Adaptive Method for Bayesian EEG/MEG Source Localization to Support Treatment of Focal Epilepsy

Joonas Lahtinen[1], Alexandra Koulouri[1], Stefan Rampp[2], Jörg Wellmer[3,] Carsten Wolters[4], Sampsa Pursiainen[1]

1 Faculty of Information Technology and Communication Sciences, Tampere University, 33720 Tampere, Finland; 2 Department of Neurosurgery, University Hospital Halle (Saale), 06097 Halle, Germany; 3 Ruhr-Epileptology, Department of Neurology, University Hospital Knappschaftskrankenhaus, Ruhr-University, 44892 Bochum, Germany; 4 Institute for Biomagnetism and Biosignalanalysis, University of Münster, 48149 Münster, Germany.

Introduction

This study introduces a new method for the localization of the epileptogenic zone (EZ) in focal epilepsy, which builds upon the established success of standardized low-resolution brain electromagnetic tomography (sLORETA). By utilizing the resolution matrix of the lead field, sLORETA ensures a highly unbiased and accurate estimation of EZ even in the presence of measurement noise. The proposed methodology further improves the accuracy of sLORETA when combined with the Hierarchical Adaptive Lp Regression (HALpR) method, which relies on a conditionally exponential prior to simultaneously localize cortical and sub-cortical activity. The resulting method, referred to as Standardized Hierarchical Adaptive Lp Regression (SHALpR), has been shown to outperform its basic counterpart, Standardized Shrinking LORETA-FOCUSS (SSLOFO), and sLORETA in localizing brain activity. We demonstrate the potential of SHALpR in improving the diagnosis and treatment of focal epilepsy, as accurate localization of EZ is essential for successful surgical interventions. By providing a robust and accurate methodology for EZ localization, this study contributes to the ongoing efforts to advance the understanding and treatment of epilepsy.

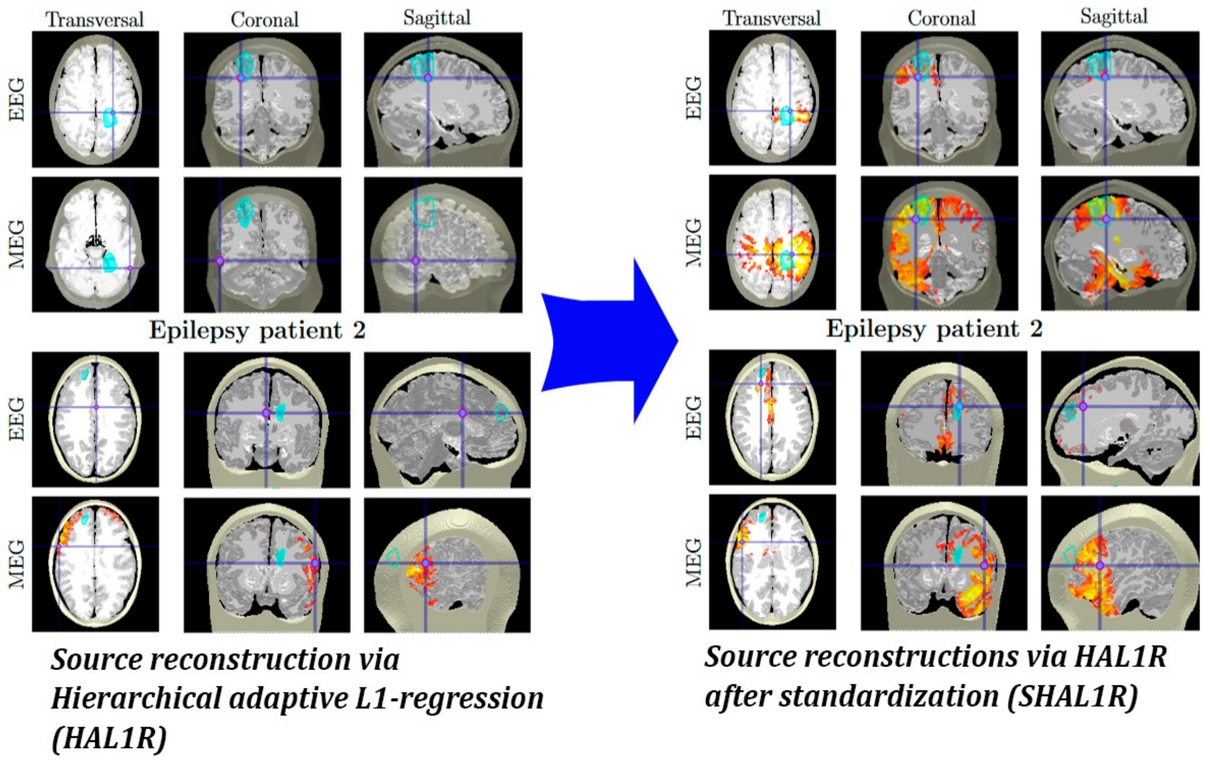

Fig 1: Reconstructed brain activity distributions for epilepsy patient 1.

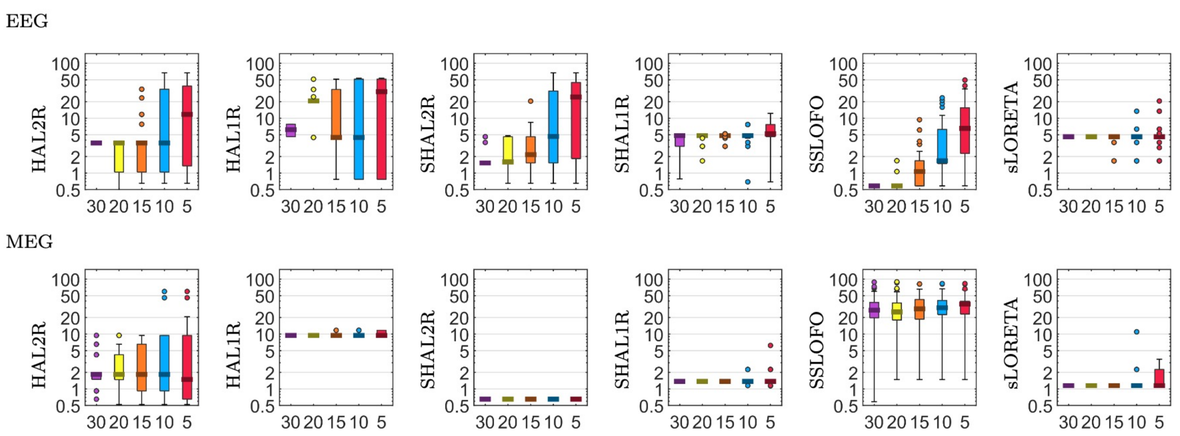

Fig 2: Source localization accuracy (y-axis) for numerically simulated data corresponding to (epilepsy patient 1) with varying signal-to-noise ratio (SNR) shown on x-axis.

Hierarchical Adaptive Lp Regularization (HALpR)

Formulation of an inverse method using a hierarchical Bayesian model (HBM) allows us to examine the brain activity distribution statistically and to explain the given prior assumptions in a probabilistic form as a prior distribution. This study contemplates the HBM with a Gaussian likelihood, conditionally exponential prior, and Gamma hyperprior, thus giving us the posterior

$$p(\mathbf{x},\boldsymbol{\gamma}\mid\mathbf{y})\propto\exp\left(-\frac{1}{2}\left(L\mathbf{x}-\mathbf{y}\right)^{T}C^{-1}\left(L\mathbf{x}-\mathbf{y}\right)\right)\times \exp\left(-\left\|\mathrm{Diag}(\boldsymbol{\gamma})^{1/q}\mathbf{x}\right\|_{q}^{q}\right)\mathrm{Ga}(\boldsymbol{\gamma},\kappa,\theta),$$

A reconstruction of the brain activity is obtained by evaluating the maximum a posteriori (MAP) estimate. In a case where q is not equal to 2 we face a mixed-norm minimization problem for which many algorithms have been developed. However, in fine resolution FEM modelling scheme, the dimension of the problem is high, and, therefore, the computational burden can often be too much. For that reason, we use fixed-point iterations with a Gaussian prior that approximates the exponential prior. In that way, we can obtain the reconstruction via linear mapping. The fixed-point iteration is continued until the duality gap reaches a certain tolerance.

Standardized HALpR (SHALpR)

To employ the standardization with HBM, we use an approach similar to SSLOFO, resulting in the following updated version of the Iterative Alternating Sequential iteration:

$$\gamma_i^{(k)}=\frac{\kappa+1/q-1}{\left|x_i^{(k)}\right|^{q}+\theta}\quad\text{for}\quad i=1,\ldots,n,$$

$$\mathbf{x}^{(k+1)}=\arg\min_{\mathbf{x}}\left\{\frac{1}{2}\left(L\mathbf{x}-\mathbf{y}\right)^{T}C^{-1}\left(L\mathbf{x}-\mathbf{y}\right)+\sum_{i=1}^{n}\gamma_i^{(k)}\left|x_i\right|^{q}\right\},$$

$$P^{(k)}=\frac{1}{2}\mathrm{Diag}\left(\left(\left|x_1^{(k+1)}\right|^{2-q}/\gamma_1^{(k)},\cdots,\left|x_n^{(k+1)}\right|^{2-q}/\gamma_n^{(k)}\right)\right),$$

$$R^{(k+1)}=P^{(k)}L^{T}\left(LP^{(k)}L^{T}+C\right)^{-1}L,$$

$$\mathbf{z}_I^{(k+1)}=\left(R_{II}^{(k+1)}\right)^{-1/2}\mathbf{x}_I^{(k+1)}.$$

Results & Discussion

Source localization results obtained for two epilepsy patients (results for patient 1 in Figs. 1 and 2) support the hypothesis that applying a focal solver yields to a greater localization accuracy than a solver providing a sparse and smooth but widespread distribution. The hypothesis is supported by the volumetrically small resection regions of studied patients. Moreover, when considering the numerical experiments, standardization seems to be the key to accurate and noise-tolerant estimates.

This finding is anticipated since sLORETA is known to be a reliable method for locating ES. In previously published studies, sLORETA has been found to localize 8 out of 9 epileptogenic zones [1], and was found to be equally accurate as connectivity measures to localize an epileptic source based on standard density EEG [2] and has provided consistent results in localizing the epileptic generators of four patients suffering from tuberous sclerosis complex [3]. The obtained localization accuracy of 1 cm can be considered useful in the planning of resection, e.g., to guide non-invasive, invasive epilepsy work-up, retrospective FLAIR-MRI and Zoomed-MRI, iEEG electrode positioning, or skull opening in neurosurgery [4,5].

In [6], the epileptic activity of the same two patients was reconstructed via dipoles scans, event-related, and averaged beamforming for a range of regularization parameters. Beamforming techniques have been shown to be able to localize the activity with zero localization error within a small interval of regularization values
However, the intervals varied between patients, and neither of the techniques had a clear advantage. The localization accuracy of averaged beamformer was around 10 mm and 5 mm with event-related beamforming. The dipole scan was able to localize the epileptic activity with around the same distance to the resection boundary as sLORETA and HAL1R in our study, but it failed with patient 2.
A broader conclusion about the usefulness of the focal standardized solver or standardization in general in localizing focal epilepsy cannot be drawn with this trial data. The sample sizes or difficulty of the patient cases is not enough to draw conclusions of the superiority between SHAL1R and sLORETA. This study demonstrated the usefulness of the standardization technique in improving the localization and suppressing the susceptibility to interference caused by measurement noise. The results suggest that the epileptic source can be localized accurately by using a standardized distributed method. In such a case, the accuracy and features of the estimations depend on the used prior model.

The original standardized method, sLORETA, is already meritorious, but the case-wise consistency and the resolution of the reconstruction could be improved by using the Laplace prior.
For further investigation, we could apply standardization for an inversion technique with richer structures, e.g., taking the temporal aspect of biopotential signals into account.

Ethical Statement

The study was conducted according to the guidelines of the Declaration of Helsinki. Both subjects of this study have given informed consent.

References

[1] Rui Li, et al., Interictal spike localization for epilepsy surgery using magnetoencephalography beamforming. *Clinical neurophysiology,* 132(4):928–937, 2021.
[2] Ana Coito, et al., Interictal epileptogenic zone localization in patients with focal epilepsy using electric source imaging and directed functional connectivity from low-density EEG. *Epilepsia open*, 4(2):281–292, 2019.
[3] Alberto J.R Leal, et al., Analysis of the dynamics and origin of epileptic activity in patients with tuberous sclerosis evaluated for surgery of epilepsy. *Clinical neurophysiology*, 119(4):853–861, 2008.
[4] Catherine J Riney, ett al., Voxel based morphometry of flair MRI in children with intractable focal epilepsy: Implications for surgical intervention. *European journal of radiology*, 81(6):1299–1305, 2012.
[5] U. Aydin, et al., Zoomed mri guided by combined EEG/MEG source analysis: A multimodal approach for optimizing presurgical epilepsy work-up and its application in a multi-focal epilepsy patient case study. *Brain topography*, 30(4):417–433, 2017.
[6] Frank Neugebauer, et al., Validating EEG, MEG and combined MEG and EEG beamforming for an estimation of the epileptogenic zone in focal cortical dysplasia. *Brain sciences*, 12(1):114–, 2022.