



Effects of sutures and fontanels on MEG and EEG source analysis in a realistic infant head model

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ABSTRACT

In infants, the fontanels and sutures as well as conductivity of the skull influence the volume currents accompanying primary currents generated by active neurons and thus the associated electroencephalography (EEG) and magnetoencephalography (MEG) signals. We used a finite element method (FEM) to construct a realistic model of the head of an infant based on MRI images. Using this model, we investigated the effects of the fontanels, sutures and skull conductivity on forward and inverse EEG and MEG source analysis. Simulation results show that MEG is better suited than EEG to study early brain development because it is much less sensitive than EEG to distortions of the volume current caused by the fontanels and sutures and to inaccurate estimates of skull conductivity. Best results will be achieved when MEG and EEG are used in combination.

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Introduction

We now have sophisticated approaches for estimating the location of active tissues in the brain and temporal course of activity at the source level in each active region on the basis of extracranial MEG and EEG measurements (Baillet et al., 2001; Dale and Sereno, 1993; Dale et al., 2000; Hämäläinen, 1995; Hämäläinen and Ilmoniemi, 1994; Lucka et al., 2012; Ou et al., 2009a; Uutela et al., 1998, 1999). Due to the ill-posed nature of the electromagnetic source estimation problem, each of these methods constrains the current sources using anatomical and physiological information and regularizes the solution to mitigate the effects of measurement noise. However, in all of these inverse approaches, a biophysical forward model is needed to relate the neural current sources to the MEG/EEG measurements. The overall task is then to search for the best estimates for the neural currents given the measurements of signals of interest, estimates of noise, selected source constraints, regularization, and the forward model. The accuracy of the solution, therefore, depends on an accurate forward model.

The required forward model accuracy can be achieved by using individual anatomical information based on MRI to define the actual

conductivity geometry of the head, combined with numerical solvers which allow the use of these data in the computation of the MEG/EEG forward solutions (Dale et al., 1999; Fischl et al., 1999a,b, 2001, 2002; Hämäläinen and Hari, 2002; Hämäläinen and Sarvas, 1987, 1989; Hämäläinen et al., 1993; Wolters et al., 2006, 2007a,b). The most advanced inverse models for interpreting MEG and EEG from the neo-cortex incorporate the exact geometry of the scalp, skull, CSF, and brain into the forward model and constrain the sources to lie in the gray matter, perpendicular to the cortical surface. It is furthermore possible to functionally constrain the inverse solutions by incorporating the map of active brain regions estimated from fMRI (Dale and Sereno, 1993; Dale et al., 2000; Ou et al., 2009b). These models have been used to identify multiple active regions in the brain, to estimate the time course of activity in each region, and to assess functional connectivity between the regions.

An accurate forward model is important for interpreting MEG/EEG signals not only from adults, but also from infants and children as the interest in human brain development continues to grow. Somatosensory activity at the early age has been investigated with ERP (EEG) methods (Karniski, 1992; Karniski et al., 1992; Taylor et al., 1996; Xiang et al., 2003). Infant language development has also been studied with ERPs (Buiatti et al., 2009; Cohen et al., 2000; Dehaene-Lambertz et al., 2006). MEG has become a new modality of studying infant brain activity in infant speech perception (Imada et al., 2006; Kujala et al., 2004), sensory perception during sleep (Kakigi et al., 2003), somatosensory development (Pihko et al., 2009), vision (Haddad et al., 2006), and auditory response as an immature brain marker (Wakai

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et al., 2007). MEG instruments optimized for the pediatric population are beginning to be developed (e.g. Okada et al., 2006).

The models for the newborns, infants and preschool children are not simple extensions of the models for adults because of the characteristic features of the human skull and brain during the early development. The cranial bones of the human skull are unfused and separated by fontanels and sutures for at least several months after full-term birth to accommodate birth and the growth of the brain. The fontanels are present at the midline junctions of the bregma and lambda. They are small during the delivery, but become larger in the first several months, up to even 3–4 cm along the coronal suture, and then eventually close. The unclosed sutures can be quite wide near the fontanels. The mean width of the coronal and lambdoidal sutures at their midpositions is 3–4 mm for infants between 0 and 60 days after birth (Erasmie and Ringertz, 1976). The sutures may not close for several years in healthy children (Hansman, 1966). In children with CNS pathology, there is a wide variation in size of the fontanels, width of the sutures, and thickness of the skull. In patients with craniostenosis (also called craniosynostosis), the cranial bones fuse prematurely. In the opposite extreme, for example in children with hydrocephalus, the width of the sutures may change during the development of the disease and become as wide as 10 mm or more (Erasmie and Ringertz, 1976). Recently, the effect of the fontanel on EEG source analysis was investigated using a three-compartment (the scalp, the skull, and the brain) volume-conductor model (Roche-Labarbe et al., 2008). The numerical solution was computed with the boundary element method (BEM). The fontanel was modeled with a thinner zone in the skull and it was found that the fontanel causes a dipole shift towards the modeled skull defect. Experimental studies show that holes in the skull, mimicking the fontanel, do not significantly affect MEG signals when they are small (Barth et al., 1986; Okada et al., 1999). However, the effect may depend on the size of the fontanel. The inverse solutions for MEG are only weakly affected by inaccurate modeling of these layers (Hämäläinen and Sarvas, 1987, 1988, 1989). However, we still do not have realistic head models of infants to assess the skull effect on MEG in human infants.

The conductivity of the skull also decreases and its thickness increases with age (Gibson et al., 2000). The thickness of the skull increases from 1 to 2 mm on the dorsal surface at term to several millimeters during the early adulthood (Hansman, 1966). The skull conductivity decreases as the external and internal hard layers become thicker and the more conductive middle layer becomes relatively thin with age. In adults the conductivity can be estimated with electrical impedance tomography (Goncalves et al., 2003). The measurements show a large variability in conductivity with a standard deviation of 48% of the mean. Therefore, it is likely that the skull conductivity is also highly variable in infants. Modeling studies have shown that the skull thickness and conductivity are quite important for correctly predicting EEG signals (Dannhauer et al., 2011; Hallez et al., 2005; Hämäläinen and Sarvas, 1987; Hämäläinen et al., 1993; Marin et al., 1998; Vallaghe and Clerc, 2009; van den Broek et al., 1998; Wolters et al., 2006). Distortion of EEG signals by a hole in the skull has been also demonstrated experimentally in the swine with a large brain (Flemming et al., 2005).

To the best of our knowledge, the effects of the infant skull on both MEG and EEG have not yet been investigated with identical realistic forward models. There are several advanced numerical methods to model the head of an infant, i.e., the finite difference method (FDM) (Hallez et al., 2005), the finite volume method (FVM) (Cook and Koles, 2006), and the finite element method (FEM) (Awada et al., 1997; Buchner et al., 1997; Lew et al., 2009; Marin et al., 1998; Thevenet et al., 1991; van den Broek et al., 1998; Wolters et al., 2007a,b). In this study, we used a high-resolution geometry-adapted five-compartment FEM model of the head of an infant, since it achieves high accuracies in multicompartiment head volume conductor modeling studies (Lew et al., 2009; Vorwerk, 2011; Wolters et al., 2007a,b).

Employing an isoparametric FEM in this geometry, the influences of the fontanels and sutures in the infant skull as well as its conductivity on the MEG and EEG source analysis were characterized using forward and inverse simulations.

Materials and methods

MRI acquisition

A female neonate with uneventful pre- and perinatal circumstances was imaged at 3 days of life on a Siemens Trio-Tim 1.5 T MRI scanner using a standard 8-channel head coil. T1 weighted MPRAGE images (Fig. 1a) were collected with the following parameters: Field of view = 200.000, TR/TE = 2530.00/3.39 ms, flip angle = 7.00°, matrix size = 200 × 200, slice thickness = 1.0 mm, number of slices = 176, and in sagittal orientation. The brain of the infant was found clinically normal by a pediatric neuroradiologist and the patient showed no persistent neurological symptoms upon discharge. In addition, a large subcutaneous fluid collection containing a small amount of blood product was observed at the vertex, most prominently in the left parietal region.

Segmentation

When the MRIs of neonates are processed, manual segmentation is usually employed because automated segmentation often cannot detect accurate structural borders in the neonatal brain due to incomplete myelination, low contrast, low signal to noise ratio, motion effects, etc. Therefore, we segmented the skull, scalp, cerebrospinal fluid, and gray and white matter manually in Freeview, a volume and surface visualization tool within the FreeSurfer software application (Dale et al., 1999). The segmentation was carried out in the coronal, axial, and sagittal planes concurrently, based on detailed neuroanatomical knowledge. The anterior fontanel was identified from a visible discontinuation of the skull in the coronal, sagittal, and axial planes. The accuracy of the segmentation was confirmed by expert review of every segmented image. Other fontanels were not easily identifiable, and were, therefore, not taken into account in the MRI based segmentation of the skull. Instead, the posterior fontanel, the sphenoidal fontanel, and the mastoid fontanel were segmented based on the knowledge of skull geometry from an infant skull atlas. In addition, the sagittal suture, the coronal suture, the lambdoidal suture, and the squamosal suture were also manually segmented based on the segmented fontanels and the atlas (Fig. 1b). The fontanels and sutures divide the skull into the frontal bone, the parietal bone, and the occipital bone (Fig. 1c).

As described above, it is, indeed, difficult to identify the fontanels in T1-weighted MRIs. We did our best to segment the anterior fontanel, which is the largest among the fontanels. All other fontanels and sutures were segmented based on an atlas because they were not clearly visible enough in the MR images. Thus, the fontanel and suture segmentation might not be exact, but this is not a critical issue in this study.

FEM mesh

A FEM volume conductor model was created based on the segmentation described above. A finite element hexahedral mesh with boundary nodes shifted was created from the segmented volume, including the fontanels and the sutures. The voxels could be used as hexahedral elements directly. However, in order to increase conformance to the real geometry and to mitigate the stair-case effects in a voxel-based mesh, Camacho et al. (1997) proposed a technique to shift nodes on material interfaces, resulting in smoother and more accurate boundaries. This approach was evaluated and validated for EEG source analysis in a multi-layer spherically symmetric conductor, where the errors reduced significantly compared to regular hexahedral approaches

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