Quantitative T2 analysis in a transgenic mouse model of AD using an optimized nonlinear digital image warping algorithm.

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Synopsis

An image warping algorithm has been implemented and applied to register volumetric and T_2 maps from MRI brain scans of transgenic mice. The algorithm successfully registered 27 mouse brain MRI volumes and T_2 maps, allowing a reliable measurement of T_2 for different regions of interest.

Introduction

Transgenic mouse models have been essential for understanding the pathogenesis of Alzheimer's disease including those that model the deposition process of Aß. Recently, we reported shortening of T_2 in the cortex and hippocampus of PS/APP mice. [Helpern et al, 2003]. In that study, for each regional image analysis, each animal was studied individually and then the results were pooled for statistical assessment. This approach involved drawing regions-of-interest (ROIs) for each brain in each of the 9 mice for each genotype, which proved to be a very time consuming process. Another approach, which is widely used in human imaging research, would be to develop a rigorous means for image registration. This would allow us to compute statistical parametric maps representing group differences of quantitative parameters (e.g., relaxation times, diffusion anisotropy) between different mouse groups.

Imaging protocol and Image registration algorithm

Twenty-seven mice 18 months old (n=9 for each genotype) and three genotypes (PS-APP, PS and NTG) were imaged on a 7 Tesla 40-cm horizontal bore magnet (Magnex Scientific, Abingdon, UK) interfaced to a SMIS console (Farnham, UK). A multi-slice multi spin-echo sequence was used to acquire the images. Imaging parameters were: one signal average, 48 slices, FOV of 2.56 x 2.56 cm^2, matrix size of 128 x 96, echo times (TE) of 15, 20,25,35,55 and 75 ms, and repetition time (TR) of 4000 ms. The in-plane resolution was 200 µm with the slice thickness of 200µm and a 100µm gap between successive slices.

The objective of the registration algorithm is to deform a subject image $I_s(r)$ to match a target image $I_t(r)$. For this purpose, a deformation field w(r) is found and the subject image is deformed as: $I_s(r+ w)$. Local template matching is employed for finding the deformation field. The algorithm follows a multi-resolution approach in which the problem is solved at different levels in the scale-space and the solution at each scale serves as the initial condition for the next higher resolution scale. Regularization of the warp field is achieved simply by Gaussian smoothing of the results at each resolution level. The deformation field components are fitted to a truncated Fourier-Legendre series at each scale. This model provides some additional regularization, allows the computation and monitoring the Jacobian of the deformation field, and achieves significant data compression for storage of the deformation field. If the Jacobian becomes zero or negative at any point in the image, then the level of smoothing is increased to alleviate the problem. Thus, it is ensured that the deformation mapping is a homeomorphism.

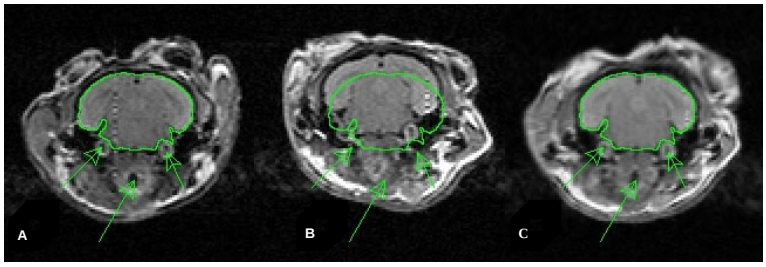

Figure 1: Registration of MRI brain scans between mice. (A) mouse brain target volume showing three easily identifiable landmarks (arrows); (B) mouse brain object volume with landmarks identified from the target mouse directly superimposed in order to highlight differences in brain shape, size and location within the imaging matrix relative to the target; (C) After warping and registration the object volume matches the target volume.

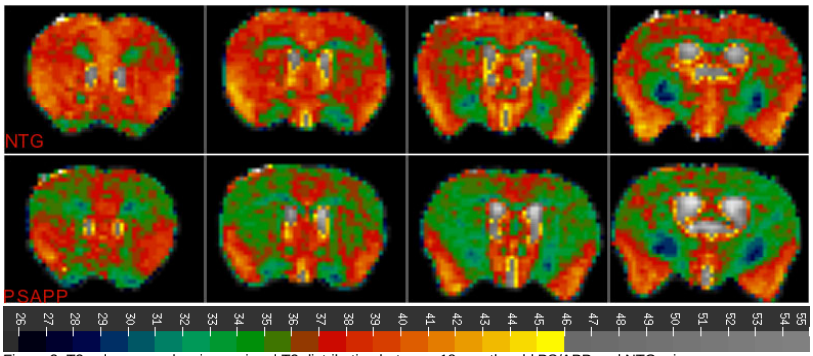

Figure 2: T2 color maps showing regional T2 distribution between 18 months old PS/APP and NTG mice.

Data analyses

A mouse target brain was chosen as the median brain volume for all 27 mice. Initially, all first echo images (48) for each mouse were warped to the target brain. The resulting image was then warped to each individual T_2 map. Using MEDx software (Sensor Systems) ROIs were manually drawn on images from each individual mouse as well as on the target brain, on regions consisting of hippocampus, cortex (cingulate and retrosplenial cortex) and corpus callosum. A mean intensity value was computed from each unwarped and warped T_2 maps.

Results and Discussion

The algorithm successfully registered all 27 image sets and their respective T_2 maps. Figure 1 shows the results of applying the program to images from two different object mice. The landmarks (in green) are extracted from the target image volume (A) superimposed on the object image before (B) and after registration (C). All landmarks are closely matched to their location on the target image. The image-warping algorithm speeded the processing time of T_2 calculations by a factor of 27. Color maps representative of the average distribution of T_2 for each specific ROI are shown in Figure 2. These images visually demonstrate the reduction of T_2 seen on the cortex of the PS/APP mouse model (p= 0.04). A comparison of T_2 measurements calculated from unwarped and warped T_2 maps showed a very high correlation although these approaches were statistically different. There was a systematic bias in the warped images (slightly lower T_2); nevertheless, the use of the warping algorithmic improved the ability to statistically discriminate between the two groups and to visually reflect intra-regional distributions of T_2.

Helpern JA at al., Mag. Reson. Med.,2003 (submitted).

Acknowledgements: Supported by the Whitaker Foundation RG-00-0350 (BAA), NIA P01 AG17617 (RN, JAH), Wyeth (JAH) and NINDS RO1 NS30899 (JAH)