Development of a Comprehensive Digital Human Brain Atlas

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Target Audience: Investigators conducting MRI research of gray or white matter of the human brain.

Purpose: An accurate, comprehensive, digital human brain atlas containing different types of high quality MRI data and anatomical labels for both white (WM) and gray matter (GM) in standardized space is desirable for a variety of brain imaging studies. The IIT2 diffusion tensor (DT) template[1] was developed recently in ICBM-152 space based on artifact-free Turboprop DT data from 67 subjects with a narrow age-range. This artifact-free template was shown to have a) higher image sharpness, b) lower noise levels, c) DT information that was more representative of single-subject human brain data, and d) improved anatomical matching to ICBM-152 space, compared to other publicly available DT templates. The goals of this work were to: a) further enhance the quality of the IIT2 DT template through the use of advanced inter-subject registration that utilizes full tensor information, and also through the use of population-based template-construction strategies, and b) extend this publicly available resource into a comprehensive WM and GM atlas of the human brain by adding anatomical MRI data from the same subjects, as well as WM and GM labels.

Methods: Turboprop-DT and T1-weighted data from 72 healthy subjects (20-40 years of age), collected on a 3T GE scanner, were used in this work. ***DT template***: Skull-stripping, motion correction, and DT estimation were conducted using TORTOISE[2]. All 72 DT datasets were registered to the IIT2 DT template using DTITK[3], and averaged to construct a temporary DT template. The 72 raw DT datasets were then registered to the temporary DT template, and the resulting datasets were averaged to obtain an updated temporary template. This process was repeated 6 times resulting in a DT template in population space. All b=0 image volumes in population-space were then registered to the ICBM-152 T2-weighted template using the Automatic Registration Toolbox (ART)[4]. The resulting ART transformations were averaged across subjects. For each subject, the transformation generated by registration of that subject's DT data from subject space to population space was combined with the averaged ART transformation from population space to ICBM-152 space, and then applied to the subject's raw DT data to transform it to ICBM-152 space. The mean and median tensors were estimated for the final DT template in ICBM-152 space. ***Skeletonized WM atlas***: The fractional anisotropy (FA) image of the final mean DT template was skeletonized using TBSS[5]. The WM skeleton was then manually divided into 39 segments per hemisphere corresponding to known WM structures, based on previously published brain atlases. ***T1-weighted template***: For each subject, the raw T1-weighted image volume was registered to the corresponding Turboprop b=0 image in subject space, using rigid body registration. The resulting transformation was combined with the final transformation applied to the subject's raw DT data to transform it to ICBM-152 space, and was then applied to the raw T1-weighted image volume. The process was repeated for all subjects. All T1-weighted volumes in ICBM-152 space were averaged to generate a T1-weighted template. ***Probabilistic GM atlas***: The raw T1-weighted images of all subjects were first segmented into 82 cortical and subcortical GM regions per hemisphere using Freesurfer[6]. The GM labels from all subjects were transformed to ICBM-152 space according to the transformations used to build the T1-weighted template. Also, the T1-weighted template was segmented into WM and GM using FAST[7]. Each voxel of the resulting GM mask in ICBM-152 space was then labeled using the transformed GM labels from all subjects and a vote-rule based on the maximum frequency of appearance of a GM label (as in multi-atlas segmentation). Additionally, a confidence index was calculated in each GM voxel, as the ratio of the number of times the final selected label was assigned to the voxel divided by the number of times any GM label was assigned to that voxel. Finally, maps of the probability a GM voxel belongs to a GM label were generated for each label separately.

Results and Discussion: ***DT template***: Inter-subject spatial normalization accuracy of DT data was increased due to the use of an advanced registration technique based on full tensor information, as well as use of a population-based template-construction approach (quantitative results not shown here). As a result, maps of the new DT template were substantially sharper than those of the IIT2 template (Fig.1). In addition, FA values in WM of the new template were higher than those in the IIT2 template and more representative of those of individual subjects (Fig.1). ***Skeletonized WM atlas***: The skeletonized WM atlas is shown in Figure 2G. It has previously been shown that, region-of-interest DT studies using atlas-based segmentation for region selection suffer from partial volume effects due to misregistration, and may benefit from segmentation using a skeletonized WM atlas[8]. Additionally, in voxel-wise TBSS studies the skeletonized WM atlas may facilitate localization of statistically significant findings. ***T1-weighted template***: The mean T1-weighted template provides complementary structural information in the same space as the DT template, since all raw data were collected on the same subjects, in the same scan session, using techniques relatively immune to magnetic susceptibility variations (Fig.2A). ***Probabilistic GM atlas***: The regions of the GM atlas are in good agreement with typical FreeSurfer segmentation results since they were generated using a multi-atlas segmentation approach based on atlases generated with FreeSurfer (Fig.2H). The confidence in GM labeling decisions was higher in the central portion of GM regions than at the borders of neighboring regions, as expected (Fig.2I).

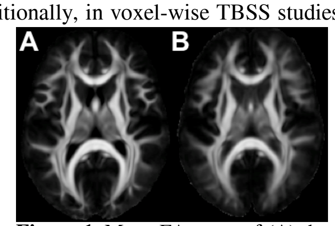

Figure 1. Mean FA maps of (A) the new DT template in ICBM-152 space and (B) the IIT2 template.

Conclusion: A comprehensive digital human brain atlas was generated in this work ["IIT Human Brain Atlas (v.3)", available at www.iit.edu/~mri]. The atlas contains high quality, artifact-free anatomical and diffusion MRI data and detailed WM and GM labels, in the same space (ICBM-152). The atlas also contains a number of supporting maps of quantities describing the quality of the information provided in different brain structures (e.g. total variance of the diffusion tensor, cone of uncertainty, standard deviation maps (Fig.2J), confidence index maps etc.). The new resource provides a flexible reference frame for integration of macro-structural, micro-structural and functional information about the human brain.

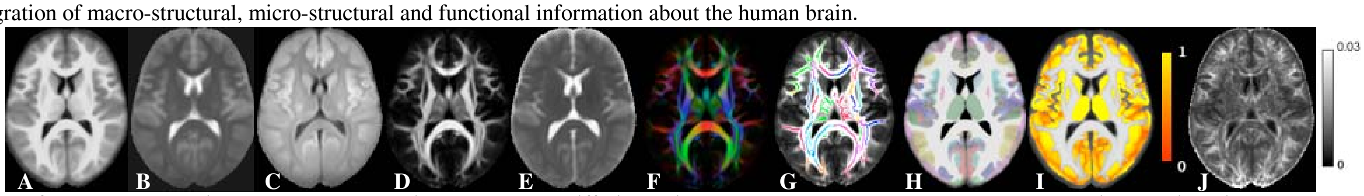

Figure 2. (A) Mean T1-weighted, (B) mean T2-weighted, (C) mean diffusion-weighted, (D) mean FA, (E) mean trace, (F) FA-weighted orientation color map, (G) skeletonized WM atlas, (H) GM atlas, (I) GM confidence index, and (J) FA standard deviation maps of the IIT Human Brain Atlas (v.3).

References: [1] Zhang S, et al., Neuroimage 2010;54:974-984. [2] Pierpaoli C, et al., ISMRM 2010; p.1597. [3] Zhang H, et al., Medical Image Analysis 2006;10:764-785. [4] Ardekani BA et al., J Neurosci Methods 2005;142:67-76. [5] Smith SM, et al., Neuroimage 2006;31:1487-1505. [6] Fischl B, Neuroimage 2012;62:774-781. [7] Smith SM, Hum Brain Mapp 2002;17:143-155. [8] Zhang S, et al., ISMRM 2012; p.3736.