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High-resolution EEG source imaging of one-year-old children

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Abstract

Recently we described an iterative skull conductivity and source location estimation (SCALE) algorithm for simultaneously estimating head tissue conductivities and brain source locations. SCALE uses a realistic FEM forward problem head model and scalp maps of 10 or more near-dipolar sources identified by independent component analysis (ICA) decomposition of sufficient high-density EEG data. In this study, we applied SCALE to 20 minutes of 64-channel EEG data and magnetic resonance (MR) head images from four twelve-months-of-age infants. For each child, we selected 15–16 near-dipolar independent components from multiple-model adaptive mixture ICA (AMICA) decomposition of their EEG data. SCALE converged to brain-to-skull conductivity ratio (BSCR) estimates in the 10–12 range and mostly compact gyral or sulcal cortical distributions for the IC sources.

I. Introduction

Electroencephalography (EEG) is the most widely used neurophysiological technique for imaging the development of functional brain activity in infants and children because of its non-invasive nature, precise temporal resolution, low cost, and relative ease of use. However, understanding and visualizing the spatiotemporal dynamics of the underlying electrical brain sources that produce the recorded scalp EEG data is challenging. In particular, accurate localization of active cortical source areas requires precise electrical forward modeling of the flow of electrical currents through head tissues. During the first year of life the infant head undergoes notable structural changes in a maturational process that continues for at least 18 years. During development, both the geometry and the conductivity of the principal head tissues (skin, skull, cerebrospinal fluid (CSF), grey matter, white matter) change continuously, and must be accurately modeled to perform precise EEG source localization [1].

It is challenging to analyze infant brain magnetic resonance (MR) images given smaller head size and lower imaging contrast of developing head tissues. We have built and released a Neuroelectromagnetic Forward Head Modeling Toolbox (NFT) to generate realistic individual head models and to solve the forward problem of EEG source localization for adult heads [2]. Here, we modified NFT segmentation routines to properly segment the T1-weighted MRI images of four twelve-months-old children. Once the head tissues are segmented, the next step is to convert geometrical information obtained by image segmentation into a numerical form, producing a set of forward model boundary meshes). The most common types of numerical models use the Boundary Element Method (BEM),

Finite Element Method (FEM), and Finite Difference Method (FDM) [3], [2]. NFT has tools for both BEM and FEM mesh generation. After generating a head mesh, the electrical forward problem can then be solved using NFT solvers.

Another important consideration EEG source localization for young children is correctly modeling head tissue conductivities, in particular the conductivity of the skull. While studies involving direct conductivity measurements have reported consistent conductivity values for scalp, brain, and CSF, skull and therefore brain-to-skull conductivity ratio (BSCR), values reported in the literature have varied between 8 and 80 in adults [4]. This variance in skull conductivity is even more dramatic in infants and young children because in them the skull is undergoing significant development from a soft and relatively wet (unossified) skull matrix to a hard and relatively dry (ossified) adult skull [5].

Our simulations showed that mis-estimating brain-to-skull conductivity ratio in adults (e.g., using an assumed value of 80:1 instead of the simulated and more modern adult value, 25:1) may cause EEG source localization errors larger than 2 cm, in particular for sources in cortical areas close to the skull surface [1]. In developmental studies, currently the most widely used tool for EEG source localization is BESA (Brain Electrical Source Analysis) software (www.besa.de) [6]. BESA provides generic age-based conductivity estimates using an exponential spline fit for children older than 3. We have previously proposed a skull conductivity estimation method using an iterative gradient-based approach, “Simultaneous tissue Conductivity And source Location Estimation” (SCALE) [7]. SCALE estimates head tissue conductivities and electrical brain source locations using a realistically shaped FEM head model and 10–30 near-dipolar sources found by ICA decomposition of sufficiently high-density EEG data. In a first test, we applied SCALE to EEG source data from two young adults. Initialized with either BSCR 80 or 25, SCALE gave BSCR estimates of 34 and 54. Here, we present results of SCALE head modeling for young children, including estimation of skull conductivity and cortical EEG source localization using EEG data from an auditory task collected from four infants. The next section describes the head modeling procedure and its results; Sections IV and V describes the skull conductivity estimation and cortical source localization.

II. Methods

III. Head modeling of one-year olds

We created realistic head models for four twelve-months-of-age subjects from available whole head MR images acquired at Rutgers University (Newark NY). T1-weighted 3-D SPGR images were collected on a GE 1.5-T Echospeed MRI scanner using a standard head coil and with the following parameters: field of view = 25 cm, TR/TE = 24/10 ms, flip angle = 30°, matrix size = 256 192, slice thickness = 1.5 mm, number of slices = 124, sagittal orientation, and bandwidth = 15.63 kHz [8], [6].

We used the NFT toolbox [2] to generate individualized realistic head models from the data (MRI plus electrode locations) and to compute numerical solutions to the forward problem of electromagnetic source imaging. NFT segmented scalp, skull, CSF, and brain tissues, thereby generating a 4-layer head model. We needed to modify NFT to allow it to generate

models for babies six-months of age and older. Before the NFT segmentation, the MR images were processed using Freesurfer (freesurfer.org) to correct inhomogeneities. NFT generated non-intersecting tissue layers for mesh generation. Normally this requires the minimum thickness to be 2 mm. Since in infants tissue layers can be thinner than in adult data, we interpolated the MR data slices to produce a voxel size of $0.5 \times 0.5 \times 0.5$ mm, then performed tissue segmentation and mesh generation using the interpolated data using adult parameters. Following BEM mesh generation, we halved the coordinates to bring the head model back to its original size. After generating a FEM mesh, for each subject, we also generated a high-resolution cortical surface source space of 80,000 voxels and computed equivalent current dipoles (ECD) for each voxel oriented normal to the cortical mesh using Freesurfer routines. Segmentation results for scalp, skull, CSF, and brain tissues obtained by NFT, and a cortical source space are shown in Figure 1.

IV. SCALE: Simultaneous tissue Conductivity And source Location Estimation

Our recently developed SCALE approach allows estimation of skull conductivity using an iterative approach while also estimating the locations of brain EEG sources whose projections to the scalp (scalp maps) are used in the estimation [7]. For each subject, SCALE uses a FEM head model constructed from their MR head image and 10–30 near-dipolar scalp maps found by ICA decomposition of their high-density EEG data. The EEG data used for SCALE can be collected in any experimental paradigm, if it can be decomposed into a sufficient number of EEG source processes that can be well represented as the projection of a single cortical-patch. We used decomposition of the continuous EEG data by adaptive mixture ICA (AMICA) for this purpose [9].

The SCALE algorithm iteratively improves the source and conductivity estimates; it can be summarized as follows [7]:

1. Generate a FEM mesh and select a starting conductivity distribution: σ_0 .
2. For each iteration $i = 0, 1, 2, \dots$,
 - a. Calculate the FEM model at conductivity σ_i .
 - b. For each IC $j = 1, 2, \dots, P$
 - i. Estimate source distribution s_j for IC_j .
 - ii. Compute estimated potentials Φ_j for s_j at σ_i .
 - iii. Calculate the sensitivity matrix, S_j .
 - iv. Find the change in conductivity distribution σ_j that maximizes the goodness of fit for IC_j .
 - c. Compute σ_{i+1} as a weighted sum of σ_j .
 - d. Update conductivity: $\sigma_{i+1} = \sigma_i + \sigma_j$.
3. Stop if $\sigma - \varepsilon$.

Note that each iteration requires generation of a new FEM model with new conductivity parameters. As this is computationally expensive, we linearize the forward problem around σ_i by computing a sensitivity matrix relating changes in scalp potentials to changes in tissue (here, skull) conductivity [3]. This avoids generation of additional head models that would be required by global optimization schemes applied to the search for the skull conductivity value that minimizes the error in representing each independent component (IC) source entered into the analysis as a single, compact cortical patch in the model source space. SCALE estimated skull conductivity for each IC. In each iteration conductivity update was then a weighted sum of these estimates. SCALE combines both residual error of the source projection to the scalp and the compactness of the estimated source patch in its goodness-of-fit measure.

V. SCALE for 1-year old data

Successful EEG source localization requires a numerical FEM or BEM model of the subject's head that accurately represents its geometry and electrical properties, a ("source space") model of allowable cortical source locations, and an inverse source localization method. The electrical head model comprises geometric information about the main head tissues and their relative conductivities. As skull conductivity changes dramatically in the first years of life, estimating skull conductivity is a major determinant of the accuracy of EEG source localization in young children.

A few published developmental studies have used the BESA software package (BESA GmbH) for infant EEG source localization. To apply source localization in infants, Benasich and colleagues used age-appropriate brain templates for 6-month-old infants in BESA Research Version 5.3, and estimated skull conductivity by fitting an exponential function to the few estimates available in the literature [8]. Here, individual BSCR estimates were not available, though simulations show that, if accurate, they could increase accuracy of source localization.

The EEG data were collected at the Infancy Studies Laboratory at Rutgers University, Newark under the supervision of author Benasich [8], [10]. The EEG data (20 min, 62 scalp channels, 250-Hz sampling rate) were collected using a EGI system during an auditory task (for further details, see [8], [11]). For each subject, after high-pass filtering the continuous EEG data above 1 Hz we removed non-brain artifact by initial likelihood-based rejection of aberrant time points (5%–10% of the data) [7]. We then applied multiple-model AMICA decomposition [12] using 1, 2, 3, and 4 models, and selected near-dipolar ICs from all decompositions and models for use in SCALE. For each subject, the scalp maps of the selected ICs were not correlated with any other above 95%. In cases when near-duplicate ICs were available in the various models, we used the IC with the most dipolar scalp map (e.g., the lowest residual variance after removing the best-fitting source-space equivalent dipole). By this means we obtained for each subject 28–29 IC scalp maps from the four AMICA decompositions. We then selected 15–16 ICs from these sets of ICs for which the equivalent dipoles were widely distributed. Figure 2 shows the ICs for the first infant (S1) that we selected to use for SCALE. Table I gives the number of ICs for each infant and the SCALE-derived BSCR values. Figure 4 shows some SCALE-generated source distributions.

For infant S1, we tested the consistency of equivalent dipole source localization when a BSCR other than the SCALE-estimated BSCR (9.8) was used to construct the lead field matrix. To do this, we performed equivalent dipole source localization for the 16 ICs for S1 using forward models assuming BSCR values of 3.3, 4.1, 6.3, 8.5, 11, 15, 20, 25, and 30. Figure 3 shows the minimum, maximum, and average localization errors over the 16 ICs. Results demonstrate that a skull conductivity error of only 5.2 mS/m (here, the difference between BSCR = 9.8 and BSCR = 8.5) can produce dipole source localization differences of up to 7.2 mm. This result is consistent with previous adult simulations [1] showing that skull conductivity estimation is a sensitive parameter that strongly affects the accuracy of EEG source localization.

VI. CONCLUSIONS AND FUTURE WORK

Here we have presented a high-resolution “source localization and skull conductivity estimation” (SCALE) approach to source-resolved imaging of EEG activity in 12-months-of-age infants. SCALE estimates conductivity while simultaneously improving the compactness and stability of estimated EEG source distributions for a set of supplied near-dipolar IC effective source processes. SCALE, applied to EEG and MRI data acquired from four one-year-old infants, found brain-to-skull conductivity ratio (BSCR) estimates in the range 9.8–12.1. The inter-individual variation here likely reflects maturational differences in bone density, electrolyte content, and/or the thickness ratio of spongiform layer to compacta layer, since all are known to affect skull conductivity [7]. The spatial distribution of brain sources may also impact the overall skull conductivity estimates returned by SCALE. Although here we estimated a single mean conductivity value for each head, it is important to note that skull conductivity is in fact not uniform across its surface [13]. This is especially true in infants, as total closure of the anterior fontanel does not occur until about two years-of-age [14].

Because of the practical difficulty of obtaining good EEG data from infants, digitized electrode locations were not available in this study. Instead, we used template electrode locations for the EGI montage and shifted, rotated, and scaled the locations to fit each head. Although the effect of non-uniform electrode co-registration error may be small [15], a uniform shift in the recorded electrode positions produces source localization errors on the order of the shift magnitude [1]. To minimize such shifts, we used a photograph of each infant wearing the electrode cap to visually verify the co-registration of the template electrodes to the infant head model. If the 3-D digitized electrode locations had been available, the source distributions found by SCALE might be more compact and the concomitant skull conductivity estimate more exact.

In this study, we used 15–16 independent components (ICs) for SCALE source localization. To test the optimum number of IC maps to use in SCALE, we have performed SCALE simulation studies using 20, 15, 10, and 5 simulated scalp maps, modeling the skull as a uniform conductivity layer. In all these (noise-free) simulations SCALE was able to estimate skull conductivity correctly. However, when we used fewer IC maps SCALE required more iterations to converge. In real heads, however, skull conductivity is not homogeneous. Accordingly, if the brain ICs used for SCALE are predominantly oriented toward one skull

region, then the skull conductivity estimated using these ICs should predominantly reflect skull conductivity in that region. We explored this in a previous study using an adult head by performing 4 simulations using 8 IC maps randomly selected from 13 available components [7]. Two of the simulations converged to the same BSCR value (34) as when all 13 ICs were used. However, others converged to BSCR values of 25, and 41. Using 18 and 22 ICs for this subject, SCALE again returned a BSCR of 34. The results are compatible with the hypothesis that so long as the ICs entered into SCALE are evenly distributed across the cortical surface, the skull conductivity estimate returned by SCALE will be consistent.

In the future, we plan to test the validity of SCALE using concurrently recorded data from modalities less sensitive to skull conductivity, e.g., from simultaneously recorded EEG and MEG, and EEG and ECoG data. We also plan to combine and compare SCALE results for EEG data sets recorded in the same individuals in separate sessions. The goal will be to further test and optimize the accuracy of the SCALE approach and its robustness across experimental sessions and paradigms. Successful validation and refinement of the SCALE approach could make EEG a portable, well tolerated, low cost modality for monitoring locally-coherent field activity in accurately localized cm^2 -scale cortical effective source areas with a time resolution on the time scale of thought and action.

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References

1. Akalin Acar Z, Makeig S. Effects of forward model errors on EEG source localization. *Brain Topography*. 2013; 26:378–396. [PubMed: 23355112]
2. Akalin Acar Z, Makeig. Neuroelectromagnetic forward head modeling toolbox. *J. of Neuroscience Methods*. 2010; 190
3. Gençer NG, Acar CE. Sensitivity of EEG and MEG measurements to tissue conductivity. *Physics in Med. and Biol.* 2004; 49:701–717.
4. Hoekema R, Wieneke G, Leijten F, van Veelen C, van Rijen P, Huiskamp G, Ansems J, van Huffelen A. Measurement of the conductivity of skull, temporarily removed during epilepsy surgery. *Brain Topography*. 2003; 16(1):29–38. [PubMed: 14587967]
5. Silau A. Normal prenatal development of the human parietal bone and interparietal suture. *J. Craniofac. Genet. Dev. Biol.* 1995; 15
6. Ortiz-Mantilla S, Hamalainen J, Benasich A. Time course of ERP generators to syllables in infants: A source localization study using age-appropriate brain templates. *Neuroimage*. 2012; 59:3275–3287. [PubMed: 22155379]
7. Akalin Acar Z, Acar C, Makeig S. Simultaneous head tissue conductivity and EEG source location estimation. *NeuroImage*. 2016; 124(Part A):168–180. [PubMed: 26302675]
8. Hämäläinen M, Ortiz-Mantilla S, Benasich A. Source localization of event-related potentials to pitch change mapped onto age-appropriate MRIs at 6 months of age. *NeuroImage*. 2011; 54
9. Delorme A, Palmer J, Oostenveld R, Makeig S. Independent EEG sources are dipolar. *PLOS One*. 2012
10. Choudhury N, Benasich A. Maturation of auditory evoked potentials from 6 to 48 months: Prediction to 3 and 4 year language and cognitive abilities. *Clin. Neurophysiol.* 2011; 122

11. Benasich A, Choudhury N, Friedman J, Realpe-Bonilla T, Chojnowska C, Gou Z. The infant as a prelinguistic model for language learning impairments: Predicting from event-related potentials to behavior. *Neuropsychologia*. 2006; 44:396–411. [PubMed: 16054661]
12. Palmer, JA., Kreutz-Delgado, K., Rao, BD., Makeig, S. Modeling and estimation of dependent subspaces; *Proc of the 7th Int Conf on ICA and Signal Separation*; 2007.
13. Law S. Thickness and resistivity variations over the upper surface of the human skull. *Brain Topography*. 1993; 6:99–109. [PubMed: 8123431]
14. Duc G, Largo R. Anterior fontanel: size and closure in term and preterm infants. *Pediatrics*. 1986; 78:904–908. [PubMed: 3763303]
15. Wang Y, Gotman J. The influence of electrode location errors on EEG dipole source localization with a realistic head model. *Clin. Neurophysiol*. 2001; 112:1777–1780. [PubMed: 11514261]

Fig. 1.

Scalp, skull, CSF, and brain surfaces for a 12-month-old infant including 64 co-registered scalp electrode locations, plus the high-resolution cortical source space.

Fig. 2.
Scalp maps of the 16 near-dipolar brain-based independent component (IC) processes used in SCALE for infant S1.

Fig. 3. Minimum, maximum and average dipole source localization differences (in mm) for 16 IC scalp maps (see Fig. 2) using forward models assuming BSCR values of 3.3, 4.1, 6.3, 8.5, 11, 15, 20, 25, and 30 instead of the SCALE-estimated 9.8 •.

Fig. 4. Selected scalp maps and SCALE-generated source distributions for infant S1 visualized on their Freesurfer-inflated cortical surface.

TABLE I

Number of ICs and BSCR values for the four infants.

	Number of near-dipolar ICs	number of selected ICs	BSCR
S1	35	16	9.8
S2	39	15	10.3
S3	30	15	12.1
S4	28	15	10.0