An Automatic Guinea Pig Brain Extraction Method

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Introduction: Guinea pigs serve as an ideal animal model in neuro-toxicology studies because their cholinergic system is similar to the humans compared to rats or mice[1]. There is a growing number of imaging studies using guinea pigs as animal models[2,3], however to our knowledge there are no automatic brain extraction algorithms available for the guinea pig, which can be very useful for preclinical studies. We previously presented an automatic rat brain extraction method, Rat Brain Deformable model method (RBD), and demonstrated that RBD reliably extracts T_2-weighted rat brains and provides superior results than any other available rat brain extraction methods[4]. In this study, we adapt the RBD method and describe a guinea pig brain deformable model method (GBD). The main modifications in GBD include adapting the guinea pig brain geometry, which is quite different from that of the rat brain, and the addition of a template based approach to generate model initialization parameters (e.g. the brain ellipsoid) specific to guinea pigs, to the RBD framework. The goal is to improve the robustness of the initialization process such that it is insensitive to the manner in which the brain imaging data is obtained.

Methods: Algorithm: GBD contains two steps. Step 1 is the preprocessing step, which involves affine registration of the guinea pig brain to a pre-defined guinea pig brain template (here we took the average of three guinea pig brains that were affinely registered to each other with further manual adjustment) to obtain model initialization parameters. Step 2 is the deformable surface model evolution to generate the brain surface, which is similar as in the RBD algorithm[4] but with adjusted parameters ($f_{n\_sup} = 0.3$, $f_{n\_inf} = 0.033$, $d_1 = 0.3$, $d_2 = 0.3$, $d_3 = 0.6$, $offset_{sup} = 0.2$, $offset_{inf} = -0.2$) to account for a few brain geometry differences between guinea pigs and rats. Briefly, f_{n_sup} and f_{n_inf} are smoothing vectors preventing a vertex moving away from its neighbors during the surface deformation (for superior and inferior regions of the brain, respectively). d_1, d_2, d_3 are distances to find local image intensity extremes at a vertex. $offset_{sup}$ and $offset_{inf}$ are used to determine a local threshold to distinguish a brain/non-brain tissue in the superior and inferior regions respectively.

Imaging: Our algorithm was tested and validated on T_2-weighted MRI images of 20 adult female Hartley Guinea Pigs. All images were acquired on a Bruker 7.0 Tesla scanner. A Bruker four-element 1H surface coil array was used as the receiver and a Bruker 154 mm inner diameter circular coil as the transmitter. A rapid acquisition with relaxation enhancement (RARE) sequence was used to obtain T_2-weighted MR images with an effective TE of 60ms, TR of 3829ms or 6900ms, RARE factor of 8, FOV of 35×40mm^2 and slice thickness of 1mm with 20 to 32 slices to cover either the central brain portion or the entire brain.

Data Analysis: The brain masks for all guinea pigs were manually delineated by an expert, based on a guinea pig brain atlas[5] using MIPAV[6], and the results served as the ground truth. Because there is no available guinea pig extraction method available, we compared our method with the direct application of the RBD method. Brain extraction performances were evaluated using the Jaccard index (J)[7], as well as the false detection rate (p_f) and miss rate (p_m)[8]. Paired t-test was used to compare results from methods.

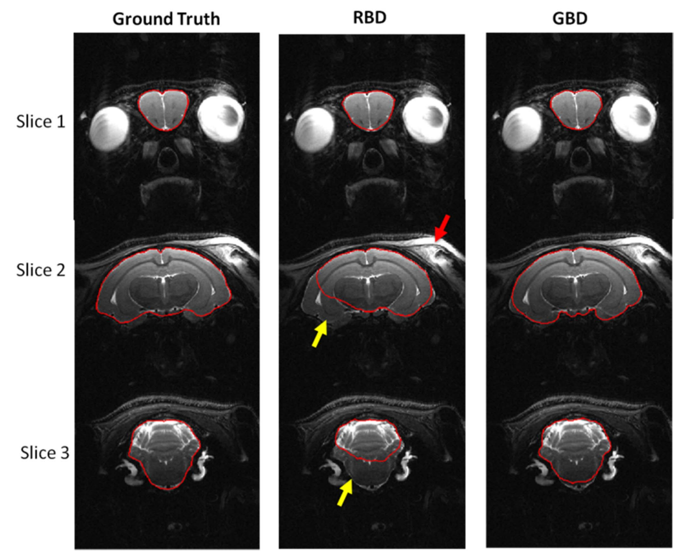

Figure 1. Brain extraction results on an example guinea pig brains. Red contours indicate the extracted brain contour on coronal slices. Yellow arrows indicate areas of misclassification from the brain extraction algorithm. Red arrow indicate strong signal from the ear that caused poor initialization.

Results: RBD failed to produce results for three out of 20 guinea pig brains (due to RBD unable to construct the initial surface because of wrong estimation of the brain ellipsoid), where the GBD produced an average J of 0.900±0.022 on the three. Figure 2 shows the brain extraction results on a representative guinea pig using the original RBD method and the new GBD method. RBD missed a big portion of brain in the left area in slice 2 and inferior portion in slice 3. The strong signal from the right ear (red arrow) likely caused a shift of estimated center-of-gravity (COG) to the right, and hence caused an asymmetric brain surface deformation and the left side of brain missed. On the other hand the COG in GBD was calculated from the template through the registration process, and hence did not suffer from this error. The quantitative brain extraction results are shown in Table 4.2. GBD showed significantly higher brain extraction accuracy than RBD ($p = 0.0006$). Both false detection rate and the miss rate did not show a significant advantage of GBD over RBD, although the performance of GBD is much more stable indicated by a smaller SD.

Method	Brain Extraction Accuracy (J)	False Detection Rate (p_f)	Miss Rate (p_m)
RBD	0.861±0.056	0.067±0.047	0.073±0.072
GBD	0.907±0.018*	0.047±0.019	0.046±0.022

Table 1. The brain extraction results for RBD and the new GBD. Values shown are mean ± SD. * indicates significant ($p < 0.05$) difference compared to RBD. RBD's J excludes failed cases.

Discussion: The improvement of GBD over RBD includes a template registration step that registers each individual guinea pig brain to a pre-defined template and then takes initialization parameters from the template. This step takes cares of one of RBD's limitations on its reliance on a good estimation of the initial brain ellipsoid to represent the guinea pig brain. This step also alleviated the COG estimation error in guinea pig brains associated with the strong MRI signals from eyes, which are now located closer to the brain. Furthermore model parameters are also adjusted in GBD to account for a few differences of guinea pig brains to rat brains: 1) a bigger brain size which affects the search region for brain boundary during surface deformation; 2) a more irregular brain shape (more elongated in the left-right axis and more geometric difference from anterior to posterior) which leads to an adjustment in the surface smoothing parameters. As guinea pig brains are larger the signal variation across the superior-inferior axis is stronger (mainly due to the use of the surface coil in the image acquisition) and tracking of the inferior surface of the brain is even more challenging due to weaker signals, so a few offset parameters are also adjusted for the model to deform properly in different sections of the brain. We demonstrate here that GBD provided an overall brain extraction accuracy of above 90% brain overlap with the ground truth. The same framework could also easily be extended to other rodent types (e.g. mice).

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References:[1] Albuquerque et al., Proc Natl Acad Sci, 2006; [2] Gullapalli et al., Neurotoxicology, 2010; [3] Mullins et al., Neurotoxicology, 2013; [4] Li et al., J Neurosci Methods. 2013; [5] Rapisarda et al., Archivio di Science Biologiche. 1977; [6] McAuliffe et al., CBMS 2001; [7] Jaccard, New Phytol, 1912; [8] Segonne et al., NeuroImage, 2004.