Digital templates and brain atlas dataset for the mouse lemur primate

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ABSTRACT

We present a dataset made of 3D digital brain templates and of an atlas of the gray mouse lemur (Microcebus murinus), a small prosimian primate of growing interest for studies of primate biology and evolution. A template image was constructed from in vivo magnetic resonance imaging (MRI) data of 34 animals. This template was then manually segmented into 40 cortical, 74 subcortical and 6 cerebrospinal fluid (CSF) regions. Additionally, the dataset contains probability maps of gray matter, white matter and CSF. The template, manual segmentation and probability maps can be downloaded in NIfTI-1 format at https://www.nitrc.org/projects/mouselemuratlas. Further construction and validation details are given in “A 3D population-based brain atlas of the mouse lemur primate with examples of applications in aging studies and comparative anatomy” (Nadkarni et al., 2018) [1], which also presents applications of

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the atlas such as automatic assessment of regional age-associated cerebral atrophy and comparative neuroanatomy studies.
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Specifications table

| Subject area          | Neuroscience                                                                 |
|-----------------------|-------------------------------------------------------------------------------|
| More specific subject area | Mouse lemur (Microcebus murinus) brain, MRI atlas                            |
| Type of data          | Template, atlas and probabilistic maps for the mouse lemur brain             |
|                       | Figure of the brain template and atlas.                                      |
|                       | Figure of probabilistic maps for the mouse lemur brain                       |
|                       | Table of animals used for template creation                                  |
|                       | Table with the list of segmented regions                                     |
| How data was acquired | in vivo 7T MRI (Agilent, Santa Clara, CA, USA)                                |
|                       | Template created with Sammba-MRI (https://sammba-mri.github.io).              |
|                       | Atlas created using ITK-SNAP (http://www.itksnap.org)                       |
|                       | Probabilistic atlas created using SPM8 (www.filion.ucl.ac.uk/spm) with the SPMMouse toolbox (http://spmmouse.org) |
| Data format           | Analyzed (NIfTI-1 format)                                                    |
| Experimental factors  | 34 mouse lemurs (22 males and 12 females; age range 15–58 months)            |
| Experimental features | 1. A brain template was constructed from T2-weighted images of 34 mouse lemurs |
|                       | 2. The template was segmented into 120 regions that covered the whole brain. |
|                       | 3. A probabilistic atlas was created from the initial brain template.        |
| Data source location  | Fontenay-aux-Roses, France                                                   |
| Data accessibility    | Data is with this article and available at NITRC:                           |
|                       | https://www.nitrc.org/projects/mouselemuratlas                               |
| Related research article | N.A. Nadkarni, S. Bougacha, C. Garin, M. Dhenain, J.L. Picq, A 3D population-based brain atlas of the mouse lemur primate with examples of applications in aging studies and comparative anatomy. Neurolmage, In press [1]. |

Value of the data

- This is the first publicly available whole brain template and atlas for the mouse lemur, an emergent model in neuroscience.
- The mouse lemur template and brain atlas can be used to study brain images of mouse lemurs recorded with various imaging modalities.
- A probabilistic atlas of the mouse lemur is also provided. It can be used as a prior for automatic segmentation studies.

1. Data

MR images of the brain of 34 healthy young adult mouse lemurs (Table 1) were acquired in a 7 T scanner. 3D images of the whole brain were mutually registered to create a template (Fig. 1A). This template was used for manual segmentation (Fig. 1, Table 2) and to create probabilistic gray matter, white matter and CSF templates of the brain (Fig. 2). The templates and atlas are available as NIfTI
volumes in an NITRC repository (https://www.nitrc.org/projects/mouselemuratlas). The dataset can be freely used for academic work upon citing this paper and [1].

### 2. Experimental design, materials and methods

#### 2.1. Animals

34 young to middle-aged adult mouse lemurs (22 males and 12 females) were used. Age range was 15–58 months, mean ± standard deviation 36.8 ± 9.2 months. Demographic information for these animals is provided in Table 1. The protocol was approved by the local ethics committee CEtEA-CEA DSV IdF (authorizations 201506051 736524 VI (APAFIS#778)) and followed the recommendations of the European Communities Council directive (2010/63/EU).

#### 2.2. MR acquisition

One T2-weighted in vivo MRI scan was recorded for each animal. Animals were anesthetized by isoflurane (4% induction, 1–1.5% maintenance). Images were recorded using a 2D T2-weighted fast spin echo sequence (7 T Agilent system) using a four channel phased-array surface coil (Rapid Biomedical, Rimpar, Germany) actively decoupled from the transmitting birdcage probe (Rapid

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### Table 1

List of mouse lemurs used for atlas creation.

| Sex | Age (months) | Age (years) |
|-----|--------------|-------------|
| M   | 28           | 2.3         |
| M   | 32           | 2.7         |
| M   | 32           | 2.7         |
| M   | 34           | 2.8         |
| M   | 35           | 2.9         |
| M   | 35           | 2.9         |
| M   | 35           | 2.9         |
| M   | 36           | 3.0         |
| M   | 39           | 3.2         |
| M   | 39           | 3.2         |
| M   | 39           | 3.2         |
| M   | 40           | 3.3         |
| M   | 40           | 3.3         |
| M   | 40           | 3.3         |
| M   | 44           | 3.7         |
| M   | 46           | 3.8         |
| M   | 46           | 3.8         |
| M   | 46           | 3.8         |
| M   | 47           | 3.9         |
| M   | 49           | 4.1         |
| M   | 51           | 4.2         |
| F   | 15           | 1.3         |
| F   | 18           | 1.5         |
| F   | 18           | 1.5         |
| F   | 26           | 2.2         |
| F   | 28           | 2.3         |
| F   | 35           | 2.9         |
| F   | 35           | 2.9         |
| F   | 36           | 3.0         |
| F   | 36           | 3.0         |
| F   | 44           | 3.7         |
| F   | 58           | 4.8         |
Fig. 1. Labeling of the mouse lemur atlas. Brain structure delineations are shown in a coronal section (B) together with the corresponding template image (A). For clarity, the label marking surrounding CSF is not displayed. Superior (C) and inferior (D) views of the three-dimensional representation of the brain atlas. Anterior views of the basal ganglia (E) and limbic structures (F). Annotations: a = amygdala, ca = caudate nucleus, f = fornix, g = globus pallidus, h = hippocampus, p = putamen. Scale bar = 1 cm.

Biomedical, Rimpar, Germany), resolution 230 × 230 × 230 μm, TR/TE = 10,000/17.4 ms, RARE factor = 4, field of view (FOV) = 29.44 × 29.44 mm with a matrix (Mtx) = 128 × 128, 128 slices, number of averages (NA) = 6, acquisition duration 32 min.
Table 2
Labels of all brain structures used in the atlas. Note that label ID corresponds to voxel intensity in the atlas file that can be downloaded from https://www.nitrc.org/projects/mouselemuratlas.

| Label ID | Brain structure name                      | Label ID | Brain structure name                      |
|----------|-------------------------------------------|----------|-------------------------------------------|
| 1        | hippocampal formation L                   | 61       | mammillary body L                         |
| 2        | hippocampal formation R                   | 62       | mammillary body R                         |
| 3        | amygdala L                                | 63       | hypophysis                                |
| 4        | amygdala R                                | 64       | pons L                                    |
| 5        | caudate nucleus L                         | 65       | pons R                                    |
| 6        | caudate nucleus R                         | 66       | nucleus accumbens L                       |
| 7        | stria terminalis L                        | 67       | nucleus accumbens R                       |
| 8        | stria terminalis R                        | 68       | basal forebrain nucleus L                 |
| 9        | CSF                                        | 69       | basal forebrain nucleus R                 |
| 10       | anterior commissure                       | 70       | cerebellum L                              |
| 11       | arbor vitae of cerebellum L              | 71       | cerebellum R                              |
| 12       | corpus callosum                           | 72       | arbor vitae of cerebellum R               |
| 13       | fasciculus retroflexus L                 | 73       | cerebral aqueduct                         |
| 14       | fasciculus retroflexus R                 | 74       | posterior commissure                      |
| 15       | fornix L                                  | 75       | cerebral cortex: area 6L                  |
| 16       | fornix R                                  | 76       | cerebral cortex: area 4L                  |
| 17       | mamillo-thalamic tract L                 | 77       | cerebral cortex: area 8L                  |
| 18       | mamillo-thalamic tract R                 | 78       | cerebral cortex: area 1–3L                |
| 19       | optic tract L                             | 79       | cerebral cortex: area 5L                  |
| 20       | optic tract R                             | 80       | cerebral cortex: area 7L                  |
| 21       | commissure of the inferior colliculus    | 81       | cerebral cortex: area 13–16L              |
| 22       | stria medullaris of the thalamus L        | 82       | cerebral cortex: area 21L                 |
| 23       | stria medullaris of the thalamus R        | 83       | cerebral cortex: area 22–(41–42) L        |
| 24       | basal forebrain L                         | 84       | cerebral cortex: area 20L                 |
| 25       | basal forebrain R                         | 85       | cerebral cortex: area 18L                 |
| 26       | substantia nigra R                       | 86       | cerebral cortex: area 17L                 |
| 27       | substantia nigra L                        | 87       | cerebral cortex: area 28L                 |
| 28       | midbrain L                                | 88       | cerebral cortex: area 24L                 |
| 29       | midbrain R                                | 89       | cerebral cortex: area 23L                 |
| 30       | subthalamic nucleus L                     | 90       | cerebral cortex: area 30L                 |
| 31       | subthalamic nucleus R                     | 91       | cerebral cortex: area 26–29 (retrosplenial area) L |
| 32       | globus pallidus L                         | 92       | cerebral cortex: area 27L                 |
| 33       | globus pallidus R                         | 93       | cerebral cortex: prepyriform and periamygdalar areas L |
| 34       | putamen L                                 | 94       | cerebral cortex: area 25L                 |
| 35       | putamen R                                 | 95       | cerebral cortex: area 6R                  |
| 36       | habenula L                                | 96       | cerebral cortex: area 4R                  |
| 37       | habenula R                                | 97       | cerebral cortex: area 8R                  |
| 38       | septum L                                 | 98       | cerebral cortex: area 1–3R                |
| 39       | septum R                                 | 99       | cerebral cortex: area 5R                  |
| 40       | claustrum L                               | 100      | cerebral cortex: area 7R                  |
| 41       | claustrum R                               | 101      | cerebral cortex: area 13–16R              |
| 42       | hypothalamus L                           | 102      | cerebral cortex: area 21R                 |
| 43       | hypothalamus R                           | 103      | cerebral cortex: area 22–(41–42) R        |
| 44       | thalamus L                               | 104      | cerebral cortex: area 20R                 |
| 45       | thalamus R                               | 105      | cerebral cortex: area 18R                 |
| 46       | central gray of the midbrain              | 106      | cerebral cortex: area 17R                 |
| 47       | inferior colliculus L                     | 107      | cerebral cortex: area 28R                 |
| 48       | inferior colliculus R                     | 108      | cerebral cortex: area 24R                 |
| 49       | superior colliculus L                    | 109      | cerebral cortex: area 23R                 |
| 50       | superior colliculus R                     | 110      | cerebral cortex: area 30R                 |
| 51       | olfactory bulb L                          | 111      | cerebral cortex: area 26–29 (retrosplenial area) R |
| Label ID | Brain structure name            | Label ID | Brain structure name                                                                 |
|---------|--------------------------------|----------|-------------------------------------------------------------------------------------|
| 52      | olfactory bulb R                | 112      | cerebral cortex: area 27R                                                            |
| 53      | cerebral peduncle L             | 113      | cerebral cortex: prepyriform and periamygdalar areas R                               |
| 54      | cerebral peduncle R             | 114      | cerebral cortex: area 25R                                                            |
| 55      | internal capsule L              | 115      | olfactory tubercle L                                                                |
| 56      | internal capsule R              | 116      | olfactory tubercle R                                                                |
| 57      | lateral ventricle L             | 117      | olfactory tract L                                                                   |
| 58      | lateral ventricle R             | 118      | olfactory tract R                                                                   |
| 59      | third ventricle                 | 119      | optic chiasm                                                                        |
| 60      | fourth ventricle                | 120      | medulla                                                                             |

Fig. 2. Template of the mouse lemur brain compared to probability maps and a representative image from a single animal. Scale bar: 5 mm.
2.3. Creation of the template

MR images from the 34 mouse lemurs were upsampled to 115 μm isotropic resolution. The template was generated using the function anats_to_common available within the sammba-mri python module (https://sammba-mri.github.io/generated/sammba.registration.anats_to_common.html#sammba.registration.anats_to_common). Most steps used tools from freely available AFNI software (https://afni.nimh.nih.gov/ [2], except for brain extraction which was done with RATS [3,4]. First, head images were bias corrected. In a second step the brains were extracted and individual brain extracted image centers were shifted to the brain center of mass. Brains were then all rigid body aligned to a previous histological atlas of the mouse lemur brain [5] and the transform was then applied to the original heads. A first brain template (Template 1) was produced by averaging the aligned heads. A second template (Template 2) was created by using the previous rigid body registration step a second time to align the 34 centered brains to the first template. A third template (Template 3) was created by affine aligning the 34 centered brains to Template 2. A final template (Template 4) was created by executing four cycles of non-linear registration: the first one to affine Template 3, the other ones to templates of heads from the previous non-linear cycle, including initialization using the concatenated transforms of the previous cycles. Corrections for systematic biases in the non-linear transforms were applied after each cycle.

2.4. Segmentation of the MRI-based atlas

The template image was up-sampled to 91 μm isotropic resolution, then brain structures manually segmented in ITK-SNAP (http://www.itksnap.org [6];) according to published histological atlases [5,7,8]. Each structure was iteratively segmented slice by slice along the coronal, axial and sagittal orientations until the three-dimensional representation of the labelled structure was found to be smooth and non-jagged. Each structure was outlined bilaterally. In total, 120 regions including 40 cortical, 74 subcortical and 6 CSF regions were drawn (Fig. 1, labels of brain regions provided in Table 2). The names of the structures were based on the NeuroName ontology (http://www.braininfo.org [9]).

2.5. Tissue probability maps

Tissue probability maps that can be used for brain morphometry analyses were created using SPM8 (www.fil.ion.ucl.ac.uk/spm) with the SPMMouse toolbox (http://spmmouse.org) [10,11]. MR images from the 34 animals of the study were registered to an SPM template of the mouse lemur brain [11]. Affine registration registered the images to control for different head positions, scanner geometry and overall brain size. Then unified segmentation iteratively warped the data whilst correcting for signal inhomogeneity. The images of the rigidly-aligned brains of each animal were then segmented using a k-means algorithm [12] with 4 segments: background, GM, WM, and CSF. These maps were then averaged across individuals separately for each tissue type to produce mean GM, WM and CSF tissue probability maps. These probabilistic maps were manually edited to correct for mis-labeling of CSF as GM or WM voxels due to partial volume effects, in particular around edges of the brain. They were also masked using masks derived from the segmented atlas, to conserve only brain and CSF structures (Fig. 2).

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Transparency document. Supporting information

Transparency data associated with this article can be found in the online version at https://doi.org/10.1016/j.dib.2018.10.067.

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