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CONSTRUCTION OF 4D NEONATAL CORTICAL SURFACE ATLASES USING WASSERSTEIN DISTANCE

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Abstract

Spatiotemporal (4D) neonatal cortical surface atlases with densely sampled ages are important tools for understanding the dynamic early brain development. Conventionally, after non-linear co-registration, surface atlases were constructed by simple Euclidean average of cortical attributes across different subjects, which leads to blurred folding patterns and therefore hampers the reliability and accuracy when registering new subjects onto the atlases. To better preserve the sharpness and clarity of cortical folding patterns on surface atlases, we propose to compute the Wasserstein barycenter, which represents a geometrically faithful population mean under the Wasserstein distance metric, for the construction of 4D neonatal surface atlases. The Wasserstein distance considers two distributions as heaps of sand, and quantifies their distance as the least cost to move all sand particles from one distribution to reshape it into the other. In our case, comparing to the direct vertex-wise Euclidean average, the Wasserstein distance takes into account the alignment of spatial distribution of cortical attributes, thus is robust to potential registration errors during atlas building. Using this method, we constructed 4D neonatal cortical surface atlases at each week, from 39 to 44 postmenstrual weeks, based on a large-scale dataset with 764 subjects. Our 4D atlases show sharper and more geometrically faithful cortical folding patterns than the atlases built by the state-of-the-art method, thus leading to boosted accuracy for spatial normalization and facilitating early brain development studies.

Index Terms

Infant surface atlases; Wasserstein distance; cortical folding

1. INTRODUCTION

Early brain development is vital for later cognitive outcomes and critical for many neurodevelopmental disorders [1]. This emphasizes the importance of constructing neonatal cortical surface atlases for providing a common space that enables spatial normalization across different subjects or studies. Hill et al. [2] constructed the first neonatal cortical surface atlas i.e., PALS-term 12 atlas, by co-registering 12 term-born neonatal cortical surfaces based on manually delineated sulcal-gyral curves. Considering the rapid brain development during neonatal stages, Kim et al. [3] used 231 scans from 158 preterm-born neonates to construct a spatiotemporal cortical surface atlas with postmenstrual age from 26 to 40 weeks based on SURFTRACC framework. Bozek et al. [4] created a spatiotemporal cortical surface atlas at each week from 36 to 44 postmenstrual weeks, based on 270 subjects, by using the MSM registration [5] in each week group.

However, certain limitations are noticed in the abovementioned atlases. *First*, these studies used relatively small-size cohorts for building atlases, thus leading to possibly biased and less generalized results. *Second*, the resulted atlases showed blurry folding patterns, due to the potential co-registration error and independent vertex-wise averaging of different subjects, which will likely reduce the accuracy when registering new subjects to the atlases. To obtain more representative atlases with sharp folding patters, Wu et al. [6] proposed to use spherical patch-based sparse representation and a large-scale dataset with >700 neonates [7] for spatiotemporal surface atlases building. Although promising, this strategy still cannot preserve sharp cortical folding patterns in some regions with large inter-subject variability, e.g., the middle frontal cortex.

To address these limitations, in this paper, we propose to use the Wasserstein barycenter [8–10] defined under the framework of Wasserstein distance to build spatiotemporal (4D) surface atlases. The Wasserstein distance under the theory of optimal transport considers two distributions as heaps of sand, and quantifies their distance as the least cost to move all sand particles from one distribution to reshape it into the other. In our application, the Wasserstein distance can measure the distance between cortical folding attribute distributions from two subjects, according to the cost of their alignment. Therefore, the resulted Wasserstein barycenter represents a geometrically and physically more meaningful group mean of the cortical folding attribute distributions over a cohort of subjects, in comparison to the conventional Euclidean average (as shown in Fig. 1), thus making it meaningful for building surface atlases. Hence, this strategy has two major advantages: 1) it respects the folding pattern, thus resulting in sharp cortical folding; 2) it is robust to possible registration errors in atlas building. Accordingly, 4D surface atlases are built at each week from 39 to 44 postmenstrual weeks using 764 neonates. Compared to atlases built with the state-of-the-art method, our 4D atlases show sharper and more geometrically faithful folding patterns and therefore increase the accuracy of aligning new subject to the atlases.

2. DATASET AND IMAGE PROCESSING

T2-weighted brain MR images were acquired from 764 neonates from 39 to 44 postmenstrual weeks. The subject information is shown in Table 1. All images were processed using the UNC Infant Cortical Surface Pipeline [11], which included skull stripping, intensity inhomogeneity correction, cerebellum and brain stem removal, tissue segmentation, masking and filling non-cortical structures, and separation of left/right hemispheres. Then, topologically correct and geometrically accurate inner and outer cortical surfaces were reconstructed using a topology-preserving deformable surface method. Each inner cortical surface was mapped onto a sphere by minimizing geometric distortion [12].

After cortical surface reconstruction and spherical mapping, we aligned all cortical surfaces into the common space using the group-wise spherical demons registration method [13], based on cortical folding attributes. After registration, all spherical surfaces were resampled using the same mesh tessellation to establish the vertex-wise cortical correspondences. One intuitive way to construct a cortical surface atlas is to simply average cortical attributes over all cortical surfaces at each age. However, due to potential registration errors and substantial inter-subject variation of cortical folds, this simple Euclidean average generally leads to over-smoothed and less faithful cortical folding patterns, which will degrade the registration accuracy when aligning new subjects onto the atlases.

3. METHOD

We propose to build cortical surface atlases by computing the Wasserstein barycenter, which represents a geometrically faithful population mean under the Wasserstein distance metric. The Wasserstein distance considers two normalized distributions as heaps of sand, and quantifies their distance as the least cost to move all sand particles from one distribution to reshape it into the other. As the toy example in Fig. 1, where the blue and green curves denote cortical attributes (e.g., curvature) from two subjects, the red and black dashed curves shows the Wasserstein barycenter and the traditional Euclidean average. As we can see the Wasserstein barycenter is a geometrically and physically more meaningful average than the simple Euclidean average, thus making it particularly meaningful for building cortical surface atlases, even in the presence of the potential registration errors. Thus, the Wasserstein barycenter provides a population mean that is more representative and faithful of the cortical folding patterns.

To build an atlas, for any cortical vertex v, we compute the Wasserstein barycenter of cortical folding attributes (e.g., curvature) in corresponding spherical patches from N surfaces. Let $\mathcal{N}^v$ denote a spherical patch centered at v with totally d vertices. The spatial location of all vertices within $\mathcal{N}^v$ is encoded in a vector $\boldsymbol{x}^v$. We first extract the cortical folding attribute on $\boldsymbol{x}^v$ for each of the N co-registered surfaces, denoting as $\boldsymbol{b}_1^v, \ldots, \boldsymbol{b}_n^v, \ldots, \boldsymbol{b}_N^v$, where $\boldsymbol{b}_n^v$ describes the cortical attributes distribution within the patch $\mathcal{N}^v$ from the n-th subject. To satisfy the framework of Wasserstein distance, we need to normalize each attribute distribution $\boldsymbol{b}_n^v$ to $\overline{\boldsymbol{b}_n^v}$ such that $\left|\overline{\boldsymbol{b}_n^v}\right|_1 = 1$ and $\overline{\boldsymbol{b}_n^v} > 0$. This is accomplished by computing $\overline{\boldsymbol{b}_n^v} = \left(\boldsymbol{b}_n^v - b_{min}\right) / \left|\boldsymbol{b}_n^v - b_{min}\right|_1$, where b_{min} is the minimum value of this attribute across all subjects.

The Wasserstein barycenter $\overline{\boldsymbol{a}^v}$ is defined as the optimal distribution $\overline{\boldsymbol{a}^v}$ of patch $\mathcal{N}^v$, which has the minimal distance to each of distributions $\overline{\boldsymbol{b}_1^v}, \ldots, \overline{\boldsymbol{b}_N^v}$ under the Wasserstein distance metric $W(\cdot,\cdot)$, such that:

$$\overline{\boldsymbol{a}^v} \in \underset{\overline{\boldsymbol{a}^v} \in \Sigma_d}{\operatorname{argmin}} \sum_{n=1}^{N} \lambda_n W\left(\overline{\boldsymbol{a}^v}, \overline{\boldsymbol{b}_n^v}\right), \quad (1)$$

where λ_n is the weight of $W\left(\overline{\boldsymbol{a}^v}, \overline{\boldsymbol{b}_n^v}\right)$. In our case, we set each $\lambda_n = 1/N$ to equally consider each subject.

More precisely, the Wasserstein distance $W(\cdot,\cdot)$ measures the distance between any two normalized distributions $\overline{\boldsymbol{a}^v}, \overline{\boldsymbol{b}_n^v} \in \Sigma_d$, where $\Sigma_d \overset{\text{def}}{=} \left\{\boldsymbol{p} \in \mathbb{R}_+^d \mid \sum_{i=1}^d p_i = 1\right\}$, under the theory of optimal transport. $\mathbb{R}_+^d$ represents the non-negative d dimensional vector space, where d is the number of vertices within the patch. $W(\cdot,\cdot)$ thus represents the cost of the most cost-efficient rearrangement from $\overline{\boldsymbol{a}^v}$ to $\overline{\boldsymbol{b}_n^v}$, using a transportation matrix $\boldsymbol{T}^{\boldsymbol{v}}$ and its associated mass cost matrix $\boldsymbol{M}^{\boldsymbol{v}}$. However, computing the Wasserstein distance is essentially as a non-convex problem. To address this issue, we employ an entropy regularized Wasserstein distance to regularize this non-convex problem and to ensure a unique optimal solution [9].

Specifically, the entropy regularized Wasserstein distance between two distributions $\overline{\boldsymbol{a}^v}$ and $\overline{\boldsymbol{b}_n^v}$ is defined as

$$W\left(\overline{\boldsymbol{a}^v}, \overline{\boldsymbol{b}_n^v}\right) \overset{\text{def}}{=} \min_{\boldsymbol{T}^v \in \mathbb{R}_+^{d \times d}} \left\{\left\langle \boldsymbol{T}^v, \boldsymbol{M}^v \right\rangle + \gamma H(\boldsymbol{T}^v) \middle| \boldsymbol{T}^v \mathbf{1}_d = \overline{\boldsymbol{a}^v}, (\boldsymbol{T}^v)^{\mathcal{T}} \mathbf{1}_d = \overline{\boldsymbol{b}_n^v}\right\}. \quad (2)$$

Where the first term $\left\langle \boldsymbol{T}^v, \boldsymbol{M}^v \right\rangle = tr\left((\boldsymbol{T}^v)^{\mathcal{T}} \boldsymbol{M}^v\right)$ stands for the trace of the product of two matrices $\boldsymbol{T}^{\boldsymbol{v}}$ and $\boldsymbol{M}^{\boldsymbol{v}}$, with symbol $\mathcal{T}$ represents the matrix transposition. The second term is the entropic penalty weighted by $\gamma > 0$, and $H(\boldsymbol{T}^v) = \sum_{i,j} \boldsymbol{T}_{i,j}^v \log\left(\boldsymbol{T}_{i,j}^v\right)$ with the convention of $0 \log 0 = 0$. The nonnegative transportation matrix $\boldsymbol{T}^v \in \mathbb{R}_+^{d \times d}$ is with the constraint such that its row and column margins are respectively equal to $\overline{\boldsymbol{a}^v}$ and $\overline{\boldsymbol{b}_n^v}$. $\mathbf{1}_d$ refers to the all-one d dimensional vector. $\boldsymbol{M}^{\boldsymbol{v}}$ is a matrix denoting the cost of transporting between any two spatial locations. We define $\boldsymbol{M}^v(i,j) = \left\|\boldsymbol{x}^v(i) - \boldsymbol{x}^v(j)\right\|_2^2$ for any two vertices i and j.

As $\overline{\boldsymbol{b}_n^v}$ is the normalized distribution of $\boldsymbol{b}_n^v$, after obtaining their Wasserstein barycenter of $\overline{\boldsymbol{a}^v}$ for vertex $\boldsymbol{v}$, we need to recover the unscaled distribution $\boldsymbol{a}^{\boldsymbol{v}}$ from $\overline{\boldsymbol{a}^v}$. This is achieved by setting $\boldsymbol{a}^v = \left(\frac{1}{N}\sum_{n=1}^N \left|\boldsymbol{b}_n^v - b_{min}\right|_1\right) \cdot \overline{\boldsymbol{a}^v} + b_{min}$. Due to patch overlapping, each vertex is covered by multiple spherical patches. Therefore, the final cortical folding attribute at the vertex $\boldsymbol{v}$ is computed as the average of its estimated values on all associated patches.

In this way, although slight misalignments could probably present among $\boldsymbol{b}_1^v, \ldots, \boldsymbol{b}_N^v$ due to possible registration errors, the resulted Wasserstein barycenter still represents a meaningful group mean respecting the cortical folding patterns, thus leading to atlases with sharp and geometrically faithful cortical folding patterns. By using this method, for each week from 39 to 44 postmenstrual weeks, the neonatal cortical surface atlas is constructed using multiple cortical attributes, e.g., average convexity and mean curvature.

4. RESULTS

In all experiments, we used the following parameters for constructing 4D atlases. The parameter γ in Eq. (2) was set as $10/median(\boldsymbol{M})$ to make the problem strongly convex, where $median(\boldsymbol{M})$ is the median of all pairwise distances in $\boldsymbol{M}$. Each patch was defined as the 4-ring neighbors on the spherical surface mesh with 163,842 vertices.

Fig. 2 shows the constructed 4D neonatal cortical surface atlases with the color-coded average convexity and mean curvature at each week on both (a) spherical surfaces and (b) average inner surfaces. As can be seen, the cortex has a remarkable non-uniform development from 39 to 44 weeks, especially in the parietal region, zoomed for better inspection in (c). To show the effectiveness of our method, we first visually compared our results with the atlases generated using two other methods in Fig. 3. The first one (denoted as 'Average') is the simple Euclidean average, and the second one is the spherical patch-based sparse representation (denoted as 'Sparse') with the state-of-the-art performance [7]. By visually comparing the curvature pattern on these three atlases at 41 postmenstrual weeks, we can see that our atlas preserves the sharpest folding patterns.

In addition, we quantitatively assessed the 4D atlases constructed by different methods. Specifically, we randomly separated the subjects at each week into two groups: one group (with 2/3 subjects) for constructing atlases, and the other group (with 1/3 subjects) for testing. Then, we aligned the cortical surfaces in the testing group onto the constructed atlases. Since there is no ground truth for the cortical surface registration, we assessed the sharpness and clarity of the folding patterns as in [14], where atlases with sharper folding patterns are expected to lead to better registration accuracy. Specifically, for any two subjects in the testing dataset, after registering them onto the same atlas, we computed the correlation coefficient of their average convexity maps. Then, for all possible pairs of subjects we obtained the average correlation coefficient. Larger correlation coefficients indicate better alignment of the cortical folding patterns. Fig. 4 shows the average correlation coefficient and its standard deviation after aligning the testing subjects onto the average atlases, sparse atlases and our OT averaging atlases. Our atlases lead to the best registration accuracy, indicating that our atlases have sharper and more meaningful cortical folding patterns compared to the other two sets of atlases.

5. CONCLUSION

In this paper, we proposed a spherical patch-based optimal transport averaging method to construct 4D neonatal cortical surface atlases from 39 to 44 postmenstrual weeks, based on a large cohort of neonates with 764 subjects, thus better characterizing the dynamic cortical development during early postnatal weeks. Benefit from the consideration of geometric information of cortical attribute distributions, our constructed 4D atlases better preserve sharp cortical folding than the state-of-the-art method, thus leading to better performance for spatial normalization of subjects. These 4D neonatal cortical surface atlases will be released to the public to facilitate early brain development studies.

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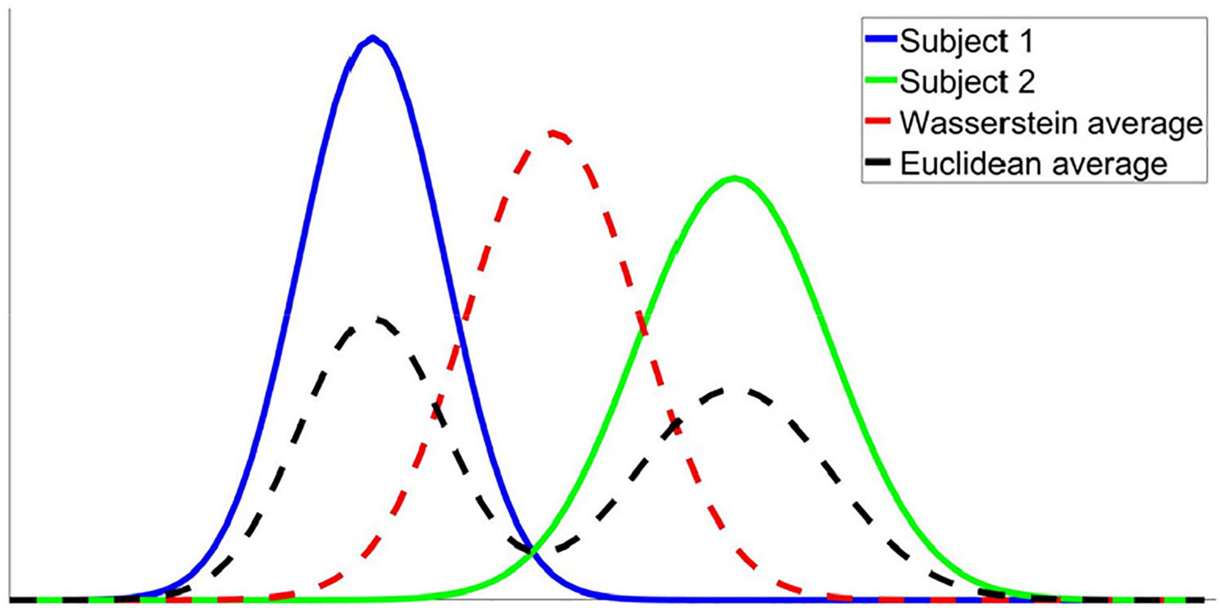

Fig. 1.
Illustration of the Wasserstein average and the traditional Euclidean average of cortical attributes (e.g., curvature) from two subjects.

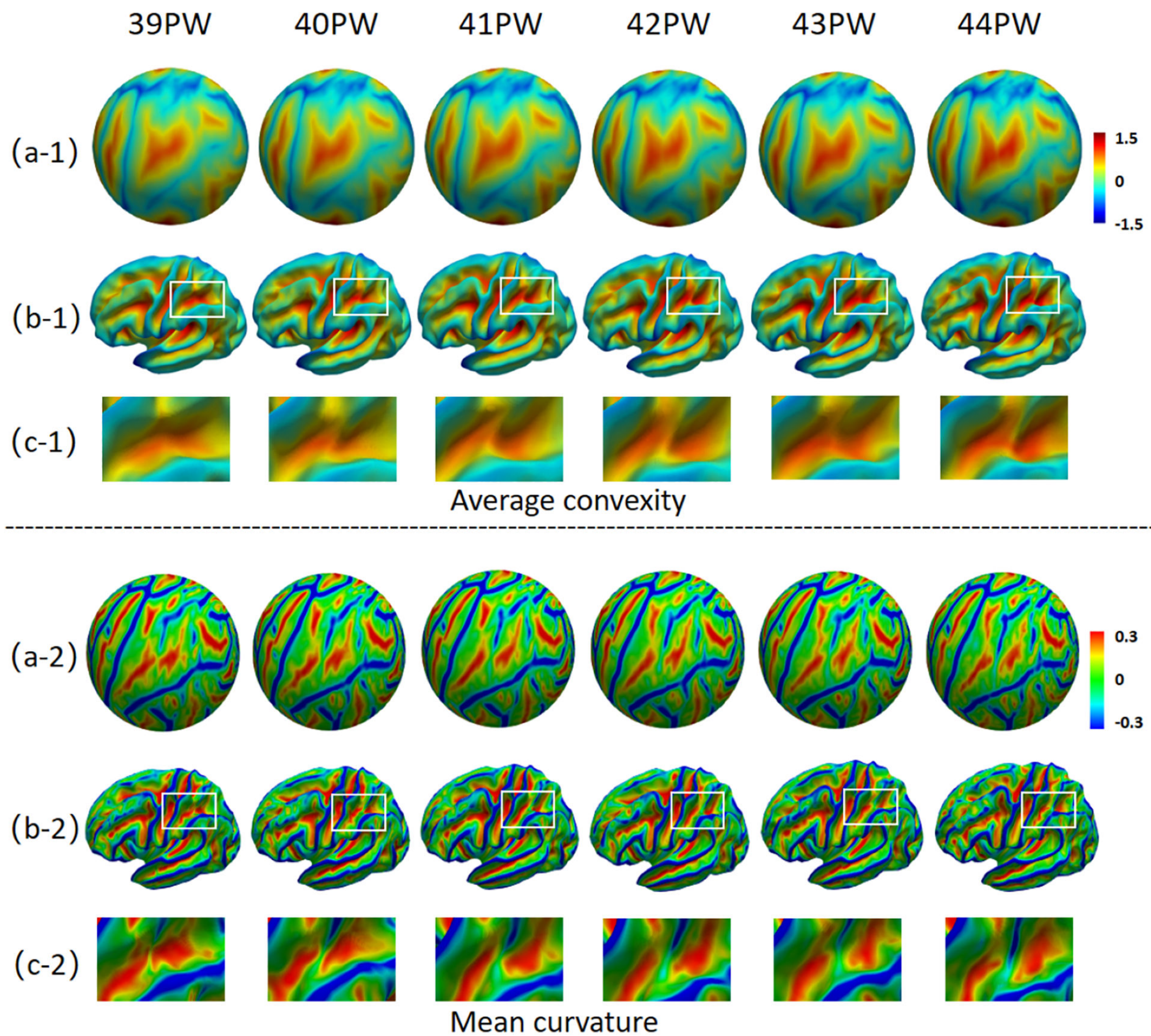

Fig. 2.

4D neonatal cortical surface atlases from 39 to 44 postmenstrual weeks (PW) constructed by the proposed method based on the Wasserstein distance. (a-1) and (a-2) are the color-coded average convexity and mean curvature in the spherical space, respectively. (b-1) and (b-2) are the average cortical surface with the folding patterns from (a-1) and (a-2). (c-1) and (c-2) zoom a respective region for better inspection of the folding development.

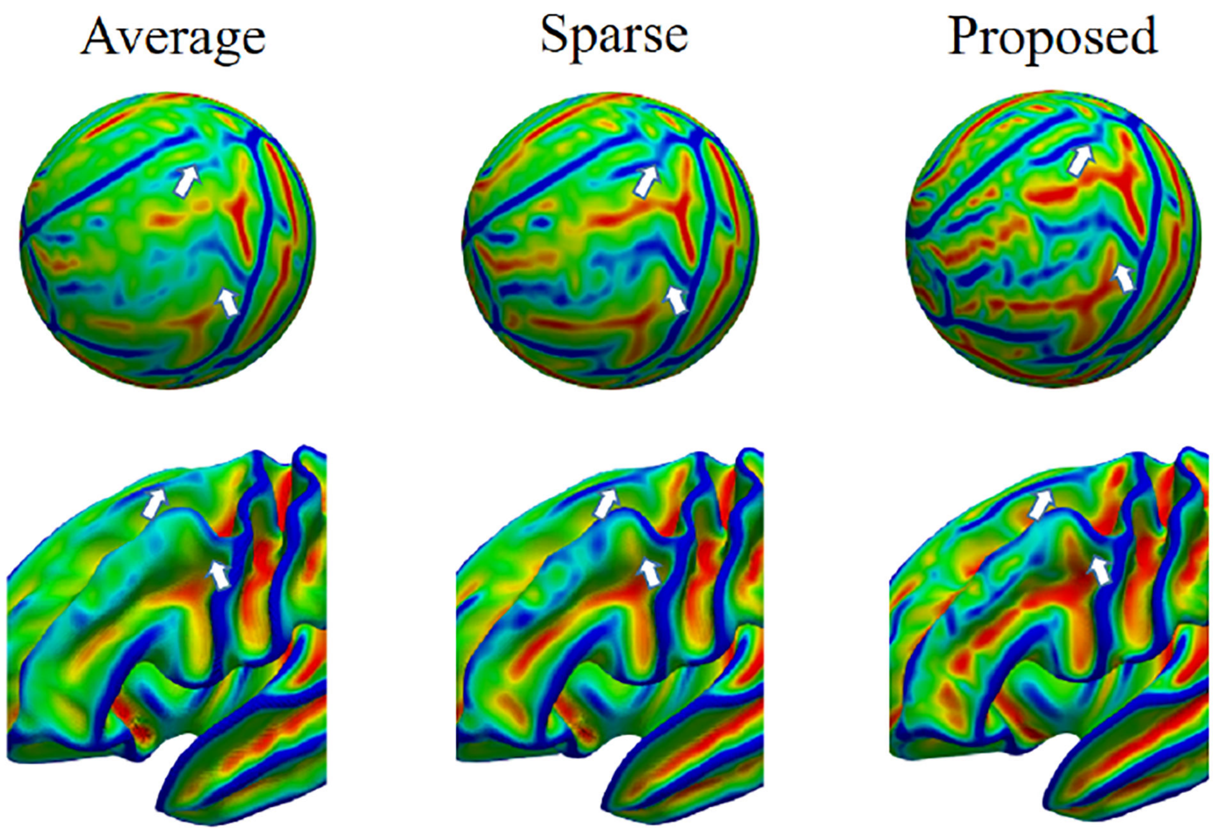

Fig. 3.
Curvature patterns on the Euclidean averaging atlas (left), sparse representation atlas (middle) and our proposed atlas using Wasserstein distance (right) at 41 postmenstrual weeks. The first row shows the color-coded mean curvature in the spherical space. The second row shows the mean curvature on the average inner surfaces.

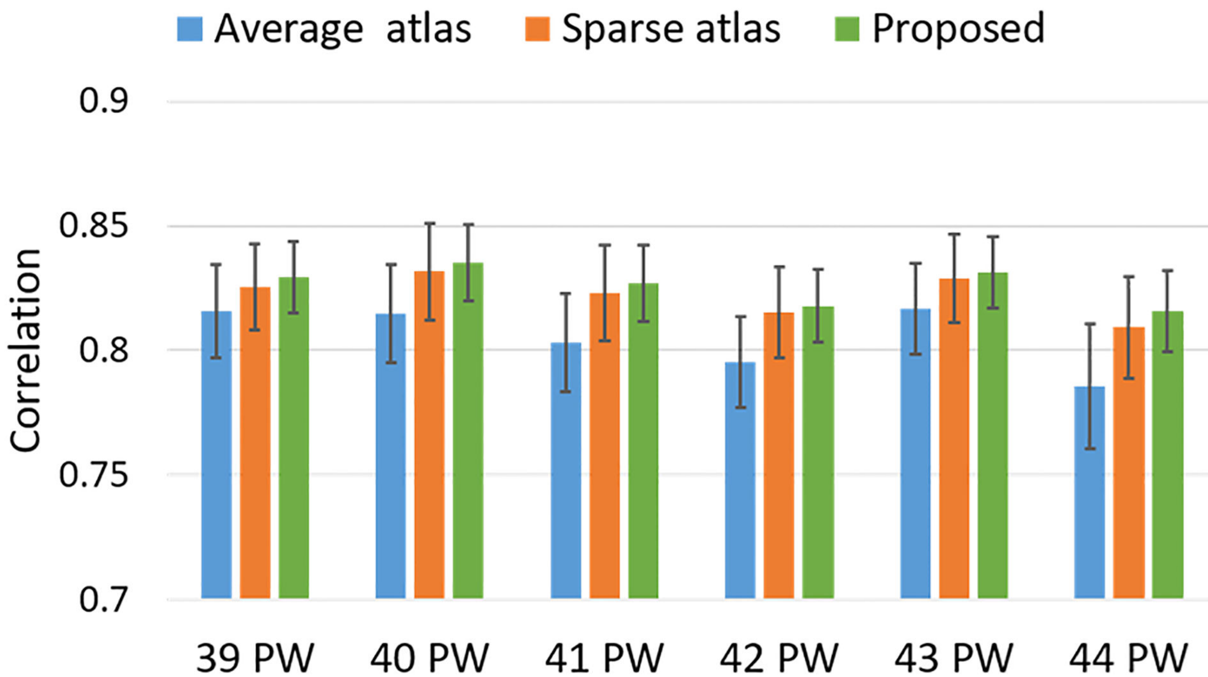

Fig. 4.

Average correlation coefficient and standard deviation after aligning individual subjects at each week onto the age-matched atlases constructed by different methods.

Table 1.

Subject information for constructing 4D neonatal cortical surface atlases.

Week	39	40	41	42	43	44	Total
Number	101	125	188	157	109	84	764
Male	62	71	98	79	50	42	402
Female	39	54	90	78	59	42	362