Automatic Mouse Brain MRM Parcellation Based on Tomographic Atlas

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Abstract. Although several MRM based mouse brain atlases have been proposed, limited work has been done on tomographic atlas based mouse brain MRM segmentation. In this study, the anatomical regions in the Paxinos and Franklin's Atlas (P-F Atlas) were first merged into 34 regions, a pseudo T2-weighted MRM was then generated from the 3D atlas based on higher order regional statistics. Finally, Geodesic-Syn approach was used to link the pseudo T2 MRM to mouse brain MRM, and the consistency between them was also evaluated. This study provides a foundation for automatic mouse brain MRM parcellation based on P-F Atlas.

Introduction

Most brain diseases are associated with subtle morphological changes within certain brain regions. Subdividing the human brain into regions of interests (ROIs) on MRIs is an essential technique in investigating brain morphology\cite{1}. Traditionally, high dimensional deformation algorithms have been developed to warp one brain MRI to another, thereby allowing one to map ROIs from a predefined atlas, to any individual's MRI. Accurate parcellation enables efficient comparison of results from different individuals and findings from different laboratories.

Nowadays, mouse models have been widely used in neuroscience research for understanding the pathobiology of complex human disorders and discovering efficient therapeutic targets. Thus, atlas based brain segmentation has also been extended from human to mouse \cite{2}. A number of groups have delineated brain ROIs in mouse MR microscopy (MRM) for atlas based parcellation. Ma et al.\cite{3} defined a parcellation scheme that divided a mouse brain MRM into 20 regions. Ali et al.\cite{4} divided the brain MRM into 21 neuroanatomical structures. Badea et al.\cite{5} segmented mouse brain MRM into 33 major structures. A refined parcellation scheme developed by Dorr et al\cite{6} has labelled the brain MRM into 62 neuroanatomical structures. The mouse brain is 3000 times as small as that of a human. The signal to noise ratio (SNR) and contrast to noise ratio (CNR) of mouse brain MRM are also much lower than those of clinical MRI. Thus, the number of regions that can be delineated in MRM is limited, and the accuracy of delineation is heavily relying on user expertise.

Paxinos and Franklin's Mouse Brain Atlas (P-F Atlas) \cite{7} is the authoritative source for the delineations of C57BL/6 wildtype mice. It consists of 100 coronal levels of feature photographic plates of Nissl- or acetylcholinesterase-stained sections as well as the matching diagrams. Due to several hundred accurately identified structures, the atlas is the most cited mouse brain atlas in neuroscience field. Unlike MRM based atlas, this tomographic atlas is based on hundreds of 2D diagrams, which limited its application in MRM parcellation.
previous study[8], we have developed a MRM parcellation scheme based on P-F atlas, but there are a number of issues can be addressed further. First, the non-linear warps in SPM99 is based on low spatial frequency basis functions (discrete cosin functions), which doesn’t have the property of inverse consistency. Second, the brain was only divided into three main regions (grey matter, white matter and CSF), and the pseudo MRM was only generated from the first order regional statistics (mean and standard deviation).

The current study is designed (1) to divide the mouse brain into 34 regions; (2) to apply diffeomorphic algorithms [9], based on large-deformation framework; and (3) to generate the pseudo T2 MRM based on higher order regional statistics. This study can provide a foundation for automatic mouse brain MRM parcellation based on P-F Atlas.

Methods

Experimental Data

The dataset used here was shared by the Computational Functional Anatomy Lab, National University of Singapore on (http://www.bioeng.nus.edu.sg/cfa/mouse_atlas.html). Five in-vivo male C57BL/6 mice T2-weighted MRM were acquired by a Bruker 7-T/20-cm ClinScan MRI, resulting in 100*98*98 µm^3 images. The original MRM was manually labeled into 39 neuroanatomical structures (Table 1) using the P-F atlas as reference. The delineation protocol is the same as protocol described by Bai et al. [10], except ROIs were extended from 19 to 39. Not all ROIs would be used in this study. In P-F atlas, cerebellar was divided as whole, so cerebellar lobules (region 9) and cerebellar cortex (region 10) were not included in the study. The hippocampus is kind of hard to be subdivided, so the four regions (region 23 to 26) were merged in to one region. Totally, 34 brain regions have been defined.

Table 1. The 39 labeled structures' name and it's corresponding numbers.

<table>
<thead>
<tr>
<th>Number</th>
<th>Structure Name</th>
<th>Number</th>
<th>Structure Name</th>
<th>Number</th>
<th>Structure Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Corpus Callosum</td>
<td>14</td>
<td>Frontal Cortex</td>
<td>27</td>
<td>Pituitary</td>
</tr>
<tr>
<td>2</td>
<td>Lateral Ventricle</td>
<td>15</td>
<td>Visual</td>
<td>28</td>
<td>Hypothalamus</td>
</tr>
<tr>
<td>3</td>
<td>Third Ventricle</td>
<td>16</td>
<td>Auditory</td>
<td>29</td>
<td>Optic Nerve</td>
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<tr>
<td>4</td>
<td>Cerebral Aqueduct</td>
<td>17</td>
<td>Somatosensory</td>
<td>30</td>
<td>Caudoputamen</td>
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<tr>
<td>5</td>
<td>Fourth Ventricle</td>
<td>18</td>
<td>Motor Cortex</td>
<td>31</td>
<td>General Basal Ganglia</td>
</tr>
<tr>
<td>6</td>
<td>Periaqueductal Gray</td>
<td>19</td>
<td>General Region of the</td>
<td>32</td>
<td>The Fornix System</td>
</tr>
<tr>
<td>7</td>
<td>Medulla</td>
<td></td>
<td>Cortex</td>
<td>33</td>
<td>Septum</td>
</tr>
<tr>
<td>8</td>
<td>Pons</td>
<td>20</td>
<td>Perirhinal Cortex</td>
<td>34</td>
<td>Internal Capsule</td>
</tr>
<tr>
<td>9</td>
<td>Cerebellar Lobules</td>
<td>21</td>
<td>Entorhinal Cortex</td>
<td>35</td>
<td>Cerebral peduncle</td>
</tr>
<tr>
<td>10</td>
<td>Cerebellar Cortex</td>
<td>22</td>
<td>Hippocampus-CA1</td>
<td>36</td>
<td>Substantia Nigra</td>
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<td>11</td>
<td>Anterior Commissure</td>
<td></td>
<td>Region</td>
<td>37</td>
<td>Thalamus</td>
</tr>
<tr>
<td>12</td>
<td>Lateral Olfactory Tract</td>
<td>23</td>
<td>Hippocampus-CA3</td>
<td>38</td>
<td>Amygdala</td>
</tr>
<tr>
<td>13</td>
<td>Olfactory System</td>
<td>24</td>
<td>Dentate Gyrus</td>
<td></td>
<td>General region of the</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>25 General Region</td>
<td></td>
<td>midbrain</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>of Hippocampus</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>26 Superior and Inferior</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Colliculus</td>
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</tbody>
</table>

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Determination of Settings for Intersubject Mouse Brain Registration

Obviously, the most famous registration algorithm in ANTs is the Geodesic-SyN[9]. A recent study of five diffeomorphic image registration algorithms have shown that Geodesic-SyN[11] is remarkable successful for mouse brain registration. Here, we used the optimal parameters proposed by Fu[12] (gradient step length at 1, time points at 2, integration time discretisation step at 0.05, the Gauss parameters for the velocity field and deformation field at [3, 2], CC as the similarity metric for diffeomorphic transform, whereas MI as the similarity metric for affine registration, the number of iterations is [100, 100, 30] , and window radius at 2).

Figure 1. Flow chart of generation of pseudo T2-weighted MRM.
Simulated MRM Based on the Mouse Brain Atlas

We used a bounding box of -8.2 to 4.2 mm in the x-direction (posterior to anterior), -1 to 7 mm in the y-direction (ventral to dorsal) and -5 to 5 mm in the z-direction (left to right) and the origin corresponds to the midline at the level of Bregma intersected by a horizontal plane passing through the interaural line. The 2D color figures, from the anterior to the posterior, were converted to gray-scale figures. The slice-to-slice realignment was also performed. Several hundred regions in diagrams were merged into 34 regions as described in Table 1. Each region was assigned an integer number as an index. By doing so, the 2D diagrams was now in the form of 3D. Then, the 3D tomographic data was interpolated to create a new 3D image with uniform inter-slice separation.

In order to co-register the mouse brain MRM with the tomographic atlas, we created a pseudo $T_2$-weighted MRM from the 3D atlas (Figure 1). For this purpose, the 34 regions were divided into two categories: The structures in the first category are small and slender, whose higher order statistics is hard to achieve. It includes structures as Corpus Callosum, Lateral Ventricle, Third Ventricle, Cerebral Aqueduct, Fourth Ventricle, Periaqueductal Gray, Anterior Commissure, Lateral Olfactory Tract, Perirhinal Cortex, Pituitary, Optic Nerve, Internal Capsule and Cerebral peduncle. The rest of structures belong to the second category.

The structures in the first category were generated by Monte Carlo method as we proposed before[8]. For the structures in the second category, we extended texture synthesis algorithm proposed by Efros and Freeman[13] from 2D to 3D, and generated the pseudo structures based on their higher order statistics. The pseudo MRM would be registered with mouse brain MRM by Geodesic-SyN.

Evaluation Criteria for the Accuracy of Registration

Surface concordance ratio (SCR) measures the boundary discrepancies between the pseudo MRM and real MRMs. The Cityblock distance was calculated to measure the distance in voxels between two regional contours. Then we determined the percentage of vertex in one contour that fall within 200 microns from another contour. This measure provided a good tool to evaluate the registration results especially for the regions with tiny volume or grotesque in shape.

Results

Figure 2 provides a visual illustration of MRM and pseudo MRM and their residual images. The pseudo MRM are visually consistent compared to mouse brain MRM. Regional misclassifications predominantly take place at the boundaries of cortical surface. The agreement of two images are also evident visually as shown in Figure 3. The outlines of the atlas external contours are shown overlaid on the MRM contours. Overall, the tomographic atlas may enable a rapid and objective selection of ROIs.
The SCR between mouse brain MRM and pseudo MRM is $0.822 \pm 0.1253$ (Figure 4). There are 41.18% of regions whose SCR is over 85%, and there are 91.2% of regions whose surface average distance is less than 200 microns.
Discussion

The central piece of this efforts was to link the P-F atlas with mouse brain MRM images. The linkage is not only feasible for those five mice with brain atlas, but also feasible for any C57BL/6 mice. In this study, we demonstrated the accuracy of the linkage by the evaluation of SCR of 34 regions, but the number of regions that can be parcellated is only depended on the regions that had been predefined in the tomographic atlas. Here, a new strategy of converting the atlas map into pseudo T2-weighted MRM based on higher order regional statistics has been proposed, which allows us to use the Geodesic-SyN to register the tomographic atlas with mouse brain MRM. The Geodesic-SyN setting was only tested with in-vivo data, so we should also be aware that the proposed procedure may not be the optimal between invivo and in-vitro due to large differences in neuroanatomy, adjustments of parameters may be required.

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References


