An in vivo tree shrew brain anatomical imaging template for tissue segmentation and morphometry analysis

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Introduction Tree shrews are special relatives of primates from evolution, with well-developed visual system and limbic brain structures [1, 2]. For years they are used as animal models in vision research [3] and in studies of social stress [4]. Few previous studies, however, have used magnetic resonance imaging to study the brain of tree shrew. Ohl et al measured the volume of hippocampus of tree shrew manually from T_2-weighted images [4, 5], and showed reduced hippocampal volume under chronic psychosocial stress [4]. As an important step to achieve automated/parametric analysis of tree shrew brain imaging data, we built a set of brain tissue probability maps of *Tupaia belangeri chinensis*. High resolution T_2-weighted images covering the whole brain were collected from 7 male tree shrews. The average probability maps of grey matter (GM), white matter (WM) and cerebrospinal fluid (CSF) were constructed, and used for semi-automated volumetric measurements of limbic brain structures.

Materials and methods Seven male tree shrews, weighing 131±16 g, were housed individually, and given access to food and water *ad libitum*. All animals were imaged on a 7 T/20 cm Bruker Biospec scanner under chloral hydrate anesthesia (10%, 400 mg/kg body weight, i.p.). A 72-mm diameter volume coil was used for radiofrequency pulse transmission, and a quadrature surface coil for signal detection. T_2-weighed images were acquired with a RARE sequence, TR 6900 ms, TE 12 ms, RARE factor 8, FOV 30 mm×30 mm, matrix size 256×256, 58 contiguous slices with a thickness of 0.5 mm, and 12 averages. All images were processed with the ANTs software (www.picsl.upenn.edu/ANTS). The non-brain tissue pixels were first removed manually, followed by correction of intensity non-uniformity resulted from surface coil reception. The preprocessed images from each individual animal were then segmented to GM/WM/CSF probability maps using the Atropos toolbox. The WM probability map from one animal was chosen as the initial template, to which the WM probability maps from all the other animals were registered first by rigid registration, and then by diffeomorphic transformation. For each animal, the registration parameters obtained were then applied to register the GM and CSF probability maps to the template space. The individual WM, GM and CSF probability maps were averaged to calculate group-average templates. The volume of bilateral hippocampus (Hip) and amygdala (Amy) were measured using both a manual method and a semi-automated method based on the templates constructed. With the manual method, bilateral Hip and Amy were traced out on the images of each individual animal. With the semi-automated method, regions of interest representing bilateral Hip and Amy were traced out only once on the template, and mapped back to the original space of each animal using corresponding inverse transformation. The volumes were then calculated in the original space.

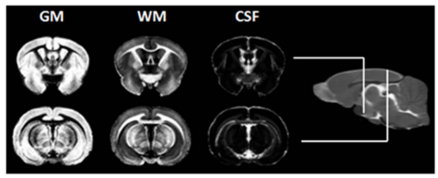
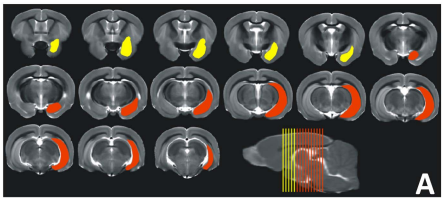
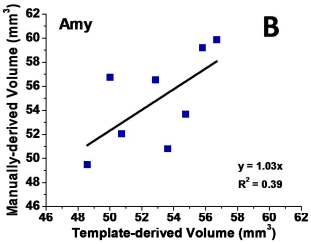


Figure 1. Group-average tissue probability maps of two axial slices, the locations of which were marked on the sagittal slice on the right.





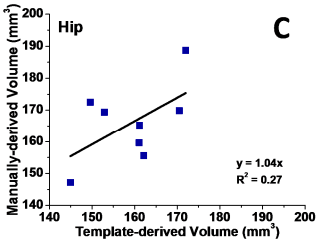


Figure 2. Volumetric measurements of amygdala (Amy) and hippocampus (Hip). The regions of interest rcprcscnting Amy (ycllow) and Hip (red) are shown in A. The correlations between the results obtained by the manual method and semi-automatic method are shown in B and C.

Results Figure 1 shows the tissue probability maps from two axial slices, representing the group-average from 7 animals. Figure 2 compares the Hip/Amy volume measured manually from each individual animal and those derived from semi-automated measurement based on regions of interest drawn on the templates (Fig. 2). The results obtained by the two methods agreed well.

Discussion High-resolution anatomical images of tree shrew brain were acquired, and used to generate population-based GM/WM/CSF probability maps for further applications such as semi-automated volumetric analysis and voxel-based morphometry (VBM). The hippocampal volume measured in this study agreed well with those reported by Ohl et al (manual: 165.9±12.5 mm^3; template: 159.3±9.6 mm^3; Ohl et al: 167.5±12.7 mm^3) [5].

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