Anatomical and Functional Neuroimaging of the Marmoset Brain

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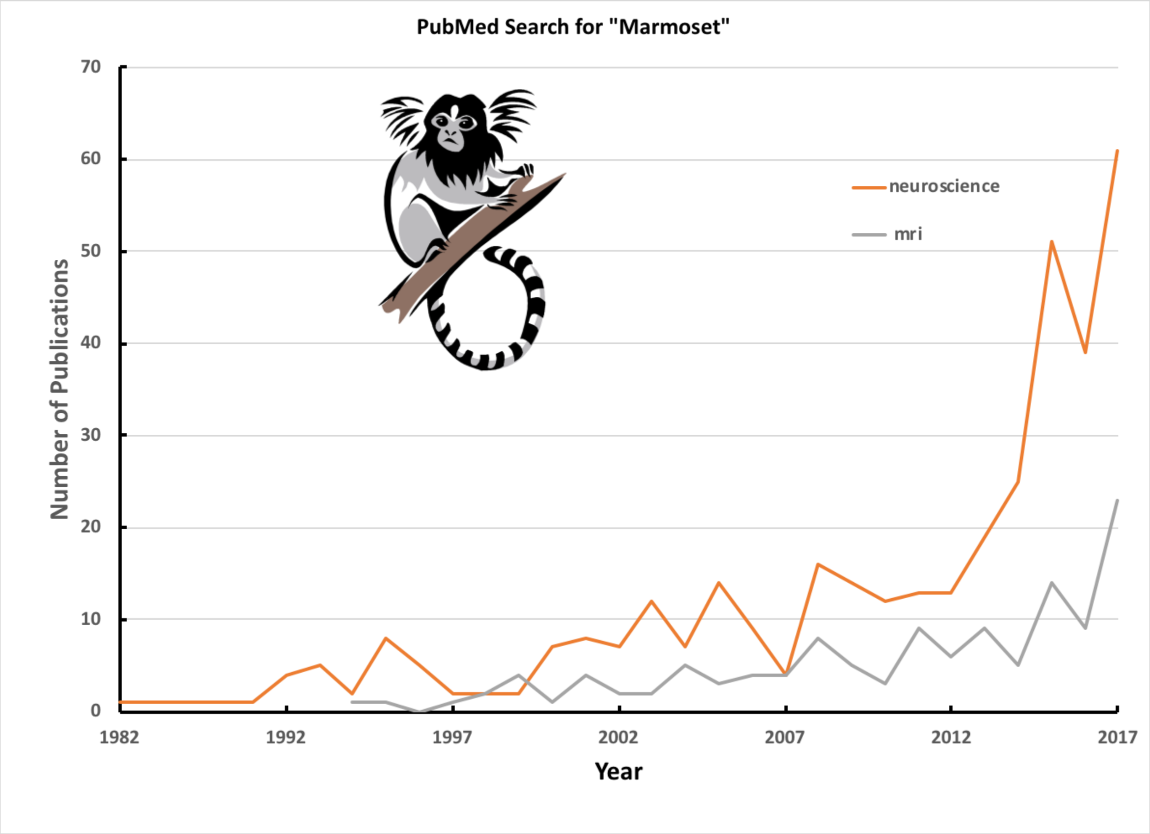
National Institutes of Health
Turning Discovery Into Health

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

Marmoset as a Model in Neuroscience



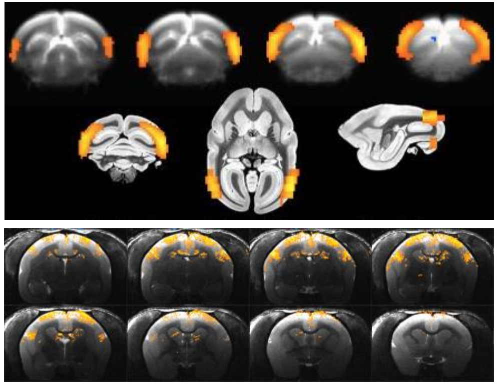
Search performed on 10/22/2018

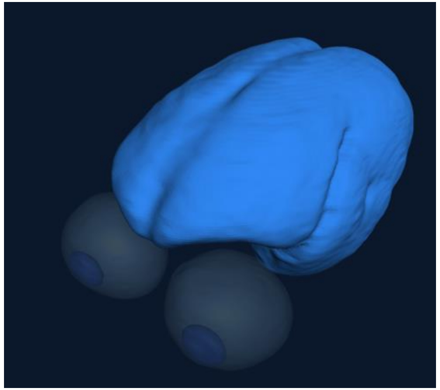
Search terms: *marmoset neuroscience*

marmoset MRI

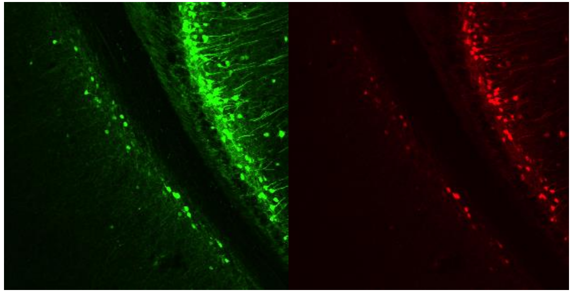
Marmosets are Lissencephalic

fMRI

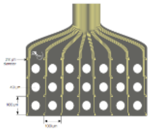


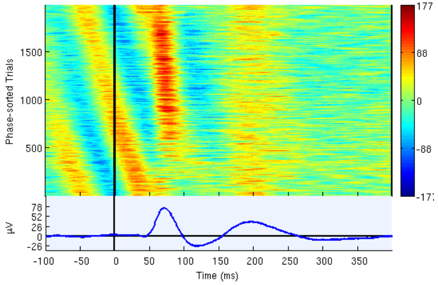


Optical Imaging



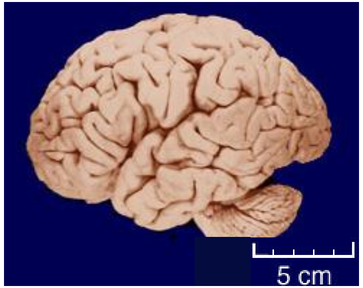
Electrophysiology



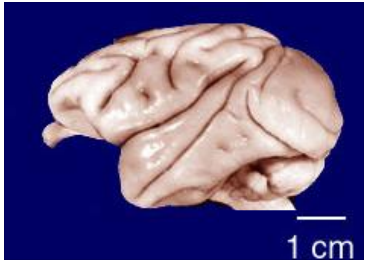


Marmosets Retain the Primate Anatomical and Functional Brain Organization

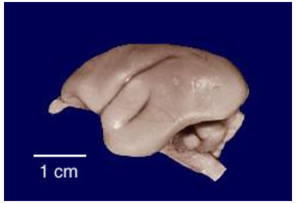
Human



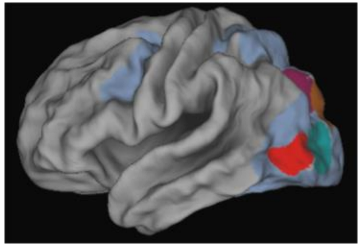
Macaque

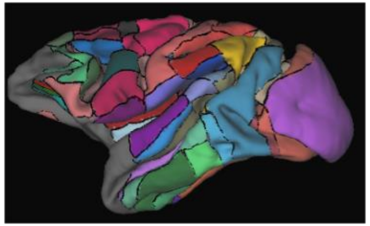


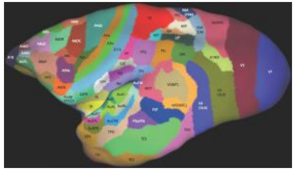
Marmoset

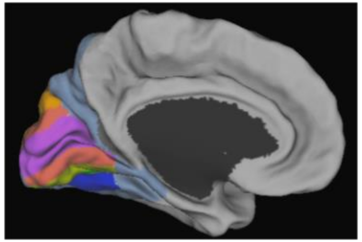


http://www.brainmuseum.org/









G. Paxinos et al. The Marmoset Brain in Stereotaxic Coordinates, 2011

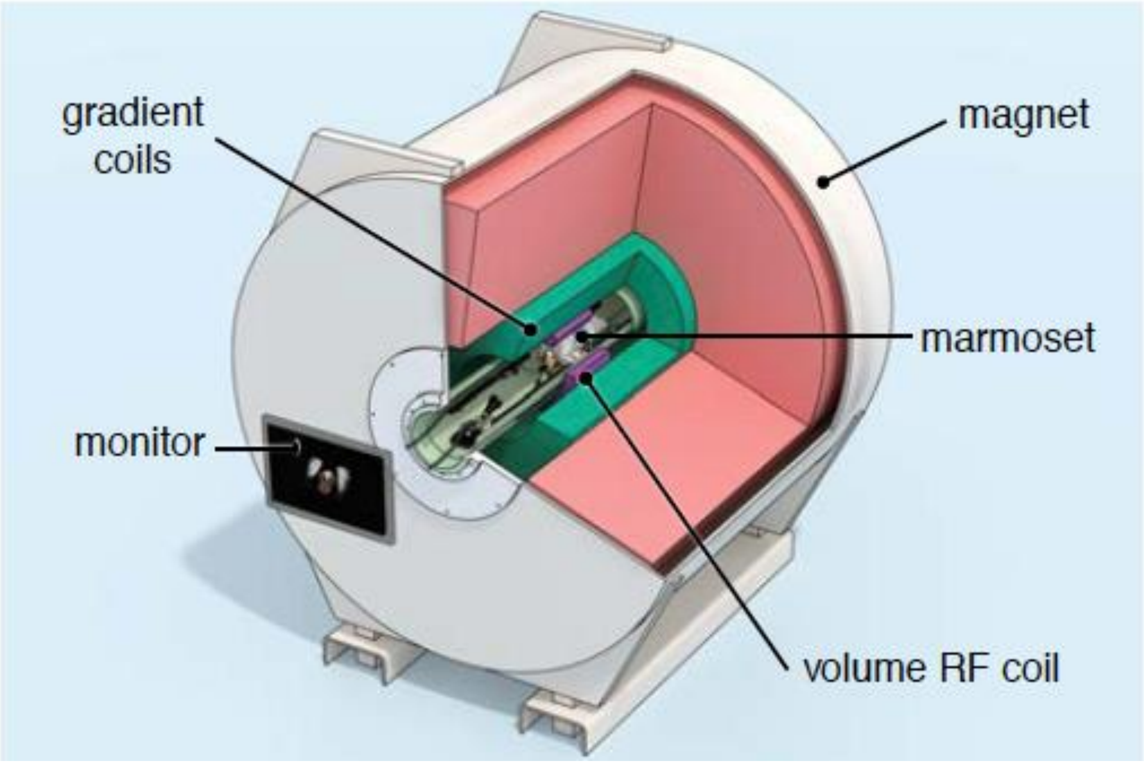
Web caret, Washington University St. Louis, MO, USA

In Vivo MRI of Marmosets

- Two basic setups:
  - Anesthetized animals
    - Isoflurane (anatomic studies)
    - MRI compatible stereotaxic head frame
  - Awake animals
    - Anatomical or functional Studies

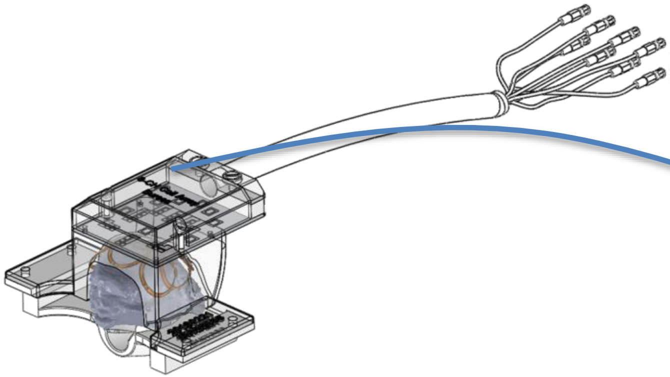
- Extensive Physiological Monitoring
  - Temperature
  - Heart Rate
  - Pulse oximetry (MR-compatible sensor)
  - Breathing (waveform acquired via pressure balloon)
  - $ETCO_2$ (anesthetized animals only)

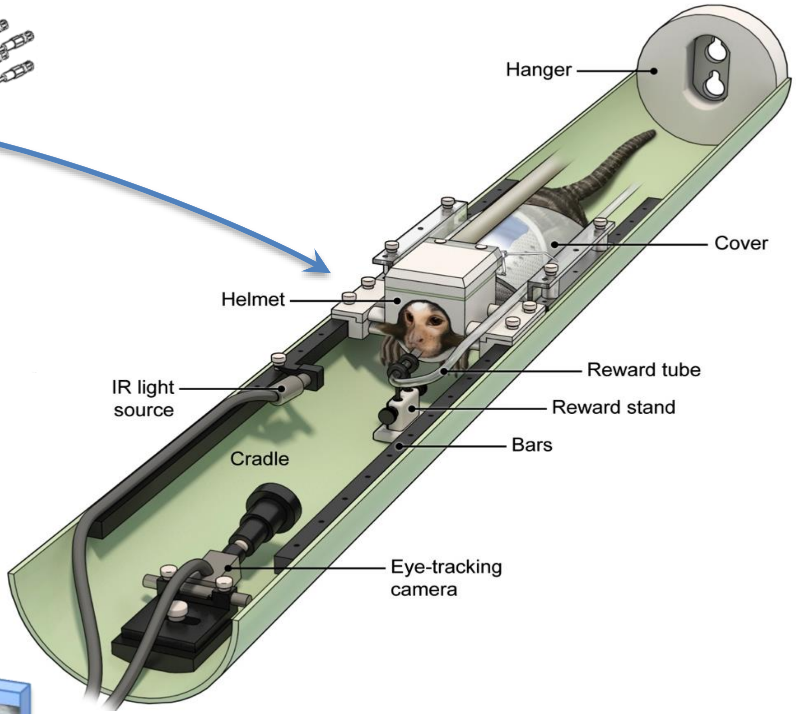
In Vivo MRI of Marmosets



** Requires 10 cm or larger clear bore (15 cm ID or larger gradient set)*

Setup for fMRI of Conscious Awake Marmosets

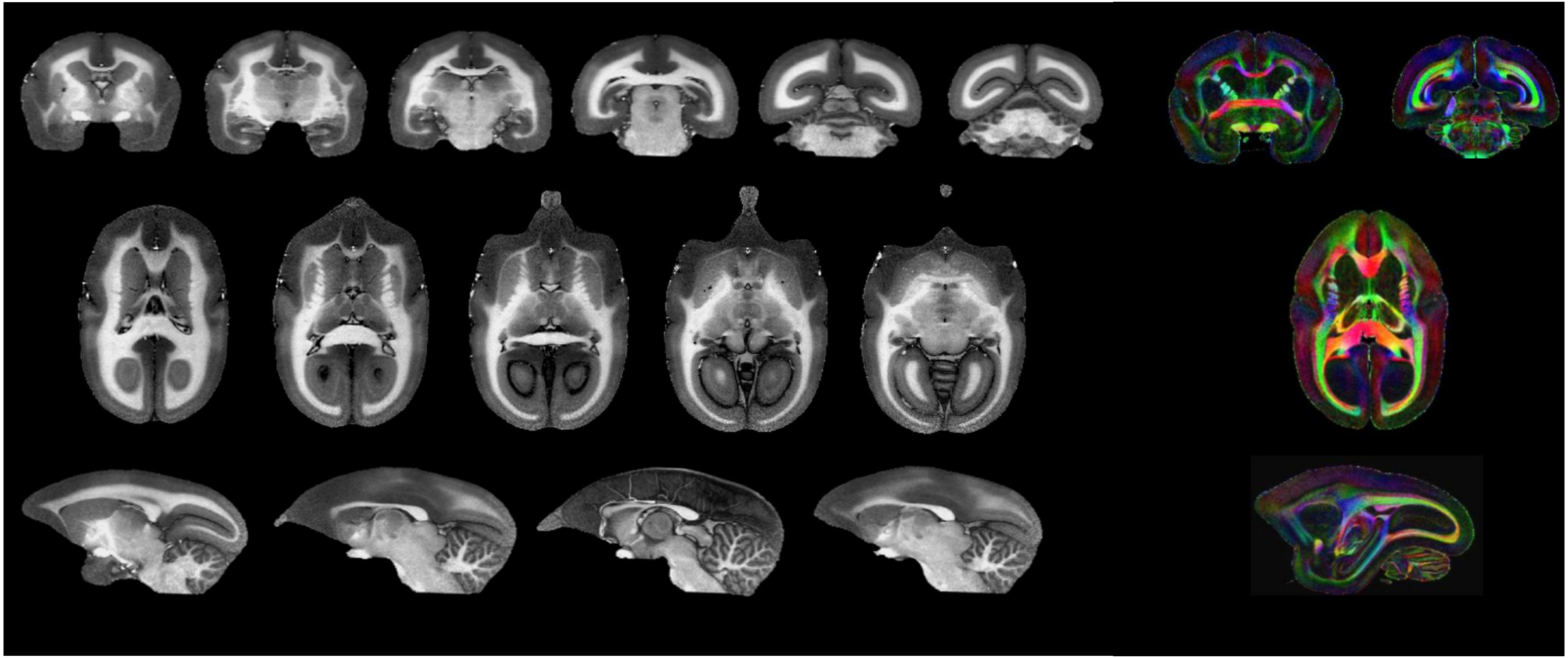




- Cradle needs to be comfortable
  - Sphinx as the natural resting position
- Training of animal to being restrained
  - Acclimatize animal
  - Non-invasive individualized helmets to hold head comfortably
- Equipment to support experiment
  - RF Coil array
  - Monitoring equipment
  - Reward delivery devices

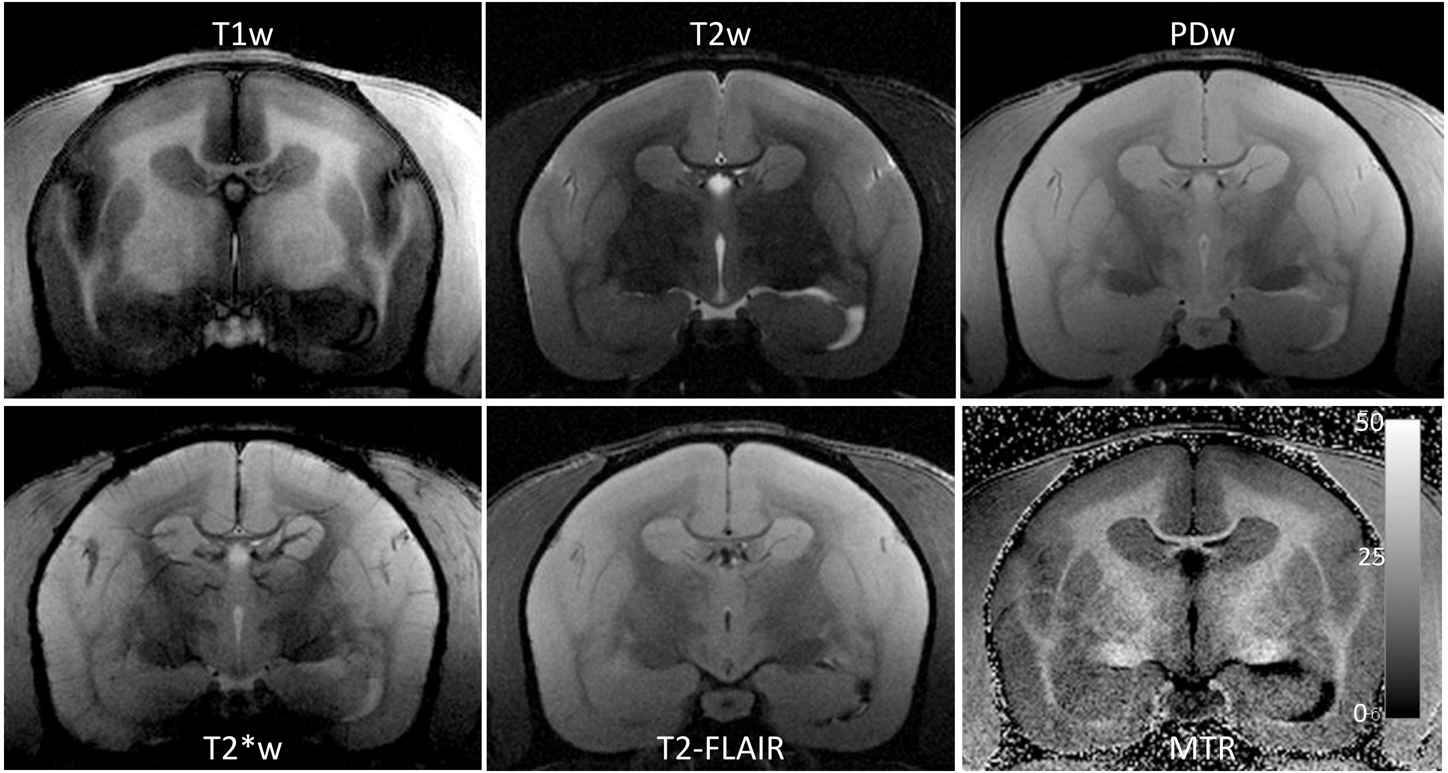
** Requires 10 cm or larger clear bore (15 cm ID or larger gradient set)*

Anatomical MRI of the Marmoset Brain



in vivo T1w-MPRAGE 150 µm^3 *ex vivo* DTI 150 µm^3

Anatomical MRI of the Marmoset Brain

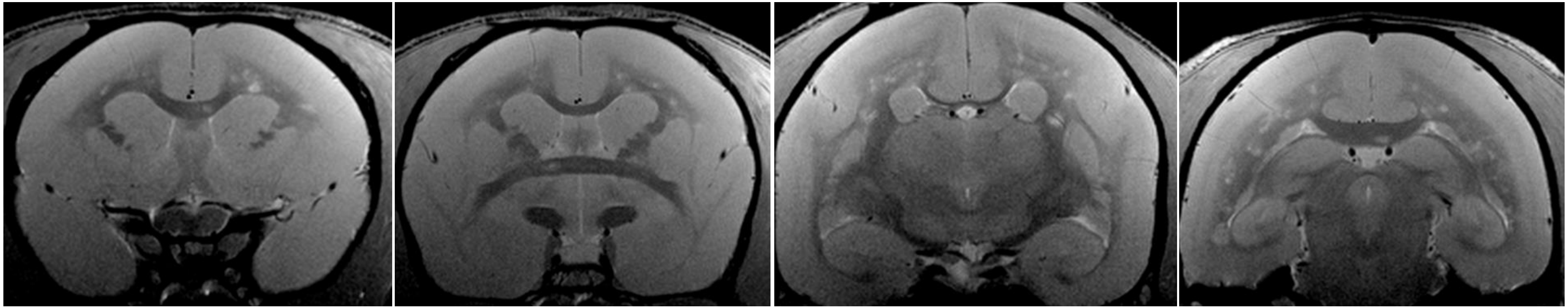


Maggi P, Sati P, Massacesi L, J Neuroimmunol (2017)

Absinta M, Sati P, Reich DS. Nat Rev Neurol. (2016);12:358-68.

125 µm x 125 µm in-plane resolution

7T MRI of a marmoset model of EAE

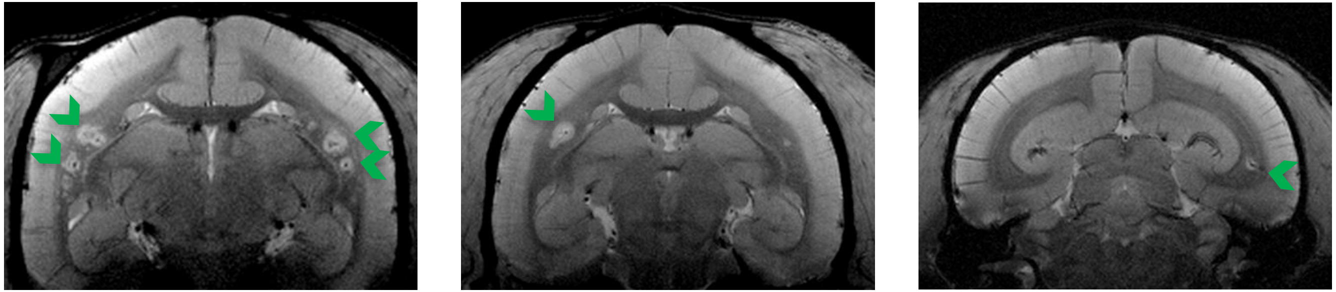


125 µm x 125 µm in-plane resolution

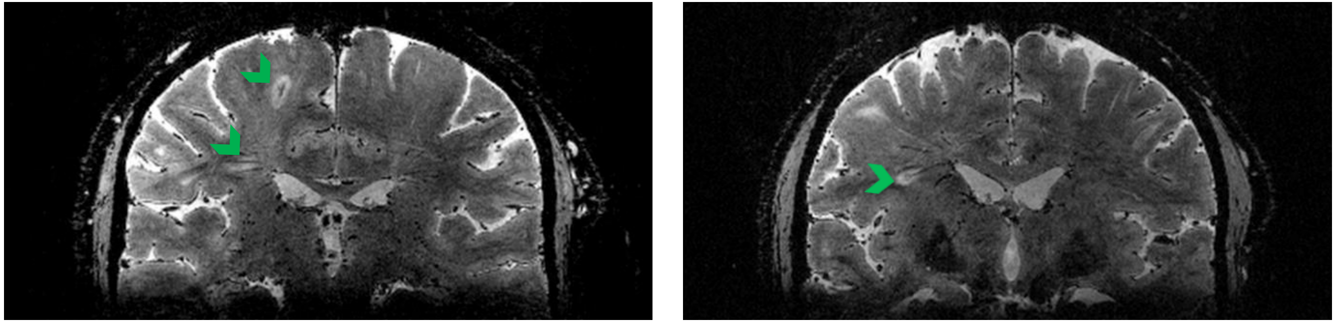
Maggi P, Sati P, Massacesi L, J Neuroimmunol (2017)
Absinta M, Sati P, Reich DS. Nat Rev Neurol. (2016);12:358-68.

Central vein in EAE and MS lesions

Marmoset EAE



Human MS

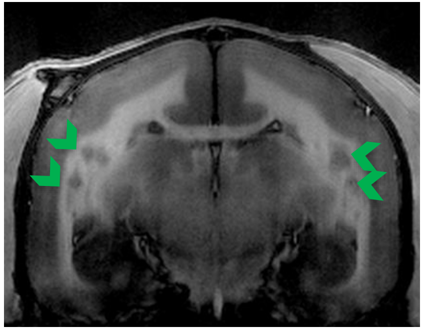


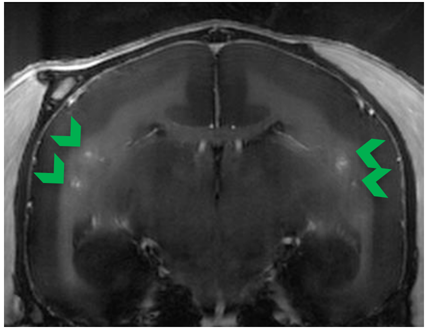
Gaitán MI et al. Mult Scler. 2014

Slide Courtesy of Dr. Pascal Sati

Enhancing lesions in EAE and MS

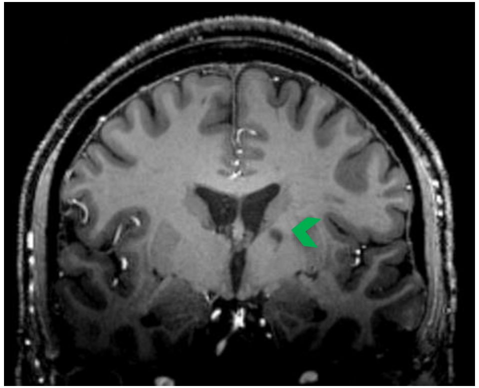
Marmoset EAE



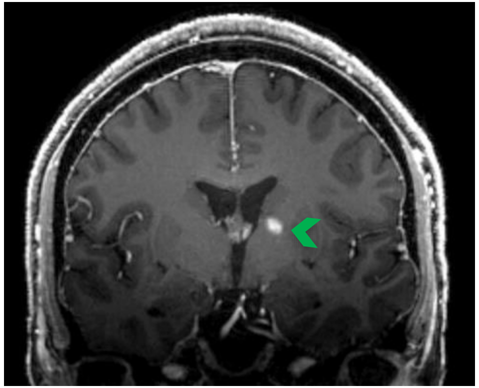


Triple-dose gadabutrol (0.3 mL/kg)

Human MS



pre-injection

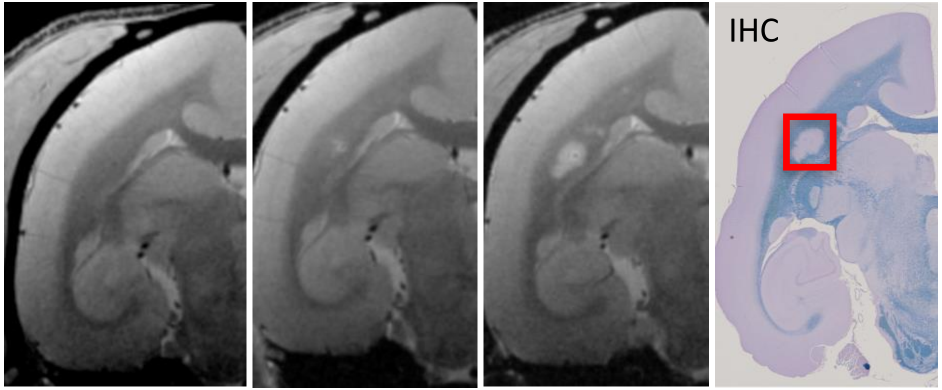


post-injection

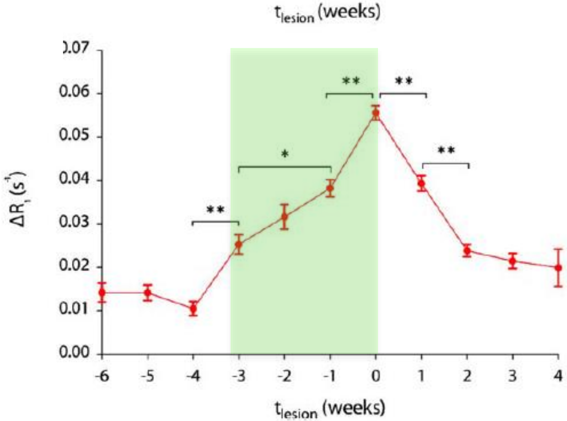
Single-dose gadabutrol (0.1 mL/kg)

Slide Courtesy of Dr. Pascal Sati

Retrospective Lesion Detection



t_{lesion} = -1 week t_{lesion} = 0 t_{lesion} = +1 week

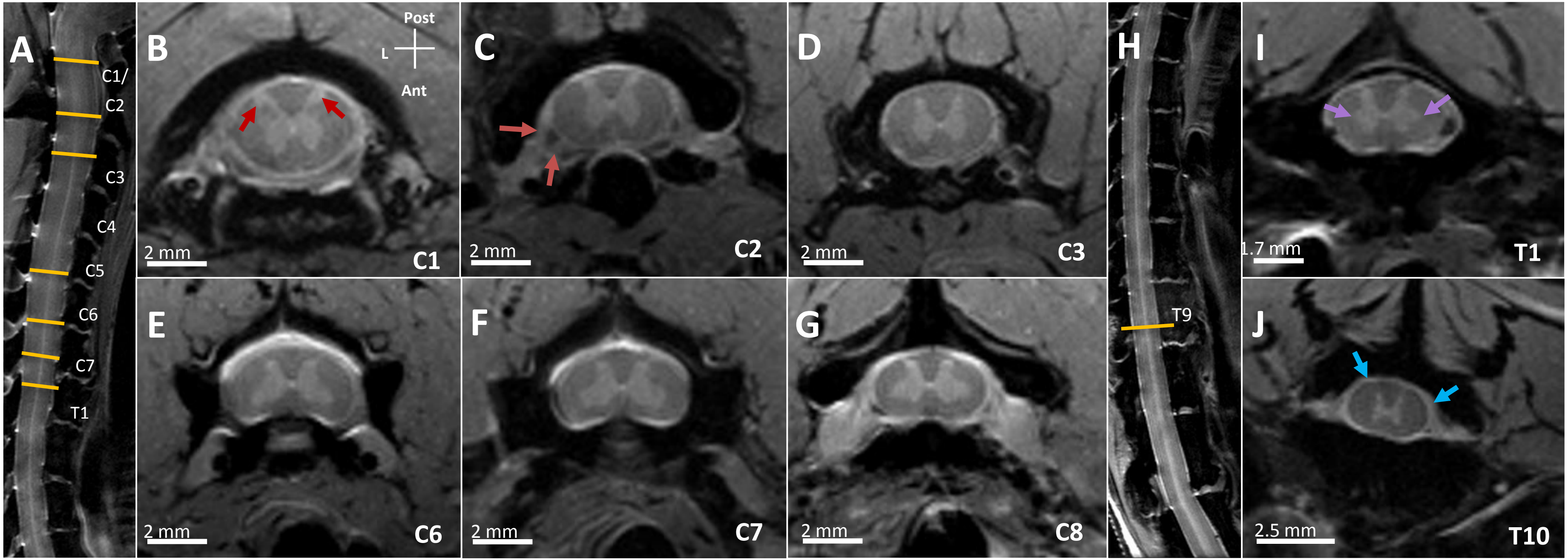


Lesion age can be determined based on serial MRI

Potential therapeutic window!

Maggi P et al. Ann Neurol. 2014

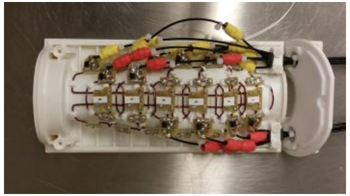
In vivo spinal cord images in marmoset EAE



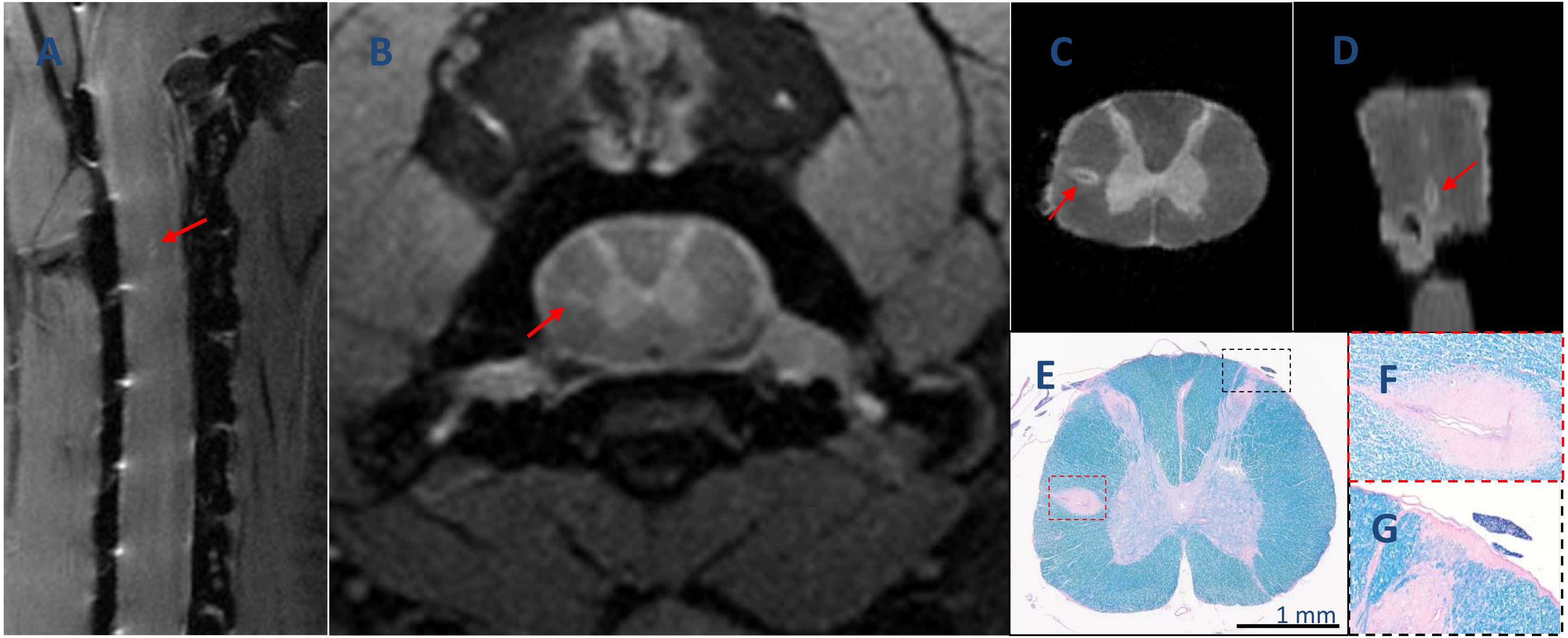
Enlarged view of the spinal cord (FOV acquired: 26x34mm; 16 slices) at the cervical levels (B-G) and thoracic levels (I,J).

PD-w FSE sequence 2D RARE: TR=3500 ms, TE= 15 ms, Rare factor= 2, NA=4, TA: ~ 30 min

Sagittal: 0.125 x 0.125 x 0.6 mm and axial plane: 0.135 x 0.135 x 0.6 mm



In vivo spinal cord images in marmoset EAE

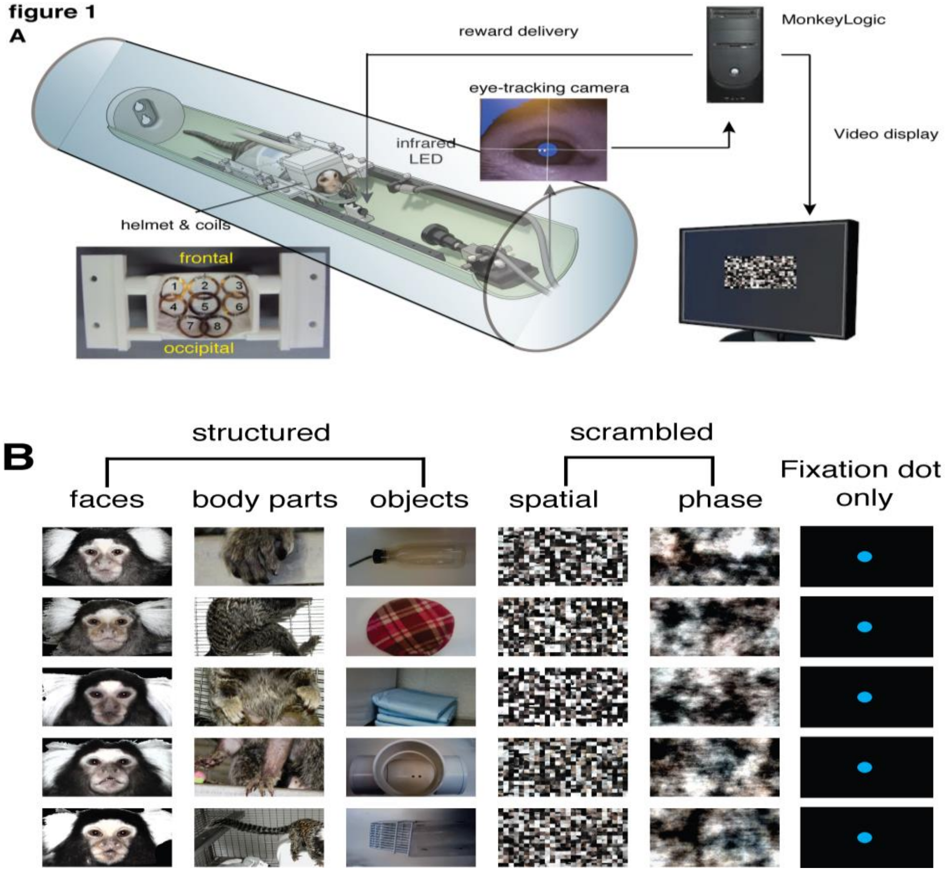


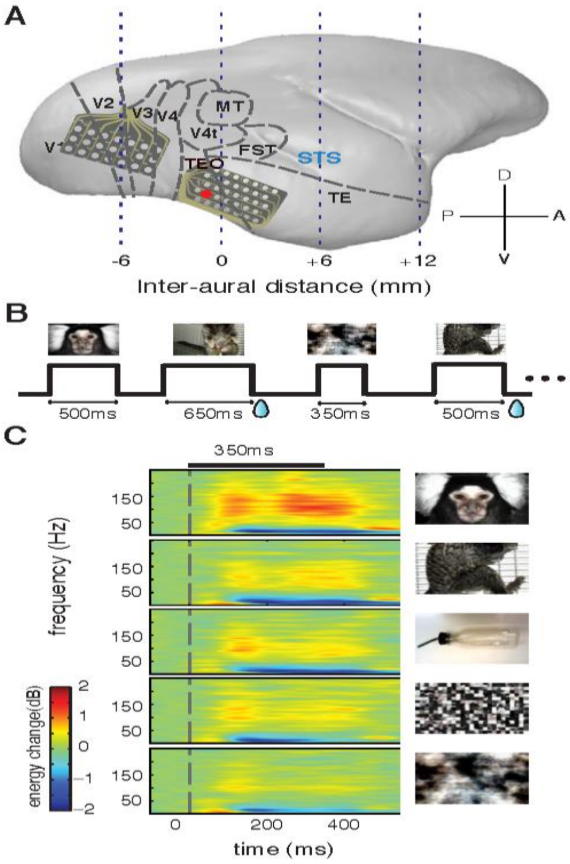
➢ **In vivo PD-w TSE (A, B):** in the EAE animal depict abnormal hyperintense signal corresponding to an area of demyelination

Ex-vivo T2* GRE 3D sequence (C, D): TR=50 ms, TE= 10 ms, FA: 12˚, NA=32, TA: 21 min per acquisition, Total TA: ~12h (entire SC), coronal slice orientation, resolution: 70 x 200x 70 µm, FOV: 11 x 38 x 11 mm

Histopathology(E-G): 5-µm thickness microtome sectioning, Luxol fast blue-Periodic Acid Shif (LFB-PAS) for myelin.

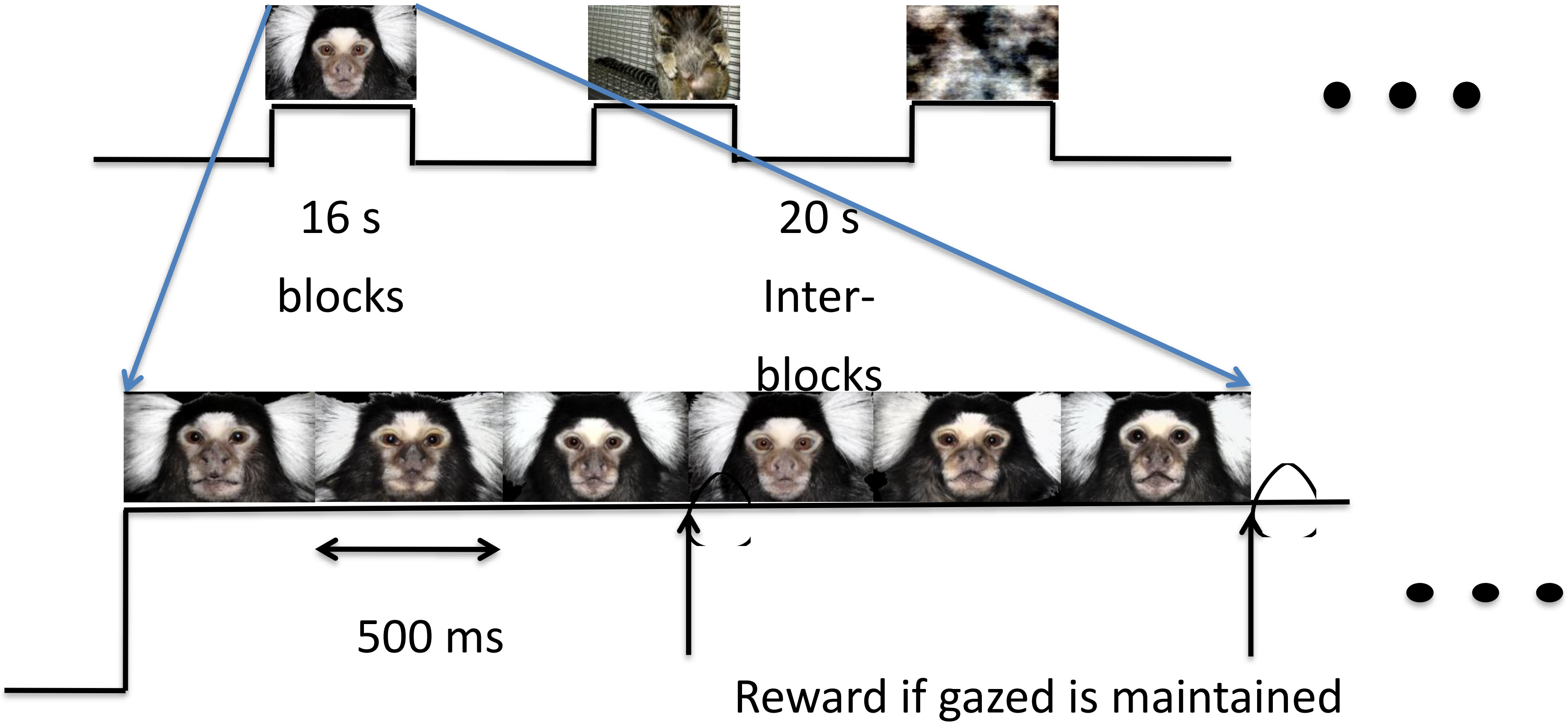
fMRI/ECoG during visual stimulation





C.-C. Hung et al Neuroimage 2015;120(10):1-11. C.-C. Hung et al J Neurosci 2015 35(3):1160-72.

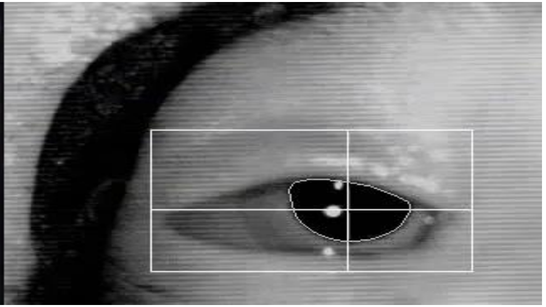
Experimental paradigm for fMRI of Visual System



C.-C. Hung et al J Neurosci 2015 35(3):1160-72.

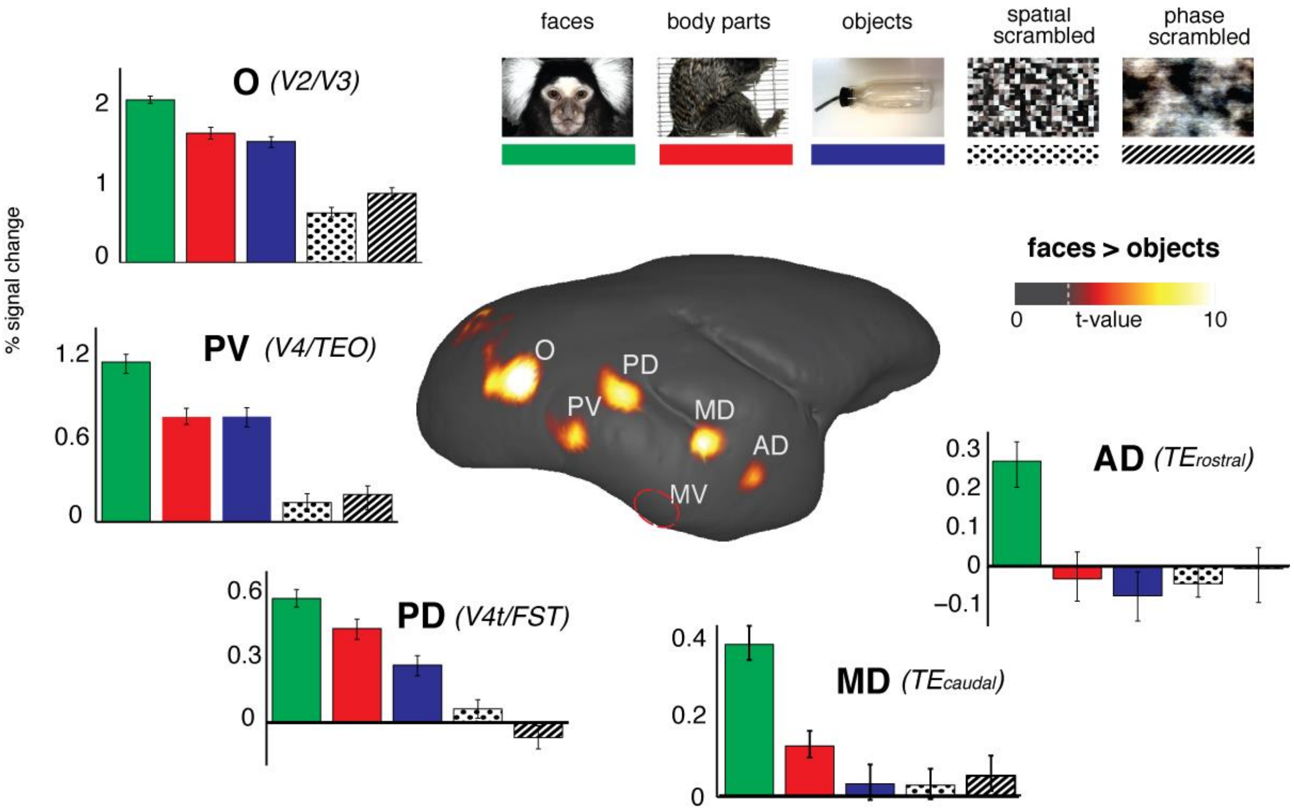
Typical behavior of awake marmoset in magnet

Positive reinforcement | Infra-red eye-tracking | Visual Stimulus



C.-C. Hung et al J Neurosci 2015 35(3):1160-72.

Face-selective patches along ventral visual pathway

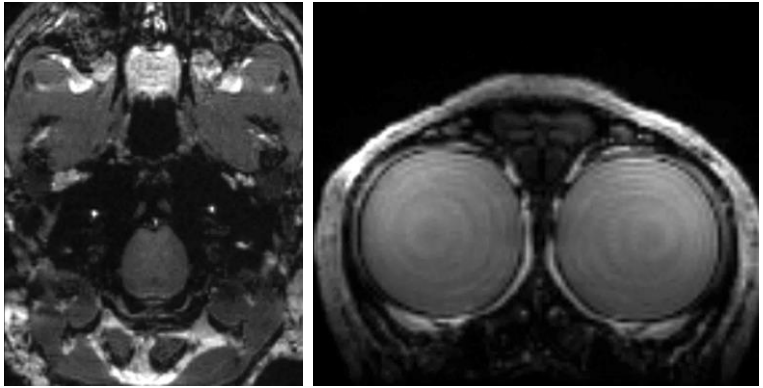


C.-C. Hung et al J Neurosci 2015 35(3):1160-72.

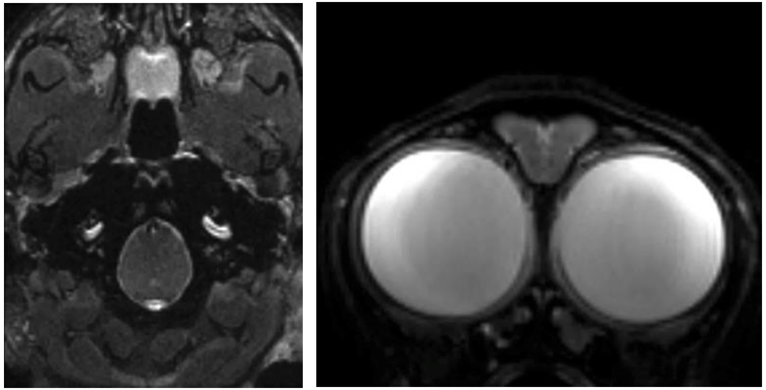
MRI Protocols for Marmoset Connectome

- Section 1: Anatomical (structural) protocol: T1, T2 and DTI
  - Data acquired under anesthesia (e.g. isoflurane) in a single 3 hour long session
  - Spatial resolution: 250 µm isotropic resolution for T1 and T2, and 500 µm isotropic resolution for DTI

Localizer 6s	AutoAlign 54s	B1-mapping 27s	Localizer for confirming alignment 24s	MAPSHIM for up to 3rd order shimming 82s	AFI for B1+ mapping 123s	MP3RAGE for T1 mapping 9.5m x 5	3RARE for T2 mapping 10.5m x 5	DTI EPI with blip up and down 2shells, 192dirs 34m	FieldMap for B0 mapping 82s
0min	1min	2min	3min	5min	8min	60min	120min	155min	160min



MP3RAGE

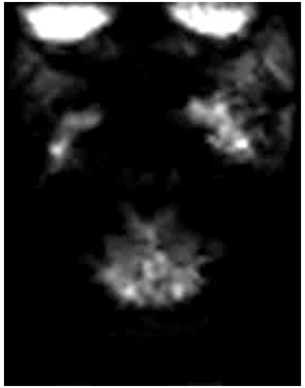
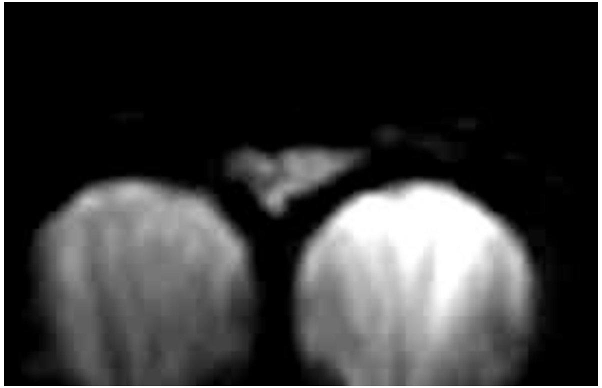


3DRARE

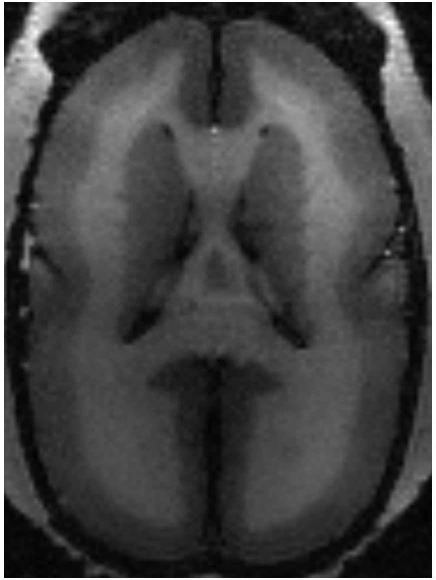
MRI Protocols for Marmoset Connectome

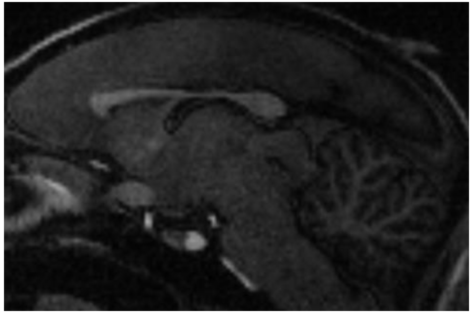
- Section 2: Functional protocol: rsfMRI
  - Data acquired under awake conditions in a single 3 hour long session
  - Spatial resolution: 500 µm isotropic resolution

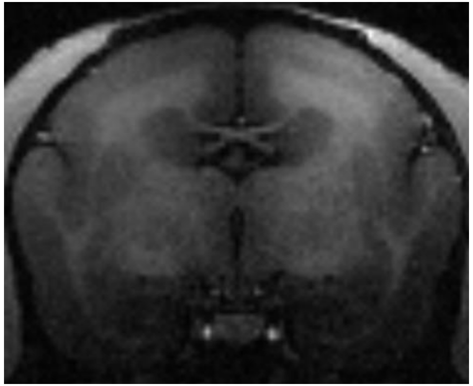
Localizer 6s	AutoAlign 54s	B1-mapping 27s	Localizer for confirming alignment 24s	MAPSHIM for up to 3rd order shimming 82s	AFI for B1+ mapping 123s	Reverse SEEPI for distortion correction 24s x 2	512 BOLD EPI with blip up and down interleaved 17m x 8	InplaneT2 144s	FieldMap for B0 mapping 82s
0min	1min	2min	3min	5min	8min	10min	150min	153min	158min

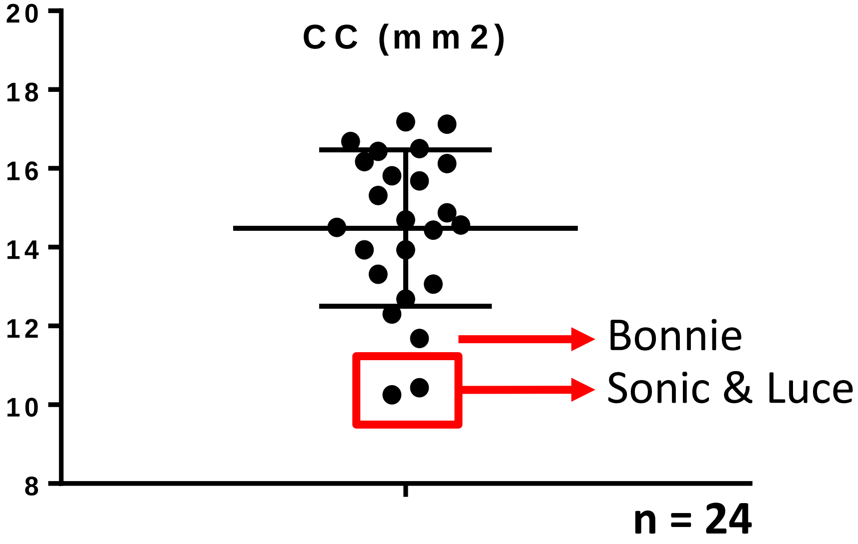



Incidental Finding: Dysgenesis of the Corpus Callosum









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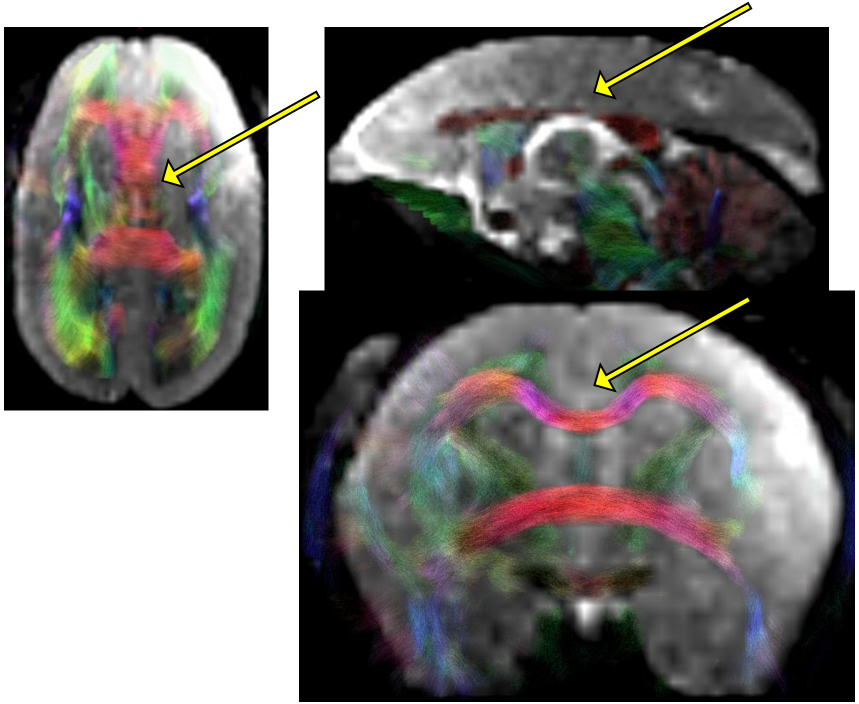
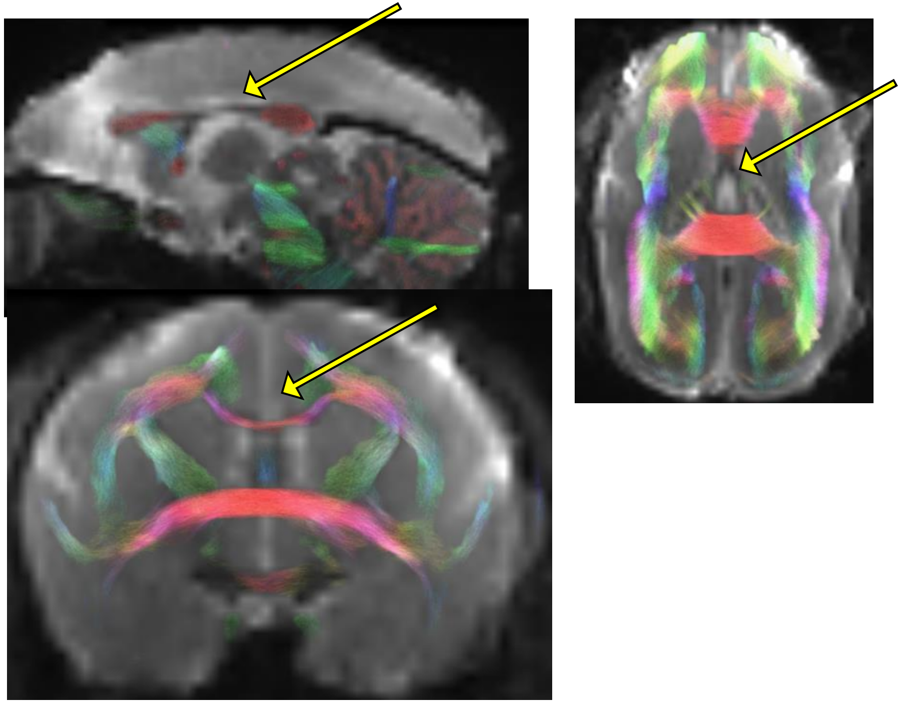


Normal CC



Hypoplasic CC

Resting State Networks In Conscious Marmosets

High Order Visual Cortex
V3, V4, A19, A19DI

Basal Ganglia

Primary Visual Cortex

Dorsomedial
Somatomotor

High Order Visual Cortex
V4, V5, V6, FST, TE3

High Order Visual Cortex
V2, A19M, V6(DM)

Default Mode Network

Salience

Orbitofrontal Cortex

Cerebellum

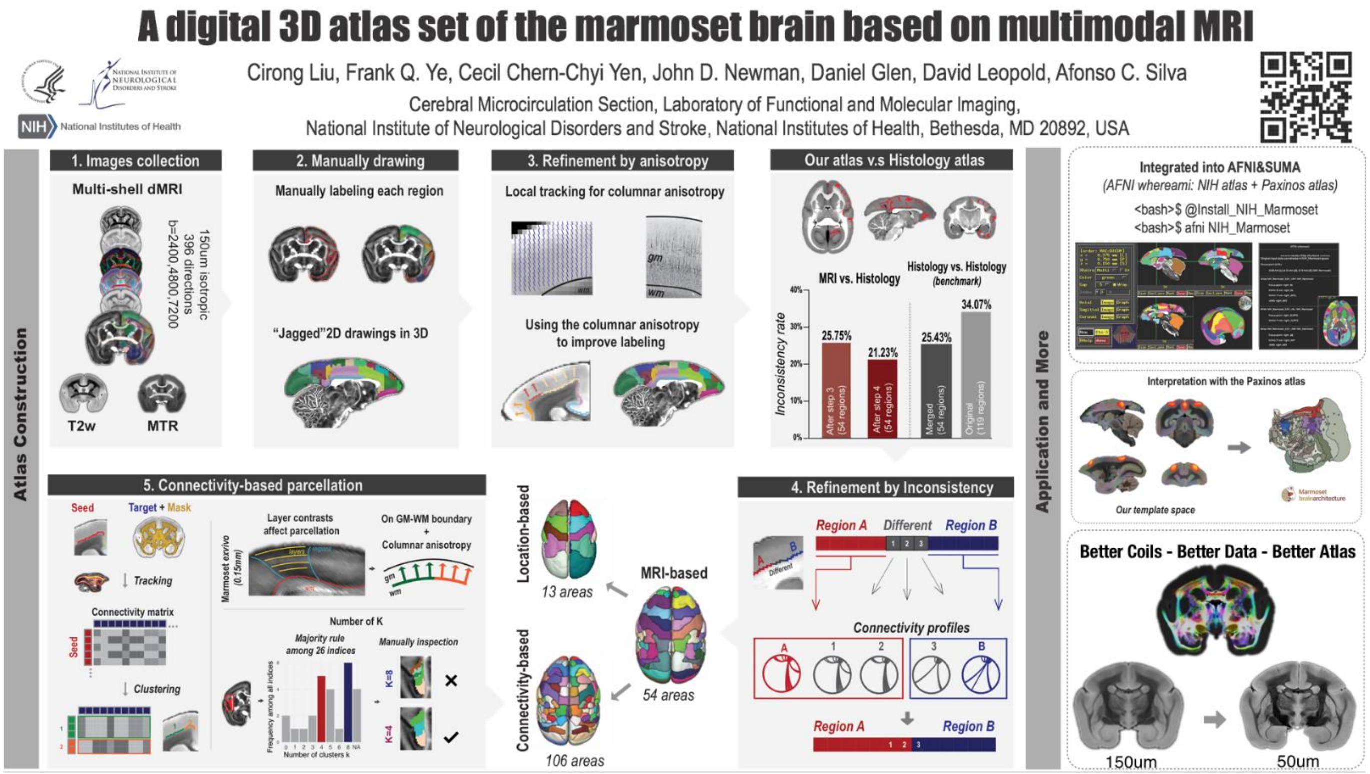
Ventrolateral
Somatomotor

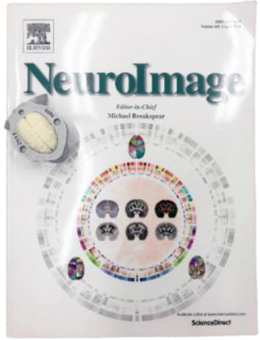
Frontal Pole

Belcher et al., J Neurosci. 2013 33(42):16796 –16804

NIH Marmoset Brain Atlas Project

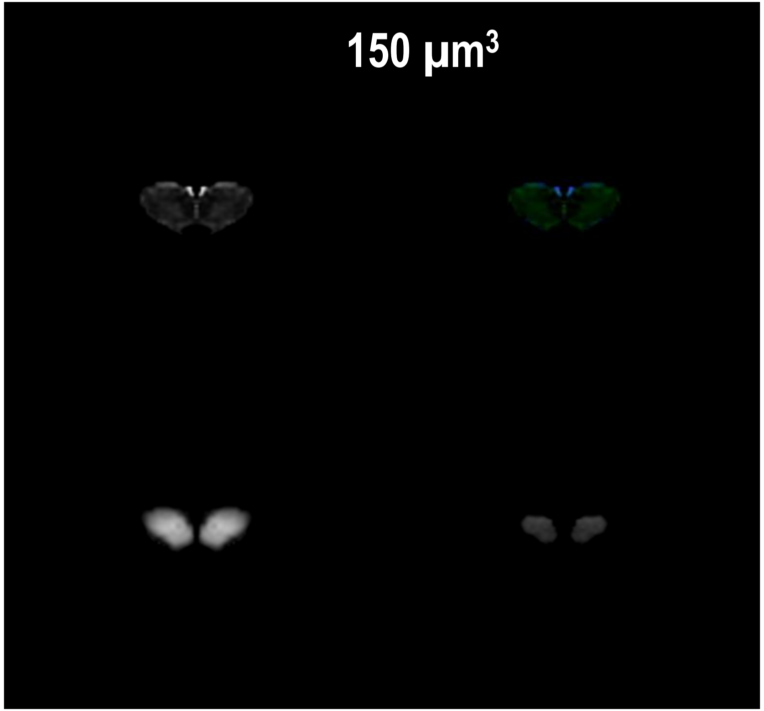
Version 1.0: **Cortical** atlas at 150um^3 *(Liu, et al, 2017)*





Cortical Atlas

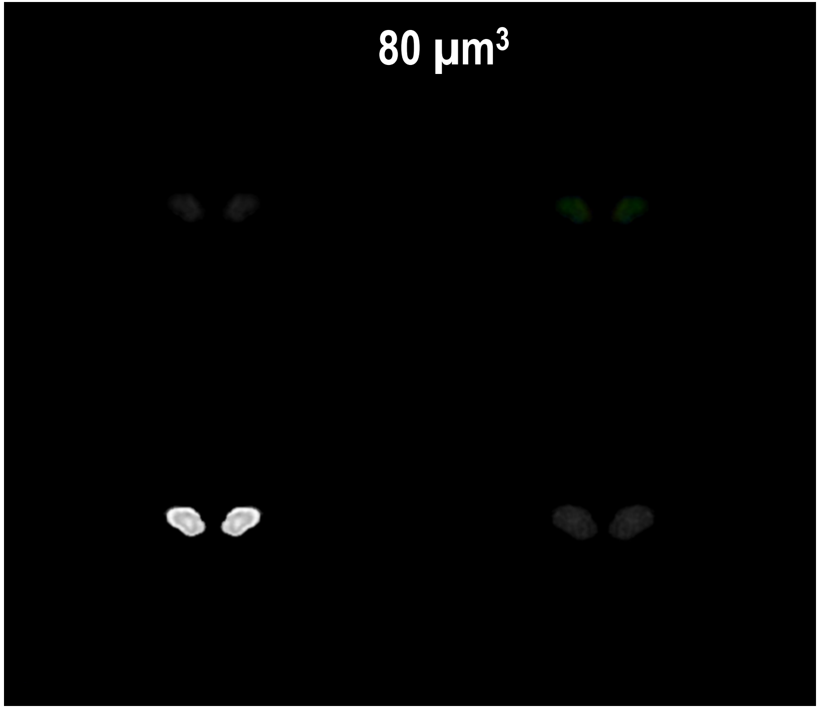
- Paxinos Atlas
- Location-based
- MRI-based
- Connectivity-based



Multi-shell Diffusion MRI

- 3D diffusion-weighted spin-echo EPI
- Three shells [b = 2400, 4800, 7200]
- 6 b0 + 126 directions per shell
- 6.25 days / 7T MRI (*Bruker 35mm linear TxRx RF Coil*)

MTR [T1-like, 3.5 hrs per image, *5 repetitions, 17.5 hrs*]



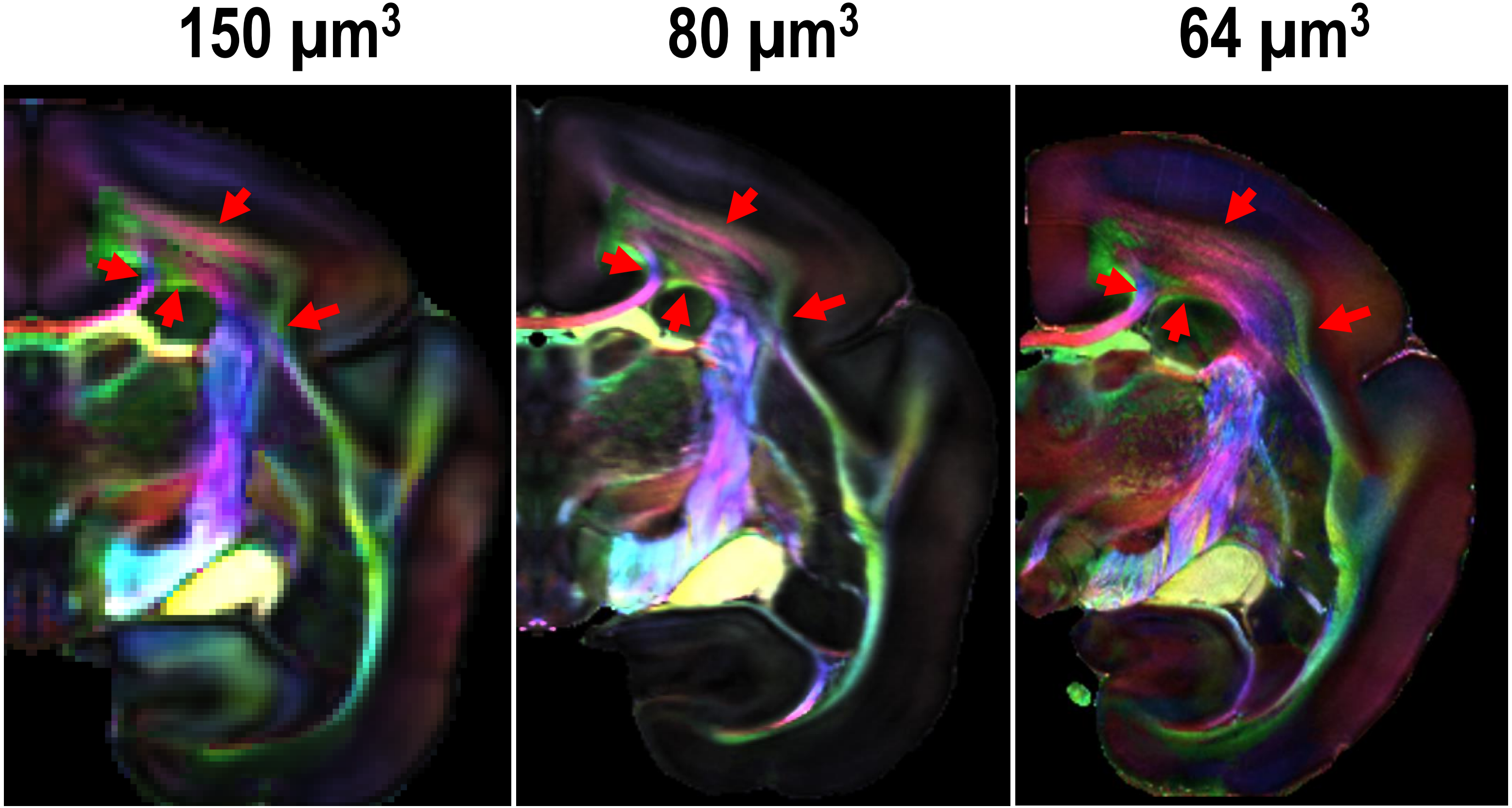
Multi-shell Diffusion MRI

- 3D diffusion-weighted spin-echo EPI
- Two shells [b = 2400, 4800]
- 6 b0 + 64 [b2400] + 126 [b4800]
- 15 days / 7T MRI **(***Quadrature Millipede TxRx Coil***)**

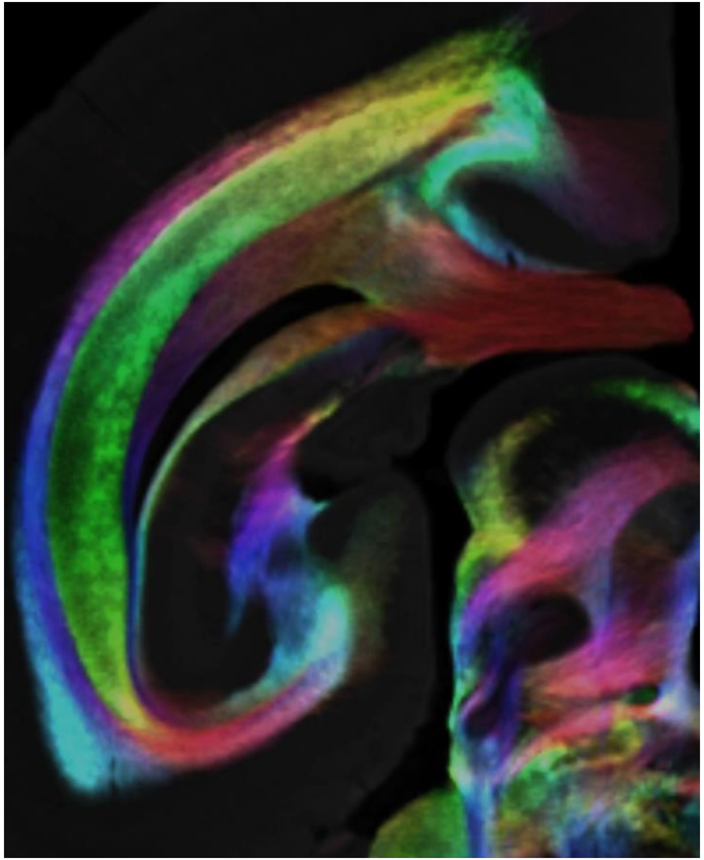
MTR [T1-like, 10 hrs per image, *5 repetitions, 50 hrs*]

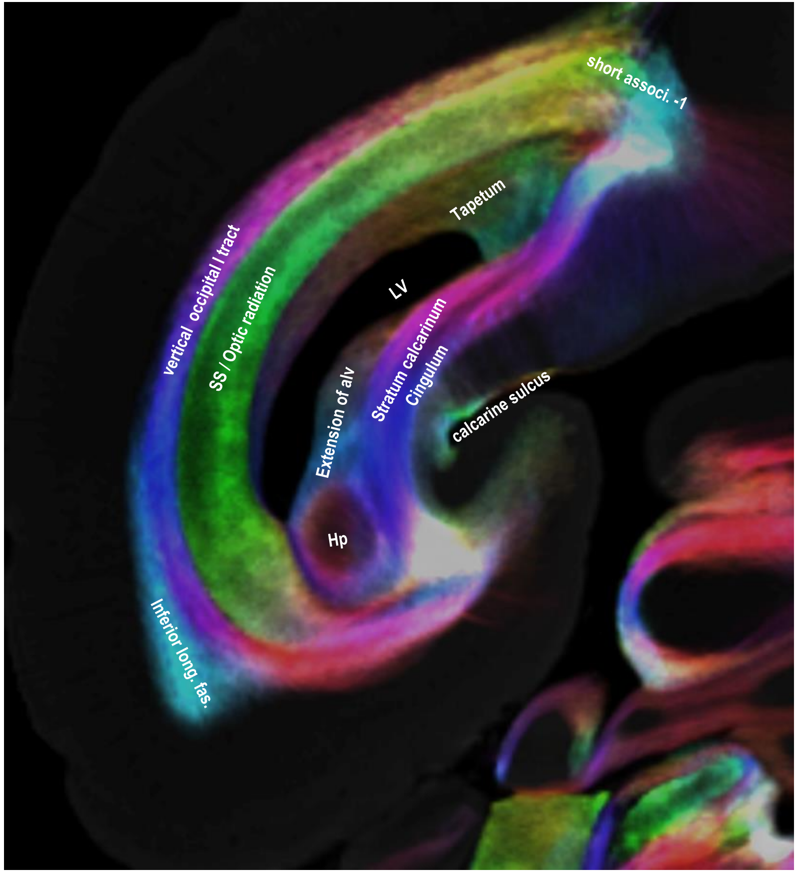
Examples: Coronal Radiation

A complex region with different fibers run different directions



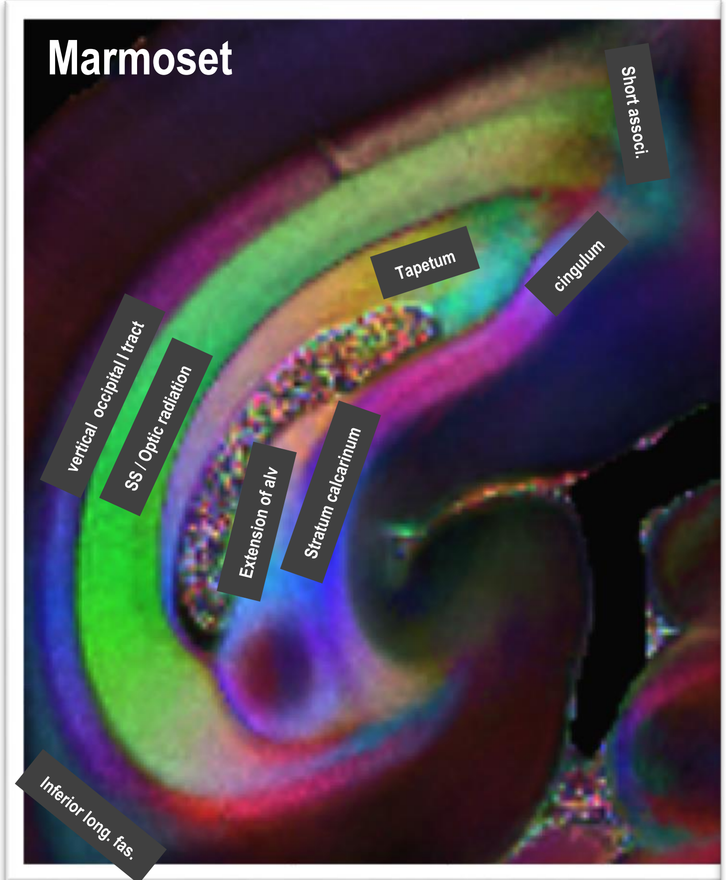
Examples: : Fibers in Occipital lobe

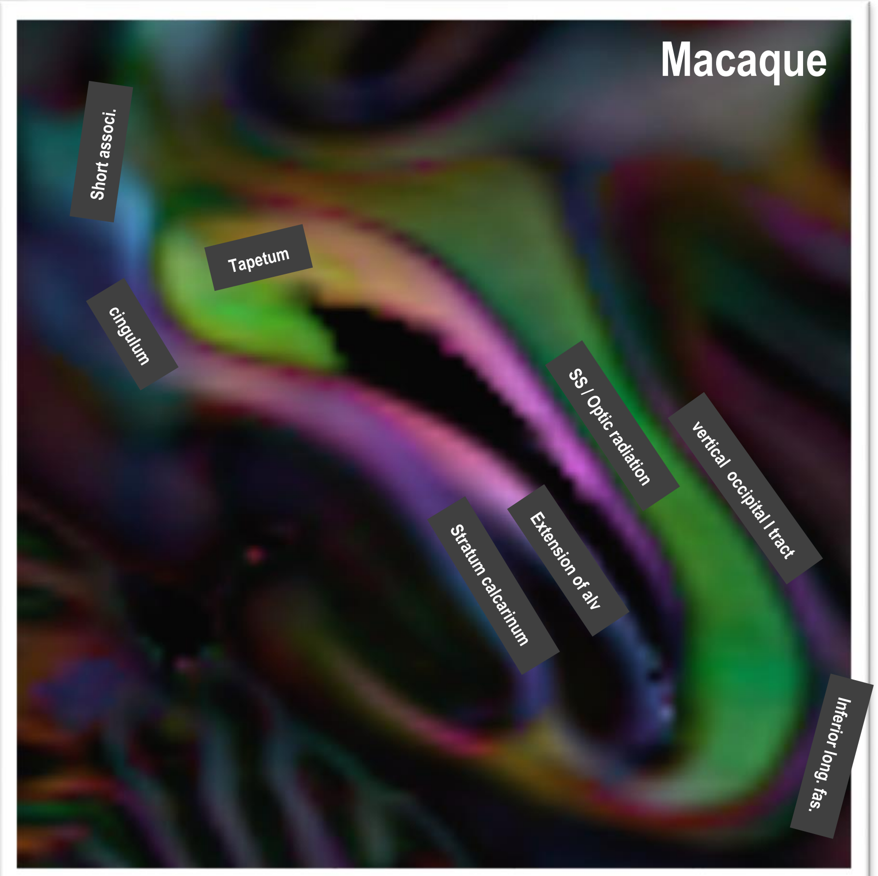




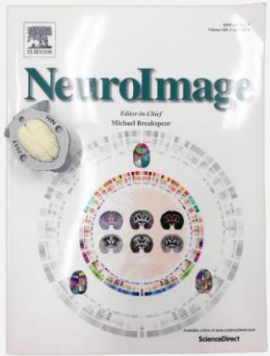
Examples: : Fibers in Occipital lobe

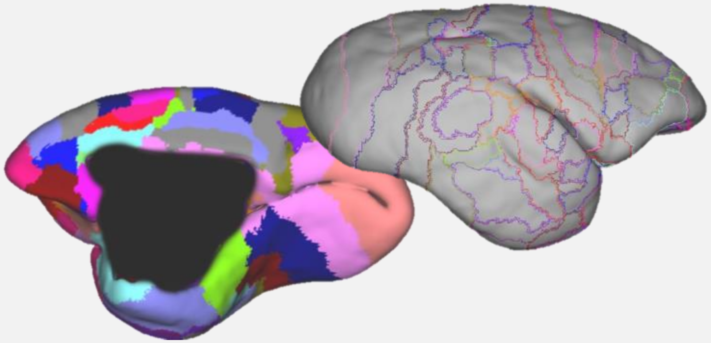
Homologous across primates





Supported by Version 1.0 – Cortical Atlas





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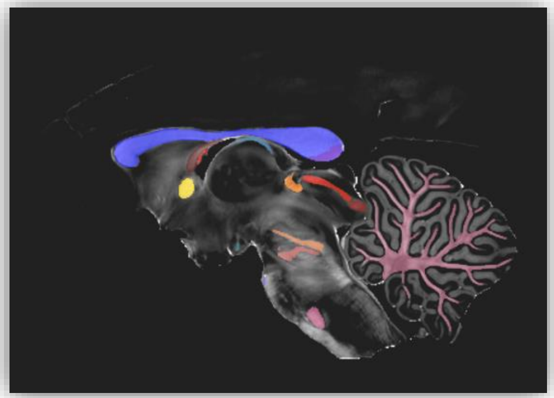
- MRI-based
- Connectivity-based



+

Version 2.0

White matter & **Fiber pathways** atlas

Supported by AFNI

Just like our old version 1.0, version 2.0 will be fully implemented in AFNI

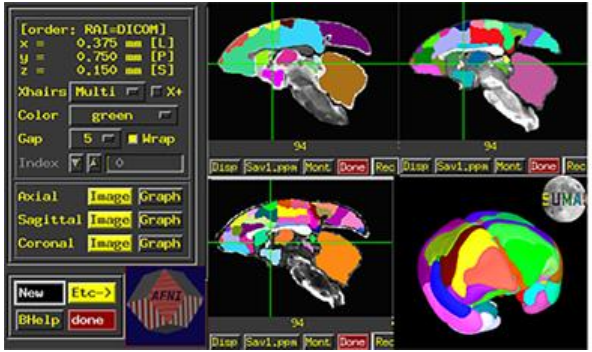
[Easy Installation]

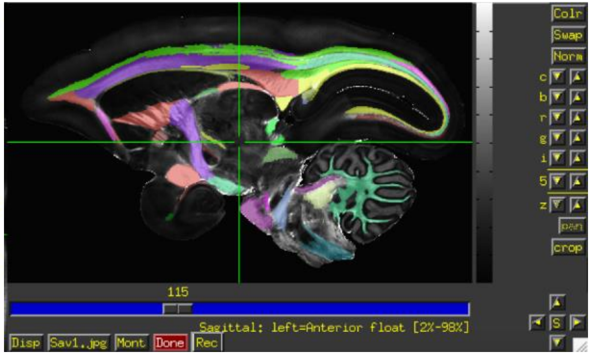
```
<bash>$ @Install_NIH_Marmoset
<bash>$ afni NIH_Marmoset
```

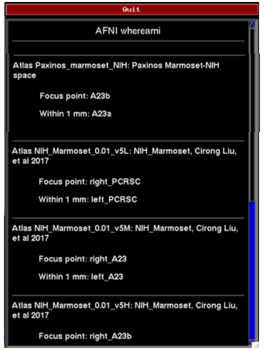
AFNI whereami: NIH cortical atlas (v1.0) +

Paxinos cortical atlas +

NIH white matter atlas (v2.0)







Conclusions

- Non-human primates are essential animal models in biomedical research and neuroscience
- Marmosets have many advantages in biomedical research, particularly as a model of aging and for the implementation of genetic tools
- The combined use of high resolution anatomical and functional MRI will allow better understanding of functional cortical organization and study of marmoset models of neurological disorders

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