UNC 4D Infant Cortical Surface Atlases, from Neonate to 6 Years of Age

Version 1.8

Updates history

Version 1.9 (May 2023)	In version **1.9**, we have released the UNC infant developmental parcellation maps, which were generated by a data driven method according to the developmental patterns of cortical surface area, using both the neonatal scans from dHCP project and infant scans from BCP project. Each hemisphere is parcellated into 17 regions. Please find the details of the parcellation maps in https://doi.org/10.1073/pnas.2121748119.
Version 1.8 (Jul 2022)	In version **1.8**, we have released a new fine-grained infant-dedicated cortical functional parcellation map, which was generated based on resting-state functional connectivity information. In this parcellation map, each hemisphere is partitioned into 300 parcels.
Version 1.7 (Nov 2021)	In version **1.7**, we have released a new fine-grained infant-dedicated cortical functional parcellation map, which was generated based on resting-state functional connectivity information. In this parcellation map, each hemisphere is partitioned into 432 parcels. Based on these generated parcels, we performed the network clustering to reveal the early development of functional network organization at age of 3, 6, 9, 12, 18 and 24 months, which are also provided on the atlases. More detailed information will be updated soon.
Version 1.6 (Feb 2020)	In version **1.6**, we have released the UNC infant developmental parcellation maps, which were generated by a data driven method according to the developmental patterns of cortical thickness during the first two postnatal years. The parcellation maps are in two different resolutions: 6 and 17 cortical regions per hemisphere. Details of these developmental parcellation maps are explained in https://doi.org/10.1073/pnas.1821523116.
Version 1.5 (Nov 2019)	In version **1.5**, we have released the latest UNC 4D infant cortical surface atlases, which improve the previous version in twofold. 1) The cortical attribute patterns in this version are sharper; 2) Different cortical attributes on the atlases are more consistent.
Version 1.0 (Nov 2017)	In this first release, we have released the UNC 4D infant cortical surface atlases, which cover the longest time range in the densest manner of the infant brain.

UNC 4D infant cortical surface atlases from neonate to 6 years of age contain 11 time points, including 1, 3, 6, 9, 12, 18, 24, 36, 48, 60 and 72 months of age, thus densely covering and well characterizing the stages of the dynamic early brain development.

0. What this is

Cortical surface atlases play a fundamental role for spatial normalization, analysis, visualization, and comparison of results across individuals and different studies. For adult MRI studies, many cortical surface atlases have been generated and widely adopted, e.g., FreeSurfer surface atlas, PALS surface atlas, ICBM surface atlas, and HCP-MMP atlas. However, the existing cortical surface atlases created for adults are problematic when applied to infant studies, due to dynamic and nonlinear changes of brain size and also different cortical folding and appearance in the infant brain. To more accurately study the early brain development, the longitudinal 4D infant cortical surface atlases are highly desired. To address this problem, for the first time, we have constructed the UNC 4D infant cortical surface atlases from neonate to 6 years of age at **11** densely sampled time points, i.e., 1, 3, 6, 9, 12, 18, 24, 36, 48, 60, and 72 months of age, based on **339** serial MRI scans from **50** healthy infants, with each being scanned longitudinally from birth. Meanwhile, we have also mapped the FreeSurfer parcellation (Desikan et al., 2006), the HCP multi-modal parcellation (MMP) (Glasser et al., 2016) and the UNC infant cortical thickness developmental parcellation (Wang06 and Wang17) (Wang et al., 2019) onto our 4D infant cortical surface atlases. Of note, these 4D cortical surface atlases have vertex-to-vertex cortical correspondences across all ages, and thus can be easily used for both cross-sectional and longitudinal analyses. These 4D infant cortical surface atlases with very dense time points will greatly facilitate cortical surface-based mapping of the dynamic and critical early brain development in many pediatric studies, e.g., the Baby Connectome Project (BCP).

1. Where to download

The package can be freely downloaded from:

https://www.nitrc.org/projects/infantsurfatlas/

It is availably free to the public for the academic research purpose. Note the ownership, copyright, and all rights are retained by UNC-Chapel Hill.

2. What it includes

Our 4D infant cortical surface atlases are distributed in three popular file formats: (1) VTK (*.vtk) format, which can be visualized and processed by any VTK supported toolkit such as ParaView; b) FreeSurfer format, which can be used by the FreeSurfer Package; c) HCP (*.gii) format, which is in accordance with the workbench toolkit developed under the HCP project.

For each of the 11 time points, we provide:

a) The corresponding spherical representation of each hemisphere of the population-average cortical structures (in a densely sampled sphere with 163,842 vertices). The left hemisphere (lh) and right hemisphere (rh) are represented in two different files.

b) The white surface (inner surface), pial surface (outer surface), and center surface (middle surface). These three surfaces are isomorphic to the spherical representation (spherical surface), with vertex-to-vertex cortical correspondences.

c) The sulcal depth, average convexity, mean curvature, and inflated mean curvature of each white/inner surface. These metrics are generally useful for cortical surface registration.

d) The MMP parcellation (Glasser et al., 2016) (with 180 ROIs in each hemisphere), the FreeSurfer parcellation (Desikan et al., 2006) (with 35 ROIs in each hemisphere) and the infant cortical thickness developmental parcellation (Wang et al. 2019) (with 6 or 17 ROIs in each hemisphere).

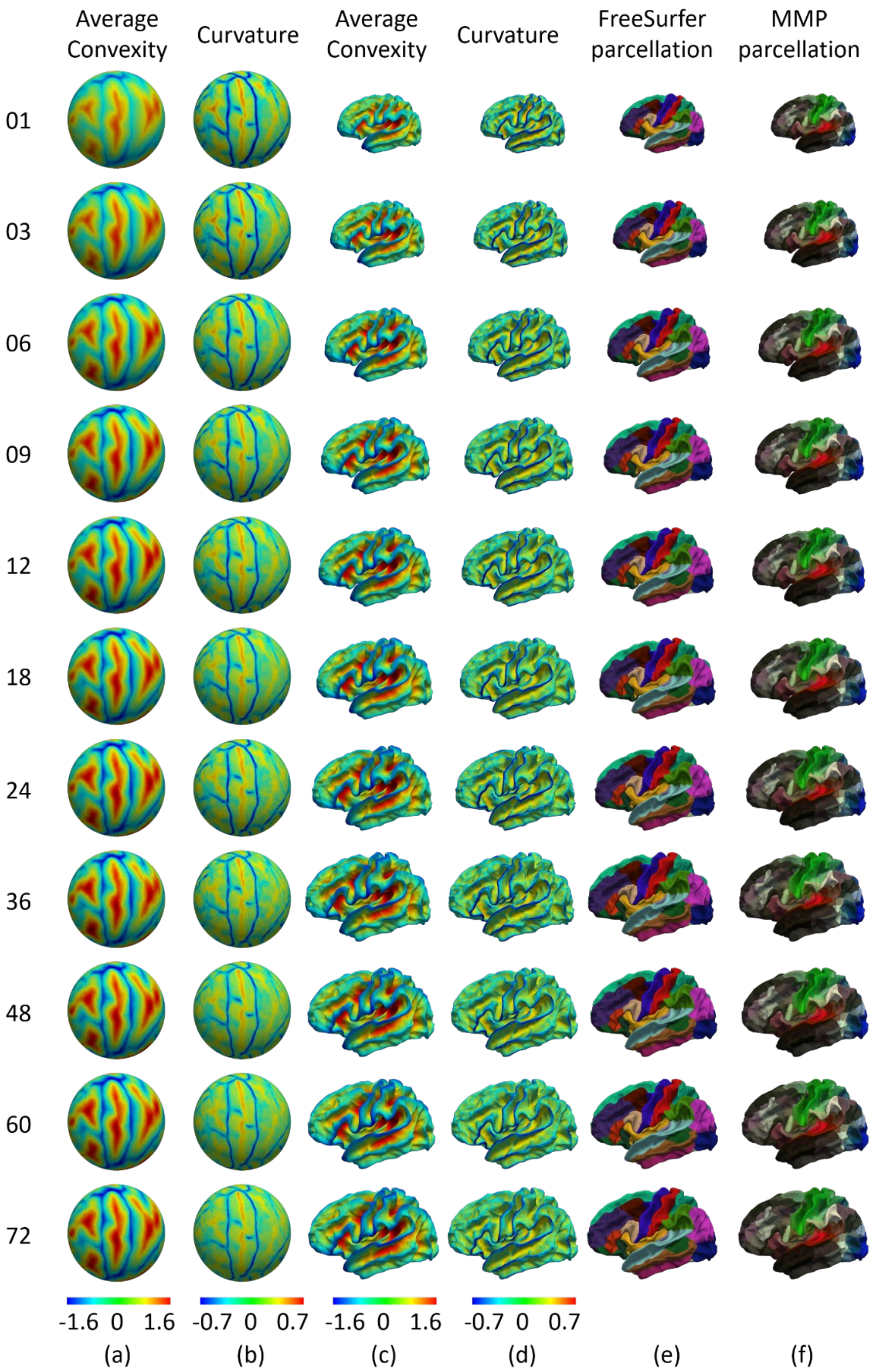
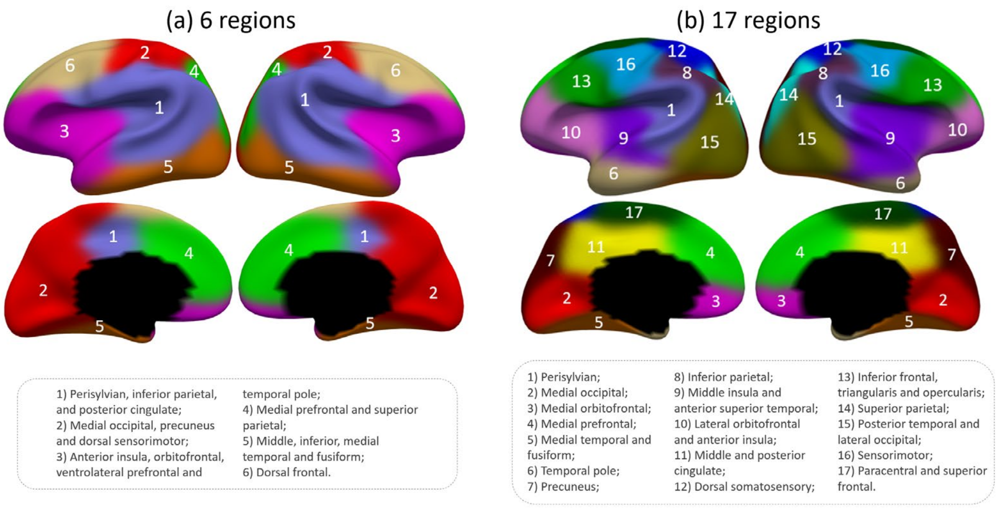


Fig. 1. UNC 4D infant cortical surface atlases and parcellations at 11 time points of age. The subject number with gender information at each time point (with M indicating male, and F indicating female) is provided on the left.

Fig. 1 shows the constructed 4D infant cortical surface atlases for the left hemisphere at each time point. Columns (a) – (b) illustrate the cortical properties on the standard sphere; Columns (c) – (d) illustrate the corresponding cortical properties on the age-specific population-average inner cortical surface; Columns (e) and (f) illustrate the FreeSurfer parcellation and the MMP parcellation at each time point. **Fig. 2** shows the infant cortical developmental parcellation with 6 and 17 ROIs per hemisphere. **Fig. 3** shows the fine-grained infant cortical functional parcellation map with 432 parcels per hemisphere. To facilitate the use of the atlas for investigating the functional networks, we have labeled the cortical surface according to the typical functional networks at age of 3, 6, 9, 12, 18 and 24 months, with each label corresponding to a major brain function region. Table 1 shows the mapping between the vertex-wise cortical label and those major function regions at different time points. These functional region labels are attached on all atlases of different ages for a consistent longitudinal study of the functional research. **Fig. 4** shows the constructed 4D infant cortical surface atlases for the left hemisphere at each time point using the cortical surface area expansion pattern.



1) Perisylvian, inferior parietal, and posterior cingulate;
2) Medial occipital, precuneus and dorsal sensorimotor;
3) Anterior insula, orbitofrontal, ventrolateral prefrontal and temporal pole;
4) Medial prefrontal and superior parietal;
5) Middle, inferior, medial temporal and fusiform;
6) Dorsal frontal.

1) Perisylvian;
2) Medial occipital;
3) Medial orbitofrontal;
4) Medial prefrontal;
5) Medial temporal and fusiform;
6) Temporal pole;
7) Precuneus;
8) Inferior parietal;
9) Middle insula and anterior superior temporal;
10) Lateral orbitofrontal and anterior insula;
11) Middle and posterior cingulate;
12) Dorsal somatosensory;
13) Inferior frontal, triangularis and opercularis;
14) Superior parietal;
15) Posterior temporal and lateral occipital;
16) Sensorimotor;
17) Paracentral and superior frontal.

Fig. 2. Infant cortical developmental parcellation with (a) 6 ROIs and (b) 17 ROIs per hemisphere. According to the number shown on each ROI, the approximately corresponding name is denoted in the dashed box.

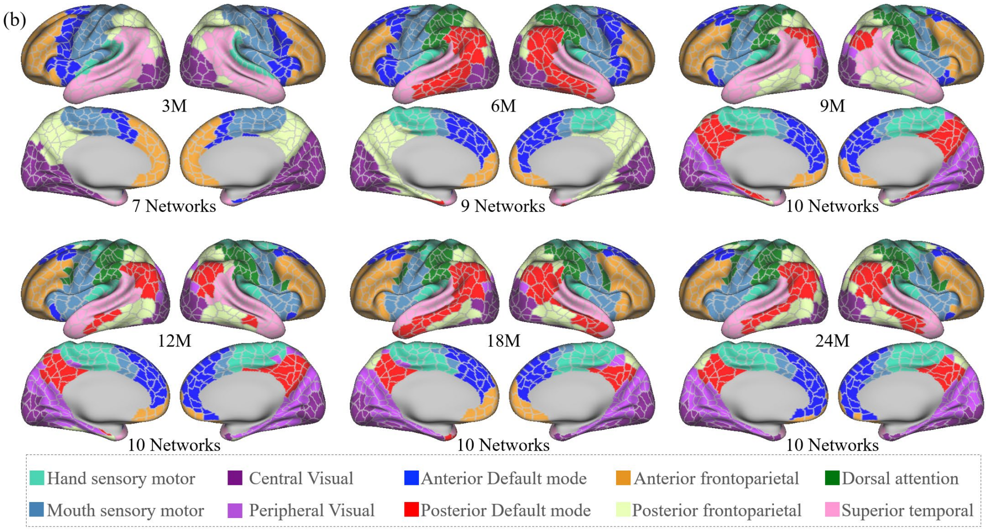


Fig. 3. Fine-grained infant cortical functional parcellation map with 432 parcels per hemisphere. Parcels are color-coded by the corresponding functional networks during infantile brain development.

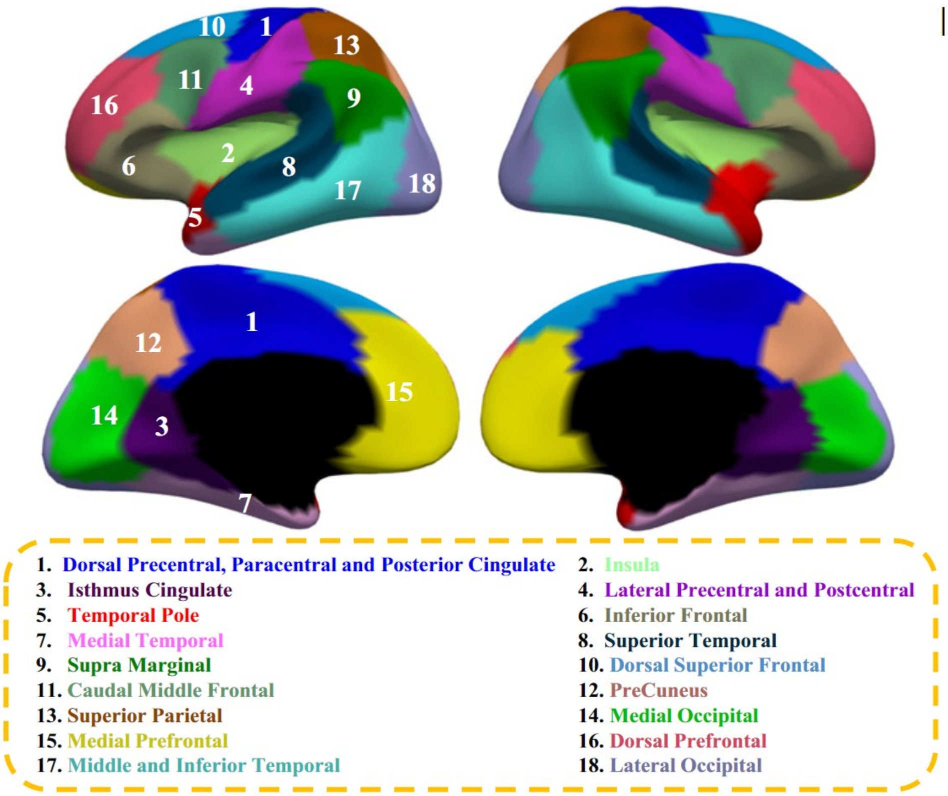


Fig. 4. Infant cortical developmental parcellation with 17 ROIs per hemisphere. Each ROI are approximately corresponding to a name denoted in the dashed box.

Table 1. Parcel label IDs and corresponding functional networks.

1	Posterior frontoparietal
2	Mouth sensory motor
3	Anterior frontoparietal
4	Central visual
5	Superior temporal
6	Medial wall and unlabeled
7	Anterior default mode
8	Hand sensory motor
9	Posterior default mode
10	Dorsal attention
11	Peripheral visual

3. File illustration

There are 3 folders, each with one format of the 4D infant cortical surface atlases.

a) For VTK format, we appended all morphological features and the parcellation labels into the surface files. Totally, for each time point, there are 8 files. The typical file name is: [***Month***]/[***Hemi***].[***Surface***].vtk. The illustration of the name field strings is listed in Table 2.

b) For FreeSurfer format, the surfaces, morphological features, and parcellations are provided in separate files. For each time point, there are 22 files. We have followed the FreeSurfer naming strategy to name our infant surface atlases. The typical surface file name is: [***Month***]/[***Hemi***].[***Surface***]; the typical morphological feature filename is: [***Month***]/[***Hemi***].[***Feature***]; and the typical parcellation filename is: [***Month***]/[***Hemi***]. *Annot*-[***Parcellation***]. All related name field strings are also listed in Table 2.

c) For HCP format, the surfaces, morphological features, and parcellations are also provided in separate files. For each time point, there are 20 files. We have followed the general HCP naming strategy to name our atlases. The typical surface file name is: [***Month***]/[***Hemi***].[***Surface***].164k.surf.gii; the typical morphological feature filename is: [***Month***]/[***Hemi***].[***Feature***].164k.shape.gii; while, the typical parcellation filename is: [***Month***]/[***Hemi***].[***Parcellation***].164k.label.gii.

Table 2. The name field value for each data format.

Name field	**VTK**	**FreeSurfer**	**HCP**
Month	{01, 03, 06, 09, 12, 18, 24, 36, 48, 60, 72}		
Hemi	{lh,rh}	{lh,rh}	{L,R}
Surface	{InnerSurf, MiddleSurf, OuterSurf, SphereSurf}	{white, center, pial, sphere}	{white, midthickness, pial, sphere}
Feature	Appended into surface {curvature, SulcDepth, InflatedCurv, Convexity}	{curv, depth, inflated.H, sulc}	{Curvature, SulcDepth, InflatedCurvature, AverageConvexity}
Parcellation	Appended into surface {par_FS, par_MMP, par_Wang06, par_Wang17, par_Wang432}	{FreeSurfer, MMP, Wang06, Wang17, Wang432}	{ParcellationFreeSurfer, ParcellationMMP, ParcellationWang06, ParcellationWang17, ParcellationWang432}

4. How it was constructed

Totally 339 serial MRI scans from 50 healthy infants, each scheduled to be longitudinally scanned at 1, 3, 6, 9, 12, 18, 24, 36, 48, 60, and 72 months of age, were used to construct UNC 4D infant cortical surface atlases. The subject number with gender information at each time point is provided in **Fig. 1**. All infant MR images were processed by the **UNC Infant Pipeline** for cortical surface-based analysis (Li et al., 2015). Briefly, it included skull stripping, cerebellum removal, intensity inhomogeneity correction, tissue segmentation, separation of left/right hemispheres, topology correction, inner, middle and outer surface reconstruction, spherical mapping, and computation of cortical properties (e.g., sulcal depth, average convexity, cortical thickness, and curvature) (Li et al., 2014a; Li et al., 2014b; Li et al., 2014c; Wang et al., 2015; Wang et al., 2014).

a) Method -- Version 1.0

To build longitudinally-consistent surface atlases, both intra-subject and inter-subject surface registrations were performed (Li et al., 2015). Specifically, to establish longitudinal cortical correspondences for each subject, first, the spherical surfaces of all time points for the same subject were registered together using an unbiased group-wise registration method (Yeo et al., 2010). Then, for each subject, a within-subject mean spherical surface was constructed by averaging corresponding cortical properties across all time points. Next, to establish inter-subject cortical correspondences, an unbiased group-wise registration was further performed to align the within-subject mean spherical surfaces of all different subjects. After that, for each age, an age-specific surface atlas (consisting of the mean and variance of cortical properties across all infants at this age) was constructed on the spherical surface, based on the inter-subject cortical correspondences defined above. Finally, a population-specific spherical surface atlas was also obtained by computing the mean and variance of cortical properties across all within-subject mean surfaces.

To equip our infant atlases with parcellations, the population-specific spherical surface atlas was aligned onto the FreeSurfer atlas. Then, for coarse parcellation, the FreeSurfer parcellation with 35 regions in each hemisphere (Desikan et al., 2006) was first propagated to our infant population-specific atlas and then further to our 4D infant cortical surface atlases at all time points. For fine-grained parcellation, the HCP multi-modal parcellation (MMP) with 180 detailed regions in each hemisphere (Glasser et al., 2016) was first mapped to the FreeSurfer atlas using the HCP workbench, and then propagated to our 4D infant cortical surface atlases.

b) Method -- Version 1.5

Due to potential registration errors and considerable inter-subject variability of cortical attributes, the average over the group-wisely aligned population cortical attributes often leads to over-smoothed cortical attributes patterns on the constructed 4D atlases, which may degrade the registration performance when aligning new subjects to our atlases. To address this issue, we propose to leverage a spherical patch-based sparse representation method to construct our 4D infant cortical surface atlases, which preserve sharper cortical attribute patterns and increase the registration performance.

The central idea includes two steps. *First*, for each spherical patch in the atlas space, we build a dictionary, which includes corresponding patches and their spatially-neighboring patches from all co-registered cortical surfaces. *Second*, for each cortical attribute on the atlas patch, we sparsely represent it using the dictionary patches. The advantages of this method include 1) by augmenting the patch dictionary with the neighboring patches, the potential registration errors can be alleviated, and 2) sparse representation is substantially more robust to noisy cortical attributes, where refers to the cortical attributes (in a patch) that have least agreement with the population's attributes (in a patch). These two advantages made the proposed atlas construction framework more robust to noise, thus preserving sharper cortical attribute patterns on our atlases. In addition, instead of treating each cortical attribute independently, we simultaneously represent all the cortical attributes in a single framework. With the group-wise sparse constraints, different cortical attributes share the similar representation weights, which preserve the consistency across different cortical attributes.

c) Method -- Version 1.6

The key idea of the infant developmental parcellation is to capitalize on spatiotemporally heterogeneous patterns of cortical thickness during infancy. This effort has been made by leveraging an infant-dedicated computational pipeline, an advanced multivariate analysis method (i.e., nonnegative matrix factorization), and a densely sampled longitudinal dataset with 210 serial MRI scans from 43 healthy infants, with each infant being scheduled to have up to 7 longitudinal scans at around 1, 3, 6, 9, 12, 18, and 24 months of age. Our resulted parcellations are in two different resolutions: 6 and 17 regions per hemisphere. These regions represent distinct clusters of vertices in terms of cortical thickness development during infancy.

5. How to use

Our 4D infant cortical surface atlases (either v1.0, v1.5 or v1.6) can be used to register an individual's cortical surface into a common space and also propagate the parcellations onto the individual's cortical surface. Here, we provide registration examples for using FreeSurfer[1] (Fischl, 2012) and Spherical Demons[2] (Yeo et al., 2010). After successful install and configuration, the pairwise alignment could be done through the following command lines.

For FreeSurfer, one can use the command:

```
    mris_register -1 individual_subject/lh.sphere 4D_altas/lh.sphere individual_subject
/lh.sphere.FS.reg
```

For Spherical Demons, one can use the Matlab code:

```
    mris_SD_pairwise_register(individual_subject/lh.sphere, 4D_altas/lh.sphere, individual_subject
/lh.sphere.SD.reg)
```

When using our 4D infant cortical surface atlases, please cite our following papers:

Li, G., Wang, L., Shi, F., Gilmore, J.H., Lin, W., Shen, D., 2015. ***Construction of 4D high-definition cortical surface atlases of infants: Methods and applications***. Medical image analysis 25, 22-36.

Wu, Z., Wang, L., Lin, W., Gilmore, J., Li, G., Shen, D., 2019. ***Construction of 4D infant cortical surface atlases with sharp folding patterns via spherical patch-based group-wise sparse representation.*** Human brain mapping 40, 3860-3880.

Wang, F., Lian, C., Wu, Z., Zhang H., Li T., Meng Y., Wang L., Lin W., Shen D., Li G., 2019. ***Developmental topography of cortical thickness during infancy.*** Proceedings of the National Academy of Sciences 116 (32), 15855-15860.

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[1] https://surfer.nmr.mgh.harvard.edu

[2] https://sites.google.com/site/yeoyeo02/software/sphericaldemonsrelease

6. Contacts

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Li, G., Wang, L., Shi, F., Lin, W., Shen, D., 2014b. Simultaneous and consistent labeling of longitudinal dynamic developing cortical surfaces in infants. Medical image analysis 18, 1274-1289.

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Wang, L., Gao, Y., Shi, F., Li, G., Gilmore, J.H., Lin, W., Shen, D., 2015. LINKS: Learning-based multi-source IntegratioN frameworK for Segmentation of infant brain images. Neuroimage 108, 160-172.

Wang, L., Shi, F., Li, G., Gao, Y., Lin, W., Gilmore, J.H., Shen, D., 2014. Segmentation of neonatal brain MR images using patch-driven level sets. Neuroimage 84, 141-158.

Yeo, B.T., Sabuncu, M.R., Vercauteren, T., Ayache, N., Fischl, B., Golland, P., 2010. Spherical demons: fast diffeomorphic landmark-free surface registration. IEEE transactions on medical imaging 29, 650-668.

Wang, F., Lian, C., Wu, Z., Zhang H., Li T., Meng Y., Wang L., Lin W., Shen D., Li G., 2019. Developmental topography of cortical thickness during infancy. Proceedings of the National Academy of Sciences 116 (32), 15855-15860.