Brain Topogr (2010) 23:46–57
DOI 10.1007/s10548-009-0117-2

ORIGINAL PAPER

Wavelet Analysis as a Tool for Investigating Movement-Related Cortical Oscillations in EEG-fMRI Coregistration

Silvia Francesca Storti · Emanuela Formaggio · Alberto Beltramello · Antonio Fiaschi · Paolo Manganotti

Received: 12 June 2009 / Accepted: 30 October 2009 / Published online: 18 November 2009

Abstract Electroencephalography combined with functional magnetic resonance imaging (EEG-fMRI) identifies blood oxygenation level dependent (BOLD) signal changes associated with physiological and pathological EEG events. In this study we used EEG-fMRI to determine the possible correlation between topographical movement-related EEG changes in brain oscillatory activity recorded from EEG electrodes over the scalp and fMRI cortical responses in motor areas during finger movement. Thirty-two channels of EEG were recorded in 12 subjects during eyes-closed condition inside a three T magnetic resonance (MR) scanner using an MR-compatible EEG recording system. Off-line MRI artifact subtraction software was applied to obtain continuous EEG data during fMRI acquisition. For EEG data analysis we used a time–frequency approach to measure time by varying the energy in a signal at a given frequency band by the convolution of the EEG signal with a wavelet family in the alpha and beta bands. The correlation between the BOLD signal associated with the EEG regressor provides that sensory motor region is a source of the EEG. We conclude that combined EEG-fMRI can be used to investigate movement-related oscillations of the human brain inside an MRI scanner and wavelet analysis adds further details on the EEG changes. The movement-related changes in the EEG signals are useful to identify the brain activation sources responsible for BOLD-signal changes.

Keywords EEG · BOLD · Wavelet analysis · Wavelet energy · Maps

S. F. Storti (✉) · E. Formaggio · A. Fiaschi · P. Manganotti
Department of Neurological and Vision Sciences, Section of Neurological rehabilitation, University of Verona, Verona, Italy
e-mail: silviafrancesca.storti@univr.it

S. F. Storti · E. Formaggio · A. Fiaschi · P. Manganotti
Policlinico "Gianbattista Rossi", Università di Verona, P.le Scuro, 37134 Verona, Italia

E. Formaggio
Department of Information Engineering, University of Padova, Padova, Italy

A. Beltramello
Department of Neurosurgery, Section of Neuroradiology, University of Verona, Verona, Italy

A. Fiaschi · P. Manganotti
IRCCS "San Camillo" Hospital, Venice, Italy

Introduction

Electroencephalogram—functional magnetic resonance imaging (EEG-fMRI) recording is a non invasive technique that is increasingly used to study human brain function. EEG phenomena are not directly visible in the fMRI, although appearance or disappearance of EEG features might cause part of the fMRI observed signal variations. Coregistration of EEG and fMRI has added value in order to investigate neurophysiological mechanisms underlying brain functional states: it could identify brain activity in motor areas and also provides information on the source of the event generator.

EEG activity recorded from the human brain at rest oscillates in various frequency bands including the theta (4–7 Hz), alpha (8–12 Hz), beta (13–30 Hz) and gamma (30–50 Hz) ranges. Movement preparation typically suppresses, with a decrease in power, the cortical oscillations in both alpha and beta rhythms starting more than 1 s before the onset of finger or hand movement (Erbil and Ungan 2007; Leocani et al. 1997; Pfurtscheller and

Aranibar 1979; Rappelsberger et al. 1994) over sensorimotor areas.

Upon movement completion, the EEG recording shows an alpha event-related desynchronization (ERD) followed a brief ''rebound'' beta event-related synchronization (ERS) over various cortical regions (Salmelin and Hari 1994). ERD indicates oscillations in cortical activation and ERS reflects a cortical idling state (Pfurtscheller 1992). These pre-movement and post-movement power changes both correspond to the somatotopic organization of the primary sensorimotor cortex (Hari and Salmelin 1997; Neuper and Pfurtscheller 1996; Stancak et al. 2000). A more recent study has described a different pattern of alpha and beta suppression band with a more persistent beta-band suppression activity during continuous finger movement (Erbil and Ungan 2007). The regional activation of cortical areas with a decrease in power has been associated with the term 'EEG desynchronization', whereas brain activation produces spontaneous synchronization of fast rhythms with high amplitudes (Steriade and Amzica 1996).

Earlier studies investigated the correlation between changes in oscillatory activity and blood oxygenation level-dependent (BOLD) activation during hand movement in separate recording sessions (Babiloni et al. 2005; Manganotti et al. 1998; Sadato et al. 1996). The recent development of digital recording methods compatible with the magnetic field surrounding fMRI scanners has enabled combined EEG-fMRI recording in human subjects. Few studies have investigated movement-related brain oscillatory activity during co-registered EEG-fMRI. One study observed a beta band synchronization during movement (Parkes et al. 2006), another analyzed the EMG activity during the coregistration EMG-fMRI (van Duinen et al. 2005). A recent study examined the EEG-fMRI relationship during bimanual motor task performance and the result was a negative correlation between Rolandic alpha (mu) rhythm and BOLD signal (Ritter et al. 2009). In a previous own study we found a significant correlation between the positive–negative ratio of BOLD signal peaks and ERD values in the electrodes over the sensorimotor area contralateral to the movement (Formaggio et al. 2008b). We investigated the effect of a motor task in fMRI activation, in a steady state motor condition following previous EEG studies (Manganotti et al. 1998) whereas we did not investigate the time course of ERD during movement (Leocani et al. 1997).

In electro-neurophysiological analysis, the frequency content of electrophysiological activity is traditionally assessed with spectrograms obtained via Fourier transform (FT) (Muthuswamy and Thakor 1998). EEG signals containing frequency components that emerge and vanish within certain intervals, however, require time as well as frequency localization. Among several solutions that can simultaneously analyze a signal in the time and frequency domains is the short-time Fourier transform (STFT). This operation nevertheless has the disadvantage that a given time window remains the same for all signal frequencies analyzed, possibly causing a substantial loss of essential information at very low or very high frequencies.

The underlying principle of the phenomena just described is due to Heisenberg's uncertainty principle, which, in signal processing terms, states that it is impossible to know the exact frequency and the exact time of occurrence of this frequency in a signal. In other words, as the time resolution improves, the frequency resolution degrades. Similarly, if the frequency resolution is increased, then the time resolution will decrease (Singer 1999).

Wavelet analysis does not require a priori selection of a narrow frequency band, and provides a better compromise between temporal and frequency resolution than time–frequency techniques based on STFT. Wavelet-based analysis of EEG signals allows the use of long time-intervals for more precise low-frequency information, and shorter regions for more high-frequency information.

In this study we investigated topographical and temporal changes in brain oscillatory activities correlated to the BOLD activity recorded during an EEG-fMRI coregistration. To do so we recorded EEG signals over the scalp and simultaneously acquired 3T fMRI signals while healthy subjects inside the scanner did a hand motor task. To calculate the spectral EEG response to hand movement we used wavelet analysis, choosing the best compromise between temporal and frequency resolution. To detect the instantaneous interaction between EEG recordings acquired under two experimental conditions (at rest and during active movement) we applied a continuous Morlet wavelet transformation (CMT). After this we used the wavelet energy as regressor of General Linear Model (GLM) in fMRI analysis.

Materials and Methods

Subjects

Data were recorded in twelve healthy subjects (seven men and five women), whose ages ranged from 21 to 34 years (mean: 32.08, SD: 5.76). All subjects, right-handed as established by the Edinburgh handedness inventory (Oldfield 1971), gave written informed consent for the study in accordance with the Declaration of Helsinki. The experiment was approved by the Local Ethics Committee of the University Department and Hospital.

Experimental Paradigm

Inside the bore of the scanner subjects were laid supine on a bed with their elbows flexed at 120° and hands pronated

in a relaxed position. The subject's head was stabilized with adjustable padded restraints on both sides. They were instructed to remain as still as possible and to keep their eyes closed throughout the experiment. While lying inside the MRI chamber the subjects performed a motor task. This task consisted of synchronous opening and closing of the right hand at a frequency of 1 Hz (metronome paced) for 26.1 s alternating with rest periods of equal duration. The metronome sound continued during activation and rest periods; and a high-pitched sound signalled subjects to start the movement task. During fMRI acquisition, 100 volumes of 2610 ms were acquired, alternating five activation and five control cycles (rest), resulting in about 5 min of echo planar imaging (EPI) recording. Each subject was trained for several minutes before the experiment to perform the task correctly at the right rate. Subjects were tested wearing earplugs. Motor performance was monitored by the EMG signal recorded inside the magnet.

EEG Data Acquisition and Analysis

The EEG was acquired using a MR compatible EEG amplifier (SD MRI 32, Micromed, Treviso, Italy) and a cap providing 32 Ag/AgCl electrodes positioned according to a 10/20 system (impedance was kept below 10 kΩ). To remove pulse and movement artifacts during scanning two of these electrodes were used to record the electrocardiogram (ECG) and electromyogram (EMG). The EMG electrode was placed on the right abductor pollicis brevis (APB) muscle.

The reference was placed anterior to Fz, and the ground posterior to Fz as in other studies (Formaggio et al. 2008a, b; Gonçalves et al. 2006; Manganotti et al. 2008) using the same system. To ensure subjects' safety, the wires were carefully arranged to avoid loops and physical contact with the subject. To minimize the variability in the EEG artifacts due to the MR sequence and avoid wire movement caused by mechanical vibration the wires rested on foam pads.

EEG data were acquired at the rate of 1024 Hz using the software package SystemPlus (Micromed, Treviso, Italy). To avoid saturation, the EEG amplifier had a resolution of 22 bits with a range of ±25.6 mV. An anti-aliasing hardware band-pass filter was applied with a bandwidth between 0.15 and 269.5 Hz.

The EEG analysis was performed by using functions implemented in Matlab 7 (The Mathworks Inc., Natick, MA) (Fig. 1a). The EEG artifact induced by the magnetic field gradient was digitally removed off-line using an adaptive filter (Micromed). The EEG artifact associated with pulsatile blood flow, ballistocardiogram (BCG), was also digitally removed offline using a simple averaging procedure (Allen et al. 1998). Reference-free recordings were then obtained by calculating the local average reference using the software EEGLAB, a Matlab toolbox (Delorme and Makeig 2004). A notch filter (50 Hz) and a baseline correction were also applied to all channels. Two subjects' data were excluded from the analysis owing to poor quality EEG recordings. Five epochs of EEG data starting one volume (2610 ms) before the active condition and one volume consecutive (epochs of 2*TR) were extracted. EEG epochs with ocular, muscular and other types of artifact were preliminarily identified and then rejected.

Time–frequency data were assessed using wavelet-based analysis. To divide the continuous-time function into wavelets we used a CMT. Unlike Fourier transform, CMT constructs a time–frequency representation of a signal that offers a time and frequency localization. The Morlet $\psi(t)$ is a function of time t consisting of a complex exponential modulated by a Gaussian envelope. It has a Gaussian distribution in both time and frequency domains. This 'mother' wavelet was then used to build a set of daughter wavelets by translating $\psi(t)$ in time, and by dilating or contracting $\psi(t)$. This operation, served to adjust the mean frequency and also the spread of the daughter wavelet.

The wavelet transform is the inner-product of the wavelet function with the signal s(t). A family of Morlet wavelets was first constructed at 1 Hz frequency intervals ranging from 8 to 30 Hz. Each wavelet has a Gaussian distribution in the time $(\mathrm{SD}:\sigma_t)$ and frequency domains $(\mathrm{SD}:\sigma_f)$ around the centre frequency f_0 (Tallon-Baudry et al. 1997):

$$w(t,f_o) = (\sigma_t\sqrt{\pi})^{-\frac{1}{2}} \exp\left(\frac{-t^2}{2\sigma_t^2}\right) \exp(2i\,\pi f_0\, t) \tag{1}$$

with

$$\sigma_f = \frac{1}{2\pi\sigma_t}. \tag{2}$$

This function depends on a parameter, the number of oscillations (f_0/σ_f), which has to be chosen by the user. Our wavelet family was computed using a ratio of 20 oscillations. To compute the time varying energy in a frequency band the recorded signal s(t) was then convolved with the corresponding set of functions generated by the mother wavelet. The convolution can be computed by using Fast Fourier Transform (FFT). Normally, the output is a real function except when the mother wavelet is complex. The power spectrum calculated from the result of convolution can be represented by (Tallon-Baudry et al. 1997):

$$E(t,f_0) = |w(t,f_0) \otimes s(t)|^2. \tag{3}$$

We computed the wavelet energy for all five epochs and for all 30 EEG electrodes using Matlab and then these five epochs of 5220 ms were average for further processing. At

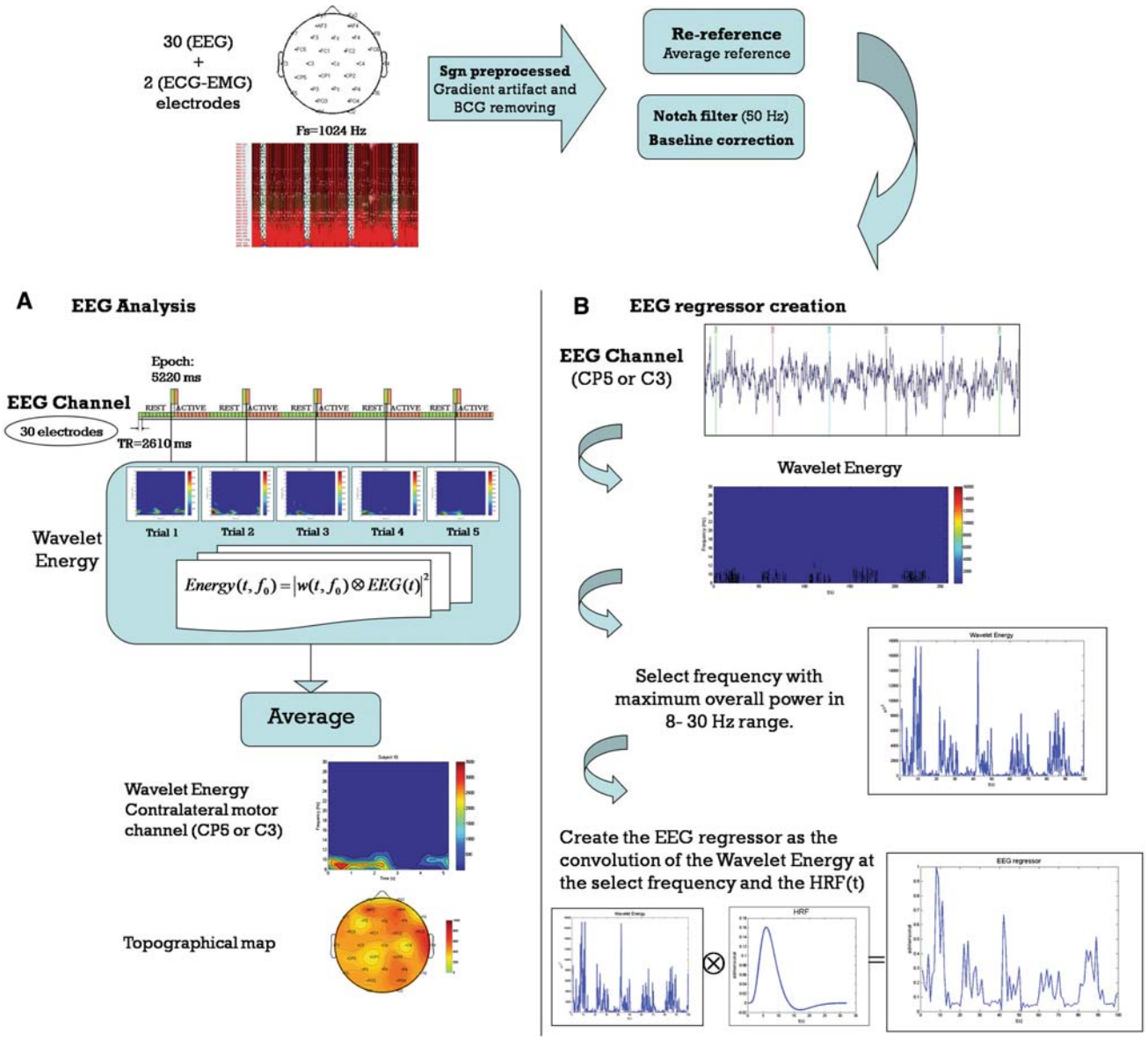

Fig. 1 Schematic representation of the different steps in EEG analysis (part *A*) and in EEG-fMRI analysis (part *B*). This procedure is in more detail described in the "Materials and Methods" section

the end we examined the wavelet trend for EEG recording channels selected for each subject (CP5 or C3). We chose these channels because they were over the sensorimotor area contralateral to the movement. The additional topographic plots were constructed with the EEGLab toolbox. The topographical maps allowed us to verify the energy distribution for all channels on the whole scalp at one specific time-point (under the two conditions). We chose the time-point from the individual subject's scalogram and it differed for each subject. Because movement preparation and execution produce ERD over the sensorimotor area at 10 and 20 Hz (Leocani et al. 1997), the frequency bands chosen for these maps were the upper alpha (10–12 Hz) and beta (13–30 Hz) for the two conditions. We also computed the grand-average scalogram and the grand mean topographic maps for the ten subjects whose data were analyzed.

We computed a two-ways ANOVA in Matlab within subjects and across subjects for alpha and beta bands both in the contralateral and ipsilateral hemisphere. The two factors are the condition (rest: 0–2610 ms versus active: 2610–5220 ms) and the subject (ten subjects for the contralateral hemisphere and three for the ipsilateral one). The electrodes providing informative data over the region of

activation in the contralateral motor area were CP5 or C3 and T4 in the ipsilateral side. For the statistical test a P value of <0.05 was considered significant.

In the wavelet results we have all values processed of ten subjects in ipsilateral side. Using EEG-fMRI analysis, described in the next paragraph "Combining EEG-fMRI signals", we had an activation of the ipsilateral sensory motor area (SM1) only in three subjects. We did not perform the statistical comparison between the ipsilateral and contralateral hemisphere because of the low number of fMRI activations in ipsilateral side.

fMRI Data Acquisition and Analysis

MRI data were acquired on a 3T MR scanner (MAGNETOM Allegra, Siemens, Erlangen, Germany) equipped with echo planar imaging (EPI) capability, a standard transient/receive head coil and foam cushions to minimize head movement. For each subject a T1-weighted anatomical scan was acquired (160 slices, repetition time (TR) = 2300 ms, time echo (TE) = 3 ms; scanning matrix 256 × 256, field of view (FOV) = 192 × 192; slice thickness of 1 mm; sagittal slice orientation). Functional images were acquired with a T2-weighted EPI sequence (36 slices, TR = 2600 ms, TE = 30 ms, 64 × 64 matrix, FOV = 192 × 192, slice thickness of 3 mm; voxel size = 3 × 3 × 3 mm, axial slice orientation). In the protocol, 100 volumes were acquired, alternating five activation and five control cycles (rest), resulting in a 5 min EPI recording. At the onset of each fMRI acquisition, the scanner emitted a trigger signal that was recorded by the EEG system and used as a volume marker.

The functional data were analyzed using BrainVoyager (QX 1.9, Brain Innovation, Maastricht, The Netherlands) running in windows VISTA environment. Preprocessing of functional MRI included three-dimensional motion correction, slice scan time correction (linear interpolation), linear trend removal by temporal high pass filtering (three cycles in time course) and transformation into Talairach coordinate space (Talairach and Tournoux 1998). Neither spatial nor temporal smoothing was used. In each subject, activated voxels were identified with a single-subject general linear model (GLM) approach for time series data (Friston et al. 1995). To account for the hemodynamic delay, the boxcar waveform representing the rest and task conditions was convolved with an empirical hemodynamic response function (HRF) (Friston et al. 1998). Brain activation was detected by comparing the signal intensity of task performance images (ON) with that of resting images (OFF) based on the changes in local BOLD signals. Images acquired during the ON condition were compared with images acquired from the same location during the OFF condition on a pixel-to-pixel basis with Student t-test. Z-score maps representing brain activation were generated. The results were displayed on parametric statistical maps in which the pixel Z value is expressed on a colorimetric scale. Individual statistical maps were thresholded at $P < 0.05$ (corrected for multiple comparisons: Bonferroni). The statistical functional maps (Z maps) were then superimposed on the respective structural scans to localize significantly activated areas.

In addition to individual subject analysis, a fixed-effect analysis (ten subjects) was used to calculate a GLM for the entire group of subjects. Group activation maps were thresholded at $P < 0.05$ (Bonferroni-corrected) and were superimposed on the (Talairach-transformed) structural scan for a representative subject.

Combining EEG-fMRI Signals

A time–frequency analysis of power was applied on the time series of the selected channel (Cp5 or C3). For the selected channel the time course of one frequency bin was used to form a regressor. This was done by selecting from the frequency bins, centered around 8 and 30 Hz, the one with the maximal power (alpha rhythm). The maximum was based on the average power in these frequency bins over the total recording session. The entire time series for the selected frequency bin (f_0) was extracted to form the basis for the regressor.

For correlation with fMRI data, the regressor $E(t,f_0)$ was convolved with the canonical two gamma HRF provided by Brain Voyager and were down-sampled to the temporal resolution of the fMRI data (TR = 2.61 s). This signal was used as a predictors for the BOLD signal in fMRI analysis:

$$x(t) = E(t,f_0) \otimes HRF(t) = \int_0^\infty HRF(\tau)p(t-\tau)\,d\tau \qquad (4)$$

where $\otimes$ denotes the convolution operation (Fig. 1b).

As single subject regressor we used the waveforms represented by wavelet energy fluctuations along the movement protocol and subsequently the regressor can be used to predict the BOLD response that have been acquired currently from the same subject (Debener et al. 2006). Single subject activation maps were calculated by using the voxel-wise student's t-test to identify activated voxels corrected P-value ≤ 0.05. In addition a fixed-effect analysis was used to calculate GLM for the entire group of subjects. Group activation maps were thresholded at $P < 0.05$ and were superimposed on the (Talairach-transformed) structural scan for a representative subject.

Results

fMRI Results

The distribution of BOLD activations in fMRI recording during hand movement were similar to that described in the literature. fMRI images showed significant BOLD activation ($P < 0.05$) in the supplementary motor area (SMA), and contralateral and ipsilateral SM1. These activations were statistically consistent ($P < 0.05$) across all the subjects.

In the single subject analysis activation clusters in the contralateral SM1 were more consistent for all subjects. In subjects #1, 2, 3, 4, 5, 7, 8 and 9 our GLM analysis showed wide activation in SMA. In subjects #1, 3, 5, 7 and 9 the statistical t-map showed a significant activation clusters also in ipsilateral SM1. Subjects #6 and 10 had no activation in ipsilateral SM1 and in SMA (see fMRI maps, Figs. 2 and 3).

In the group analysis (fixed effect analysis), fMRI showed significant BOLD activation ($P < 0.05$) in SMA, and SM1 and also in ipsilateral cerebellum (Fig. 4).

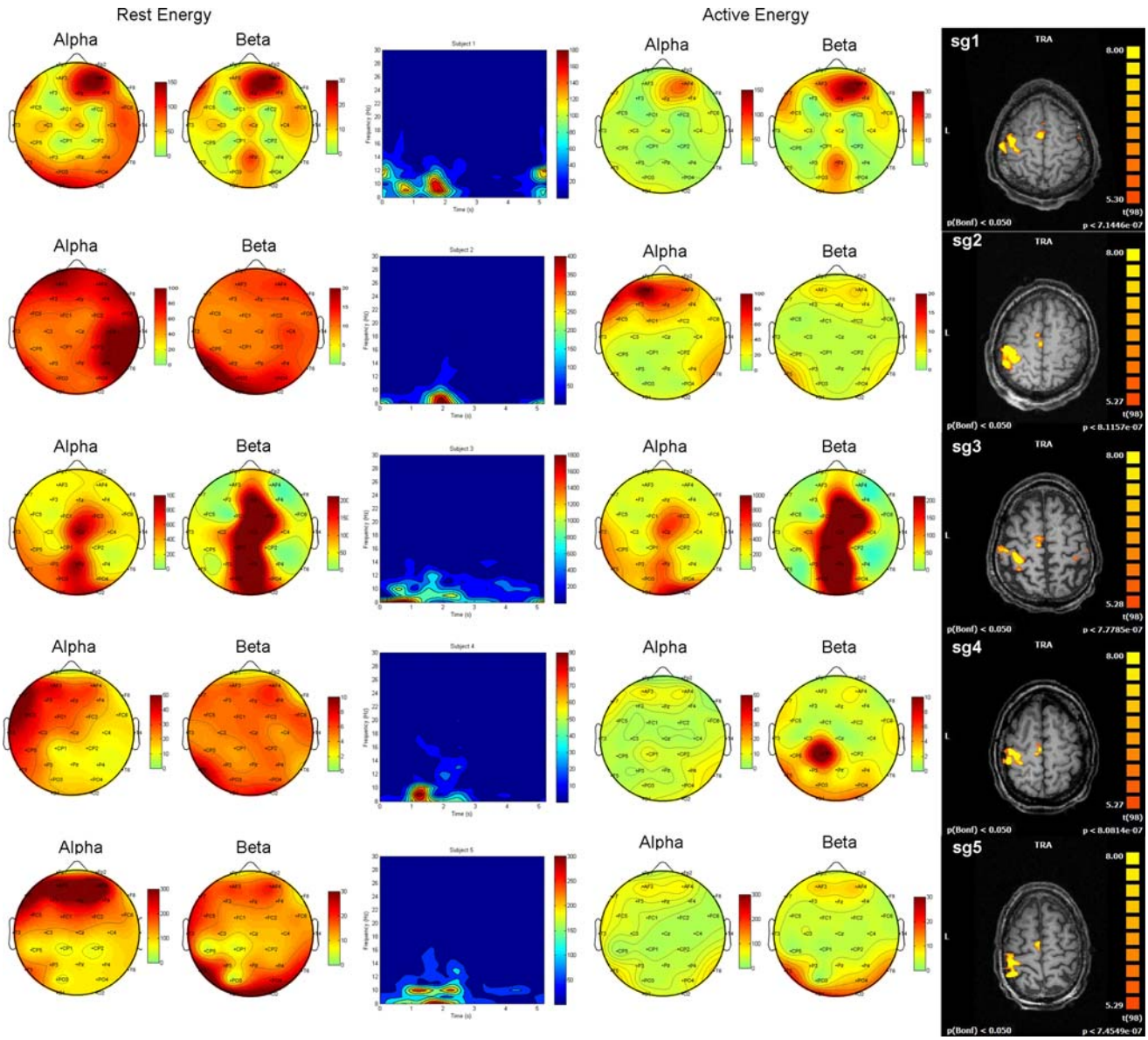

Fig. 2 Individual time–frequency plots for the 1–5 subjects; *blue* areas indicate low power values whereas *red* areas show high power, and their alpha (10–12 Hz) and beta (12–30 Hz) topographies obtained under the two experimental conditions: at rest and during active movement. Units are μV^2. On the *right* side the transaxial images show activation of the sensorimotor area (SM1) in the *left* hemisphere for each subject. The *color* bar shows the *Z* score scale

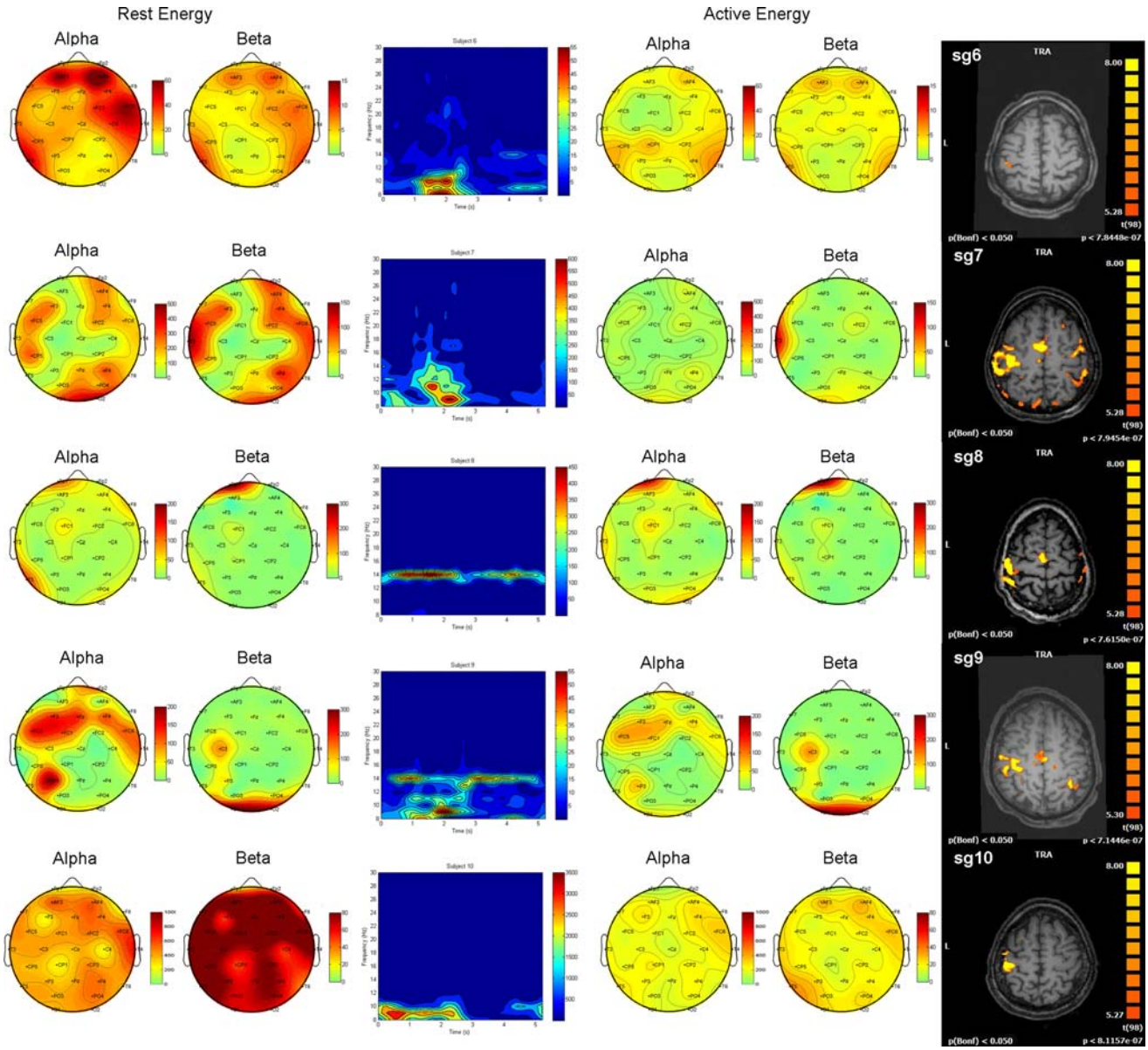

Fig. 3 Individual time–frequency plots for the 6–10 subjects; *blue* areas indicate low power values whereas *red* areas show high power, and their *alpha* (10–12 Hz) and *beta* (12–30 Hz) topographies obtained under the two experimental conditions: at rest and during active movement. Units are μV^2. The transaxial images on the right show activation of the sensorimotor area (SMI) in the *left* hemisphere for each subject. The *color* bar shows the Z score scale

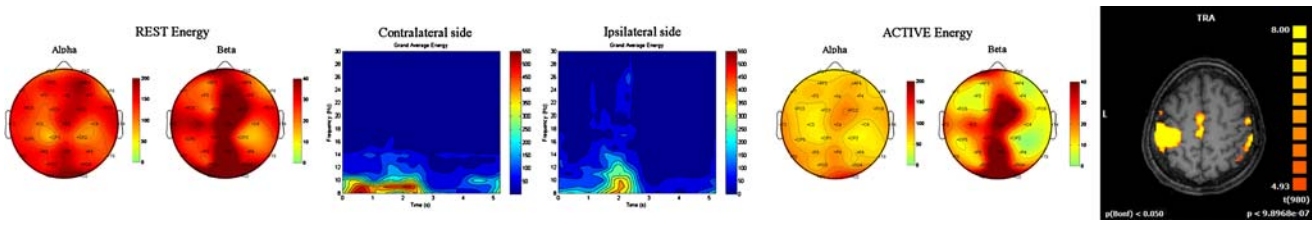

Fig. 4 Grand-averaged time–frequency energy plot for the ten subjects recorded from EEG electrodes over the contralateral sensorimotor cortex, CP5 or C3 (*left* wavelet image) and over the ipsilateral sensorimotor cortex, T4 (*right* wavelet image) in the rest condition (from 0 to 2610 ms) and during active movement (from 2610 to 5220 ms). On the *left* side of the panel, *alpha* (10–12 Hz) and *beta* (12–30 Hz) topographies from the rest condition (t = 1300 ms) and on *right* side from the active condition (3900 ms). Units are μV^2

EEG Results

EEG results generally agreed with the pattern of BOLD activation in the contralateral and ipsilateral motor areas as reported in the previous study (Formaggio et al. 2008b). The individual EEG data showed that the motor task invariably activated the contralateral central-temporal electrodes over the SM1. The scalograms show a common trend, although temporal dynamics differed, and energy values, especially those in the alpha range, changed rapidly from rest to the active condition (Figs. 2 and 3). Changes in time–frequency energy from rest to active condition in the alpha (10–12 Hz) and beta (13–30 Hz) frequency bands were prominent over the central parietal and central temporal areas contralateral to the movement (see the topographical maps, Figs. 2 and 3). Alpha maps showed a decrease in energy distribution from rest to the active condition located especially in the electrodes over the sensorimotor area contralateral to the movement.

In beta maps the effect was less perceptible over the electrodes of interest whereas it was topographically more restricted to temporal and posterior areas; except for subjects 2, 7, 8 and 10 in whom there was a significant difference between conditions in CP5 and C3. Despite the technical problems related to filtering and MRI artifacts, we observed that in all subjects central temporal electrodes were especially sensitive to the EEG changes and were close to the activated cortical areas corresponding to Brodmann areas 4 and 3, 1 and 2 of the hand representation over the cortex.

The most clearly visible feature in the contralateral grand-averaged scalogram was that alpha and beta energy decreased from rest to active condition (0–2610 vs. 2610–5220 ms) (Fig. 4). Associated with the hand movement there is an increase of energy over the contralateral electrodes (CP5 and C3 time of rest block), while in $t = 3900$ ms (half time of active block) the energy decreased significantly in alpha band especially over contralateral and ipsilateral electrodes as represented in the topographical maps.

In the contralateral hemisphere the alpha and beta energy for CP5 or C3 differed significantly both across subjects (alpha: $F = 20.01$, $df = 9$, $P < 0.05$; beta: $F = 7.69$, $df = 9$, $P < 0.05$) and within subjects (alpha: $F = 8.37$, $df = 1$, $P < 0.05$; beta: $F = 12.11$, $df = 1$, $P < 0.05$).

In the ipsilateral hemisphere the alpha energy for T4 differed significantly in alpha and beta band (Across subjects. Alpha: $F = 5.95$, $df = 2$, $P < 0.05$; Beta: $F = 32.56$, $df = 2$, $P < 0.05$; Within subjects. Alpha: $F = 14.66$, $df = 1$, $P < 0.05$; Beta: $F = 26.2$, $df = 1$, $P < 0.05$).

As shown in the statistical results during the movement we obtained an asymmetry in the modulation of EEG oscillations with an energy decrease for the active versus the rest condition, mostly on the left hemisphere contralateral to the finger abduction. This asymmetry is only a trend because it was not possible to compare contralateral vs. ipsilateral side using a statistical analysis due to the low number of subjects (3) which activated ipsilateral SM1 in EEG-fMRI analysis.

EEG fMRI Results

Alpha rhythm was chosen since it was most intensely modulated by motor task and since it was identified over both hemispheres. As expected, alpha rhythm was suppressed during hand movement and reappeared during rest; the power of this rhythm is inversely correlated to the motor task. As a consequence, voxels that are activated during motor task will tend to be deactivated during periods of desynchronization. The negative correlations between alpha rhythm and BOLD signal are shown in Fig. 5 with the respective wavelet time course. Our fMRI maps based on alpha energy regressor are very similar to the maps obtained with the previous fMRI block analysis.

Confirming earlier findings during fMRI block analysis, eight subjects of ten showed a negative correlation between the BOLD signal and the wavelet energy in motor areas. In subjects #1, 2, 3, 4 and 7 our GLM analysis showed activation in SMA. In subjects #2, 5 and 7 the statistical z-map showed a significant activation clusters also in ipsilateral SM1. Subjects #6 and 10 had no activation in ipsilateral SM1 and in SMA. Region of interest's number of voxels in each subject are reported in Table 1.

In the group analysis (fixed effect analysis), fMRI showed significant BOLD activation ($P < 0.05$) in SMA, and contralateral SM1 and also in ipsilateral cerebellum (Fig. 5).

Discussion

Using combined EEG-fMRI we obtained useful new information on the temporal and topographical changes in brain oscillatory activity in the alpha and beta frequency bands during voluntary movement. We also extended current knowledge on the sites of BOLD activity as the possible sources generating these rhythms. While healthy subjects did the motor task inside the scanner, EEG recordings showed a movement-related alpha and beta rhythm desynchronization over the bilateral sensorimotor area predominantly on the side contralateral to the movement. Despite the technical problems related to filtering and MRI artifacts we were able to detect brain oscillatory changes during hand movements and to map this activity.

In this study, the EEG-fMRI method based on CMT we used for data analysis provided excellent temporal

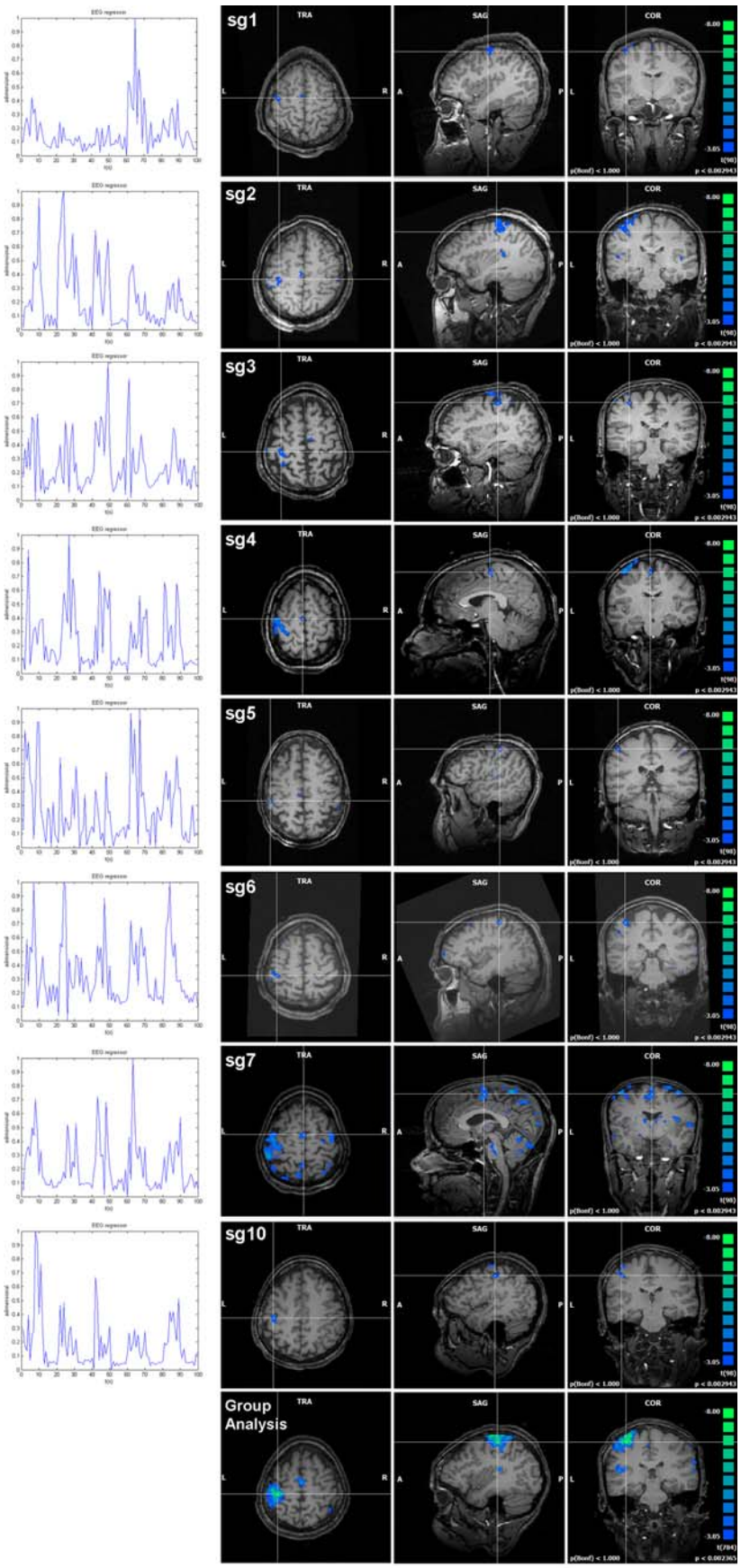

Fig. 5 Single subject (eight of ten subjects, 1, 2, 3, 4, 5, 6, 7, 10) and group analysis fMRI-EEG activations overlaid on 3D anatomical images in the *Talairach* space. The *colorbar* on the *right* indicates the statistical Z scores. The wavelet time course, on the *left*, was strongly anti-correlated with the motor areas

Table 1 Region of interest's number of voxels in each subject in EEG-fMRI analysis. Ipsilateral (i) and controlateral (c) refer to the hemispheric side with respect to the hand moved

Subject	Nr of voxels		
	SMIc	SMIi	SMA
1	555	0	179
2	4591	38	152
3	957	0	144
4	7072	0	367
5	195	52	17
6	553	0	0
7	6522	895	1251
8	0	0	0
9	0	0	0
10	735	0	0

localization, far more accurate than that obtained by analyzing frequency alone. A time–frequency representation based on CMT of EEG data was used to identify stimulus-induced amplitude modulations in oscillatory activities.

When fMRI showed BOLD activation in sensorimotor areas energy in the alpha and beta bands of the EEG signal decreased significantly. Despite using a 3T MR scanner, which produces a large BCG, we could easily detect the temporal energy changes in oscillatory activity during movement. These findings are supported by studies showing that BOLD activity correlates with activity in the alpha and beta EEG frequency bands (Babiloni et al. 2005; Brookes et al. 2005; Formaggio et al. 2008b; Singh et al. 2002). A study combining fMRI and EEG (Parkes et al. 2006) studying the time course of this oscillatory activity during finger abduction reported that the BOLD activity in the postcentral sulcus is related to post-movement beta rebound (PMBR). Unlike Parkes et al., in this study, EEG recordings showed reliable, consistent alpha and beta suppression during the finger movements in the fMRI recording. As documented by the topographical maps, we noted in most subjects a reliable suppression of both rhythms correlating with the BOLD activation.

The wavelet-based analysis we used in this EEG-fMRI study had several other advantages. It clearly showed the pattern of energy development while two fMRI volumes (during the two condition) were acquired and distinguished the temporal changes over a motor electrode on the contralateral and ipsilateral sides. A decrease of wavelet energy could be the result of the involvement of a larger neural network or cell assemblies in information processing. These findings could suggest that activity in primary sensorimotor areas increases when the motor task begins and decreases when it ends. The increase in BOLD signal with a decrease in EEG alpha and beta energy mainly in the contralateral motor areas suggests that the mean rate of synaptic activity measured at baseline increased in the local neuronal population during the movement. Using a multi-trial wavelet analysis of EEG, we previously study the temporally components related to the finger movement, then we use the information derived from EEG recordings to inform the analysis of fMRI data recorded for the same motor task. The localisation of the alpha band generators using EEG/fMRI did not require assumptions on the number of dipoles, their geometry and spatio-temporal smoothness. So using this technique we were able to identify the cortical regions that correlated with the EEG temporally and in doing so we demonstrated the two different regressors (block protocol and EEG regressor) captured activations from the same number of regions in somatosensory cortex.

The correlation between the BOLD signal associated with the EEG regressor provides further evidence that sensory motor region is a source of the EEG.

Topographic maps are probably sensitive to MRI artifacts, despite the filtering different MRI effects may affect the EEG maps. Gradient effects can induce a diffuse EEG signal increase that may mask slight EEG changes during a motor task (Menon and Crottaz-Herbette 2005). Hand movements themselves could induce slow activity over the scalp electrodes that is more evident under a gradient effect. Generally, because the BCG artifact becomes larger from occipital to the frontal sites (Allen et al. 1998) it could have affected responses in frontal regions in most of our subjects. After we subtracted MRI artifacts the brain oscillatory activity nevertheless persisted during both experimental conditions, rest and active movement.

Overall our findings in this study and our previous study (Formaggio et al. 2008b) suggest that investigating the correlation between brain oscillatory activities and BOLD activity recorded during fMRI recording is a suitable method for studying movement in healthy subjects and in patients. Using combined EEG-fMRI in healthy subjects is an important research tool that provides new information on the neural activity underlying the hemodynamic changes (BOLD signals). We reported the results of EEG/fMRI combination for the evaluation of the underlying neural correlates in terms of fine functional cortical topography (fMRI) and fine time course of the activation (EEG) and related modulation of alpha rhythms.

These findings must nevertheless be interpreted carefully because the fMRI signal is an indirect measure of synaptic activities or action potentials from cortical neurons. fMRI signals arise from the so-called BOLD effect (De Yoe et al. 1994; Kim and Ugurbil 1997; Ogawa et al. 1998), characterized by an excellent spatial resolution (1–2 mm) but limited temporal resolution (TR timing correlated).

We conclude that wavelet energy reflects the degree of synchronization in brain rhythm generators and we

investigate brain oscillatory activity in time during fMRI recording. During EEG signal processing, quantifying wavelet energy—a measure indicating the degree of synchronization in brain rhythm generators—helps to clarify possible sources of movement-related brain activation. Using the time course of the oscillatory activity we provide information on the relationship between EEG recordings and the fMRI results. This relationship is quantitatively described by fMRI activation maps, obtained using a regression analysis. This new approach enables the study of dynamic properties of motor processing relating to hemodynamic response.

In healthy subjects, fMRI topographic maps correlate closely with EEG energy findings. In the study of functional deficits in patients with motor disorders, the wavelet-based technique could help to analyze brain responses more reliably and may also tell us more about their dynamics.

References

Allen PJ, Polizzi G, Krakow K, Fish DR, Lemieux L (1998) Identification of EEG events in the MR scanner: the problem of pulse artifact and a method for its subtraction. Neuroimage 8(3):229–239

Babiloni F, Cincotti F, Babiloni C, Carducci F, Mattia DL, Astolfi L, Basilisco A, Rossini PM, Ding L, Ni Y, Cheng J, Christine K, Sweeney J, Heg B (2005) Estimation of the cortical functional connectivity with the multimodal integration of high-resolution EEG and fMRI data by directed transfer function. Neuroimage 24:118–131

Brookes MJ, Gibson AM, Hall SD, Furlong PL, Barnes GR, Hillebrand A, Singh KD, Holliday IE, Francis ST, Morris PG (2005) GLM-beamformer method demonstrates stationary field, alpha ERD and gamma ERS colocalisation with fMRI BOLD response in visual cortex. Neuroimage 26(1):302–308

De Yoe EA, Bandettini P, Neitz J, Miller D, Winans P (1994) Functional magnetic resonance imaging (FMRI) of the human brain. J Neurosci Methods 54:171–187

Debener S, Ullsperger M, Siegel M, Engel AK (2006) Single-trial EEG–fMRI reveals the dynamics of cognitive function. Trends Cogn Sci 10(12):558–563

Delorme A, Makeig S (2004) EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J Neurosci Methods 134:9–21

Erbil N, Ungan P (2007) Changes in the alpha and beta amplitudes of the central EEG during the onset, continuation, and offset of long-duration repetitive hand movements. Brain Res 1169:44–56

Formaggio E, Avesani M, Storti SF, Milanese F, Gasparini A, Acler M, Cerini R, Pozzi Mucelli R, Fiaschi A, Manganotti P (2008a) Effect of a static magnetic field (1.5T) on brain oscillatory activities in resting state condition. Neuroradiol J 21(5):629–635

Formaggio E, Storti SF, Avesani M, Cerini R, Milanese F, Gasparini A, Acler M, Pozzi Mucelli R, Fiaschi A, Manganotti P (2008b) EEG and fMRI coregistration to investigate the cortical oscillatory activities during finger movement. Brain Topogr 21(2):100–111

Friston KJ, Holmes AP, Worsely KJ, Poline JP, Frith CD, Frackowiak RSJ (1995) Statistical parametric maps in functional imaging: a general linear approach. Hum Brain Mapp 2:173–181

Friston KJ, Fletcher P, Josephs O, Holmes A, Rugg MD, Turner R (1998) Event-related fMRI: characterizing differential responses. Neuroimage 7(1):30–40

Gonçalves SI, de Munck JC, Pouwels PJW, Schoonhoven R, Kuijer JPA, Maurits NM, Hoogduin JM, Van Someren EJW, Heethaar RM, Lopes da Silva FH (2006) Correlating the alpha rhythm to BOLD using simultaneous EEG/fMRI: inter-subject variability. Neuroimage 30:203–213

Hari R, Salmelin R (1997) Human cortical oscillations: a neuromagnetic view through the skull. Trends Neurosci 20:44–49

Kim SG, Ugurbil K (1997) Functional magnetic resonance imaging of the human brain. J Neurosci Methods 74:229–243

Leocani L, Toro C, Manganotti P, Zhuang P, Hallett M (1997) Event-related coherence and event-related desynchronization/synchronization in the 10 Hz and 20 Hz EEG during self-paced movements. Electroencephalogr Clin Neurophysiol 104:199–206

Manganotti P, Gerloff C, Toro C, Katsuta H, Sadato N, Zhuang P, Leocani L, Hallett M (1998) Task-related coherence and task-related spectral power changes during sequential finger movements. Electroencephalogr Clin Neurophysiol 109(1):50–62

Manganotti P, Formaggio E, Milanese F, Gasparini A, Storti SF, Cerini R, Bongiovanni LG, Pozzi Mucelli R, Baraldo A, Fiaschi A, Avesani M (2008) Continuous EEG-fMRI study in patients with partial epilepsy and focal interictal slow-wave discharges on EEG. Magn Reson Imaging 26(8):1089–1100

Menon V, Crottaz-Herbette S (2005) Combined EEG and fMRI studies of human brain function. Int Rev Neurobiol 66:291–321 Review

Muthuswamy J, Thakor NV (1998) Spectral analysis methods for neurological signals. J Neurosci Methods 83(1):1–14

Neuper C, Pfurtscheller G (1996) Post-movement synchronization of beta rhythms in the EEG over the cortical foot area in man. Neurosci Lett 216:17–20

Ogawa S, Menon RS, Kim SG, Ugurbil K (1998) On the characteristics of functional magnetic resonance imaging of the brain. Annu Rev Biophys Biomol Struct 27:447–474

Oldfield RC (1971) The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9(1):97–113

Parkes LM, Bastiaansen CM, Norris DG (2006) Combining EEG and fMRI to investigate the post-movement beta rebound. Neuroimage 29:685–696

Pfurtscheller G (1992) Event-related synchronization (ERS): an electrophysiological correlate of cortical areas at rest. Electroencephalogr Clin Neurophysiol 83:62–69

Pfurtscheller G, Aranibar A (1979) Evaluation of event-related desynchronization (ERD) preceding and following voluntary self-paced movement. Electroencephalogr Clin Neurophysiol 46:138–146

Rappelsberger P, Pfurtscheller G, Filz O (1994) Calculation of event-related coherence–a new method to study short-lasting coupling between brain areas. Brain Topogr 7:121–127

Ritter P, Moosmann M, Villringer A (2009) Rolandic alpha and beta EEG rhythms' strengths are inversely related to fMRI-BOLD signal in primary somatosensory and motor cortex. Hum Brain Mapp 30:1168–1187

Sadato N, Campbell G, Ibanez V, Deiber M, Hallett M (1996) Complexity affects regional cerebral blood flow change during sequential finger movements. J Neurosci 16(8):2691–2700

Salmelin R, Hari R (1994) Spatiotemporal characteristics of sensorimotor neuromagnetic rhythms related to thumb movement. Neuroscience 60:537–550

Singer P (1999) Uncertainty inequalities for the continuous wavelet transform. IEEE Trans Inf Theory 45(3):1039–1042

Singh KD, Barnes GR, Hillebrand A, Forde EME, Williams AL (2002) Task-related changes in cortical synchronization are

spatially coincident with the hemodynamic response. Neuroimage 16:103–114

Stancak A Jr, Feige B, Lucking CH, Kristeva-Feige R (2000) Oscillatory cortical activity and movement-related potentials in proximal and distal movements. Clin Neurophysiol 111:636–650

Steriade M, Amzica F (1996) Intracortical and corticothalamic coherency of fast spontaneous oscillations. Proc Natl Acad Sci USA 93:2533–2538

Talairach J, Tournoux P (1998) Co-planar stereotaxic atlas of the human brain. Thieme, New York

Tallon-Baudry C, Bertrand O, Delpuech C, Pernier J (1997) Oscillatory gammaband (30–70 Hz) activity induced by a visual search task in humans. J Neurosci 17(2):722–734

van Duinen H, Zijdewind I, Hoogduin H, Maurits N (2005) Surface EMG measurements during fMRI at 3T: accurate EMG recordings after artifact correction. NeuroImage 27(1):240–246