Are Sources of EEG and MEG rhythmic activity the same? An analysis based on BC-VARETA

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Abstract

In the resting state (closed or open eyes) electroencephalogram (EEG) and the magnetoencephalogram (MEG), rhythmic brain activity is very evident, typically the 10 Hz alpha rhythm. It has a topographic frequency spectral distribution that is, at first sight, quite similar for both modalities-- something not surprising since both EEG and MEG are generated by the same basic oscillations in thalamocortical circuitry which produce primary current densities (PCD). However, different aspects (divergence and curl) of this PCD vector field underpin the two types of signals. Does this difference lead to a different distribution of reconstructed sources for EEG and MEG rhythms? This question is important for the transferal of results from one imaging modality to the other but has surprisingly received scant attention till now. We address this issue by comparing eyes open EEG source spectra recorded from 77 subjects from the Cuban Human Brain Mapping project with the MEG of 63 subjects from the Human Connectome Project. Source spectra for each voxel and frequency were obtained via a novel sparse-covariance inverse method: BC-VARETA based on individualized BEM head models with subject-specific regularization parameters (noise to signal ratio). While curtailing source leakage, the sparse BC VARETA estimator produces a large number of zero activations (zero inflation or ZI) which generates severe problems for traditional statistical methods. We circumvent the ZI problems by employing a novel dimensionality reduction technique known as Zero-inflated Factor Analysis (ZIFA). Both

minimum energy and Hotelling's T-2 tests showed that ZIFA scores for MEG and EEG sources were significantly different at all frequency bands. These results exclude a simple identification of the MEG and EEG sources of resting-state EEG rhythms. Further study is required to determine the relative contribution of instrumental, physical or physiological mechanisms to these differences.

Keywords: EEG, MEG, BC-VARETA, Electrophysiological Source Imaging, alpha rhythm

1. Introduction

At resting state EEG and MEG readings show an evident rhythmic activity in frequency spectra, specifically alpha band. Postsynaptic potentials (PSP) are continuously happening even in resting state (both eyes open and closed). These PSPs are generated from the same cortical networks (thalamocortical, cortical-cortical, etc.) PSPs generate primary current densities (PCD) at the cortical surface and these PCDs are measured as electric potential or magnetic field by EEG electrodes and MEG magnetometers respectively. Since both phenomena are generated from the same cortical activity, there should not be any differences in these rhythms which seems evident at first sight. However, both modalities are physically different in nature, so they suffer from different effects of volume conduction. Moreover, the measurement noise in the recorded signals might be different since the engineering and physics behind the signal and sensors that are used for acquiring those signals is different for both modalities.

These biological and instrumental factors affect the M/EEG signals. However, it's an ongoing discussion that whether the sources of the acquired rhythmic activities are the same or different. The term source localization is used to define the process of reconstructing the cortical source spectra or to localize the cortical activity from the electromagnetic rhythms. While comparing source localization, there are different results based on a variety of experiments. Some claimed EEG source localization is better than MEG (Liu, Dale, & Belliveau, 2002), (Gavaret, Badier, Bartolomei, Bénar, & Chauvel, 2014) (Klamer, et al., 2014) others found in their experiments that MEG has better source localization accuracy (Cohen & Cuffin, 1991) (Cuffin, 1983), while others did not find significant differences (Hedrich, Pellegrino, Kobayashi, Lina, & Grova, 2017) (Waldert, et al., 2008) (Cuffin, 1983) between two modalities performance on source localization. There is a significant amount of research that claims combining EEG and MEG outperforms individual modality in terms of source localization and spike detection (Lin, et al., 2003) (Knake, et al., 2006) (Sharon, Hämäläinen, Tootell, Halgren, & Belliveau, 2007) (Muthuraman, et al., 2014) (Plummer, et al., 2019).

One major difference between EEG and MEG is the sensitivity to source orientation and source Signal-to-Noise Ratios (SNR) at different brain areas. Evidence for the sensitivity of EEG to tangential and MEG to radial sources are found in many studies (Cuffin, 1983) (Haueisen, Funke, Güllmar, & Eichardt, 2012). However, there are results showing the opposite case and that opens the discussion of the sensitivity of EEG and MEG to different

source orientation (Hunold, Funke, Eichardt, Stenroos, & Haueisen, 2016) (Rossi, Luria, Sommariva, & Sorrentino, 2017). The sensitivity of EEG and MEG to deep and superficial sources has been discussed in many studies claiming MEG is not able to give high SNRs for deep sources while EEG is successful in that (Hunold, Funke, Eichardt, Stenroos, & Haueisen, 2016).

As mentioned earlier that volume conduction effect has influence on the readings of both modalities. This is demonstrated in the experiments conducted by many researchers for different head models (Vorwerk, et al.) (Siems, Pape, Hipp, & Siegel, 2016). They also found that tissue anisotropy and the white matter has major conduction effect for EEG while MEG is only affected by white matter anisotropy (Haueisen, et al., 2002) (Siems, Pape, Hipp, & Siegel, 2016). These two phenomena also affect source reconstruction accuracy where EEG is more susceptible to muscle artifacts and different head models while MEG is less prone to both factors (Wolters, et al., 2006).

There are some shortcomings in almost all the current studies. The comparative studies were not based on a statistical analysis of source spectra. Real head models were not used in many studies, the number of subjects was not significantly high, modern inverse solutions were not used to incorporate the effects of cortical activity as well as connectivity estimation techniques. All these aspects are very important to achieve a transferal between these two modalities. In this study, we discuss this issue by comparing the resting state (eyes open) of 77 subjects from Cuban Human Brain Mapping project and MEG of 63 Human Connectome Project. Figure 1. shows a flowchart for the methodology that has been used for statistical comparison of two modalities. We have used a novel inverse method BC-VARETA which works on the individual head model based on Boundry Element Method (BEM). We perform statistical testing on the results of the inverse solution we used and found both modalities significantly different. These results may be helpful in achieving the cross-modality transfer of information.

2. Materials and Methods

2.1. Dataset

The EEG data we analyzed is from Cuban Brain Mapping Project (Hernandez-Gonzalez, et al., 2011). EEG was recorded using 58 channels, electrodes were placed according to the international 10/20 electrode system. The EEG data was acquired from 77 healthy subjects (64 male and 13 females, ages between 19 to 50 years old) in resting state with eyes open. The sampling frequency was 200 Hz.

The MEG data that has been studied in this work is from the Human Connectome Project (Van Essen, et al., 2011) (Behrens, et al., 2013)(Van Essen et al., 2011) (Behrens et al., 2013), led by Washington University, University of Minnesota, and Oxford University (https://www.humanconnectome.org/) (Hileman, et al., 2013). MRI for the anatomical data

was collected using a 3 Tesla (3T) Siemens Skyra scanner. The MEG data was acquired using 248 magnetometer channels and 23 reference channels of a whole head MAGNES 3600 (4D Neuroimaging, San Diego, CA) system. The sampling frequency of the preprocessed data was 508 Hz. We analyzed 63 healthy subjects (33 male and 30 females, ages between 22 to 35 years old) with eyes open resting-state condition.

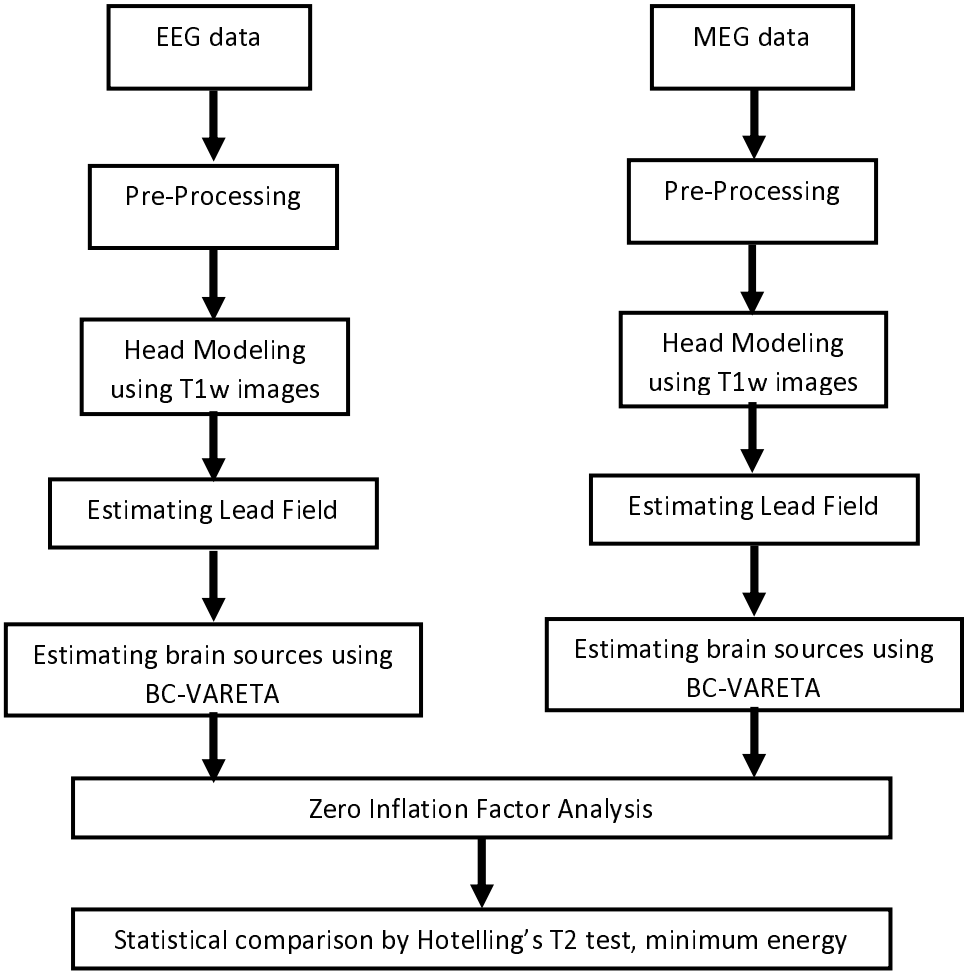

Figure 1:Flowchart of research methodology

2.2. Preprocessing

The EEG data was filtered using a band-pass filter of 0.5 Hz to 60 Hz. Furthermore, Independent Component Analysis (ICA) (Comon, 1994) was applied on the time series data, to remove the artifacts.

The MEG data were preprocessed by the Human Connectome Project teams using MEG Connectome pipeline (Van Essen, et al., 2011) . A high-pass filter of 1.3 Hz and a low-pass filter 150 Hz was applied to the data with two additional notch filters of 59-61 Hz and 119-121 Hz. Moreover, ICA was used for artifact removal.

2.3. Forward model

To estimate the realistic head models of individual subjects, Freesurfer toolbox was used(http://www.freesurfer.net/) (Dale, Fischl, & Sereno, 1999) (Fischl, 2012) (Dale, Fischl, & Sereno, 1999) (Fischl, 2012) on T1w images. Brainstorm (https://neuroimage.usc.edu/brainstorm/) (Tadel, Baillet, Mosher, Pantazis, & Leahy, 2011) (Tadel, Baillet, Mosher, Pantazis, & Leahy, 2011) was used to apply Boundary Element Method (BEM) (Fuchs, Kastner, Wagner, Hawes, & Ebersole, 2002) for head modeling and estimation of the lead field for each subject. The lead field was computed for 6002 sources.

2.4. Brain Connectivity Variable Resolution Tomographic Analysis (BC-VARETA)

Furthermore, the Data Empirical Covariance was computed using Fourier Transform (48 equispaced frequency components between 0-19 Hz were used). The time-series data, lead field matrix and Data Empirical Covariance was used to apply BC-VARETA and the source activity and connectivity along the whole spectra were obtained.

The Brain Connectivity Variable Resolution Tomographic Analysis (BC-VARETA) (Gonzalez-Moreira, Paz-Linares, Martinez-Montes, & Valdes-Sosa, Third Generation MEEG Source Connectivity Analysis Toolbox (BC-VARETA 1.0) and Validation Benchmark, 2018)(Gonzalez-Moreira et al., 2018) is a recently proposed technique to reconstruct source distribution from M/EEG rhythms. This method rests on a Bayesian identification approach of linear dynamical systems in the frequency domain. The M/EEG generative model underlying BC-VARETA is expressed in terms of spectral equations of a Linear State Space Model (LSSM), which is estimated by Hidden Gaussian Graphical State-Model (HIGGS) (Paz-Linares, Gonzalez-Moreira, Martinez-Montes, & Valdes-Sosa, 2018)(Paz-Linares et al., 2018a). BC-VARETA uses a univariate version of HIGGS that allows searching the sparse subspace with statistical guarantees, an instance of SSBL based on the Elastic-Net model (Paz-Linares et al., 2017). The synergy of these algorithms (HIGGS and SSBL) turns BC-VARETA in a high-resolution technique for source activity estimation that outperforms state-of-the-art methods by several orders of magnitude (Gonzalez-Moreira, et al., 2018)(Paz-Linares et al., 2018b).

2.5. Frequency scaling

Outliers in the data could add bias to the results of the statistical comparison between sources of M/EEG rhythmic activity. To deal with outliers, frequency scaling was applied according to the characteristics of the data. Following are the steps:

(1) The values smaller than 10^{-3} were discarded (were set to 0).
(2) $\log_{10}$ was applied to the non-zero values of source spectra. This was to obtain ZIFA scores (explained in next section).
(3) An arbitrary number was added to deal with negative values generated due to log transformation in step 2.
(4) For each subject and each frequency component, normalization was done by dividing with the maximum value.
Finally, we obtained the scaled source spectra, refer Figure 2(b).

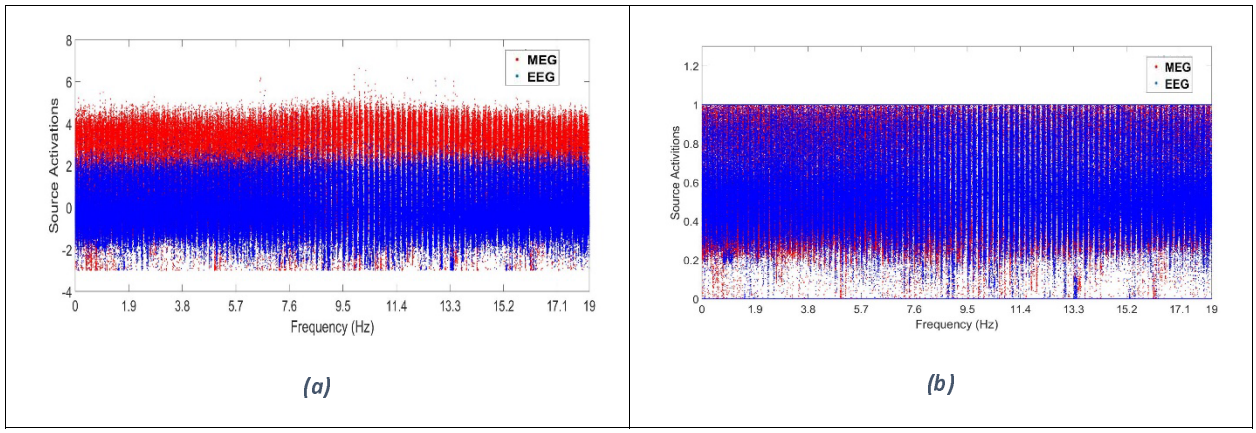

Figure 2: M/EEG source activity (a) before frequency scaling (b) after scaling data

2.6. Zero inflation Factor analysis (ZIFA)

When data is highly sparse due to a large number of unobserved values this is known as Zero Inflation. While dealing with source leakage and to minimizes the False Positive sources, BC- VARETA use Sparse Hermitian Sources Graphical Model (Paz-Linares, Gonzalez-Moreira, Martinez-Montes, & Valdes-Sosa, 2018). This generates a large number of zero activations. Thus, the resultant source spectra were highly sparse or Zero-Inflated. The histogram of source activations is shown in Figure 3. which demonstrates zero inflation in reconstructed source space.

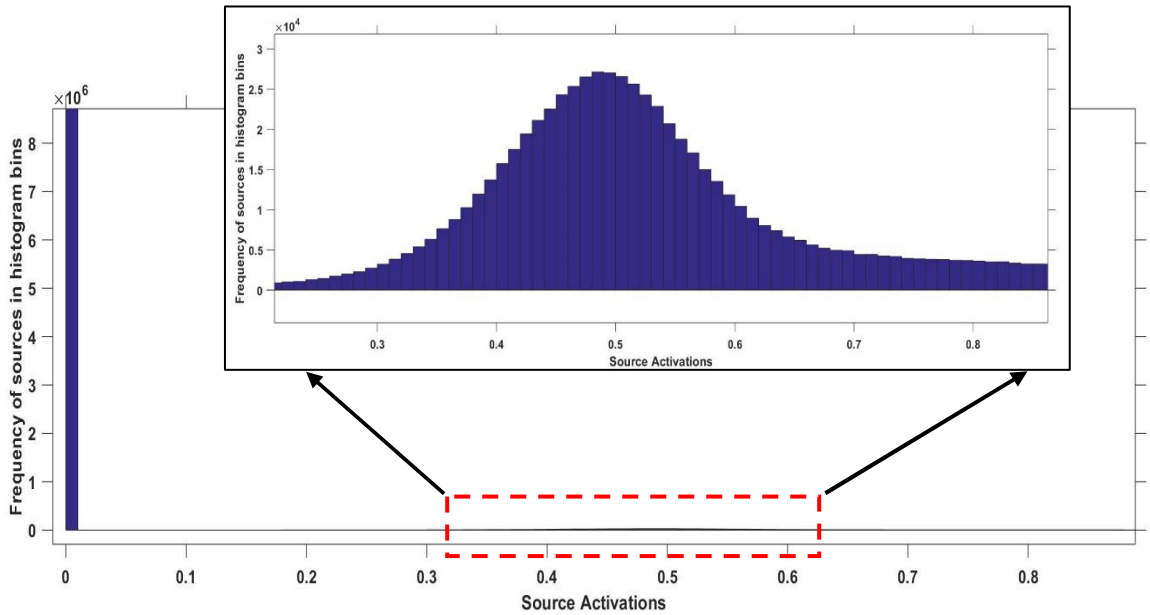

Figure 3: histogram for source activations shows Highly sparse or Zero inflated source space

Principal components analysis (PCA) (Pearson, 1901) (Harold Hotelling, 1933) (Ku, Storer, & Georgakis, 1995) is the most frequently used method in the literature for data cleaning and dimensionality reduction. PCA finds the direction of the largest variances as principal components and uses a linear transformation to model a latent space. However. it does not account for a large number of zero or null values in the data. Specialized statistical methods are needed to deal with zero-inflated data. Therefore, for the comparison of M/EEG rhythms in the reconstructed zero-inflated source spectra, we applied a novel method known as Zero-inflated factor analysis (ZIFA) (Pierson & Yau, 2015). It is an extension of probabilistic principal components analysis (PPCA) (Michael, E. Tipping & Christopher M. Bishop, 1999). The main idea is to reduce the dimensionality of data while considering the effect of zeros. It suggests that zeros in the data are generated by a separate process. Hence, it models zero and non-zero source activations independently. A Python-based software implementation and source codes are available online via an MIT License: https://github.com/epierson9/ZIFA. (Pierson & Yau, 2015).

ZIFA was applied for dimensionality reduction on highly sparse source space. Based on the variance explained by each factor, it was decided to retain only the first 40 factors as the dimensions of latent space and the rest were discarded (refer Figure 4).

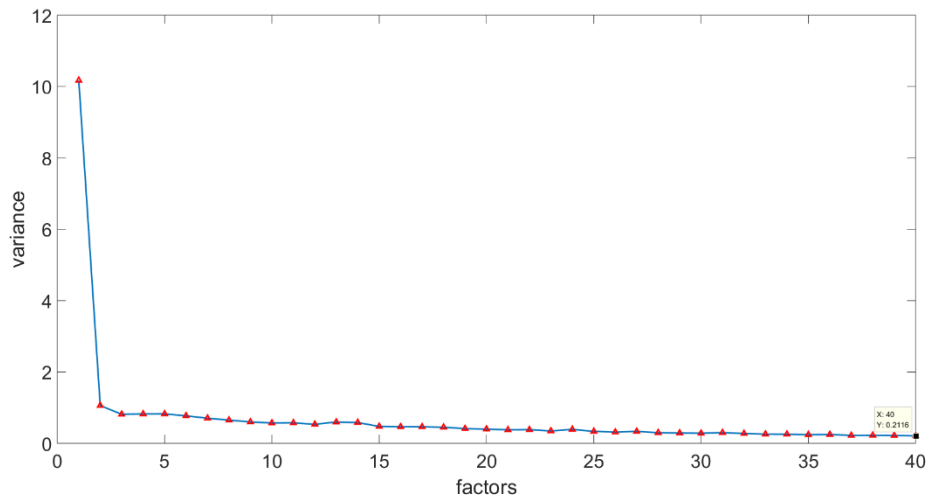

Figure 4: Explained variance of each factor obtained by ZIFA

2.7. Statistical Testing for Comparing Sources of M/EEG rhythmic activity

After the dimensionality reduction, we have applied two multivariate non-parametric statistical tests Hotelling's T-2 test and Minimum Energy Norm test, to identify the statistically significant difference in the ZIFA scores, generated by the sources of the rhythms in the two modalities.

3. Results

Applying BC-VARETA on the EEG and MEG time series, we have obtained the source activations for the M/EEG rhythms. As BC-VARETA maps activity and connectivity in the frequency domain. The results of BC-VARETA for each subject were source spectra for each voxel(6002) in 48

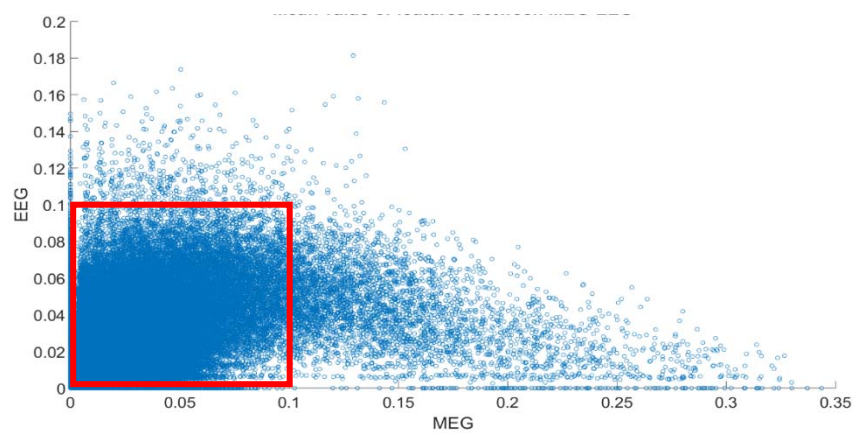

Figure 5:The mean value in each frequency bin resulting from BC_VARETA for MEG versus EEG

equispaced frequency bins between 0-19 Hz. Figure 5 shows the distribution of source activity of MEG and EEG after rescaling, the mean values of each frequency bin are plotted. It is

evident, that the range of mean MEG source activations has a larger spread than EEG. However, most of the mean values of both modalities are in the red squared region.

Later, Zero Inflated factor analysis (ZIFA) was applied for dimensionality reduction in highly sparse source activations. The results are shown in Figure 6. The histogram of ZIFA factors in latent space shows a normal distribution which is almost symmetrical around zero. Furthermore, ZIFA was also applied separately on frequency band-specific source spectra (i.e. delta: 0.7812 Hz to 3.9060 Hz, theta: 4.2966 Hz to 7.8120 Hz, alpha: 8.2026 Hz to 13.6710 Hz, beta: 14.0616 Hz to 18.7488 Hz).

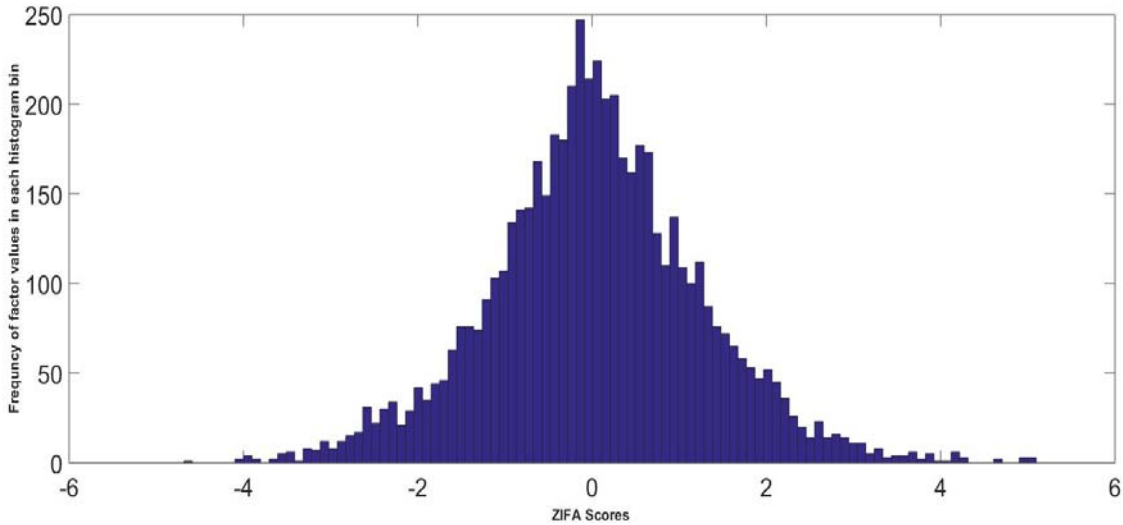

Figure 6: The histogram of factors from ZIFA

To answer the question about the generators/sources of EEG and MEG rhythms, that if these sources are essentially the same or different, the statistical tests were applied on the scores of ZIFA, to find out any significant differences in the two modalities. The results are shown in Table 1.

Test / Band	Energy statistical test		Hotelling's T-squared test	
	P-value	Energy statistic	P-value	Hotelling statistic
All bands	0.001	32.18	0	970
Delta band	0.001	25.44	9.56e-13	319
Theta band	0.001	35.13	2.35e-14	361
Alpha band	0.001	36	0	838
Beta band	0.001	39.23	0	1004

Table 1: Results of the T-2 test and Minimum Energy Test

With all frequency components (0 Hz to 19 Hz), the P-value of the energy test is 0.001 (less than 0.05) and Hotelling's test is 0 (less than 0.001). Furthermore, when each frequency band is compared separately, the results have shown that the P-values of energy test and Hotelling's test are all less than 0.001 (delta: 0.7812 Hz to 3.9060 Hz, theta: 4.2966 Hz to 7.8120 Hz, alpha: 8.2026 Hz to 13.6710 Hz, beta: 14.0616 Hz to 18.7488 Hz).

4. Discussion

The results have shown that the source of EEG and MEG rhythms are different when BC-VARETA was used as inverse methods. The comparison was done using the non-parametric multivariate statistical test. The mean distribution for sources of M/EEG rhythms for all the subjects is shown in Figure 7, where x-axis corresponds to (6002) sources in each frequency component. It clearly suggests that in the high-frequency bands, the values of MEG are much higher than EEG. Whereas. for the low-frequency bands, the values of MEG and EEG sources are similar.

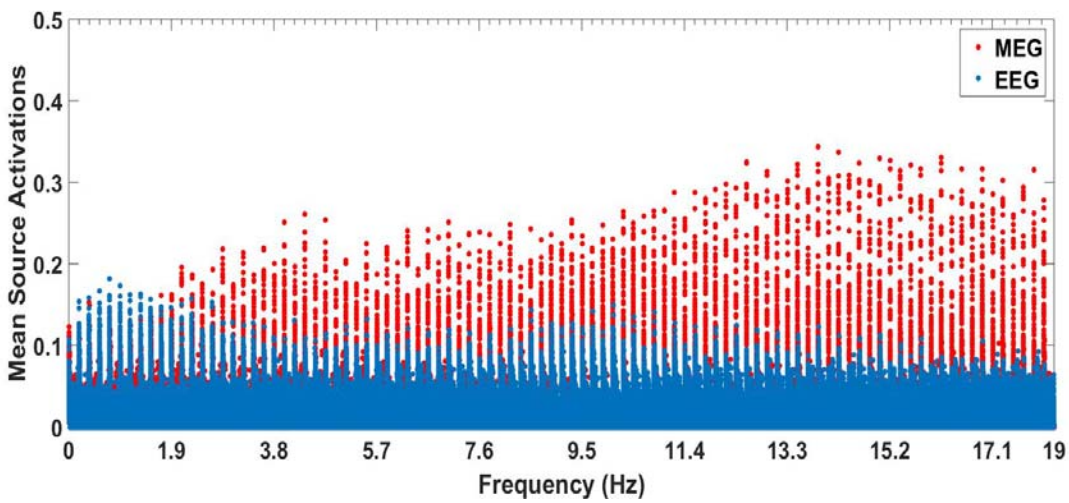

Figure 7: Mean value of each feature from the source activity of EEG and MEG for different frequencies (Hz)

However, the topographical map for the mean value of alpha band (Figure 8), shows that the activation region of EEG and MEG is almost the same, that is occipital area, except some activation in the frontal area of MEG. It is evident that the source activations of EEG and MEG rhythms are very similar. The previous studies in the literature, shows that there should be some similarities/overlap between sources of both modalities (Burgess, et al., 2005) (Hamalainen, Hari, Ilmoniemi, Knuutila, & Lounasmaa, 1993) (Stam, Breakspear, Van Cappellen van Walsum, & Van Dijk, 2003) (Nakasatp, et al., 1994) (Van Der Meij, et al., 2001) (Paul L. Nunez, 2019).

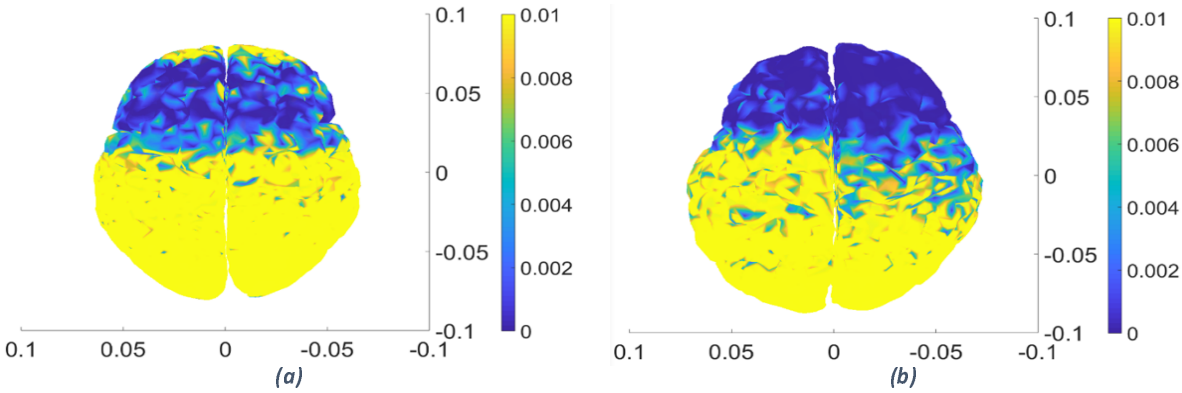

Figure 8: Topographical map for the mean source activations of the alpha band (a) EEG (b) MEG

The possible reasons for the P-value to be so small even though the topographical maps are quite similar can be due to the following factors. Firstly, the number of channels of EEG and MEG are different (58 channels in EEG while about 240 channels in MEG). This difference in channels can have some effect on the spectra of the scalp signals. Secondly, the EEG and MEG signals are from different subjects as well as the data is not simultaneously recorded for EEG and MEG. This can result in individual differences. Thirdly, the preprocessing steps were also different because the data is from different datasets and different systems. There are some preprocessing aspects that can create a difference or expand the difference, for example, the different filters of EEG (band-pass filter, 0.5-60 Hz) and MEG (high-pass and low-pass filtering (cutoff frequency 1.3 Hz and 150 Hz), notch filters (59-61 Hz and 119-121 Hz)). Furthermore, the MEG data from HCP was only recorded in the resting state with the eyes open while the EEG data from Cuban dataset was recorded in the resting state, but with alternate conditions of open and closed eyes. However, we have chosen only the eyes open condition from the original dataset. All these different aspects may have some influence on the results.

Nevertheless, our research and results have stated that the source spectra of M/EEG are statistically different, it agrees with the recent paper by Christian Benar at el. They provided some initial evidence that MEG and EEG differ in terms of background activity (C . G. Bénar, 2019) and this leads to further analysis on the understanding of the physiological mechanism and activation state of M/EEG.

5. Conclusion

To the best of our knowledge, this is the first study to perform a statistical comparison between the sources of EEG and MEG rhythms, with a large number of healthy subjects in resting state, using a novel inverse solution of BC-VARETA. Furthermore, to deal with highly sparse source spectra generated by BC-VARETA, a novel dimensionality reduction method

for sparse data named Zero Inflated Factor Analysis was applied before statistical testing. The P-values of Minimum Energy Norm test and Hotelling's T-squared test were both very small (less than 0.05), which means that the sources responsible for MEG and EEG rhythmic activity are significantly different. This is a very important finding however, to achieve transferal of results between two modalities, the requirement is to underpin the contributions of different instrumental, physical or physiological factors, which demands further investigation. The possible future directions are: Comparing sources of simultaneous EEG and MEG rhythms and their connectivity and checking if the differences persist when other inverse methods are used. Moreover, exploring the found differences to find out possible causes whether these are due to the biophysical nature of the brain or due to different hardware aspects involved in signal acquisition.

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8. Data availability statement

The dataset (EEG) from Cuban Brain Mapping Project for this study is available on request to Denys Buedo Hidalgo (buedo@neuroinformatics-collaboratory.org) or Iris Rodriguez (iris.rodriguez@neuroinformatics-collaboratory.org).

The dataset (MEG) from the Human Connectome Project for this study can be accessed on request at https://www.humanconnectome.org/ .

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