Technical Note

Simultaneous recording of MEG, EEG and intracerebral EEG during visual stimulation: From feasibility to single-trial analysis

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Abstract

Electroencephalography (EEG), magnetoencephalography (MEG), and intracerebral stereotaxic EEG (SEEG) are the three neurophysiological recording techniques, which are thought to capture the same type of brain activity. Still, the relationships between non-invasive (EEG, MEG) and invasive (SEEG) signals remain to be further investigated. In early attempts at comparing SEEG with either EEG or MEG, the recordings were performed separately for each modality. However, such an approach presents substantial limitations in terms of signal analysis. The goal of this technical note is to investigate the feasibility of simultaneously recording these three signal modalities (EEG, MEG and SEEG), and to provide strategies for analyzing this new kind of data. Intracerebral electrodes were implanted in a patient with intractable epilepsy for presurgical evaluation purposes. This patient was presented with a visual stimulation paradigm while the three types of signals were simultaneously recorded. The analysis started with a characterization of the MEG artifact caused by the SEEG equipment. Next, the average evoked activities were computed at the sensor level, and cortical source activations were estimated for both the EEG and MEG recordings; these were shown to be compatible with the spatiotemporal dynamics of the SEEG signals. In the average time–frequency domain, concordant patterns between the MEG/EEG and SEEG recordings were found below the 40 Hz level. Finally, a fine-grained coupling between the amplitudes of the three recording modalities was detected in the time domain, at the level of single evoked responses. Importantly, these correlations have shown a high level of spatial and temporal specificity. These findings provide a case for the ability of trimodal recordings (EEG, MEG, and SEEG) to reach a greater level of specificity in the investigation of brain signals and functions.

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activity is seen on the two recordings. Simultaneous recording would allow the comparison of average responses from the very same neural events across the different modalities. Most importantly, it is the only method that allows the combined analysis of signal fluctuations evoked by individual stimuli, referred to as “single trials”. This is a prerequisite for an optimal use of multimodal recording, where fine-grained co-variation across modalities can be exploited as a new and major source of information on the links between modalities (Bénar et al., 2007).

A few recent studies have reported simultaneous recordings of MEG-SEEG or EEG-SEEG in epilepsy (Kakiskila et al., 2012; Pacia and Ebersole, 1997; Santìuste et al., 2008) or in cognition (Dalal et al., 2009), but neither the quality of the non-invasive signals nor the possibility of recovering evoked activity at the single trial level has been addressed. Moreover, the complementary information provided by MEG and EEG (Dehghani et al., 2010) has not been considered in these studies.

The enterprise of combining MEG, EEG and SEEG recordings within a single “trimodal” session is not without technical challenges. Besides physical constraints, such as fitting the bulky electrode connections within the MEG dewar, the recording session requires a tight organization in order to ensure the smoothness of the operations and to reduce the amount of time during which the patient is in the MEG laboratory (and therefore not in the monitoring unit). Despite these precautions, the quality of non-invasive recordings can be affected by the presence of the SEEG equipment. This can in turn compromise single-trial analyses, which do not compensate for low signal-to-noise ratio through averaging.

The goal of this technical note is to report on the feasibility of simultaneously recording three signal modalities (EEG, MEG and SEEG), and to provide strategies for analyzing this kind of data. To our knowledge, this is the first report of such a trimodal recording. The evidence comes from a patient case study involving a visual stimulation paradigm.

Material and Methods

Patient

The recordings were performed on a 19-year-old female patient with intractable epilepsy undergoing an intracerebral EEG pre-surgery evaluation. The locations of implantation were strictly imposed by clinical indications. The trimodal recording session was performed on the last (10th) day of clinical evaluation. Several weeks after SEEG de-implantation, the patient was re-tested on the same task in a separate session during which only MEG signals were recorded. This was intended to evaluate the impact of the SEEG equipment on the spatial distributions (topographies) and on the time courses of the evoked field. We compared the first session (with SEEG) and the second session (without SEEG). The patient gave a written consent for both sessions. This research has been approved by the relevant Institutional Review Board (i.e. the “Comité de Protection des Personnes, CPP”).

Stimulation paradigm

The paradigm consisted in the presentation of a full screen reversing checkerboard pattern during 5 min. The checkerboard was composed of 8 by 8 black and white squares covering the whole screen with a small central yellow fixation point. The patient was passively watching the screen in a supine position at a distance such that every square unit represented an angle of 1.5°. The pattern reversed every second such that a total of 300 checkerboard reversals were presented. A photocell was flashed at each reversal to allow precise timing. This stimulation experiment was developed using Presentation® software (www.neurobs.com).

Recording set-up

The data were acquired at La Timone hospital in Marseille on a 4D Neuroimaging MEG/EEG system at a sampling rate of 2035 Hz. The recording included 20 s of background activity followed by 5 min of stimulation and further background activity to reach a total duration of 10 min. A total of 248 MEG magnetometers were recorded with an online correction based on reference channels. The electrocardiographic activity was recorded on a bipolar EEG channel. Scalp EEG was recorded from twenty-three GRASS silver-chloride EEG electrodes positioned on a 10–20 montage slightly modified to avoid any overlap with the implantation sites. A right mastoid reference was used for both EEG and SEEG. Intracerebral EEG electrodes were implanted stereotactically orthogonally to the midline vertical plane. The location of the electrodes was bilateral with predominance in the left hemisphere (11/13 left-sided electrodes) exploring the temporal-parieto-occipital junction. The electrodes had a diameter of 0.8 mm, and contained 10 to 15 recording sites (also referred to as “contacts”), each 2 mm long and separated from each other by 1.5 mm (Alcis, Béasançon, France). This resulted in a total number of 190 contacts. The electrodes were labeled (from the most posterior to the most frontal); CL, CU, CA, P1, P2, P3, P4 (right), OT, OT, GC, PT, GPH, B, TB and contact numbers start from the most mesial one to the most lateral one (for an overview of the implantation sites see Figs. 1c and 4). The recording equipment used in the present study constrained the number of recorded SEEG contacts to 72. The neurolgists selected contacts based on the patient epileptic activity and the planned functional mapping of the primary visual areas.

Anatomical co-registration

Co-registration of the EEG electrodes was performed manually based on pictures of the patient taken during the placement of these electrodes. Anatomical MRI pre-implantation, MRI intra-implantation and CT scan intra-implantation were all co-registered using Medinria software (http://www-sop.inria.fr/asclepios/software/MediINRIA/index.php). Each electrode contact was identified on the CT scan performed during the implantation and all electrodes were reconstructed in 3D using Brainvisa (http://brainvisa.info) combined with our own code in MATLAB 2012a (Mathworks, Naticks, MA). The co-registration between the MRI and MEG coordinate systems was based on three fiducials: nasion, left and right pre-auricular points for the trimodal recording and on the head shape for the separate session. The quality of the co-registration was checked using the digitization of the facial mask.

Spectral analysis and signal pre-processing

Based on the observation of the continuous signals, we identified two groups of 8 MEG sensors each near the SEEG implantation site that presented different types of artifacts: low and high-frequency noise. Another set of 8 sensors on the contralateral side was taken as a reference (see Fig. 1). In order to characterize the MEG artifacts, the power spectral density of each of the three groups (averaged over sensors) was computed over 10 s of background data (no stimulation) using Welch’s method (Welch, 1967).

The continuous data of all channels was band pass filtered with a fourth order forward-backward Butterworth filter (Anywave software, MEG laboratory, INS, http://meg.univ-amu.fr.). We used a 1–40 Hz bandpass for time domain analysis and an 1–120 Hz bandpass for time-frequency analysis. The scalp EEG data was additionally filtered with a notch filter between 45 Hz and 55 Hz in order to remove the 50 Hz contamination. Artifacts and channel rejection, segmentation into epochs, averages and source localizations were performed with Brainstorm Matlab toolbox (Tadel et al., 2011). For visualizing the averaged evoked activity we used the 40 Hz low pass filter between 45 Hz and 55 Hz in order to remove the 50 Hz contamination. Artifacts and channel rejection, segmentation into epochs, averages and source localizations were performed with Brainstorm Matlab toolbox (Tadel et al., 2011). For visualizing the averaged evoked activity we used the 40 Hz low pass filter implemented in Brainstorm.

The continuous data were inspected in order to identify artifacts, either physiological (blinks, epileptiform discharges) or instrumental (bad or noisy sensors). Blinks and epileptiform discharges were detected manually on continuous data (respectively on MEG and SEEG signals). Epochs free of artifact were extracted around the checkerboard reversal, from 200 ms to 500 ms for the time domain analysis and
from −500 ms to 800 ms for the time–frequency analysis (in order to take into account the edge effects).

Time domain averages at sensor level

Signal averages were computed separately for each modality of the trimodal session as well as for the MEG data of the separate session. A baseline correction was performed on a pre-stimulus window [−200 ms; 0 ms].

To quantify the overall similarity of the averaged signals across the three modalities, we computed the global field power (GFP) (Lehmann and Skrandies, 1980) of the average signal of each modality separately and calculated the Pearson correlations of their time courses. Since the artifact rejection procedure did not leave the same number of trials in the two sessions, we randomly selected from the largest dataset the same number of trials as in the smallest dataset to compute the GFP and the correlation. We repeated this procedure 500 times and, after observing that the distribution of the correlation coefficient was Gaussian, reported the average of their values.

Signal to noise ratio

We quantified the MEG signal quality degradation introduced by the EEG/SEEG equipment during the trimodal session by computing the signal to noise ratio (SNR) of the evoked responses separately for each session. For MEG sensors, two SNR measures were computed with our own code in MATLAB. One SNR aimed at evaluating the signal quality at the average level (SNRaverage, Eq. (1)), and another one at the single trial level (SNRtrials Eq. (2)).

\[
\text{SNR}_{\text{average}} = 20 \log_{10} \left( \frac{A_{\text{max}}}{\sigma_{\text{average}}} \right)
\]

(1)

\[
\text{SNR}_{\text{trials}} = 20 \log_{10} \left( \frac{A_{\text{max}}}{\sigma_{\text{trials}}} \right)
\]

(2)

with \(A_{\text{max}}\) the maximum amplitude of the averaged evoked response between 50 ms to 100 ms after stimulation, and \(\sigma\) the estimated standard deviation, computed either on the baseline of the averaged signal (\(\sigma_{\text{average}}\)) or across trials (\(\sigma_{\text{trials}}\)). The values obtained at all MEG sensors were imported into Brainstorm in order to visualize them on a topographic view (interpolated with 10 contour lines) (Fig. 2).

Source localization

The 3D reconstruction of the patient’s cortex was performed with BrainVisa (Rivière et al., 2003) and down-sampled to 15,000 vertices. The Minimum Norm Estimate source localization method was used (Hämäläinen and Ilmoniemi, 1994), for which the regularized linear inverse operator is given by

\[
M = R'G'\left( G'R' + \lambda^2C \right)^{-1}
\]

(3)
where \( G \) is the lead field matrix, \( R \) is the source covariance matrix, \( \lambda \) is the regularization parameter set to \( \lambda^2 = \text{SNR}-1 \) with signal to noise ratio defined as the ratio of variances computed on the whitened noise, and \( C \) is the noise covariance matrix. The MEG lead fields were computed using an overlapping-sphere head model (Huang et al., 1999) based on the patient's individual anatomy, whereas the EEG lead fields were computed using a Boundary Element Model (Gramfort et al., 2010). The noise covariance \( C \) was computed from 30 s of recording post stimulation with the patient inside of the MEG array with no stimulation. It was regularized with a factor of 0.1. The SNR parameter was set to 2 for the MEG during simultaneous recordings and to 3 for the MEG only. No constraint on the orientation of the dipoles was used. We corrected the bias of the method towards superficial currents by adjusting the matrix \( R \), performing a depth weighting (order 0.5, max amount 10). Further details are available at http://martinos.org/mne/manual/mne.html.

**Time–frequency analysis**

The EEGLAB Matlab toolbox (Delorme and Makeig, 2004) was used to compute the time–frequency analysis of the three modalities (bipolar SEEG, EEG and MEG). We used a seven cycle Morlet wavelet to compute the event related spectral perturbation (ERSP) (Makeig, 1993). The gain model described by Delormé and Makeig (2004) was used to perform the baseline correction over the pre-stimulus period (–500 ms to 0). Maps were thresholded using False Discovery Rate (FDR) correction (\( q < 0.05 \)) (Genovese et al., 2002).

In the three modalities, the time–frequency planes of the posterior sensors were reviewed visually in order to identify representative patterns. For each pattern we selected the sensors showing a local peak, either positive or negative.

**Single trial correlation across modalities**

At each time point, we computed a robust linear regression (Holland and Welsch, 1977) across trials between SEEG contacts and non-invasive data. The details of this procedure are as follows.

For each time \( t \in [-200, 500 \text{ ms}] \) and each SEEG contact \( x \) we estimated \( \beta_1 \) in

\[
\text{data}_{\text{depth}}(k, t, x) = \beta_1(t, x) \times \text{data}_{\text{surface}}(k, t) + \beta_0(t, x) + \varepsilon
\]

using robust regression (Matlab function `robustfit`). With \( k = 1...\text{trials} \), data vectors \( \text{data}_{\text{depth}} \) and \( \text{data}_{\text{surface}} \) had previously been standardized by removing the mean and dividing by the standard deviation.

For each surface time series, we defined the inter-trial correlation index (\( \text{Itcor} \)) as being the \( t \)-test of significance at each time point \( t \) and each SEEG location \( x \):}

\[
\text{Itcor}(t, x) = |t_{\text{stat}}(t, x)| = \frac{\beta_1(t, x)}{\sigma_{\text{Itcor}}(t, x)}
\]

with \( \sigma \) estimated standard deviation.

The threshold of significance of the \( \text{Itcor} \) index was determined using the False Discovery Rate (Genovese et al., 2002) with a level of \( q = 0.05 \). This addresses the issue of multiple comparisons jointly in time (one test per time sample) and in space (one test per pair of surface and intracerebral contacts). Additionally, a threshold on the length of significant time windows was set to 10 ms in order to further reduce the number of false detections.

To avoid capturing spurious correlations driven by the use of a common reference between EEG and SEEG, we computed a bipolar montage on the SEEG signals. The bipolar montage construction consisted in subtracting all pairs of recorded and not rejected consecutive contacts within each electrode.

The \( \text{Itcor} \) was estimated over independent components extracted from ICA (Bell and Sejnowski, 1989) performed on the non-invasive signals, in order to increase the signal-to-noise ratio (critical for single trial analysis). The EEGLAB Matlab toolbox (Delorme and Makeig, 2004) was used to compute ICA separately on the MEG and EEG data. As a first step, we selected visually for each modality (EEG and MEG) the ICA component corresponding to the visual evoked response. This component was selected on the basis of its temporal mean timecourse and its

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topography across sensors. We confirmed the visual selection by performing a t-test for each component at each time point. This allows assessing whether the evoked response on a given component differed significantly from zero. In a second step, we ran the single trial correlation analysis on all ICA components as well as all sensors in an exploratory manner. There, the FDR correction accounted for multiple comparisons not only across time and SEEG contacts but also across sensors/ICA components.

The approach was used to perform the single-trial correlation analysis in the time–frequency domain. We computed the Morlet transform (see Time–frequency analysis section) for each trial and summed the activities for bands of interest: beta 12–30 Hz, gamma1 35–45 Hz, gamma2 60–90 Hz, and gamma3 90–110 Hz.

Results

Preprocessing and spectral characterization of the recordings

The artifact rejection left 242 trials spanning [−200 ms; +500 ms] for the first session and 161 trials of similar length for the simultaneous MEG session (without simultaneous SEEG nor EEG). One flat and two noisy MEG channels (3/248) were excluded from the analysis of both sessions. Five EEG (5/23) and five SEEG channels (5/72) were rejected from the trimodal analysis because they were either not showing any signal (5 EEG and 3 SEEG contacts) or were noisy (2 SEEG contacts).

We compared the MEG signals recorded during two sessions (with and without SEEG and EEG equipment). During trimodal recording, a left posterior group of sensors located above the patient’s shoulder showed a low frequency artifact (<1 Hz) directly observable on the raw data, presumably following the patient’s breathing rhythm. In contrast, a left central group of sensors, above the SEEG implantation site, showed a high frequency component (>15 Hz). The separate recording from the MEG-only session did not show such artifacts. The contralateral sensors to the implantation site showed similar amplitudes and spectra across sessions (Fig. 1).

Evaluation of the quality of MEG signals

The spatial pattern of the SNR values (Fig. 2) was rather symmetric for the separate session. In contrast, for the trimodal session we observed a decrease of SNR in the left posterior region presumably due to the presence of SEEG connectors. This effect was more prominent at the single trial level.

Still, the maximum values of the SNR on the right side were of the same order. The SNRaverage was 30.9 dB versus 28.9 dB respectively for trimodal and separate sessions. The SNRtrial was −2.4 dB versus 3 dB respectively for trimodal and separate sessions.

Concordance of time-domain average responses

We compared the responses evoked by the visual stimulus (a reversing checkerboard) in the three recording modalities. The average evoked responses of the three modalities showed main peaks at the same latency (80 ms), as presented on Fig. 3 (left panel). In addition, an early response was observed on MEG signals at 35 ms (both sessions). At the same latency, a peak of low amplitude (relative to the main peak) was also observed on the medial contacts of the posterior SEEG electrodes (GL′, FCA′, OT′) as indicated by a star on Fig. 3a, but no peak was observed on the EEG signals. The average evoked response obtained during the separate MEG-only session (Fig. 3d) showed a waveform and a spatial pattern similar to those obtained during the simultaneous recording.

The overall similarity of the signals across the three modalities was quantified as the temporal correlation of the global field power (GFP) of each signal averaged separately. We compensated for the different numbers of trials between the two MEG sessions as described in the Material and methods section. Within the simultaneous session, the correlation coefficient between SEEG and EEG was 0.95. It was 0.86 between SEEG and MEG, and 0.86 between MEG and EEG. The MEG signals of the separate session showed a correlation of 0.70 with the MEG signals (of the simultaneous session), 0.75 with the SEEG signals and 0.73 with EEG signals.

Concordance of reconstructed sources

To visualize the activity at the cortical level, we computed the source localization of the MEG and EEG averaged evoked responses. In Fig. 4 we present source activations at three latencies (35, 80, and 120 ms), along with the corresponding SEEG potentials. These latencies were chosen for being representative of the spatiotemporal dynamics of the evoked response.

SEEG activations were mainly observed on four occipito-temporal electrodes exploring the lingual gyrus (GL′ and FCA′), the cuneus (CU′) and the fusiform gyrus (OT′). The activations progressed within these electrodes towards the lateral occipital cortex. In EEG, the first latency revealed no substantial activation. At the later latencies (80 and 120 ms) a broad posterior temporo-parieto-occipital region was activated, as well as the left lateral occipital region. In MEG, the reconstructed activations from both sessions were similar for the three latencies. Firstly (35 ms), a small activation was observed in the medial part of left and right occipital poles. Then (80 ms), the activation spread through the bilateral ventral pathway and the first steps of the dorsal pathway in the lateral occipital cortex. Finally (120 ms), the polar activity disappeared while the lateral activity remained present.

Time–frequency analysis

The artifact rejection procedure left 217 trials for time–frequency analysis in the trimodal session and 140 in the separate session. The rejected channels were the same as in the time domain analysis.

The visual inspection of the time–frequency planes across all modalities (in both sessions) revealed four main patterns (Fig. 5). The first pattern was an increase of energy in the 20–40 Hz band before 100 ms that was visible both in MEG and SEEG. In EEG a similar pattern was observed at a slightly higher frequency (around 40 Hz). The second pattern was a decrease of energy around 20 Hz. This pattern was clearly visible in the SEEG signals and in the MEG signals of the separate session. It was present but less visible on the EEG and MEG sensors of the trimodal recording. The third pattern was a broadband increase of energy in the high gamma range (>50 Hz) clearly visible on SEEG contacts, but scarce and inconsistent for the non-invasive data. The fourth pattern was an increase of energy in the 20–40 Hz band at around 300 ms and was visible in the MEG and EEG signals of the trimodal session.

Correlations between modalities at the single-trial level

We performed the inter-trial correlation analysis (Itcor) on the selected ICA components. Within each modality, the component that was visually selected corresponded to the maximum t-value in the t-test analysis across trials for each time point and each component (IC #9 for EEG and IC #26 for MEG). The inter-trial correlation (Itcor) was computed between these two ICA components and each SEEG contact. The MEG ICA component showed a significant correlation with seven SEEG contacts from three bilateral posterior electrodes (GL′ to GL′3, CU′4, CU′6, OT′8, and OT′11) (q < 0.05 FDR corrected). Notably, the correlation occurred earlier (starting around 80 ms) for the most posterior contacts (on electrode GL′), and later (starting around 150 ms) for the most anterior contacts (on electrode OT′). This pattern was consistent with peak activity progression as seen on the source localization data. The EEG ICA component showed a significant correlation with two contacts from two SEEG electrodes (TB′2, Cu′4) (q < 0.05 FDR corrected). On all raster plots (Fig. 6), the column corresponding to the main evoked
response clearly appeared. In SEEG, two additional columns were visible following the main peak (indicated by arrows in Fig. 6a), but only the last one was clearly visible on EEG and MEG. The increase in correlation occurred at the time of the secondary peaks. By construction, these correlations reveal the co-variation of the signals around their respective means and not only the increase of signal amplitude at the evoked potential (see Material and methods for details).

The correlations in the time–frequency domain were computed in 4 frequency ranges (beta, gamma1, gamma2, gamma3) between the selected ICA components (based on the visual response as described in Single trial correlation across modalities section) and the SEEG contacts. No significant correlation was observed.

As a final step we computed the single trial correlations exhaustively over all sensors and ICA components both in temporal and time–frequency domain. The results are shown as supplementary material on Fig. S1. In the time domain, correlations were observed in EEG both on sensors (statistically significant on 10 electrodes) and ICA components (statistically significant on 4 ICA components, including that selected based on the visual response, IC#9). They mainly occurred after 100 ms post stimulation. The two ICA components with the most significant correlations (IC#8 & IC#13) showed a posterior spatial pattern (Fig. S1a). Correlations between SEEG and MEG were only observed on the ICA components, specifically on two of them: the component previously selected based on the visual response (IC#26), and another component also showing a posterior spatial pattern compatible with a brain response in the visual areas (IC#14; Fig. S1b). Finally, the computation of the time–frequency correlations per frequency band for EEG and MEG data did not show any significant correlations in the gamma
bands. Two significant correlations appeared in the beta band for ICA components extracted from EEG data (Fig. S1c).

**Discussion**

We recorded SEEG, EEG and MEG in a patient within a single trimodal acquisition. We described the signals obtained in the three modalities both in time and time–frequency domains. We characterized the artifact observed on the MEG signals due to the presence of SEEG/EEG equipment. Most importantly, we provided strategies aimed at revealing the presence (or absence) of correlations between depth and non-invasive signals at the single trial level.

**Signal quality**

As expected, the presence of the SEEG equipment resulted in characteristic artifacts in the raw MEG signals. A low frequency component was presumably caused by the presence of the SEEG connectors in contact with the patient’s shoulder, which moved with breathing. A high frequency component was more likely due to the presence of the bolts holding the depth SEEG electrodes in place on the scalp of the patient. This is consistent with previous studies that described artifacts caused by metallic parts within the MEG array (Hämäläinen et al., 1993; Hillebrand et al., 2013; Volegov et al., 2004).

Ball and colleagues investigated the signal quality degradation on simultaneous recordings of EEG and intracerebral EEG (Ball et al., 2009). However they focused a specific type of physiological artifact (eye blinks). In our recordings, the SEEG induced artifacts impacted the signal to noise ratio of the MEG signals in the posterior left region, especially at the single trial level. In order to improve the signal quality (for general MEG guidelines see Gross et al., 2013), future efforts should be made when positioning the patient and the equipment in the MEG system. The SEEG connectors should be placed as far as possible from the MEG array and as far as possible from the region(s) of interest. Also, every effort should be made to avoid contact them with the patient’s body.

In spite of these constraints, non-invasive signals (both MEG and EEG) were interpretable. Previous clinical studies have demonstrated that non-invasive signals (either MEG or EEG) recorded along with SEEG could be processed and interpreted. However, these studies only

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Fig. 4. Concordance of reconstructed cortical activations for the three modalities at three notable timestamps of the evoked response (corresponding to those shown on Fig. 3). (a) Activity recorded from depth electrode contacts (absolute values) mapped on a 3D representation of all electrodes within the cortex. (b–c) Cortical source localizations for EEG and MEG signals, respectively. (d) Cortical source localization for the separate MEG session of the same patient without SEEG or EEG. For each modality, the maximum color scale value was set to the maximum value of activation over the whole time window. The threshold on source estimates was set to 10% of the maximum value.
focused on epileptiform discharges (Kakisaka et al., 2012; Santiuste et al., 2008) and epileptic oscillations (Rampp et al., 2010), which are activities that have a high signal-to-noise ratio within their respective frequency bands (Zelmann et al., 2012).

Evoked responses

The evoked responses that we obtained were comparable to those generally observed for EEG, MEG, or SEEG recorded separately (Barbeau et al., 2008; Hatanaka et al., 1997; Nakamura et al., 1997). In our study, the average waveforms were consistent between non-invasive (MEG, EEG) and depth (SEEG) recordings. The only notable difference was an early response observed at 35 ms on SEEG and MEG but not on EEG, presumably because of the underlying source orientation (Ahlfors et al., 2010; Merlet et al., 1997). The net benefit of simultaneous compared to separate recordings (Godey et al., 2001) is readily apparent in the correlation coefficients between non-invasive and depth signals; these were substantially larger within the trimodal session than across sessions.

Identification of time–frequency patterns

The visibility of specific frequency bands in the three modalities has largely been discussed on separate recordings (Lachaux et al., 2005; Michel and Murray, 2009; Vidal et al., 2010). While MEG studies

Fig. 5. Time–frequency analysis of the visual response. (a) SEEG bipolar channel located on two posterior electrodes. (b) Posterior EEG electrodes. (c) posterior MEG sensors in the trimodal recording, and (d) posterior MEG sensors in the separate session. Circle one indicates the 20–40 Hz increase of energy pattern. Circle two indicates a decrease of energy around 20 Hz visible in the three modalities as well as in the separate session after 100 ms. Circle three indicates a broadband increase of energy above 50 Hz visible on SEEG. Circle four indicates increase of energy in the 20–40 Hz band at around 300 ms visible in MEG and EEG signals of the trimodal session.

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Adjamian et al., 2004; Hoogenboom et al., 2006; Schwarzkopf et al., 2012) have shown an increase in the gamma band during visual paradigms, our data did not reveal such activity neither in the trimodal nor in the separate session. However the gamma activity was clearly present in the SEEG data. This indicates that strong oscillatory activity in the cortex can go unnoticed on non-invasive data. The absence of high gamma on MEG and EEG could arise from the fact that our stimulation protocol only induced the synchronization of small areas of cortex in this frequency band (Schwarzkopf et al., 2012). Alternatively, other signal processing methods could help enhance the detection of gamma-band activity (e.g. beamforming Dalal et al., 2009, 2013).

**Reconstructed sources**

The cortical sources estimated from the non-invasive signals revealed sources that were consistent with the location of the SEEG contacts that detected the evoked potential, similarly to Dalal et al. (2009). In addition, we showed that the temporal evolution of SEEG activity, starting from primary areas and propagating to secondary areas, could be retrieved from the non-invasive recordings. This spatiotemporal pattern is consistent with the previous findings (Hagler et al., 2009).

Importantly, our results demonstrate that, within the trimodal recording, the precise spatiotemporal dynamics of evoked neural processes (Adjamian et al., 2004; Hoogenboom et al., 2006; Schwarzkopf et al., 2012) have shown an increase in the gamma band during visual paradigms, our data did not reveal such activity neither in the trimodal nor in the separate session. However the gamma activity was clearly present in the SEEG data. This indicates that strong oscillatory activity in the cortex can go unnoticed on non-invasive data. The absence of high gamma on MEG and EEG could arise from the fact that our stimulation protocol only induced the synchronization of small areas of cortex in this frequency band (Schwarzkopf et al., 2012). Alternatively, other signal processing methods could help enhance the detection of gamma-band activity (e.g. beamforming Dalal et al., 2009, 2013).

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Importantly, our results demonstrate that, within the trimodal recording, the precise spatiotemporal dynamics of evoked neural processes

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The full benefit of simultaneous recordings, however, only comes from the single-trial analyses. This has been shown in the field of EEG-fMRI, where trial-to-trial signal fluctuations were a fruitful source of information on the coupling between modalities (Bénar et al., 2007; Debener et al., 2005).

At the level of sensors, results were either not significant (MEG) or without clear spatial or temporal pattern (EEG). In contrast, independent component analysis allowed retrieving meaningful response fluctuations at the level of single-trial (Jung et al., 2001). Most importantly, it allowed us to observe significant correlations between the amplitudes of non-invasive and depth signals. This confirms the usefulness of ICA for capturing single trials correlations on multimodal data as done previously in the field of simultaneous EEG-fMRI (Debener et al., 2005; Eichele et al., 2005). Moreover, the correlation patterns revealed a high level of specificity in space and time: only a few SEEG contacts and time points were statistically significant. Most interestingly, MEG correlations were observed rapidly after the stimulation (i.e. within 150 ms post-stimulation) on SEEG contacts located in the visual cortex, although not precisely at the peak of the evoked response.

Concerning the small number of SEEG contacts presenting correlations, a factor to take into account is the relatively low spatial sampling of SEEG, both across the brain and within a given region. Many of the electrodes that we sampled were not located in visual areas. The absence of correlation on their contacts is not surprising, and is in fact reassuring regarding the selectivity of the correlation measure. In MEG, the significant correlations that we observed on the ICA corresponding to the visual response reproduced the spatiotemporal patterns seen at the source level. However, our analysis did not consider the possible impact of source orientations on bipolar SEEG (for discussion see Lachaux et al., 2004, p. 615) or on MEG and EEG. Variations in the local cortical orientation may promote or dampen the relationship with the non-invasive signals. This effect might vary from MEG to EEG signals because of the different sensitivities to source orientations of the two recording techniques: MEG being less sensitive to radial sources than EEG (Ahlfors et al., 2010; Merlet et al., 1997).

The fact that correlations occurred later than the main peak of evoked activity (Fig. 6) is somewhat unexpected. A tentative explanation can be built on the fact that the three modalities have different volumes of sensitivity. While intracranial electrodes measure a focal activity, especially in a bipolar montage (Lachaux et al., 2004), MEG and EEG record a mixture of synchronous activities over a broad area (Cosandier-Rimélé et al., 2012). If a focal activation such as the earliest peak of the visual response has spatial variability across trials (arising, for example, from small differences in eye fixation), this would have a more direct impact on SEEG amplitude than on MEG/EEG amplitude. In contrast, a less focal activation (for example, the one observed slightly after the peak) might be more homogenous across trials both in depth and surface sensors. While only tentative, this account could explain why the correlations are not strongest at the peak. This proposal is compatible with previous findings by Cohen et al. (2008), who reported a modest amplitude coupling along with consistent phase coupling between scalp and depth EEG signals.

A limitation of our study is that only 23 electrodes were placed on the scalp because of physical and clinical constraints. This could negatively impact detectability at the EEG sensor level, as well as the separability of ICA components. Despite this limitation, EEG presented more significant correlations with depth signals than MEG. Still, it is worth noting that the correlated SEEG contacts with MEG and EEG were different; those correlating with MEG being located within the primary visual areas. The differential capacities of EEG and MEG are a controversial topic (Malmivuo et al., 1997); our results suggest that the two modalities are best used in combination (Zijlmans et al., 2002).

Conclusion and perspectives

This technical note reports a procedure for recording MEG, EEG, and SEEG signals within a single session. Our results show the feasibility of such trimodal recordings, and the tractable SNR of the signals. For the reported case, the data revealed clear and meaningful correlations between certain signal components, as well as a notable degree of specificity. The main limitation of this study is that a single case was explored. Thus, it is premature to translate the findings to other cases or the general population.

In addition, the complexity of this procedure is not negligible. For this reason, the current findings are not intended to provide arguments against unimodal recordings, as these are to be preferred in most contexts. Still, trimodal recordings shall provide unique information on the coupling between signals while controlling for the fluctuations of brain activity across trials or recording sessions. There are numerous sources of such confounding fluctuations when signals are not recorded concurrently: spontaneous changes of the brain state, attention levels, learning, consequences of pathological activity, etc.

In this context, trimodal recordings could be used to address several issues. One is to investigate the visibility of gamma oscillations (Michel and Murray, 2009), or epileptic discharges (Alarcon et al., 1994) across the three modalities.

This is directly relevant for unimodal research. A better understanding of how and to what extent surface signals capture activities directly seen within the cortex should constrain the interpretation of surface empirical phenomena. Another perspective is to fuse the three modalities into a common model, such as in joint source-localization procedures or joint connectivity analysis.

In sum, this preliminary study shows that, despite its complexities, trimodal recordings have the potential to address specific neurophysiological questions from a new perspective.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.neuroimage.2014.05.055.

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