Atlas-based segmentation for quantitative analysis of brain structures in the rhesus monkey

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Animal models are often used in pre-clinical studies of potential pharmaceuticals to study physiological mechanisms or evaluate efficacy or toxicity. Such models are also used in anatomical and functional studies that are impossible to complete with humans due to practical or ethical considerations. The rhesus macaque, a species of non-human primate, is often used to create models of human diseases and infections. Such studies can yield very important data that can be translated to humans. Both anatomical and functional studies often require identification of specific regions to evaluate structure size or quantify functional activity within a region. Since manual segmentation of multiple structures from a large number of MRI brain images from different individuals is prohibitively time consuming and subject to inter- and intra-observer variability, we have designed and implemented an automated atlas-based segmentation (ABS) procedure. The ABS procedure is derived from an image-processing pipeline originally designed for the analysis of human brain MRI data at the Montreal Neurological Institute [1]. This study briefly describes the image processing pipeline and presents initial results from the analysis of a group of rhesus macaques.

Subjects and image acquisition: MRI scans were performed all animals (28f, 27m) using previously described procedures[1]. The age range was somewhat bimodal (24 animals less than or equal to 15yo, mean 6.9y, inter-quartile 3.25-9.5yo, 7 females; 31 animals greater than 15yo, mean 25.0, inter-quartile 24-26, 21 females). Monkeys were intubated under ketamine anesthesia, and maintained with 1.5% isofluorane and mechanical ventilation during scanning. Scans were performed on a 3T Siemens/Trio and using Siemens eight-channel array head coil. A total of four structural scans were performed, but this study focuses on data from 3D MPRAGE sequences acquired with the following specifications: TR/TE/NA/FA 1.47s/4.38ms/4/12o, 128x128x64 mm3 FOV, 256x256x80 matrix. All animal handling procedures were approved by the Institutional Animal Care and Use Committee at Merck Research Laboratories.

Processing: In the ABS approach, an average brain image is used as a template (or registration target). The template was manually segmented into 20 structures (e.g., lateral ventricles, corpus callosum, putamen, caudate, globus pallidus, hippocampus, entorhial cortex, perirhinal cortex, cerebellum) to form an atlas [2]. In short, segmentation is achieved by mapping atlas labels through the inverse of the non-linear spatial mapping function that aligns each voxel of a subject's MRI with the corresponding voxel in the target. The pipeline consists of the following steps, customized to account for differences between rhesus and human MRI. First, RF non-uniformity is corrected using N3 [4]. We reduced the default spline distance to 100mm to account for the smaller head size. The brains were extracted using BET [5]. Intensities are normalized to a range of 0.0-100.0 by mapping the 0.01 and 99.9 percentiles of the original T1 histogram. Registration is achieved in a two step process, first computing a linear registration to the template, followed by estimation of a non-linear mapping to the template. Both are achieved using minctracc from the mni_autoreg software [3]. Labels from the template are mapped through the inverse of the estimated transformation, thus segmenting structures on the individual MRIs. Volumes for each structure are computed by counting voxels with the same label and multiplying by the voxel size. In addition to absolute volumes, a relative metric of brain size known as BICCR (brain to intra-cranial capacity ratio) was computed. To account for differences in head size, all volumes were normalized to the intracranial volume.

Results: Figure 1 shows a transverse slice through a typical segmentation. Overall, WM increased (0.14%/y, r^2=0.25, p=0.0002), GM decreased (-0.1%, r^2=0.49, p<0.0001) and lateral ventricular volume increased with age (0.39%/y, r^2=0.17, p=0.0025). (Note that % change is reported relative to the structure in question.) BICCR in the younger group was larger than the older group (p<0.05). The cerebellum decreased slightly (-0.20%, r^2=0.10, p=0.024). Two of basal ganglia structures decrease with age, putamen (-0.7%/y, r^2=0.38, p<0.0001) and caudate (-0.4%/y, r^2=0.24, p=0.0003), while the globus pallidus increases (1.8%/y, r^2=0.54, p<0.0001). In the medial temporal lobe, the perirhinal cortex decreased with age (-0.37%/y, r^2=0.20, p=0.001). Entorhinal and hippocampal volume increased slightly with age (0.7%/y, r^2=0.25, p=0.0102 and 0.4%/y, r^2=0.09, p=0.029), respectively.

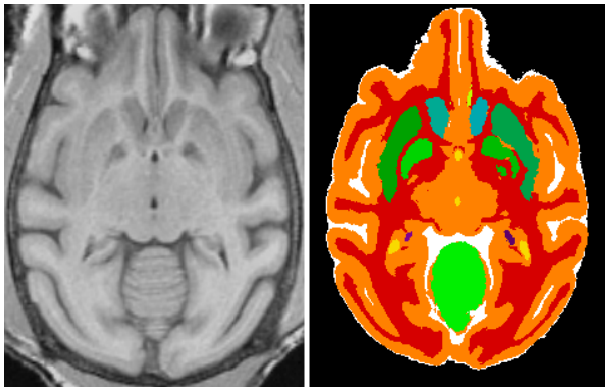

Figure 1: Example of T1 weighted MPRAGE image from a rhesus monkey (left) and corresponding ROIs.

Conclusions: This study shows feasibility of automatic regional segmentation of brain MRI data from rhesus monkeys.

1: Collins et al, Human Brain Mapping, 1995; 2: Frey, Collins, Human Brain Mapping abstract. 3: Collins, et al. Journal of Computer Assisted Tomography, 1994. 4: Sled, et al. IEEE Trans Med Imaging, 1998. 5: Smith, Human Brain Mapping, 2003