Dog's Whole Brain Probabilistic Diffusion Tensor Imaging Tractography Normalization: A Solution for Brain Image Normalization Difficulty Problems

Witaya Sungkarat[1], Jiraporn Laothamatas[1], Boonlert Lumlertdacha[2], Supaporn Wacharapluesadee[3], and Thiravat Hemachudha[4]

[1]Advanced Diagnostic Imaging and Image-Guided Minimal Invasive Therapy Center and Radiology Dept., Ramathibodi Hospital Faculty of Medicine, Mahidol University, Rajataewe, Bangkok, Thailand, [2]Queen Saovabha Memorial Institute, Thai Red Cross Society, Bangkok, Thailand, [3]WHO Collaborating Center for Research and Training on Viral Zoonoses, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [4]Department of Medicine and WHO Collaborating Center for Research and Training on Viral Zoonoses, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Introduction

In order to conduct group analyses of diffusion tensor imaging (DTI) upon rabid against normal dogs, a new normalization technique has been developed and presented here. In general, fractional anisotropy (FA) maps are unsmooth and have unusually high values at brain borders and in susceptibility artifact areas. Moreover, at brain areas with crossing fibers, the FA values are low, not representing the axonal densities. Thus an FA template is not an ideal choice for normalization. In dog's structural MRI images, typically, there are very high degree of distortion and variability (worse than those found in MRI brain images of elder people and Alzheimer's Disease). Thus whole brain probabilistic DTI tractography maps were used for dog brain's normalization in this study. A whole brain probabilistic DTI tractography map is generally smooth and represents relative axonal densities. Based on the probabilistic tractography maps, all warping and registration parameters could be calculated and then applied to individual FA and mean diffusibility (MD) maps before voxel-wise group analyses could be performed.

Materials and Methods

Dogs (6 normal and 5 rabid) were recruited and scanned with a 3-Tesla MRI scanner (Achieva, Philips Healthcare, Best, the Netherlands). A whole-brain single shot echo planar imaging (EPI) pulse sequence (8-element phased array RF coil, TR=10.3s, 128x128 matrix, 30 contiguous slices at 2-mm thick, one b=0s/mm^2 and 16 isotropic gradient directions with b=800s/mm^2, NEX=2) was used to get DTI image data (at voxel size of 1.41x1.41x2.00 mm^3). Manually, on each subject data set, a brain mask of the DTI data was drawn on the b=0 EPI images using MRIcro (Chris Rorden, http://www.cabiatl.com/mricro). FSL (The Oxford Centre for Functional Magnetic Resonance Imaging of the Brain -- FMRIB Software Library, http://www.fmrib.ox.ac.uk/fsl), specifically, FDT (FMRIB's Diffusion Toolbox) module, was then utilized to process the DTI data. The data processing steps using FSL were as follows: correcting Eddy current artifacts; computing FA and MD maps with FDT 'DTIFIT' sub-module; estimating diffusion parameters (with crossing fiber model) with FDT 'BEDPOSTX' sub-module; calculating a whole brain probabilistic DTI tractography map with FDT 'PROBTRACKX' sub-module (using the drawn whole brain mask). A normal dog at about the averaged size of all subjects was selected to be a reference in order to make a template. The template making steps are as follows: all probabilistic DTI tractography maps of all normal subjects were smoothed with a Gaussian kernel of 4-mm full width at half maximum (FWHM) using SPM (Statistical Parametric Mapping, http://www.fil.ion.ucl.ac.uk/spm), specifically, SPM2; the smoothed probabilistic maps of all other 5 normal subjects were co-registered (6-parameter affine transformation) to the smoothed reference map; voxel-by-voxel across all maps, the 6 smoothed coregistered probabilistic DTI tractography maps were averaged, resulting in a dog brain probabilistic DTI tractography template (after being smoothed with a Gaussian kernel of 4-mm FWHM). All resultant probabilistic DTI tractography maps of 6 normal and 5 rabid dogs were then normalized to the new template using SPM2, while the estimated warping and affine transformation parameters were also applied to individual FA and MD maps to create normalized FA and MD maps, which then smoothed with a Gaussian kernel of 4-mm FWHM. Finally, voxel-by-voxel, the smoothed normalized FA and MD maps of normal dogs were compared against those of rabid dogs using the two-sample t-test analysis module of SPM2.

Results and Discussion

Even being smoothed, the dog's whole brain probabilistic DTI tractography template, representing axonal densities, still shows sufficient anatomical details (**Fig. 1**). For FA group comparison, at $p < .05$, there were significant decreased FA areas in the rabid dog brain group (**Fig. 2 (a)**). **Fig. 2 (b)** shows example slices of the decreased MD map in the rabid dog brain group at $p < .05$.

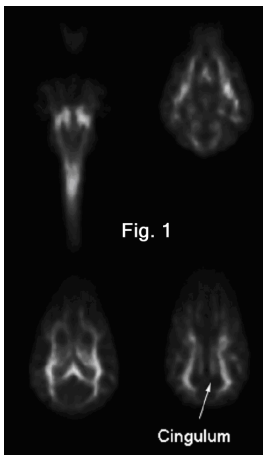
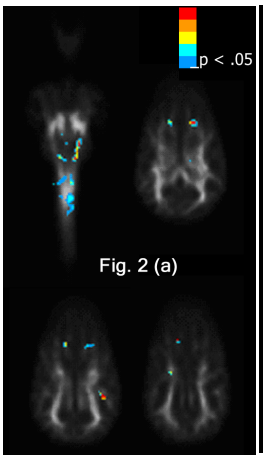
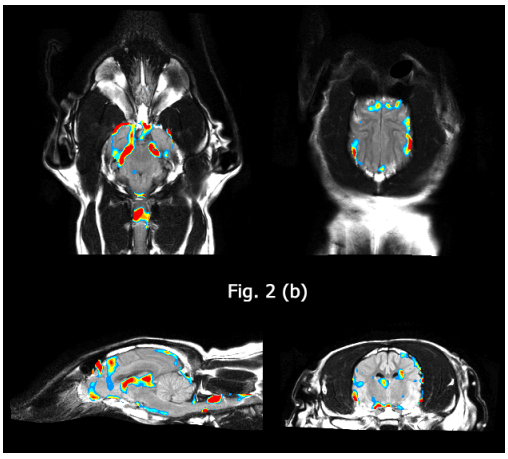


Fig. 1: Selected slices of the smoothed normal dog's whole brain probabilistic DTI tractography template are shown. Cingulum can be clearly observed (but not prominent compared to white matter).

Fig. 2: (a) Example slices of FA reduction map of rabid dog group at $p < .05$ threshold, superimposed on the probabilistic DTI tractography template. **(b)** Example slices of decreased MD map of the rabid dog group at $p < .05$ threshold, superimposed on FLAIR images (coregistered to the template).





Using whole brain probabilistic DTI tractography maps and template in brain image normalization seems to be very robust. It can address the immense variability of dog's brain shape and size. However, it is very time consuming. Thanks to the success of the normalization, voxel-based group comparisons could be conducted. The decreased FA findings confirmed that there was impairment of neural tract integrity in brainstem and upper spinal cord of paralytic rabies infected dogs. This may explain the clinical manifestations, differences in viral load and MRI findings in human furious and paralytic rabies [1, 2]. Moreover, the decreased (not increased) MD values confirmed that there was cytotoxic (neuronal cell swelling) brain edema with preserved blood-brain barrier. The findings support that DTI can serve as a sensitive measure to detect early/minimal changes in central nervous system diseases. The method presented herein using whole brain probabilistic DTI tractography normalization may be applicable for functional and structural brain studies in very young, elderly people, and patients with encephalitis and Alzheimer's disease.

References

[1] Hemachudha et al. (2002), Lancet Neurology 1: 101–09; [2] Laothamatas et al. (2003), AJNR Am J Neuroradiol 24:1102–1109