This measure can be considered as simple and reliable. Repeated within subjects GSR measurements exhibit common features in wave shapes and habituation patterns. However, in the context of a simultaneous EEG/fMRI experiment, EDA measures are more difficult to obtain and safety issues are pertinent. We performed extensive tests on the

Figure 1: EDA measurement
new EDA sensor in 3T scanner (Trio, Siemens, Erlangen, Germany). We investigated 12 healthy male subjects, all right-handed. A total of 60 painful laser stimuli (using a thulium laser, duration 1ms, intensity 600mJ) were applied to the dorsum of the left hand. The pseudo-randomized interstimulus interval was 8-12 seconds. Every third stimulus was skipped to allow the hemodynamic response to return to baseline. The fMRI BOLD response as well as continuous EEG and EDA data were recorded simultaneously.

EDA was measured as a skin conductance response in constant voltage technique. Silver-silver chloride electrodes were placed at the palmar middle phalanges of the index and middle finger of the hand contralateral to the stimulation side (Figure 1). The measurement site was prepared according to recommendations given by Fowles et al. (1981). Electrode paste and the MR-capable sensor (Brain Products GmbH, Germany) were subsequently applied.

The skin conductance response (SCR) signal was recorded in DC mode by means of a bipolar BrainAmp ExG MR amplifier (Brain Products GmbH, Germany) simultaneously with the continuous EEG.

As EDA and EEG data were recorded together in the same file, the same artifact correction procedures were applied to the EEG and EDA raw data: gradient artifact correction was performed using modified versions of the algorithms proposed by Allen et al. (2000), where a gradient artifact template is subtracted from the EEG using a baseline-corrected sliding average of 20 MR volumes. In addition a bandpass filter of 0.016 Hz to 5 Hz was applied to the EDA data. Data was then downsampled to 250 Hz. Laser stimulus-related EDA data processing was performed in a time frame of between 1 and 8s after laser stimulus onset. The single-trial EDA amplitude was calculated as the peak-to-peak difference between the negative and positive extreme value within this window.

![Graphs](image)

*Figure 2: A single-subject, single-trial EDA measurement (red: after gradient artifact correction). a: prototype EDA sensor; b: new sensor with long electrode cables; c: new sensor with shorter electrode cables*
We observed an event-related increase in skin conductance (EDA) that peaked 4860 ms after painful stimulation. A single-subject, single-trial experiment is depicted in Figure 2. A sample EDA stack plot of a single-subject experiment is shown in Figure 3.

We used the EDA data in two different ways for BOLD modelling. First we sorted trials according to their EDA amplitude into trials with a high vs. trials with a low EDA response. The fMRI contrast trials with high EDA vs. trials with low EDA at group level showed activation in areas consistent with pain processing. See Mobascher et al., NeuroImage 2008 for further details. We next used the single-trial EDA response as an additional regressor for fMRI BOLD to clarify which brain regions would covary with the EDA response from trial to trial. Again, structures that were previously shown to be involved in cortical pain processing were activated. For further details and discussion of the findings see Mobascher et al., NeuroImage 2008.

In our pilot study published in NeuroImage (2008) we used a prototype EDA sensor. At that stage of the project data analysis required the above-mentioned gradient artifact correction procedure to obtain a high-quality EDA signal that could be analyzed at single-trial level. Subsequent optimization of the hardware, namely improved shielding and shorter electrode cables, resulted in an EDA raw signal that was already largely artifact-free and did not require any gradient artifact correction procedures.

![Figure 3: Stack plot of a single-subject experiment](image-url)
**References**


BrainAmp MR series is the first Siemens tested system for combined EEG/fMRI worldwide!

A report on the BrainAmp MR and Siemens Magnetom compatibility test

Since its foundation, Brain Products has identified the capabilities of combined EEG/fMRI measurements to provide groundbreaking insights in neurophysiology. MR compatibility was an essential principle for the design of the BrainAmp MR series from day one. Our hardware developer team therefore consists not only of medical device engineers but also of radio frequency experts. And this mix has paid off: More than 200 BrainAmp MR amplifiers have been sold worldwide. Although a huge number of BrainAmp MR related publications have already illustrated the success of combined measurements, Brain Products decided to go one step further and substantiate this specific EEG/fMRI expertise by testing leading MR imager manufacturers.

Siemens was selected as the first candidate. The objective of the Siemens test was to verify the impact and influence of the BrainAmp MR system on the stability, image quality and safety of Siemens MR systems. On January 24th, this test took place at the Max Planck Institute (MPI) for Human Cognitive and Brain Science in Leipzig, Germany, on a Siemens TRIO system: Our special thanks go to Professor Arno Villringer, who provided scanner time for the practical part of the test. The Siemens-appointed external referee was Dr. Günther Wetzler, an engineer with more than ten years of 3rd party device testing experience of Siemens scanners. All measurements were conducted by Dr. Wetzler with the assistance of Dr. Petra Ritter and her enthusiastic and highly EEG/fMRI experienced staff. My humble self took care of the EEG system and provision of realistic test conditions.

The test subject was a complete and fully operational 64-channel BrainAmp MR plus system including PowerPack, the most recent version of BrainCap MR 64, controlled by BrainVision Recorder and running a real time gradient correction from BrainVision RecView. Test criteria and tolerance ranges were specified in advance by Siemens engineers and consisted of elementary safety tests, such as magnetostatic forces, the measurement of magnetostatic properties, magnetic field interference, MR muteness, measurement of the electromagnetic frequency-stable and stray radiation, measurement of electromagnetic noise, measurement of dynamic magnetic effects, gradient eddy fields and many other critical imaging properties. The test procedure itself was an elaborated show-jumping course with different phantoms, special diagnostic sequences, alternating blank measurements and scans using the operating BrainAmp MR system. Needless to say, the BrainAmp MR system fulfilled all the test criteria with flying colours and very narrow tolerances. Next, the measurement results were subjected to
an in-depth review at the Siemens Medical Solutions headquarters in Erlangen, Germany. By March 13th the expected result was made official: The complete BrainAmp MR 64 system does not interfere with the safety and functioning of the Siemens 3T systems TIM Trio and Verio.

The certificate obtained again demonstrates the well-engineered quality of the BrainAmp MR concept. Experience makes the difference: Some competitors offer their amps even for use in MRI experiments, but only Brain Products markets a BrainAmp MR series certified for professional research.

The complete certificate is available at www.brainproducts.com.

We are grateful to Professor Arno Villringer, who made the MPI scanner available and set it up for the tests, as well as hosting the measurements, to Dr. Petra Ritter and her research fellows for their technical assistance and to Dr. Günther Wetzler for his precise work and fair judgment and collaboration.
Brain Products and Philips Healthcare cooperate on EEG/fMRI: BrainAmp MR/MR plus compatibility with Philips 3T MRI officially confirmed

Given the galvanically isolated, non-magnetic and completely RF-proof design of the BrainAmp MR, this amp will probably work directly in every imager bore if boundary conditions (meaningful Tx coil configuration, GRE-EPI sequence) are met. This has been empirically proved and is no longer in question. If the EEG cap is properly mounted and the imager gradient system timing is reliable, good EEG during a BOLD sequence will always be achieved.

A more crucial question is how the overall EEG system affects imaging quality. Important research on this issue has been conducted (Krakow et al 2000, Mullinger et al 2008, Carmichael 2009, Mullinger et al 2010). However, the ultimate test of compatibility remains the confirmations issued by individual scanner manufacturers. Only if a scanner manufacturer confirms compatibility with a given third-party product can there be certainty of obtaining high-quality imaging data during the combined EEG/fMRI session.

Siemens confirmed the BrainAmp MR’s compatibility with their 3T Magnetom series early in 2008 (see Brain Products’ Press Release, Vol. 28, 2/2008). Even though several dozen units of the BrainAmp MR/MR plus are already in use on Philips platforms ranging from 1.5 to 7T, we were curious to learn more by observing the Philips compatibility test at first hand.

As the Philips MR neuro team and the Brain Products MR team are always meeting at the same conferences, Elizabeth Moore (Senior MR Clinical Scientist, Philips Neuro) and Pierluigi Castellone (General Manager, Brain Products) were soon able to arrange an on-site test at the Philips headquarters in Best, the Netherlands.

Eventually, in November 2009 a complete 64-channel BrainAmp MR plus system, our certified distributor in the Netherlands, Dr. Harm-Jan Wieringa (MedCat NL), and I arrived at the centre of testing operations, Philips’s

The Achieva 3.0T X-series MRI combines simple operation with fast scanning and superb image quality
MRI R&D facility in Best. It was certainly an impressive spectacle for us EEG guys to see dozens of Philips Achievas side by side.

Philips test engineer Filip Vuigts selected one of the 3T Achievas and quickly explained the test procedures. In particular, he detailed the steps that made up the compatibility test: a safety check followed by checks for spurious signals, LF B fields, Bo homogeneity, RF coil influence, the influence of eddy currents, spurious signal generation by protons, susceptibility to RF fields/switching gradient fields, ECG lead conductivity, susceptibility to static magnetic fields, connectivity between the BrainAmp MR plus system and the Philips MR system, and patient isolation.

Our contribution was to analyze the EEG data acquired during the compatibility tests and to evaluate the impact of the various sequences on it. Filip Vuigts’ report and our report underwent an appropriate review process and ultimately resulted in the compatibility statement covering the Philips Intera 3.0T, Achieva 3.0T, Achieva XR@3.0T, and Achieva 3.0T TX. The certificate is available for download at www.brainproducts.com/product_approvals.php?aid=4.

The production of joint outcome documents and certificates is only one aspect of the collaboration between our two companies. Even more important for our customers are the practical improvements which emerge from teaming up at the working level. During the same meeting Liz Moore presented the prototype of the brand-new 32-channel Philips SENSE head coil, which is the very first coil in which the needs of combined EEG/fMRI were considered. Beyond its outstanding imaging capabilities, right from the start this 32-element SENSE coil (Fig. 1) was designed with a cable channel in the Z-direction for the EEG cables of a 128-channel BrainAmp MR system. For further information please visit: www.healthcare.philips.com/in/products/mri/options_upgrades/coils/achieva3t/coils_neuro.wpd

This is an excellent solution which prevents loops involving the BrainCap MR cable harness in the scanner.

Other improvements for Achieva users will soon follow.

Mandelkov et al (2007) have worked out that perfect scanner/EEG synchronization...
requires consideration to be given to sequence timing.

Liz Moore quickly decided to attack the root of this problem and asked Philips’s developers to design a console application (Fig. 2) which automatically calculates an optimized volume/slice timing parameter for combined EEG/fMRI using the Achieva with BrainAmp MR/MR plus systems.

We are very pleased to see Philips’s awareness of the needs of the fast-growing Achieva/BrainAmp MR user community, and we look forward to a fruitful collaboration in the future.

Fig. 2: The new Philips console application provides optimized sequence timing parameters for combined EEG/fMRI and will be available soon.

References


BrainAmp MR:
Superior solution for combining EEG and fMRI

Over the course of the last number of years the combination of EEG and fMRI to investigate the electrophysiological as well as the hemodynamic information of cerebral dynamics has become an extremely popular technique. The first BrainAmp MR system for EEG/fMRI simultaneous acquisition was manufactured by Brain Products almost 7 years ago and it represented a real technological breakthrough.

The extremely high data quality, ease of use, long lasting experience of our developers and the unparalleled scientific and technical support made the BrainAmp MR amplifier the first choice for researchers all over the world. Many scientific publications refer to EEG/fMRI co-registration studies performed with the BrainAmp MR systems.

Technical reasons for the great success achieved by Brain Products with this system are as follows: The BrainAmp MR is a shielded amplifier which can be taken directly inside the MRI chamber and placed right behind the subject’s head. From the amplifier the digitized signal is sent via fiber optic cable to the USB interface located in the control room. Therefore no artifacts can be added along the way to outside of the MRI chamber. The short length required for the electrical cables used to connect the electrode cap with the amplifier complies with all safety requirements for the experimental subject.

The sturdy and compact BrainAmp MR can be stacked one on one to acquire up to 128 EEG channels with ease. The MR-usable rechargeable batteries make this system a truly portable solution even for outdoor recordings.

The BrainAmp MR can be combined with the MR-usable ExG amplifiers to add the capability to record bipolar and peripheral signals (e.g. Galvanic Skin Response) in an extremely compact setup.
BrainAmp MR plus extends the borders of the technically possible

Since the design of the first BrainAmp MR, the neurophysiology research world moved forward and started to look at new techniques of investigating the brain in action. In light of this it was obvious that there was a need to develop a more advanced amplifier which could cover a wider range of applications and be as flexible as required by its users.

The BrainAmp MR plus enhances the already outstanding features of the BrainAmp MR thanks to the multiple hardware signal resolution options settable via the recording software. Based on the recording needs, with just one “click” it is possible to switch from AC to DC mode acquisitions as well as to extend the hardware bandwidth.

The result is an amplifier that can be placed inside of the MRI bore for simultaneous EEG/fMRI acquisitions as well as used in the EEG lab for EEG/TMS co-registrations, EEG/ERP studies and Brain Computer Interface applications. There is no need for different amplifier types as the Brain Products’ flagship represents the state of the art solution for all of the aforementioned applications.

BrainAmp MR plus systems can be stacked on top of each other to increase the number of available channels up to 128 for recordings in the MRI environment and up to 256 channels for laboratory applications. Powered with rechargeable batteries, this amplifier can be used in any environment even for outdoor recordings. The BrainAmp MR plus system can be combined with the BrainAmp ExG MR amplifier to record EEG, EOG, EMG, ECG, GSR (Galvanic Skin Response) and many other types of bipolar and auxiliary signals.

BrainAmp ExG MR: MR-usable bipolar amplifier with unparalleled design

The increasing interest in simultaneous EEG/fMRI recordings to investigate the brain’s activity very quickly led to the need to also co-register other types of physiological data such as bipolar and peripheral signals. The BrainAmp ExG MR bridges this gap and makes the recording of bipolar and polygraphic signals in the MRI environment a simple procedure.
The magnetically shielded BrainAmp ExG MR system can be taken inside the magnet bore and placed right next to the experiment subject minimizing the length of the cables to meet all safety requirements.

The available MR usable auxiliary sensors (GSR MR) are powered directly through the battery supplied amplifier which ensures patient safety and product portability.

The two existing versions with 8 or 16 channels can be purchased as extension to the BrainAmp MR and BrainAmp MR plus, but also as fully independent units.

SyncBox: Solution designed to boost data quality for concurrent EEG and fMRI recordings

The SyncBox is a unique tool which significantly reduces timing related errors and boosts the quality of MRI artifact correction by synchronizing the clock of the BrainAmp MR system with the clock driving the MRI scanner’s gradient switching system.

Phase synchronization between the EEG equipment and the MRI scanner results in temporal stability of the EEG acquisition in relation to the switching of the gradients during the MR acquisition. This leads to significant improvement of the recorded data quality.

The SyncBox's scanner interface and the appropriate clock output available in the scanner electronics cabinets are physically connected by using a galvanic coupling device to avoid any potential influence on the MR scanner system. More than 100 Brain Products users have already chosen this solution and are experiencing the added advantage in using it together with all major commercial MRI scanners available on the market. If you want to optimize your data quality then - join the crowd!
Sensors for MR: Brain Products GSR (Galvanic Skin Response) module for fMRI

Skin conductance (SC) has for decades been one of the most employed measures in psychophysiological research. As a sensitive parameter for emotional and cognitive states, stress and pain, SC has also been widely used in psychiatric research. With the growing availability of EEG for functional MRI, we have seen increasing demand for the capability to measure the established psychophysiological parameters in addition to EEG in the scanner. At the very top of the wish list came EDA/GSR. The initial market survey revealed that there are already some allegedly MRI-usable GSR devices on the market: These consist of essentially MR incompatible amplifiers, placed in the control room with long electrode cables extended to reach the subject though the wave guide - a hole in the wall traversing the scanner room and the control room.

In our experience of EEG/fMRI in practice, we are convinced that the concept of short resistive electrode wires meets safety requirements and promotes safety in a superior way to other solutions currently available. As an EEG company, we are aware of EMC and noise problems which may be caused by galvanically connected devices located outside the scanner room. With these considerations in mind we instigated the development of a competely RF proof sensor for use inside the scanner bore.

Our MR amplifier development team devised an extremely compact but heavily shielded DC instrumentation amplifier capable of measuring conductance directly using 5V constant voltage. Because of this instrumentation amplifiers high CMRR properties, the gradient artifact emerges remarkably suppressed so that in many cases smoothing is sufficient to get a laboratory-like GSR signal. The sensor interfaces with the bipolar BrainAmp ExG MR via the ExG AUX box and the GSR is recorded synchronously with the EEG.

The device was electically and EMC tested to IEC 60601-1. The new sensor has been extensively tested in various 3T scanners. The first publications have already been submitted. It is now possible to add the GSR MR module to your already existing BrainAmp ExG MR system and record GSR of laboratory-standard quality even during functional MRI.
PowerPack:
MR-usable rechargeable batteries

The PowerPack is an MR-usable rechargeable battery designed for use with BrainAmp MR, BrainAmp MR plus and BrainAmp ExG MR systems.

The PowerPack is the perfect solution for safe EEG recordings in the MR. It is also a valid alternative to the mains power systems for standard EEG/ERP recordings as it fully eliminates problems with 50/60 Hertz mains noise. The PowerPack can be used for continuous acquisitions of up to 30 hours and allows for more than 1000 recharging cycles.

How to keep your PowerPack well and fit
PowerPack was originally designed to feed the BrainAmp in MR environments. Over the years the PowerPack enjoyed increasing popularity even for laboratory applications, in faraday cages, MEG cabins and mobile use. In labs where the mains tends to destroy the BrainAmp mains power supply by voltage peaks or where the mains voltage dips if the neighbor lab charges the TMS coil, is the PowerPack the method of choice.

Given correct operation, the PowerPack is an extremely economic and long-lasting purchase.

The maintenance is simple:
Use it. Preferably the whole day. It feeds two amps >15h and has a deep discharge protection.
Charge it. Charge it directly after use. Don’t worry about memory effects. You can’t overcharge the PowerPack, even over the weekend.

There is only one certain way to destroy the PowerPack within weeks: If you forget it in your cupboard. This misuse is not covered by warranty.
BrainCap MR: Important safety aspects for combined EEG / fMRI recordings

The technique of combined EEG & fMRI recordings has been explored and improved over the last couple of years. Since the release of our first products for this purpose devices have been improved in terms of quality, handling and safety. This means that the electrode cap and electrodes, which are connected directly to the subject, have been continuously modified in line with our increased experience in this field. Below we would like to give you an understanding of the improvements and further development of the BrainCap MR.

Safety Aspects

- Electrodes must not touch the skin. Our new electrodes are pin type sensors which are placed inside a plastic holder mounted on the cap. The holder is filled with gel to reduce skin conductance and to establish contact between the sensor and the subject's skin.
- Every electrode contains safety resistors between the sensor and the connection wire. Connection between the components is performed by gluing, not soldering.
- Additional safety resistors are placed inside the cap connector, acting like an additional RF-filter.
- Wires are located on the outside of the cap to ensure isolation between skin and wire according to FDA patient safety regulations.
- High temperature isolating tubes around the ECG electrode cable avoid contact between skin and wire.
- ECG electrodes contain higher resistors than normal electrodes to compensate for the technical characteristics of longer wires.
- All wires are fixed into the cap to avoid loops.
- Wire length from electrode to the amplifier input is fixed to a minimal required length.
- Wire outlets for the cable tree at central positions avoid loops due to cable routing.
- Extra electrodes (for e.g. EMG recordings) are surrounded by tubes to avoid contact between wire and skin as well as to avoid cable loops occurring by mistake.
- Serial number sticker ensure easy tracking and support/service issues.

Image Artifacts

- The new pin sensor design reduces the amount of Ag/AgCl in the cap.
- Reducing the number of extra electrodes hanging out of the cap reduces possible image artifacts.
- Wire outlets for the cable tree at central positions ensure short cable routing distances through the head coil.
Comfort

- Extra flat electrode holders for extra comfort, especially when resting on electrodes.
- Extra spare electrode holders for extra comfort to compensate for gaps between electrodes especially when using less than 64-channels.
- Soft cap fabric to increase comfort and to widen the fit to accommodate different head sizes.

Serviceability

- Serial number sticker for easy tracking, assembly and layout questions.
- Colored electrode holders for easy access/clarification of assembly affiliation (e.g. 10-20, 10-10).
- Name labels on every electrode for easy recognition.
- Special gel adds electrode visualization capabilities (similar to vitamin E capsules).
BrainVision Analyzer 2: 
Our answer for today and tomorrow

Our market leading complete EEG & ERP processing software with 10 years on the market and in use by more than 1.000 labs all over the world. Its unique history tree structure for analysis and powerful features with Matlab integration, Wavelet analysis, ICA and many more makes it the perfect tool for analyzing data from nearly any EEG amplifier available on the market.

BrainVision Recorder: 
Easy to use multifunctional recording software

The BrainVision Recorder controls all of our amplifiers, displays and saves the incoming data. Various options such as online averaging or video integration are available. Direct output of incoming data to the network via TCP/IP protocol makes the Recorder a BCI realtime-server.

BrainVision RecView: 
Software for real time data analyses

BrainVision RecView is an advanced solution designed for real time analysis of data received over the Ethernet network via TCP-IP directly from the Recorder software. BrainVision RecView is widely used in the EEG/fMRI co-registration to remove both the gradient and the ballistocardiogram artifact permitting experimental control during the scan. The innovative Template Drift Compensation algorithm remedies template jitter caused by imperfect synchronization between the EEG amplifier and the scanner clocks and thus ensures optimal data correction at any time.

By using the same history tree concept already implemented in BrainVision Analyzer, RecView can also be used for FFT analysis, data filtering, mapping of the surface potentials as well as BCI and bio-/neurofeedback on the incoming data.

For more information please visit www.brainproducts.com
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