Consistency of local activation parameters at sensor- and source-level in neural signals

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Abstract

Objective. Although magnetoencephalography and electroencephalography (M/EEG) signals at sensor level are robust and reliable, they suffer from different degrees of distortion due to changes in brain tissue conductivities, known as field spread and volume conduction effects. To estimate original neural generators from M/EEG activity acquired at sensor level, diverse source localisation algorithms have been proposed; however, they are not exempt from limitations and usually involve time-consuming procedures. Connectivity and network-based M/EEG analyses have been found to be affected by field spread and volume conduction effects; nevertheless, the influence of the aforementioned effects on widely used local activation parameters has not been assessed yet. The goal of this study is to evaluate the consistency of various local activation parameters when they are computed at sensor- and source-level.

Approach. Six spectral (relative power, median frequency, and individual alpha frequency) and non-linear parameters (Lempel-Ziv complexity, sample entropy, and central tendency measure) are computed from M/EEG signals at sensor- and source-level using four source inversion methods: weighted minimum norm estimate (wMNE), standardised low-resolution brain electromagnetic tomography (sLORETA), linear constrained minimum variance (LCMV), and dynamical statistical parametric mapping (dSPM).

Main results. Our results show that the spectral and non-linear parameters yield similar results at sensor- and source-level, showing high correlation values between them for all the source inversion methods evaluated and both modalities of signal, EEG and MEG. Furthermore, the correlation values remain high when performing coarse-grained spatial analyses.

Significance. To the best of our knowledge, this is the first study analysing how field spread and volume conduction effects impact on local activation parameters computed from resting-state neural activity. Our findings evidence that local activation parameters are robust against field spread and volume conduction effects and provide equivalent information at sensor- and source-level even when performing regional analyses.

1. Introduction

Neural signals are generated by the synaptic activity of the neurons when transmitting and processing information. They reflect brain function, thus containing valuable information that can lead us to achieve a better understanding about cerebral dynamics. In this regard, neural activity has proven to be useful to associate certain complex cognitive processes with brain regions or their interactions, understand brain maturation, and analyse the neuropathological development of diseases affecting the central nervous system [1–3].

Different neuroimaging methods can be used to measure brain activity non-invasively, such as functional magnetic resonance imaging (fMRI),
functional near-infrared spectroscopy (fNIRS), electroencephalography (EEG) or magnetoencephalography (MEG). Radiological techniques have usually higher spatial resolution, whereas electrophysiological techniques provide higher temporal resolution that allows them to capture faster brain signal oscillations [4]. Accumulating evidence indicates that the study of time-varying oscillatory brain activity is of paramount importance to further understand a complex and dynamical system, like the brain [5]. Magnetoencephalography and electroencephalography (M/EEG) provide indeed the ability to analyse neural activity in the range of milliseconds, claiming their role in clinical and research environments [1, 2, 6]. The analysis of M/EEG signals poses notwithstanding new methodological challenges. This is the case of the source inversion techniques that provide a plausible distribution of locally synchronised neurons (i.e. neural sources) responsible of the electromagnetic activity observed in the acquisition sensors [7, 8]. Many source localisation methods have been developed in the past few decades, turning this into a flourishing topic in the brain signal processing field [8, 9].

Source inversion is, however, an ill-posed problem, thus not having a unique solution. Different types of assumptions are therefore applied to restrict the results, thus yielding different solutions [10]. There are two main methodological approaches that can be used to localise brain sources: equivalent current dipole (ECD), and linear distributed (LD) methods. ECD approaches assume that brain signals are generated by a small number of dipoles, being used to localise focal sources, such as interictal epileptic discharges [10]. On the other hand, LD methods do not limit the number of neural sources that can be considered simultaneously [10]. LD approaches are often used when sources across all the brain can be active or there is no a priori hypothesis about source distribution, which is the case for resting-state studies [10].

Localising brain sources is not straightforward, because electromagnetic signals suffer from distortion, attenuation, noise, and source mixing when travelling through the different head tissues. These issues are reflected in the field spread and volume conduction effects [11]. To overcome these problems, source inversion pipelines apply different modelling procedures. First of all, an anatomical model is required: it can be constructed using your own anatomical data or a template. In this step, the sensor positions has to be defined, as well as the modelling procedure (spheres-based, boundary element method modelling, finite element method modelling, among others). Secondly, another model must specify the number of sources, their localisation and orientation. Next, both models are integrated to generate the so-called forward model, which defines how the signals travel from the neural sources to the acquisition sensors. Lastly, a source inversion algorithm has to be selected, and its setting variables optimised. Using the information from the forward model, the inversion algorithm can finally be applied to M/EEG data. Although different software tools provide semi-automatic solutions to simplify the pipeline associated to inverse modelling [4, 12], the application of source localisation algorithms is a complex, time-consuming, and computational expensive procedure [13, 14]. Source inversion has therefore to be carefully carried out to accurately interpret the results obtained using source reconstructed data.

M/EEG are recorded at sensor-level, thus they suffered from field spread and volume conduction effects. Recently, Lai and colleagues demonstrated that global functional connectivity metrics (amplitude envelope correlation and phase lag index) at sensor- and source-level are strongly correlated [15]. On the contrary, they also found that network-related parameters defined using the minimum spanning three are sensitive to field spread and volume conduction effects [15]. According to the classification defined by Stam and van Straaten in [16], connectivity studies correspond to 'first order' analyses, while network studies encompass 'second and higher order' analyses. Nonetheless, they also defined another category: 'zero order' analyses, corresponding to local activation studies. Of note, local activation metrics include a variety of methods, such as spectral and non-linear parameters, which are extensively used in different neural signal processing studies to summarise the activation of functional units (i.e. synchronised neural pools) [16]. The influence of field spread and volume conduction on local activation metrics (i.e. 'zero order' analyses) has not been assessed yet. This lack of evidence on the consistency of zero order metrics computed at sensor- and source-level puts forth indeed a relevant challenge to avoid the potential bias in the physiological interpretation of the research findings, and motivates new research on this unexplored problem.

To the best of our knowledge, this is the first study analysing the influence of field spread and volume conduction effects in (zero order) local activation parameters. We pose the hypothesis that neural oscillatory activity at sensor level reflects the global time-varying properties of the underlying neural generators; consequently, local activation parameters, based on the analysis of the oscillatory, dynamic content of a given neural signal, should exhibit a similar distribution when they are computed at sensor- or source-level. The purpose of the work is then to evaluate the influence of field spread and volume conduction effects on local activation parameters by addressing: (i) the consistency of diverse spectral and non-linear parameters computed at sensor- and source level for M/EEG...
3. Methods

3.1. Source reconstruction

Time courses of M/EEG signals at source level were obtained using Brainstorm, which is documented and freely available for download online under the GNU general public license (http://neuroimage.usc.edu/brainstorm) [12]. The forward model was created using anatomical information from the template ICBM152 head (Montreal Neurological Institute), which is a non-linear average of 152 magnetic resonance images from different subjects [19, 20]. A head-shaped forward model with 15 000 sources was created using a boundary elements method based on the aforementioned template in order to obtain a common source space for M/EEG signals. This model might not be the most convenient due to its computational complexity, especially for MEG where simpler models have been proven to achieve adequate results [12]; nevertheless, its choice was done trying to select a model that fits both EEG and MEG signals [21]. The source-level was restricted to the cortex, and the volume was segmented in three tissues: brain, skull, and scalp, with conductivities: 1, 0.0125 and 1, respectively [4]. Neural sources were restricted to be normal to the cortex [15]. OpenMEEG software was employed to generate the head model [21]. As noise recordings were not available, an identity matrix was used as noise covariance [15].

Given that in the study we considered M/EEG resting-state recordings, the number and location of the neural sources were not constrained. Furthermore, in order to avoid the bias introduced by assuming the restrictions derived from only one source localisation method, four different LD source inversion algorithms were applied to M/EEG signals. They are listed below.

- **Weighted Minimum-Norm Estimation (wMNE):** The wMNE method restricts the solutions to those with the minimum energy (L2 norm). This method weights deeper sources to ease their identification. More information regarding the wMNE algorithm can be found in [22].
- **Standardised Low-Resolution Brain Electromagnetic Tomography (sLORETA):** This method restricts the solutions assuming that nearby neurons are synchronised; therefore, the correlation between neighbouring sources is maximal. Deeper insights about sLORETA algorithm are described in [23].
- **Linearly Constrained Minimum Variance (LCMV):** The LCMV method limits the solutions by minimising the variance in the output of a spatial filter. More information regarding LCMV can be found in [24].
- **Dynamic Statistical Parametric Mapping (dSPM):** This procedure uses *a priori* physiological and anatomical information from different imaging modalities to restrict the solutions. Additional
information regarding dSPM algorithm is provided in [25].

### 3.2. Segmentation in Regions of Interest (ROI)

The high dimensionality of the source-level signals was limited using the Desikan-Killiany atlas to project the signals from the 15 000 sources on 68 cortical areas [15]. The projection was done by averaging the signals of the voxels included in each cortical area after flipping the sources of opposite direction [15]. Subsequently, the 68 cortical areas were grouped using the information provided by the atlas into five regions of interest (ROIs): left frontal (LF), right frontal (RF), left temporal (LT), right temporal (RT), and occipital (O). This process was performed by averaging all the local activation parameters belonging to each ROI.

To compare the parameter distributions at sensor- and source-level, M/EEG sensors were also grouped into five ROIs with a spatial topography similar to that used at source-level. Table S1 and figure S1 from supplementary material (stacks.iop.org/JNE/17/056020/mmedia) provide detailed information about the cortical areas and sensors belonging to each ROI for M/EEG signals.

### 3.3. Local activation parameters

Local activation parameters are widely applied to many signal processing problems to characterise the activation of synchronised neural pools. The assessed metrics can be grouped into two main categories: spectral and non-linear. Spectral parameters evaluate different characteristics of the time-frequency content, such as the proportion of neural oscillators in each band, the signal slowing, or the dominant frequency of the most common brain activity in eyes-closed resting-state condition (i.e. alpha). Complementary, non-linear local activation parameters measure fundamental properties of neural signals, such as irregularity, complexity, and variability.

#### 3.3.1. Spectral parameters

Spectral parameters are used to quantify the properties of the normalised power spectral density ($PSD_n$) of the signals. The $PSD_n$ was calculated using the Blackman-Tukey approach [26–28]. Next, the spectral parameters computed in the current study are briefly summarised.

- **Relative Power (RP):** The RP is likely the most widely used spectral parameter. It quantifies the activation of the neural oscillators in a given frequency range in relation to the global brain activity [27, 28]. The RP was calculated using the conventional frequency bands for neural signals: delta ($\delta$, 1–4 Hz), theta ($\theta$, 4–8 Hz), alpha ($\alpha$, 8–13 Hz), beta 1 ($\beta_1$, 13–19 Hz), beta 2 ($\beta_2$, 19–30 Hz), and gamma ($\gamma$, 30–70 Hz) [27, 28].

- **Median Frequency (MF):** This parameter summarises in one measure the distribution of the spectral content content of the signal. Specifically, it is commonly used to quantify whether there is a global slowing of the oscillatory neural activity [27]. Its definition is based on the computation of the frequency that accumulates half of the power of the $PSD_n$ [29].

- **Individual Alpha Frequency (IAF):** Alpha oscillations play an important role in the modulation and control of diverse higher cognitive functions [30] and, consequently, much attention has been devoted to their characterisation. In this study, we implemented the IAF definition that quantifies the frequency at which the alpha peak can be found. In particular, it is estimated as the median frequency in the extended alpha frequency range (4–15 Hz) [27, 29].

#### 3.3.2. Non-linear parameters

The brain is a complex system in which non-linear interactions can be found at different levels and, consequently, non-linearity arises as an intrinsic property of neural signals [31, 32]. Non-linear parameters are usually computed on zero order analyses to provide complementary information to spectral metrics by quantifying diverse properties of M/EEG signals. The non-linear parameters assessed in the present study are summarised below.

- **Lempel-Ziv Complexity (LZC):** This parameter is a ‘coarse-grain’ complexity measure, which assigns higher values to more complex time series. In order to calculate the LZC, each M/EEG epoch is transformed into a binary sequence using a threshold defined as the median of the signal. LZC algorithm estimates the complexity of the time series counting the number of different subsequences in the aforementioned binary sequence [33].

- **Sample Entropy (SampEn):** SampEn quantifies the irregularity of a time series, so that larger values are assigned to signals with higher irregularity [27]. SampEn has two setting parameters: the length of the sequence, $m$, and the tolerance, $r$ [34]. According to previous M/EEG studies, they were set to: $m = 1$, and $r = 0.25 \cdot SD$, where $SD$ is the standard deviation of the time series [35, 36].

- **Central Tendency Measure (CTM):** This parameter is commonly used to quantify the variability of a time series using second-order difference plots [37]. The definition of CTM is based on computing the second-order difference diagram of the signal and counting the number of points within a radius $\phi$ [37]. Based on previous studies on neural signals, the radius, $\phi$, was set to 0.075 [27].
3.4. Statistical analysis
An exploratory data analysis was initially performed to evaluate the distribution of the parameters. Normality and homoscedasticity of the data were tested by applying Lilliefors and Bartlett tests, respectively. The data did not meet the normality and homoscedasticity hypotheses, thus non-parametric statistical tests were used.

For independent distributions, Kruskal-Wallis tests were employed to assess the differences for three or more distributions, whereas Mann-Whitney U-tests were applied to pairwise comparisons. Besides, Wilcoxon tests were used to evaluate the differences between two paired distributions. The differences between the shape of the data distributions were evaluated using the Kolmogorov-Smirnov test after mean subtraction.

The association between parameters calculated at sensor- and source-level was assessed using the non-parametric Spearman rank correlation to detect linear and non-linear monotonic relationships.

It is important to note that sampling frequency and epoch length were assessed as possible confounding factors. For this purpose, a stability evaluation procedure was applied [38]. First of all, Friedman test was used to assess the global effects of confounding factors [38, 39]. If statistically significant differences were shown by Friedman test, the lowest sampling frequency or epoch length that did not show statistically significant differences with any higher frequency or epoch length was considered as the lowest stable frequency or epoch length, respectively (applying Dunn’s test of multiple comparisons) [38].

4. Results

4.1. Influence of sampling frequency and epoch length
In a first analysis, the role of sampling frequency and epoch length as possible confounding factors was assessed. For this task, all the spectral and non-linear local activation parameters were calculated using different sampling frequencies and epoch lengths.

For MEG signals, we considered the sampling frequencies: 125, 250, and 500 Hz, and the epoch lengths: 1, 2.5, 5, and 10 seconds. Both sampling frequency and epoch length showed an increment in correlation values between sensor- and source-level local activation parameters as they increase. Dunn’s test showed that for all parameters and source inversion methods, the first common stable sampling frequency was 250 Hz, whereas the first common stable epoch length was 2.5 seconds. Figures S2-S12 in supplementary material show the distribution plots for the different sampling frequencies and epoch lengths assessed for MEG signals, whereas table S2 summarises the corresponding Friedman statistics. As can be observed, the original sampling frequency (1000 Hz) and epoch length (5 seconds) fall within the stability region; therefore, they were used for subsequent analyses.

In the case of EEG signals, we considered the sampling frequencies: 125, 250 and 500 Hz, and the epoch lengths: 1, 2.5, 5, and 10 seconds. Again, epoch length and sampling frequency showed a progressive increment in the correlation values between sensor- and source-level local activation parameters as they increase. The first common stable sampling frequency was 250 Hz, and the first common stable epoch length was 2.5 seconds, as can be seen in figures S13–S23 and table S3 in supplementary material. The original sampling frequency (500 Hz) and epoch length (5 seconds) were within the stability region; they were then selected for further analyses.

4.2. Correlation between sensor- and source-level local activation parameters
In order to assess the association between local activation parameters computed at sensor- and source-level, we initially carried out a so-called epoch-wise analysis [15]. Specifically, we computed the Spearman correlation between both levels by averaging all the channels (M/EEG sensors or cortical areas) for each epoch and subject. Figures 1 and S24 show, for each local activation parameter and source inversion method, scatter plots of MEG data at sensor- and source-level. The correlation values are included in the legend of the figures. Figures S25 and S26 depict similar analyses for EEG signals. Remarkably high correlations ($\rho > 0.92$, $p < 0.00001$) were obtained for all the local activation parameters ($\text{RP}$, $\text{MF}$, $\text{IAF}$, $\text{LZC}$, $\text{SampEn}$ and $\text{CTM}$), inversion methods ($\text{wMNE}$, $\text{sLORETA}$, $\text{LCMV}$, and $\text{dSPM}$), and modality of signal (MEG and EEG). No local activation parameter nor source localisation method provided noticeable higher (or lower) values than the others. The mean ($\pm \text{SD}$) $\rho$ value is $0.972 \pm 0.009$ for MEG-based parameters, and $0.970 \pm 0.016$ for EEG-based parameters. These values are remarkably higher than those obtained by Lai and colleagues, where the maximum $\rho$ value obtained was 0.933 [15]. All the $\rho$ values for the epoch-wise analysis are included in table 1.

In the case of MEG analyses, it can be appreciated in figures 1 and S24 that all the local activation parameters exhibited a linear relationship. Besides, it can be observed a drift in the data, with LCMV showing slightly lower $\text{LZC}$, and $\text{SampEn}$ values than the other source localisation methods. LCMV also provided slightly higher values for $\text{CTM}$ than the other source inversion methods. This result implies that LCMV affects to source-level time series, eliciting a slight loss of complexity, irregularity and variability when compared to sensor-level signals. It can be also observed that $\text{RP}_{\text{Gamma}}$ obtained lower values for LCMV than for the other source inversion algorithms. Additionally, we tested the differences between the local activation parameters computed at sensor- and source-level
Figure 1. Spearman correlation (\(\rho\)) between sensor- and source-level \(RP\) values computed from MEG signals for each source inversion method and frequency band: (a) delta, (b) theta, (c) alpha, (d) beta 1, (e) beta 2, and (f) gamma. For each figure, the X-axis includes the distribution of \(RP\) at sensor-level, whereas Y-axis includes the distribution of \(RP\) for the different source localisation methods.

for MEG signals. Statistically significant differences were only found for \(RP_{\text{gamma}}\) (\(Z = 3.253, p = 0.0498\), Bonferroni corrected Wilcoxon test), \(\text{LZC}\) (\(Z = 3.331, p = 0.0380\)) and \(\text{SampEn}\) (\(Z = 3.253, p = 0.0498\)) when using LCMV. Nevertheless, the distribution of the local activation parameters at sensor- or source-level was similar; there were no statistically significant differences in the shape of the distributions for any parameter nor source localisation method (\(p > 0.05\), Kolmogorov-Smirnov test). This result can be observed in figure 2 that summarises the data distribution for each local activation parameter and source inversion algorithm for MEG signals.

Regarding EEG analyses, figures S25 and S26 show that, as for the case of MEG signals, all the local activation parameters fit a linear regression. Statistically significant differences were found for \(\text{LZC}\) (\(Z = 3.874, p = 0.0047\)) and \(\text{CTM}\) (\(Z = -3.948, p = 0.0035\)) when using LCMV, and for \(RP_{\text{gamma}}\) for all source inversion methods (\(w\text{MNE}: Z = 4.224, p = 0.0011; \text{sLORETA}: Z = 3.567, p = 0.0159; \text{LCMV}: Z = 4.486, p = 0.0003; \text{dSPM}: Z = 3.839, p = 0.0054\)). Notwithstanding non-significant differences were found in the distribution of the local activation parameters for any source inversion method (\(p > 0.05\), Kolmogorov-Smirnov test), as can be observed in figure 3.

The previous results were obtained by applying the epoch-wise analysis (see table 1); however, a subject-wise analysis was also performed by averaging the epochs of each subject (see table 2). As it could be appreciated by comparing tables 1 and 2, subject-wise analysis provided slightly higher \(\rho\) values than the epoch-wise one. The average difference between \(\rho\) values is less than 1% for both MEG and EEG signals.

4.3. Field spread and volume conduction effects according to the modality of signal

The Spearman correlation values obtained for MEG and EEG were compared to assess whether they can be influenced by the type of recording. Tables 1 and 2 show that, in general, the correlation values were very similar, with MEG providing slightly higher values than EEG. These observable differences in the Spearman correlation values between MEG and EEG were assessed using t-tests for all parameters.
Table 1. Spearman correlation values ($\rho$) of the epoch-wise analysis between sensor- and source-level local activation parameters for each source inversion algorithm and type of signal. All the $\rho$ values are statistically significant ($p < 0.0001$). Tables S4 and S5 in supplementary material include the corresponding confidence intervals for each correlation value.

| EPOCH LEVEL | wMNE | sLORETA | LCMV | dSPM |
|-------------|------|---------|------|------|
|             | MEG  | EEG     | MEG  | EEG  | MEG  | EEG  | MEG  | EEG  |
| $RP_{\text{Delta}}$ | 0.970 | 0.964  | 0.965 | 0.970 | 0.956 | 0.931 | 0.971 | 0.967 |
| $RP_{\text{Theta}}$ | 0.983 | 0.984  | 0.978 | 0.985 | 0.981 | 0.963 | 0.982 | 0.985 |
| $RP_{\text{Alpha}}$ | 0.984 | 0.987  | 0.981 | 0.988 | 0.976 | 0.970 | 0.984 | 0.987 |
| $RP_{\text{Beta1}}$ | 0.983 | 0.984  | 0.974 | 0.984 | 0.975 | 0.965 | 0.984 | 0.984 |
| $RP_{\text{Beta2}}$ | 0.983 | 0.984  | 0.977 | 0.986 | 0.978 | 0.971 | 0.982 | 0.985 |
| $RP_{\text{Gamma}}$ | 0.971 | 0.975  | 0.968 | 0.978 | 0.965 | 0.951 | 0.972 | 0.976 |
| MF           | 0.966 | 0.957  | 0.952 | 0.961 | 0.949 | 0.921 | 0.968 | 0.960 |
| IAF          | 0.970 | 0.984  | 0.966 | 0.986 | 0.951 | 0.968 | 0.968 | 0.985 |
| LZC          | 0.974 | 0.967  | 0.969 | 0.971 | 0.963 | 0.941 | 0.975 | 0.970 |
| SampEn      | 0.974 | 0.970  | 0.970 | 0.974 | 0.962 | 0.944 | 0.976 | 0.972 |
| CTM          | 0.973 | 0.970  | 0.969 | 0.974 | 0.963 | 0.942 | 0.975 | 0.972 |

Figure 2. Data distribution of all local activation parameters and source inversion methods for MEG signals. Each circular sector contains all the distributions of one of the local activation parameters assessed, whereas the concentric circles in white divide sensor- and source-level distributions. Thus, each one of the subdivisions represent the distribution for a given parameter (circular sector) and a sensor- or source-level (concentric divisions). All values have been z-transformed. The lower colorbar depicts the correspondence between colours and z-values. Each circular sector shows the data distribution centred in zero with ±4 standard deviations (SD) in each side of the distribution.

and inversion methods. Most of the comparisons (81,82%) showed statistically significant differences ($p < 0.05$, Bonferroni corrected Wilcoxon tests) with MEG showing higher $\rho$ values. Table S8 in supplementary material summarises the corresponding statistics

4.4. Influence of field spread and volume conduction effects in different ROIs
To evaluate the spatial robustness of the local activation parameters, the 68 cortical areas were grouped into five ROIs: left frontal, right frontal, left temporal, right temporal, and occipital.
A spatial coarse-grained analysis was performed by joining the correlation values from all the available parameters and source inversion methods. Then, the distribution of the $\rho$ values (which contains the correlation values for the 11 parameters and 4 source inversion methods for each ROI) were compared across ROIs using Mann-Whitney $U$-tests. Figure 4 shows the distribution of the $\rho$ values in each ROI for M/EEG. The $\rho$ values decrease in comparison with those obtained in the global analyses, though they are still high and statistically significant ($p < 0.0001$). It can be observed that right temporal ROIs provide the highest correlations. On the contrary, occipital and frontal regions showed the lowest correlation for MEG and EEG signals, respectively.

**Table 2.** Spearman correlation values ($\rho$) of the subject-wise analysis between sensor- and source-level local activation parameters for each source inversion algorithm and type of signal. All the $\rho$ values are statistically significant ($p < 0.0001$). Tables S6 and S7 in supplementary material include the corresponding confidence intervals for each correlation value.

| SUBJECT LEVEL | wMNE | sLORETA | LCMV | dSPM |
|---------------|------|---------|------|------|
| MEG           |      |         |      |      |
| EEG           | 0.977| 0.972   | 0.970| 0.978|
| $R_P_{\text{Delta}}$ | 0.988| 0.990   | 0.985| 0.991|
| $R_P_{\text{Theta}}$ | 0.983| 0.991   | 0.980| 0.992|
| $R_P_{\text{Alpha}}$ | 0.988| 0.990   | 0.976| 0.991|
| $R_P_{\text{Beta1}}$ | 0.987| 0.986   | 0.983| 0.987|
| $R_P_{\text{Beta2}}$ | 0.976| 0.978   | 0.974| 0.980|
| $R_P_{\text{Gamma}}$ | 0.972| 0.969   | 0.959| 0.973|
| $R_P_{\text{MF}}$ | 0.979| 0.991   | 0.975| 0.992|
| $R_P_{\text{IAF}}$ | 0.970| 0.973   | 0.969| 0.977|
| $R_P_{\text{SampEn}}$ | 0.969| 0.973   | 0.971| 0.977|
| $R_P_{\text{CTM}}$ |      |         |      |      |

Figure 3. Data distribution of all local activation parameters and source inversion methods for EEG signals. Each circular sector contains all the distributions of one of the local activation parameters assessed, whereas the concentric circles in white divide sensor- and source-level distributions. Thus, each one of the subdivisions represent the distribution for a given parameter (circular sector) and a sensor- or source-level (concentric divisions). All values have been $z$-transformed. The lower colorbar depicts the correspondence between colours and $z$-values. Each circular sector shows the data distribution centred in zero with $\pm 4$ standard deviations (SD) in each side of the distribution.
5. Discussion

In the current study we explored the robustness of local activation parameters of neural activity to field spread and volume conduction effects. Our results support two main findings: (i) the local activation parameters assessed in the study provide consistent estimations of diverse spectral and non-linear properties of neural oscillations measured both from MEG or EEG activity, independently whether they are computed at sensor- or source-level; and (ii) the regional patterns of the local activation parameters are strongly correlated at sensor and source-level, though spatial resolution at sensor-level plays a role that barely depends on the neuroimaging modality.

5.1. Consistency of local activation parameters

Local activation parameters correspond to the zero order analysis according to the classification made by Stam and van Straaten [16]. They are extensively applied in a high number of neural signal processing studies, since they provide relevant insights to characterise brain function. In line with our results, previous studies found that relative power at sensor- and source-level exhibited similar activation patterns [40]. Furthermore, Lai et al [15] observed that global connectivity (corresponding to first order analyses according to Stam and van Straaten [16]) was highly correlated between sensor and source levels, though it remarkably decreased for minimum spanning tree parameters (second order analyses). These results suggest that global oscillatory neural patterns and synchronous firing of neural populations can be observed both at sensor and source levels. M/EEG recordings at scalp-level are able to reflect the ‘coarse’ underlying neural fluctuations and coupling patterns, though field spread and volume conduction effects modify the ‘fine’ spatio-temporal properties of brain activity. Local activation parameters computed from M/EEG signals at sensor- and source-level rely on different assumptions and restrictions. Therefore, they should be different, depending on the approach used to calculate them. Nevertheless, as we hypothesised, the parameters calculated at both levels are strongly related, and the shape of the distributions is similar.

For MEG signals, statistically significant differences were obtained for LZC, and SampEn when using LCMV, which suggests that the highest deviances between sensor- and source-level occur for non-linear parameters and that particular source inversion method. Sensor-level signals showed higher LZC and SampEn; this means that complexity and irregularity decrease for signals at source level using LCMV. In line with our results, a number of studies analysing scalp level signals obtained higher LZC values at scalp level for the control group [36, 41–46] than those focused on source-level analysis using LCMV [47]. These studies used different databases and processing pipelines notwithstanding; hence, the results should be carefully interpreted. Comparisons with SampEn at source-level using MEG cannot be established, since to the best of our knowledge no study...
has addressed this kind of analysis. Nonetheless, the results obtained by Echegoney and colleagues [48] provide some evidence in line with our findings. They observed that complexity and irregularity of MEG activity, quantified by means of statistical complexity and permutation entropy, were slightly lower at source-level using LCMV than at sensor-level.

In the case of EEG signals, statistically significant differences were found in LZC, SampEn, and CTM for LCMV, and in $RP_{\text{Gamma}}$ for all source localisation methods. Similarly to the MEG analyses, the loss of complexity, irregularity and variability with EEG signals at source-level can be due to the source inversion method. Also, the decrease in gamma power may be caused by higher frequencies attenuating when being projected across the different head tissues. A number of EEG studies computed LZC at scalp level [27, 49–53], whereas only one focused on source-level using sLORETA [54]. Their results are in agreement with our findings: the complexity values obtained by the control group at sensor-level were higher than those reached at source-level. Comparisons with EEG studies applying SampEn or CTM at source-level cannot be established, though it can be hypothesised that irregularity and variability values should show a similar complexity pattern. Regarding $RP_{\text{Gamma}}$ results, previous EEG studies at sensor-level [27, 55–58] also obtained activation values for controls higher than those reached at source-level using eLORETA [59]. Certainly, eLORETA is an improved version of sLORETA, but they both rely on similar assumptions. Therefore, the results can be directly compared [23, 60], supporting our findings.

Performing a source localisation pipeline involves applying a transformation to the sensor-level signals and, by extension, to the local activation parameters extracted from them. This was reflected by the statistical analyses, where significant differences were found for some parameters when comparing them at sensor- and source-level. Nonetheless, the high correlations obtained for all the parameters indicate that the shapes of the distribution of the local activation parameters at sensor-level are very similar to those at source-level. Kolmogorov-Smirnov statistics supported these results, since no statistical differences were obtained for any comparison. The statistical significant differences observed are therefore due to an offset of the local activation parameters, which depends on the source localisation method. In order to avoid the bias of assuming the restrictions of only one source inversion method, four different source localisation algorithms were applied to M/EEG signals. Although some methods are rarely used with certain modality of signal (e.g. sLORETA in MEG, or LCMV in EEG), this study is not intended to unveil the real underlying sources; it is focused on comparing the influence of field spread and volume conduction effects in local activation parameters. It is noteworthy that source localisation methods and local activation parameters are affected differently by epoch length and sampling frequency; thus the first stable sampling frequency and epoch length are different across parameters and source inversion methods. These results are in line with previous studies, which reported that different connectivity measures stabilise at different epoch lengths [38, 39]. Our results suggest that higher sampling frequencies and epoch lengths improve the robustness of the source estimates. Using short epoch lengths may avoid to capture the slow signal activity adequately, because the number of available oscillations is not enough to accurately estimate the PSDn, thus biasing the spectral parameter calculation [61]. Also, although stability is less affected by sampling frequency, small sampling frequencies may cause distortion at high frequencies. Interestingly, it can be appreciated that LCMV provide slightly lower Spearman correlation values, specially for non-linear parameters. This source localisation method is a beam-forming technique that involves a spatial filtering [24]. It can be hypothesised that this process may be causing higher frequencies to attenuate, or noise bandwidth to decrease, which are associated with a complexity loss [62, 63].

5.2. Influence of field spread and volume conduction effects on spatial patterns

Our results show a high correlation between sensor- and source-level local activation parameters, even when performing a regional analysis. Nonetheless, we have performed a ‘coarse-grain’ segmentation; it is likely that ‘fine-grain’ spatial segmentation would unveil remarkable differences between sensor- and source-level activation patterns. In this regard, source-level analyses are indeed useful to accurately assess activation or coupling patterns from single cortical areas or even single voxels. The spatial resolution of our EEG setting (19 sensors) prevented us to perform a higher resolution spatial segmentation, but it was enough to conclude that regional analyses provide very similar results at sensor- and at source-level, even though the sensor relative position might influence our results, especially for MEG where there is not a standard sensor layout.

Both MEG and EEG local activation parameters yielded remarkably high correlation between sensor- and source-level. Nonetheless, MEG parameters have higher $\rho$ values than EEG-derived parameters. There are five factors that could explain this outcome. First, it has been proven that the accuracy of the source localisation methods increases with the spatial resolution [15, 64]. This hypothesis agrees with the results obtained by Coquelet and colleagues that obtained similar results when analysing static resting-state functional connectivity using MEG and EEG layouts with a similar number of sensors [65]. As the number of sensors, and thus the spatial resolution, is almost ten times higher for the MEG signals,
it is expected the associated $\rho$ values to be higher [5]. Additionally, we are analysing the activity from 68 cortical areas, which is a higher dimensionality than the provided by the 19 EEG sensors. This issue could be hindering the reconstruction of neural sources. The selection of the reference electrode has also been proven to have influence on the analysis of EEG signals [66]. The choice of the EEG signal referencing was robustly done based on previous studies [11, 39, 67, 68], though this factor could influence the correlation values yielded by EEG-derived parameters. The fourth potential factor that could influence those differences is the fact that EEG and MEG are sensitive to different types of neural sources; while EEG mainly records extracellular currents, MEG also reflects the neural activity of primary intracellular currents [69, 70]. Nonetheless these neural sources are often considered essentially the same and would likely have little impact in our results [69, 71]. Finally, magnetic signals are less sensitive to field spread and volume conduction effects than EEG signals because magnetic permeability is roughly constant across all head tissues and the free space [15, 72]. This will make the source inversion process to be carried out more accurately for MEG signals and, consequently, the $\rho$ values obtained should increase.

Statistically significant differences between ROIs ($p < 0.05$, Bonferroni-corrected Mann-Whitney $U$-tests) were observed for all pairwise comparisons except between LF and RF regions, and between LT and RT regions, for both MEG and EEG. Many factors could be contributing to the differences found in the $\rho$ values for the ROIs assessed. Some of them, such as anatomical features or brain activity heterogeneity, are difficult to take into account. Nevertheless, it can be observed that symmetric areas depict similar correlation values, being the only comparisons that not obtained statistically significant differences. As brain has a high degree of mid-sagittal symmetry [73], this suggests that the anatomy could influence the impact of field spread and volume conduction effects in local activation parameters. Interestingly, the left temporal ROI exhibited slightly lower values than the right one for both MEG and EEG. It is known that language processing is located in temporal brain areas, with a strong left lateralisation [74]. As the resting-state condition does not involve direct language processing, it could be producing lower neural activity in the left temporal than in the right temporal ROI. Thus, due to the decreased signal-to-noise ratio, the source inversion process for the left temporal area could be hampered, yielding lower $\rho$ values.

5.3. Limitations and further steps

Our findings indicate that the analysed local activation parameters provide robust estimations of spectral and non-linear properties of neural activity; nevertheless, some methodological considerations should be taken into account. Firstly, only five different ROIs were defined, as we wanted to perform a robust segmentation to analyse the consistency of the local activation parameters across brain regions. It would be interesting for future work to analyse in-depth the spatial extent of the robustness of local activation parameters against field spread and volume conduction effects by increasing the spatial resolution of the segmentation performed in this contribution.

Secondly, our results illustrate how field spread and volume conduction effects influence local activation parameters only in resting-state signals. This kind of analysis is a widely used paradigm; however, it would be of great interest to address how the aforementioned effects influence those parameters in task-related protocols [3].

Thirdly, although the employed head model fits MEG and EEG signals [21], it would be of great interest to assess how different head models (e.g. single-layer, sphere-based, Finite Element Models, etc) perform differently regarding field spread and volume conduction effects.

Besides, some interesting differences have been found between MEG and EEG correlation values. It would be interesting to perform a further analysis to get deeper insights on how different parameters and source inversion methods perform differently against field spread and volume conduction effects on the different recording techniques (MEG and EEG).

Finally, we have used anatomical templates because the source reconstruction process is minimally biased [15, 19]. The use of anatomical MRIs notwithstanding along with the M/EEG recordings would allow to accurately assess how different factors, as the head shape or the tissue thickness, affect spatial patterns of local activation parameters.

6. Conclusions

To the best of our knowledge, this is the first study analysing how field spread and volume conduction effects impact on local activation parameters computed from resting-state neural activity. Our findings evidence that spectral and non-linear parameters yield similar results at sensor- and source-level for four different source inversion methods, being strongly correlated at both levels and showing similar distributions. Furthermore, our results indicate that the correlation remains high when segmenting the brain in ROIs. These findings support the idea that local activation parameters are robust against field spread and volume conduction effects, even when performing regional analyses.

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