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A Novel Framework for the Local Extraction of Extra-Axial Cerebrospinal Fluid from MR Brain Images

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Abstract

The quantification of cerebrospinal fluid (CSF) in the human brain has shown to play an important role in early postnatal brain developmental. Extr a-axial fluid (EA-CSF), which is characterized by the CSF in the subarachnoid space, is promising in the early detection of children at risk for neurodevelopmental disorders. Currently, though, there is no tool to extract local EA-CSF measurements in a way that is suitable for localized analysis. In this paper, we propose a novel framework for the localized, cortical surface based analysis of EA-CSF. In our proposed processing, we combine probabilistic brain tissue segmentation, cortical surface reconstruction as well as streamline based local EA-CSF quantification. For streamline computation, we employ the vector field generated by solving a Laplacian partial differential equation (PDE) between the cortical surface and the outer CSF hull. To achieve sub-voxel accuracy while minimizing numerical errors, fourth-order Runge-Kutta (RK4) integration was used to generate the streamlines. Finally, the local EA-CSF is computed by integrating the CSF probability along the generated streamlines. The proposed local EA-CSF extraction tool was used to study the early postnatal brain development in typically developing infants. The results show that the proposed localized EA-CSF extraction pipeline can produce statistically significant regions that are not observed in previous global approach.

Keywords

Cerebrospinal Fluid; Laplace Partial Differential Equation; Magnetic Resonance; and Brain Development

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1. INTRODUCTION

Produced by the brain, cerebrospinal fluid (CSF) is a clear, colorless fluid that circulates around the brain in the extra-axial space acting as a cushion or buffer for the brain, providing basic mechanical and immunological protection to the brain inside the skull. CSF also serves regulatory functions, including the distribution of growth factors critical to brain development. In addition, CSF circulation provides a means to filter solutes from the brain interstitium washing away waste particles that would otherwise build up. In fact, interruption of typical CSF circulation is shown to contribute to the development of many diseases, including neurodegenerative conditions such as Alzheimer's disease, ischemic and traumatic brain injury, and neuroinflammatory conditions such as multiple sclerosis.[1]

Extra-axial CSF (EA-CSF) is characterized by the cerebrospinal fluid in the subarachnoid space, particularly over the frontal lobes. EA-CSF enlargement is believed to provide an early sign that CSF is not filtering and draining when it should; which can provide an early biomarker detection of children at risk for neurodevelopmental disorders (e.g., autism spectrum disorder (ASD)). Shen et al.[2,3] indicated that the amount of EA-CSF detected as early as 6 months was predictive of more severe ASD symptoms at 24 month. A quantitative protocol was developed to objectively measure the volume of the total EA-CSF in each participants' magnetic resonance (MR) brain scan. Results indicate that the quantification of total EA-CSF could be key to characterizing the nature of the pathology and its relation to autism symptoms, particularly its more severe forms. The total EA-CSF measure though does not provide a localization of the effect. A more sophisticated, localized EA-CSF extraction would provide measurements suitable for localized group analysis or localized discriminative analysis. One way to extract local measurements is through voxel-based morphometry (VBM) analysis. VBM methods are usually computationally efficient as they do not involve surface reconstruction of complex surfaces. However, the accuracy and precision of the local VBM CSF measurements are limited by the voxel resolution, as well as are sensitive to volumetric registration errors, which are known to be abundantly present in most cortical areas due to the inherent cortical folding variability. In addition, such voxel-based measurements cannot be easily correlated with other surface-based measurements (e.g., cortical thickness), limiting our understanding of how these different biomarkers interact.

To overcome the limitations mentioned above, we propose a novel framework for extracting surface-based local EA-CSF measurements from MR brain images (Figure 1). The proposed framework relies on a standard tissue segmentation approach to generate a CSF probability map. This is followed by the reconstruction of the outer CSF hull surface as well as white matter (WM) and gray matter (GM) surfaces. A Laplacian partial differential equation (PDE) is solved between the WM and the CSF hull surfaces to generate a vector field that is used to create streamlines connecting the surfaces. Along these streamlines, the CSF space is sampled and CSF probability values are accumulated to generate local EA-CSF measures at each cortical vertex. To our knowledge, this is the first surface based method to quantify local extra-axial CSF measures.

2. METHOD

2.1 Data and Image Processing

We used images from 153 MRI scans from 51 typically developing subjects assessed at age 6, 12 and 24 months available as part of the IBIS (Infant Brain Imaging Study) network acquired at 4 different sites, each equipped with 3T Siemens Tim Trio scanners. The scan sessions included T1 weighted (160 slices with TR=2400ms, TE=3.16ms, flip angle=8, field of view 224 × 256, and identical head coils) and T2 weighted (160 slices with TR=3200ms, TE=499ms, flip angle=120, field of view 256 × 256) MR scans. All datasets possess the same spatial resolution of $1 \times 1 \times 1\text{mm}^3$.

All the image preprocessing was performed with an adapted version of the ”Constrained Laplacian-Based Automated Segmentation with Proximities (CLASP)” pipeline.[4,5] The cortical surface model consisted of 81,920 high-resolution triangle meshes (40,962 vertices) in each hemisphere, and the smoothed middle surface was obtained by averaging gray and white matter surfaces, followed by a single iteration of one-neighborhood averaging based surface smoothing. Cortical surface correspondence was established via spherical registration to an average surface template, which performs a sphere-to-sphere warping by matching crowns of gyri.[6] Tissue segmentation was performed using a population atlas based classification in AutoSeg,[7] and the outer CSF hull was generated by first dilating the intracranial mask followed by a surface reconstruction using standard marching cubes algorithm.

2.2 Local extraction of EA-CSF

Following the reconstruction of the inner (WM) and outer (CSF hull) surfaces, the next step of the proposed framework is to solve a Laplaces equation. Laplaces equation is a second-order partial differential equation solved for a scalar field $u(x)$ that can be written as the form of $\Delta u = \nabla^2 u(x) = 0$; where $u(x) = u_L$ for $x \in \Omega_{WM}$ and $u(x) = u_H$ for $x \in \Omega_{BG}$. Ω_{WM} and Ω_{BG} denote the WM-GM interface and the CSF hull-background interface respectively. The solution domain is bounded by the Dirichlet condition and the Neumann condition. The interface with the Dirichlet condition defines the inner and the outer surface where streamlines start and arrive, and yet the Neumann condition defines an open boundary that is parallel to streamlines. To ensure consistent boundary map generation, surface-based pre-processing steps are applied.[8]

The proposed streamlines are then constructed explicitly by integration of the Lagrangian vector field. To minimize local truncation error and provide faster convergence, a Runge-Kutta (RK) integration method is used to solve the PDE. Finally, to achieve sub-voxel accuracy, we process the starting and ending segments of the streamlines in order to fit them perfectly within the boundary of the defined inner and outer surfaces.

3. RESULTS

Figure 2 shows the mean local EA-CSF maps, averaged across all subjects, on the central brain surface at the 3 ages of 6 months, 12 months and 24 months. Vertex-wise heat kernel smoothing with FWHM of 20 mm was applied before computing the mean local EA-CSF.[9]

Overall the patterns at the three ages look quite similar. the highest levels of extracted local EA-CSF are observed in the medial and ventral temporal areas. Aside from that, wide sulcal fundus regions display the highest levels of local EA-CSF, whereas gyral saddle regions display lowest levels of local EA-CSF. As expected, local EA-CSF is larger in the central and precentral sulci, since the arachnoid granulations are located just above these cortical regions, so local EA-CSF may remain transiently elevated there before draining. This is consistent with our visual inspection of hundreds of 6-month MR infant brain images.

Figure 3 shows the mean local EA-CSF change between 6 and 12 months, while Figure 4 provides the mean local EA-CSF change in the 2nd year of life of a typically developing infant. Consistent with our previous global EA-CSF report,[3] we see a larger negative change in local EA-CSF from 6 to 12 months as compared to from 12 to 24 months. As shown in Figure 3 (c), several regions show statistically significant local EA-CSF changes ($p < 0.05$) including right posterior cingulate gyrus, right cuneus, right superior occipital gyrus, right middle occipital gyrus, left angular gyrus and left middle frontal gyrus. As indicated by Figure 4, fewer number of regions showed significantly significant ($p < 0.05$) differences between 12-months and 24-months including right inferior parietal, superior temporal gyrus, and right superior occipital gyrus.

4. CONCLUSIONS & FUTURE WORK

In this paper, we have described a novel framework for the local extraction of accurate local EA-CSF measurements along the brain cortex. To the best of our knowledge, the proposed framework is the first to address the problem of extracting local EA-CSF measurements in a way that is suitable for localized surface based analysis. The quantitative analysis of local EA-CSF was used to study the early postnatal brain development in typically developing infants. The stability of the proposed method is indicated by the consistency in local EA-CSF patterns across the 3 studied ages. We are in the process of computing human phantom based reliability measures of our method.

Currently, we are also applying the proposed method to a dataset of infants at high risk of developing autism spectrum disorder (ASD). This will enable us to study localized differences within the high-risk population associated with ASD, as well as differences between the low-risk and high-risk groups. In addition, we are investigating the use of local EA-CSF measurements combined with other cortical shape measurements (e.g., local surface complexity) in the early prediction of ASD using structural MR brain images.

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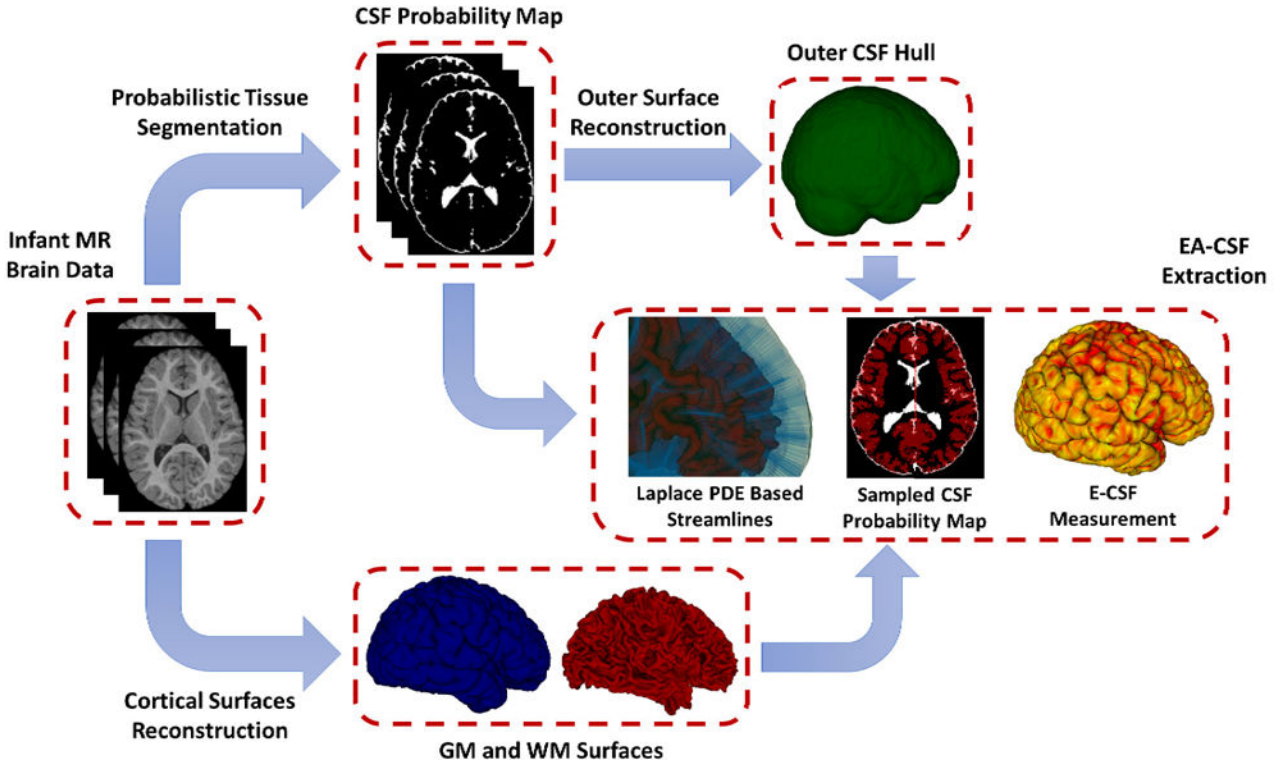
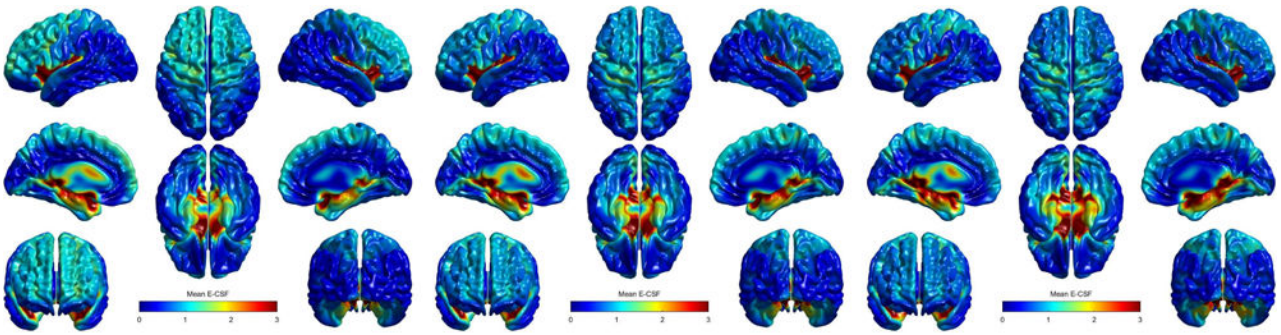
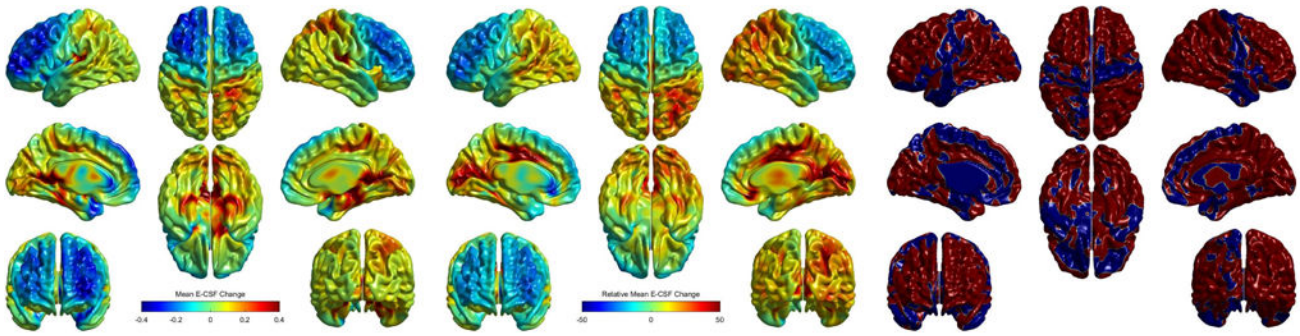


Figure 1.
The proposed framework for the local extraction of local EA-CSF.



(a) 6-Months (b) 12-Months (c) 24-Months

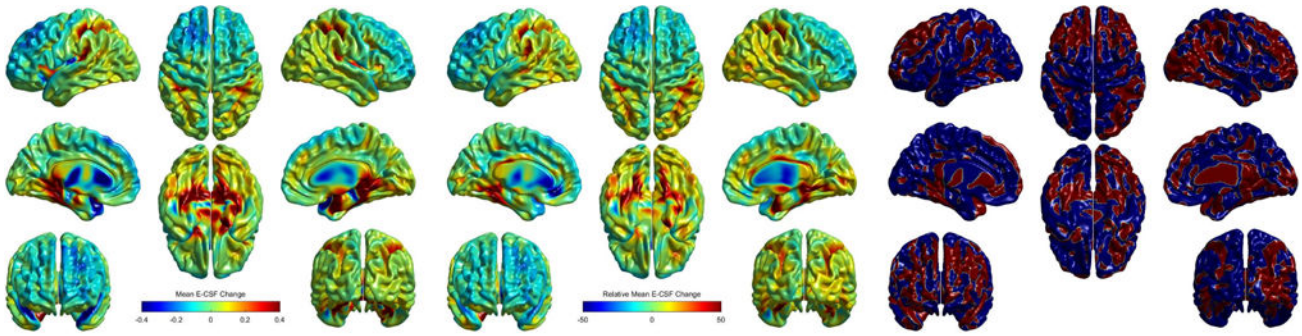
Figure 2.
Mean local EA-CSF measured over age.



(a) Local EA-CSF Change (b) Relative local EA-CSF Change (c) Significant local EA-CSF Change

Figure 3.

Mean local EA-CSF change between 6-months and 12-months MR brain images. Note that regions that show statistically significant differences are shown in red, while other regions are shown in blue.



(a) Local EA-CSF Change (b) Relative local EA-CSF Change (c) Significant local EA-CSF Change

Figure 4.

Mean local EA-CSF change between 12-months and 24-months infant MR brain images. Note that regions that show statistically significant differences are shown in red, while other regions are shown in blue.