Template images for neuroimaging in *Macaca fascicularis*

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**Introduction**

- Combining functional neuroimaging data across different subjects in a common atlas space provides several benefits.
- In humans, atlas registration of 3D images is done by automated voxel-based methods.
- This requires a high-quality, representative and preferably atlas-registered 3D template image, not previously available for cynomolgus monkeys (*M. fascicularis*).

**Methods 1.**

- MRI template was constructed from images of 9 male and 2 female radiologically normal *Macaca fascicularis* monkeys, ~5kg
- 8 additional lower-quality or radiologically abnormal scans to test generalizability.
- Sagittal 3D MPRAGE images with known spatial accuracy.
- Validated custom software for cross- and within-modality affine and rigid-body image registration.
- Template image development:
  1. Reference was Martin RF, Bowden DM: Primate Brain Maps: Structure of the Macaque Brain. Amsterdam: Elsevier, 2006. (*"PBM"*)
  2. Create 3D image from digital PBM coronal atlas images.
  3. Register each original MPRAGE to the 3D PBM image, then average.
  4. Register original MPRAGEs to this first average and average these aligned images; then realign this new average to the PBM image to preserve atlas correspondence.
  5. Repeat this process (x 20) until transformation matrices describing registration are consistent. Resample from original images.

**Methods 2.**

- Note: The PBM atlas used one brain for the middle sections of the Template Atlas (those showing subcortical structures) and another animal for the most anterior and posterior sections. We registered MR images to the PBM atlas based only on the center sections from a single animal.
- Validation:
  - Absolute 3D error compared to PBM atlas, at 5 subcortical and 2 cortical sulcal landmark test points (identified by expert).
  - Test points were: AC, PC, L & R center of caudate on coronal slice best showing foramen of Monro, center of corpora quadrigemina on best coronal slice, lateralmost point of L & R lateral sulcus.
  - Hand-traced brain boundary in new MRI template was back-registered to individual MR images for automatic brain volume estimate.

**Results**

- MRI template images, (0.5mm)^3, available at http://purl.org/net/kbmd/cyno
- Subcortical test points: mean error vs. atlas (11 normal subjects), 1.2mm; max 2.5mm
- Cortical test points: mean error vs. atlas (11 normal subjects), 2.7mm, max 4.2mm
- Brain volume in these living animals is 22% larger than the brain used for the published atlas.

**Conclusions**

- We developed an MRI template image of the cynomolgus brain needed for automatic, voxel-based image registration methods.
- It is averaged from multiple subjects to better represent the species than would a single brain (compare the human MNI template).
- Individual MR images can be registered accurately to this template and to the PBM photomicrographic atlas (available online at http://braininfo.rprc.washington.edu).
- Can be used with SPM99 or similar software to refer functional imaging findings to the atlas.
- Complementary tools are described at braininfo.rprc.washington.edu/indexotheratlas.html & brainmap.wustl.edu/resources/caretnew.html

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**Other species**

- Pig-tailed macaque
- M.nemestrina
- Other primates
- VV63
- Vervet
- Cercopithecus aethiops
- J. nemestrina