

## Creation of a population-representative brain atlas with clear anatomical definition

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**Introduction:** MRI and modern image analysis techniques have greatly enhanced our abilities in detecting abnormalities in diseased brains. An MR based brain atlas, serving as the template for image mapping and the anatomical framework of statistical analysis, is a key component in image analysis. Typically, there are two types of atlases with different characteristics: the population-averaged atlas that has an unbiased representation of average brain anatomy and the single-subject (SS) atlas that has sharp anatomical definitions. Highly elastic image transformation tools require a template with sharp anatomical definition, but employment of a sharp SS atlas may introduce bias in anatomical quantification. Using newly developed computational techniques on image mapping and metric distance of images, we employed a continuous fluid dynamic, image metric based method<sup>[1]</sup> to generate an unbiased atlas with sharp tissue contrast. The new atlas was compared with an existing SS atlas, the affine based group-averaged template (AGA), and the non-linear mapping based group-averaged template (NGA). The results suggested that the new atlas was unbiased and with fine anatomical details.

**Methods:** MRI data from 20 healthy subjects (age  $32.1 \pm 5.8$  years old; 10 males, 10 females) were included in the study. T2-weighted images (imaging parameters from [2]) were skull-stripped, distortion corrected, affine transformed to the ICBM152 coordinate, and resampled to  $90 \times 108 \times 90$  with 2 mm isotropic resolution. We first selected one subject's image as an initial template, and the weighted-LDDMM image matching algorithm was applied to estimate the template (Est.T) based on the observed population<sup>[1]</sup>. The AGA and NGA images were generated by averaging after affine and nonlinear mapping of the 20 images to an SS atlas<sup>[3]</sup> (also in ICBM152 coordinate), respectively. Volumes of the brain and lateral ventricle (LV) were obtained via manual segmentation in the atlas and subject images. Metric distances<sup>[4]</sup> between each subject image and the four types of atlases were also calculated.

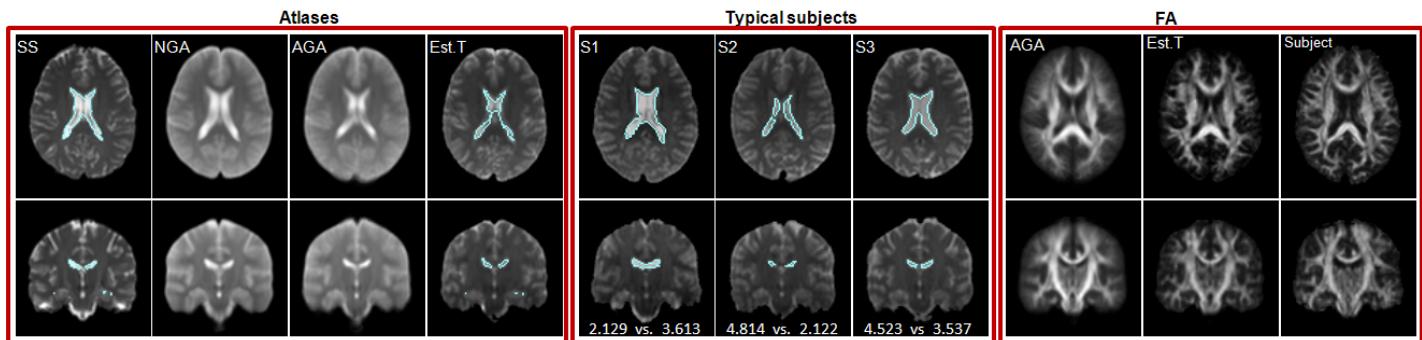


Fig.1. Four types of brain atlases (Col. 1-4), selected subjects images(Col. 5-7), and the FA results (Col. 8-10). The numbers in the subject images (S1-S3) are the metric distances of each image to the SS and Est.T, respectively. S1 is "closer" to the SS than to the Est.T, S2 and S3 are "closer" to the Est.T than to the SS. Lateral ventricles were delineated in the SS and Est.T and subject images. In the right three columns, the Est.T of FA image has the group-based structural geometry similar to the AGA image and reserves fine structural definitions similar to the individual subject image.

**Results and Discussion:** In Fig.1, the SS and Est.T atlases of T2-weighted images had sharper contrast than the AGA and NGA atlases. Anatomical bias of the SS and Est. T atlases was evaluated using volumes of various brain structures. While the mean brain volumes of the 20 subjects after affine normalization were close to the brain volumes of the SS and Est.T atlases, the LV volume in the Est.T atlas approximated the mean LV volume of the 20 subject, which was significantly lower than the LV volume in the SS atlas (see Fig.2). As expected, metric distances between subject and atlas images, which characterize the variation in geometric difference, showed significantly shorter distances for the Est.T atlas than the SS atlas (see Fig.3 & Fig.4). The results suggested that the proposed Est.T atlas was less biased than the SS atlas with respect to the 20 subjects. The estimated template from FA images (Fig.1, Column 9) also illustrates that it retains both an unbiased structural geometry of the averaged image (Col. 8) and the detailed structural definitions of a single-subject image (Col. 10). If a highly elastic transformation method is used for brain mapping, sharp anatomical definition of the template brain is essentially important. The presented technique provides a way to generate a population-averaged anatomical definition with sharp anatomical definitions of a single-subject atlas.

**References:** 1. J. Ma, et al., Neuroimage 42 (2008) 252-261. 2. Y. Zhang, et al., Neuroimage 52 (2010) 1289-1301. 3. K. Oishi, et al., Neuroimage 46 (2009) 486-499. 4. M.F. Beg, et al., Int. J. Comput. Vis. 61 (2005), 139-157.

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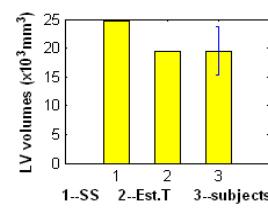


Fig.2. lateral ventricle volumes of single subject atlas, the estimated atlas and subjects.

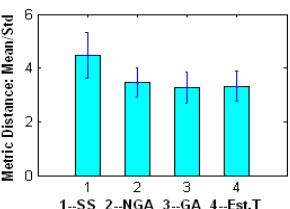


Fig.3. mean metric distances from subjects to SS, NGA, AGA and Est.T.

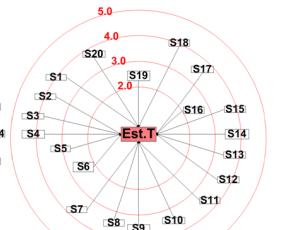
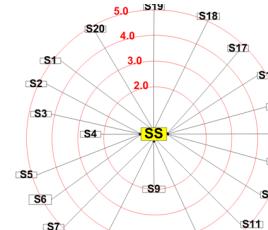


Fig.4. the proportional metric distance map of SS (left) and Est.T (right). Red rings marked the metric distance scales.