

# A MR Brain Template of Young Children

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## Introduction:

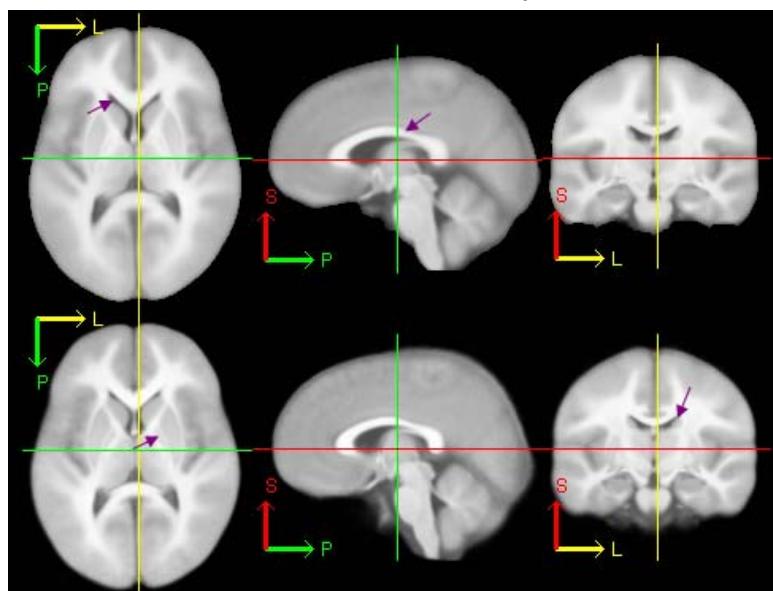
A probabilistic brain atlas plays an important role in interpreting results, visualizing information, and processing data in neuroimaging research. Extensive efforts have been made to develop such brain atlases on the basis of magnetic resonance (MR) images. However, these efforts have focused primarily on adult brains. Studies have shown considerable differences between adult and pediatric brains in gray matter (GM) and white matter (WM) ratios, cortical thickness, and sulcal patterns.<sup>1,2</sup> Even though use of an adult brain atlas/template can introduce severe bias into pediatric neuroimaging studies,<sup>3,4</sup> few studies have focused on constructing pediatric brain atlases.<sup>5,6</sup> The purpose of this study is to develop a pediatric brain template on the basis of 3D T1 MR head images.

## Methods:

We constructed a reference image on the basis of MR data from 96 normal individuals in the pediatric brain database created as part of the Pediatric MRI Study of Normal Brain Development project.<sup>7</sup> The 3D T1 MR data, brain mask, and tissue classification images from children ages 6–8 years were retrieved from the database. However, if multiple studies of a single subject were available, only 1 study was included. A free registration toolkit of VTK CISG was used for rigid, affine, and nonlinear registration.<sup>8</sup> The reference image was averaged from individual brain MR data as follows. First, brain mask and tissue classification images were mapped back to the original head image to generate brain images ( $I_{bi}$ ,  $i = 1\dots 96$ ) in the original size and position. Because the brain mask and tissue classification images were based on images linearly transformed to Talairach space, we did this to avoid the scale effect introduced by linear registration. Second, brain images ( $I_{bi}$ ) were aligned by a rigid body registration-based normalized mutual information (NMI) to a standard atlas space, using the ICBM452 atlas (<http://www.loni.ucla.edu/Atlases>). Third, the intensity of each aligned brain image ( $I_{bi\_aligned}$ ) was normalized to 0–1024; a brain image ( $I_{A1}$ ) was generated by averaging all intensity-

normalized brain images ( $I_{bi\_aligned\_si}$ ). Fourth, brain images ( $I_{bi}$ ) were normalized by an affine registration-based NMI to the average brain image ( $I_{A1}$ ). Fifth, the procedure described in step 3 was repeated using the normalized brain images ( $I_{bi\_normalized}$ ) to create a brain image ( $I_{A2}$ ). Sixth, brain images ( $I_{bi}$ ) were warped by free form deformation (FFD)-based NMI to the average brain image ( $I_{A2}$ ). The final brain reference image ( $I_B$ ) was derived by repeating the procedures in step 3, using the warped brain images ( $I_{bi\_warp}$ ). The tissue classification image of each subject was mapped to  $I_B$  by using the transformation matrix found during the brain registration. The tissue probability map of GM, WM, and CSF were generated by summing the warped tissue classification of all subjects.

We used this brain reference image and ICBM452 for spatial normalization of positron emission tomography (PET) images of 25 patients treated for soft-tissue tumors using an affine registration in the Automated Image Registration (AIR) toolkit.<sup>9</sup> GMs on aligned PET image were segmented using a fuzzy c-mean algorithm. The similarities (kappa indices) between the GM from the aligned PET and those on MR atlases were calculated to evaluate the accuracy of registration.



**Fig. 1.** Comparison of ICBM452 atlas (upper row) and the reference image of young children (lower row). The two images are in the scale, dimension, and voxel size. Although these 2 images are similar, differences are visually recognizable in corpus callosum, putamen, and ventricle system.

normalization process when ICBM452 was used as the template, but none failed when the reference image of children was used. The agreement of GM between the aligned PET images and MR atlases is significantly higher ( $P < 0.05$ , two tails) using developed brain template (averaged kappa index 0.73) than those using ICBM452 (averaged kappa index 0.70).

## Discussion:

This study differs from similar studies performed by Wilke et al.<sup>5,6</sup> in that we have used an iterative approach by which brain images are normalized to their own average instead using affine registration to an adult space.

## Conclusion:

We developed a brain atlas of young children on the basis of MR images and used it for spatial normalization of PET images. The spatial normalization results showed that a pediatric brain atlas is more appropriate for pediatric neuroimaging research than the adult brain atlas.

## References:

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