ANATOMICAL AND FUNCTIONAL MRI IN ANIMAL MODELS

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8/21/2017

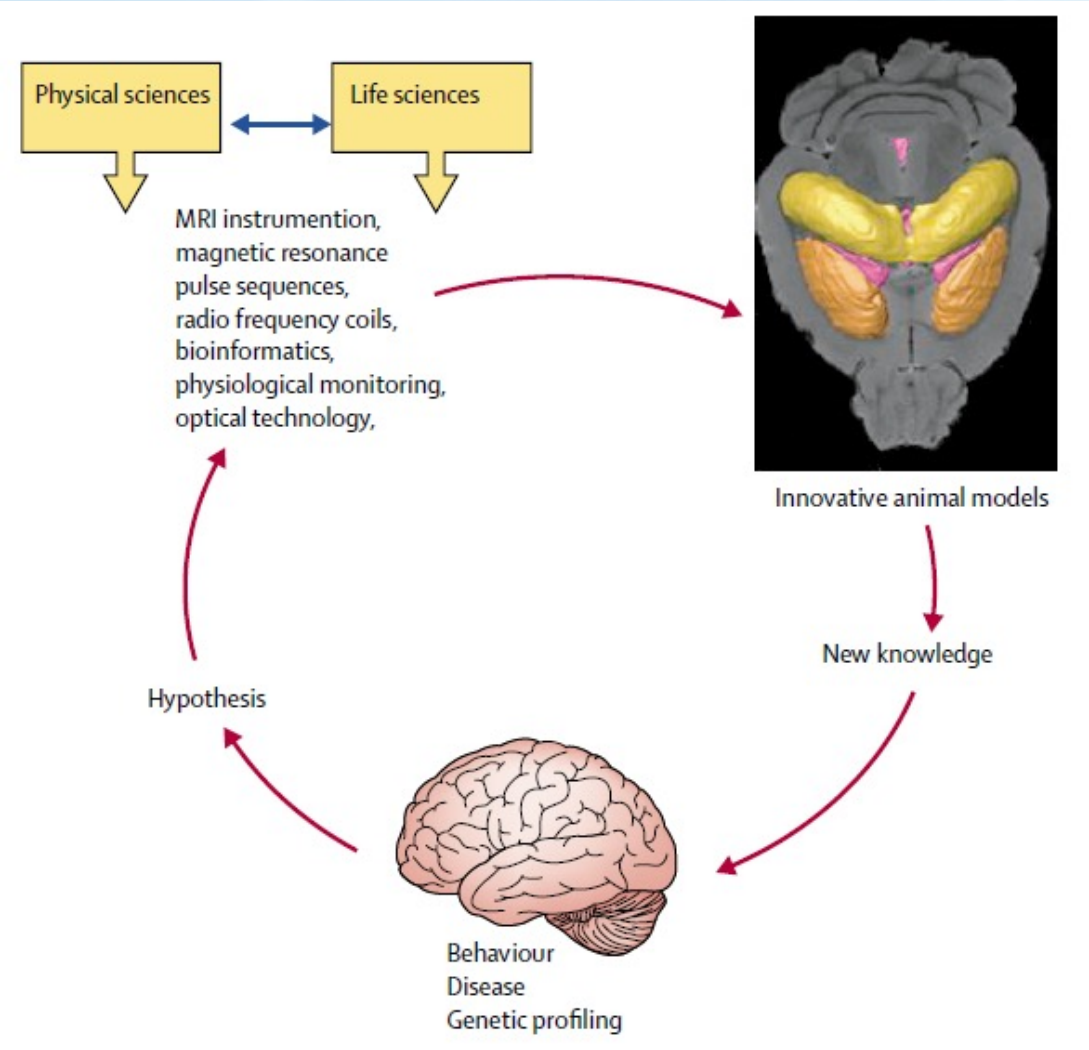
Outline

- Animal Models
  - Translational MRI
  - Multi-modal Investigations
  - Advantages over clinical MRI

- Anatomical MRI
  - T_1 Myelination Map
  - Marmoset MRI Atlas
  - Diffusion Tensor Imaging
  - T_2* Map

- Functional MRI
  - Resting-state fMRI
  - Somatosensory fMRI
  - Auditory fMRI
  - Visual fMRI

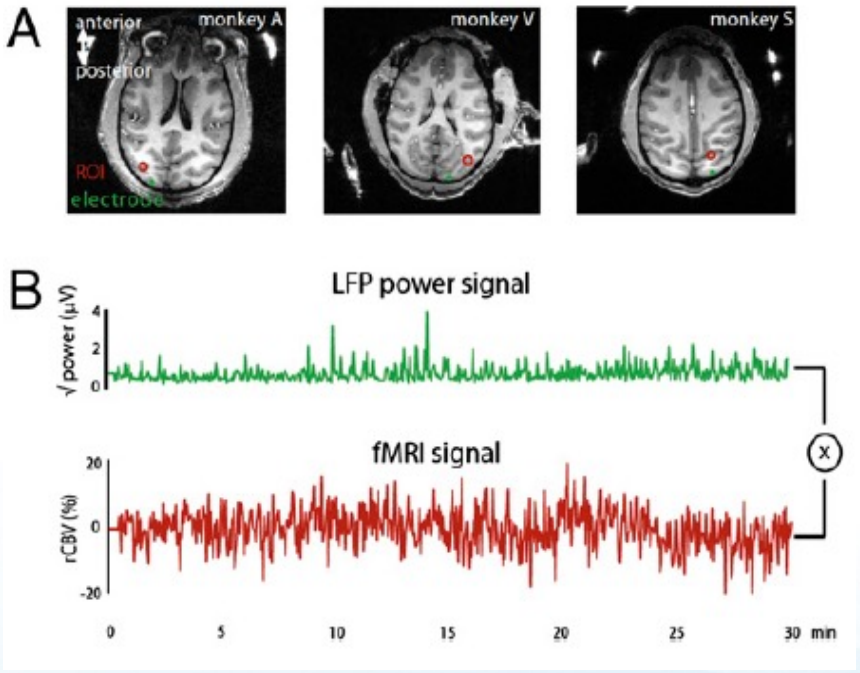
Translational MRI



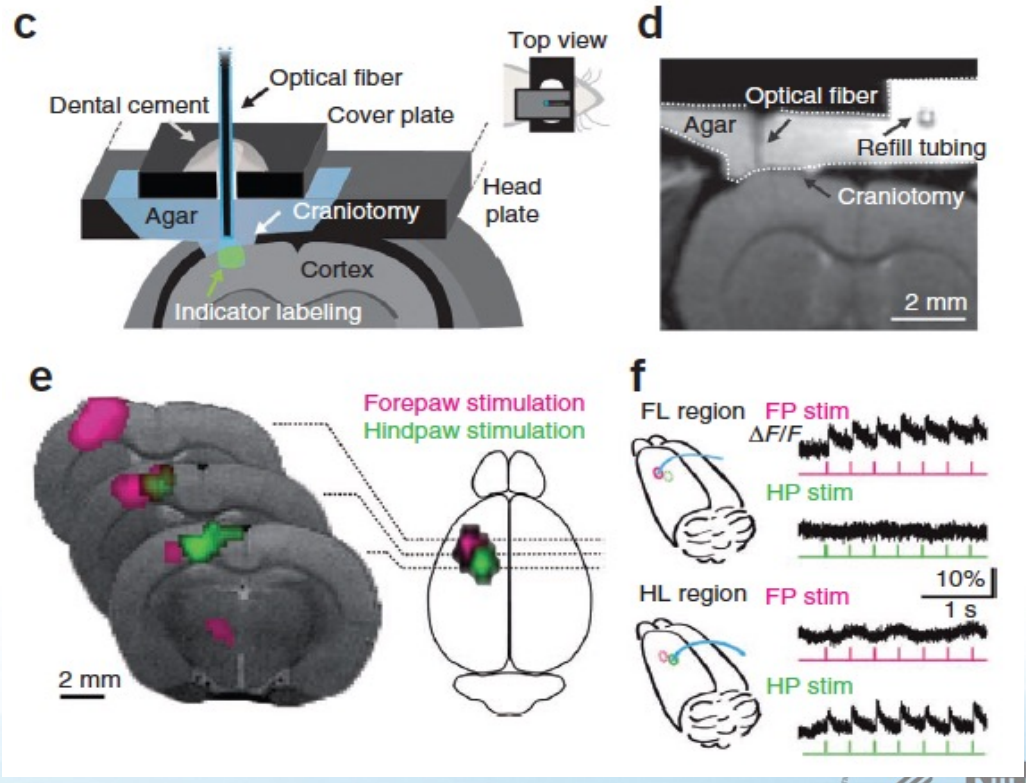
Benveniste, Blackband. **Lancet Neurol**, 2006; 5:536–44

Multi-modal Investigations

- Simultaneous fMRI and electrophysiology
- Simultaneous fMRI and optical Imaging
- Pharmacological manipulations
- Transgenic animal models

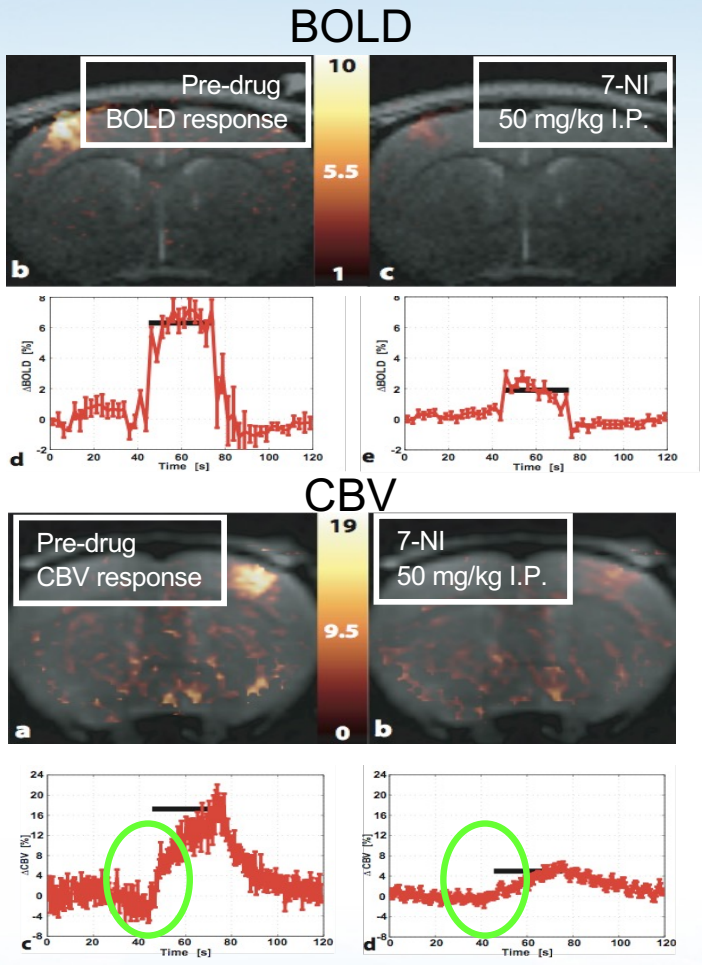


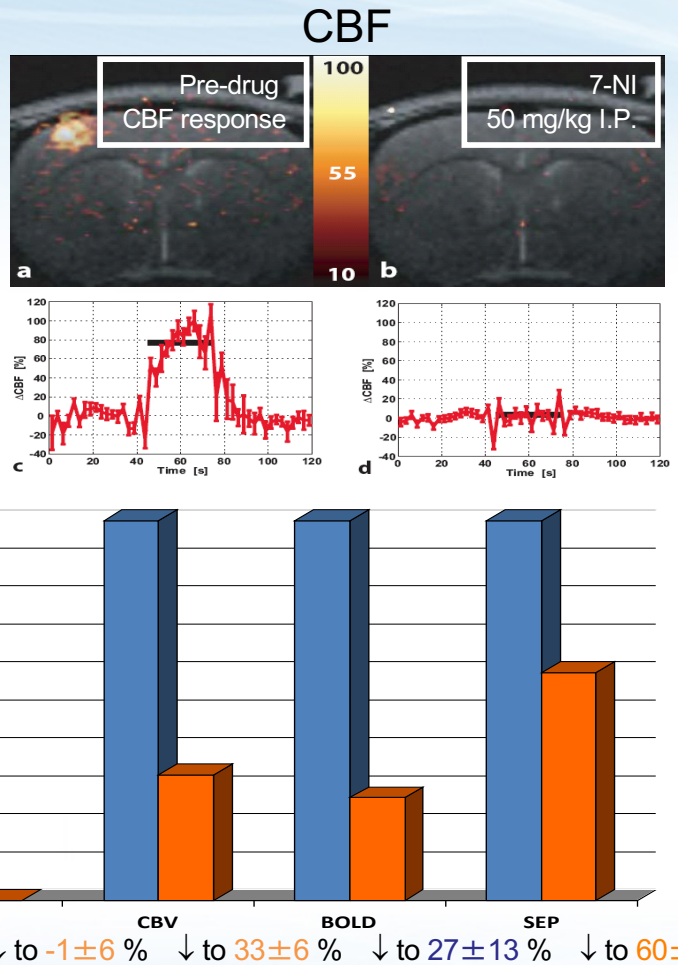
Schölvinck et al. PNAS. 2010;107(22):10238-43



Schultz et al. Nat Methods. 2012;9(6):597-602

Pharmacological Inhibition of Nitric Oxide Uncouples BOLD from CBF

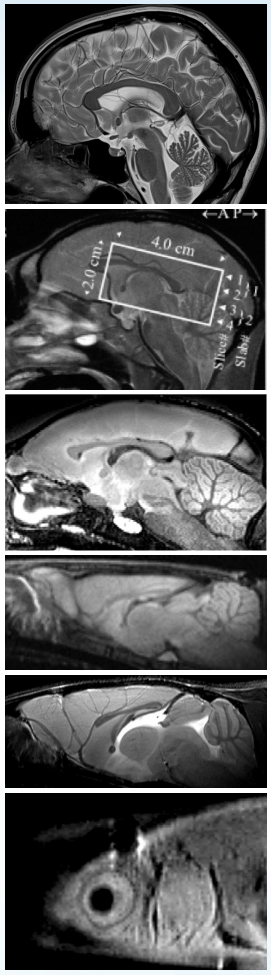




CBV = Cerebral Blood Volume
CBF = Cerebral Blood Flow
7-NI = 7-Nitroindazole

Stefanovic et al. J Cereb Blood Flow Metab. 2007;27(4):741-54.

Transgenic Animal Models



Human

Macaque

Marmoset

Rat

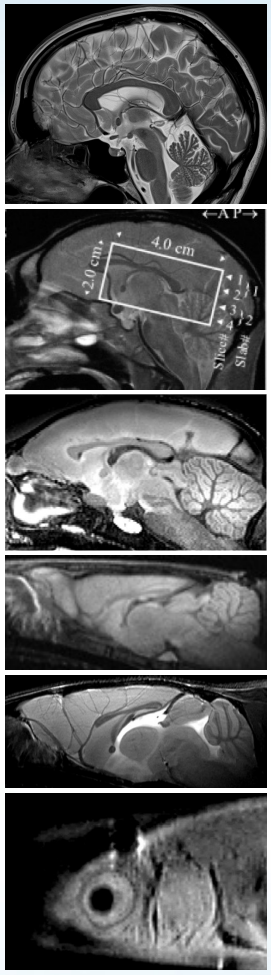
Mouse

Zebrafish

Neural circuitry

Genetic manipulation

Transgenic Animal Models



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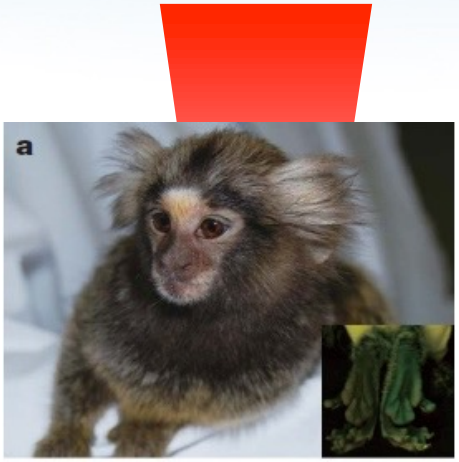
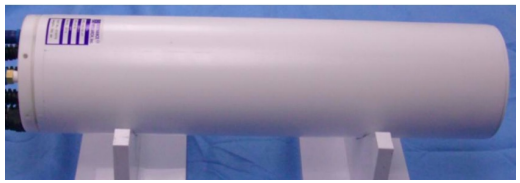


Sasaki et al, Nature. 2009

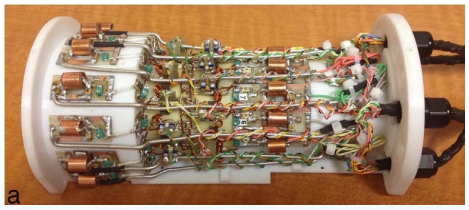
Advantages Over Clinical MRI

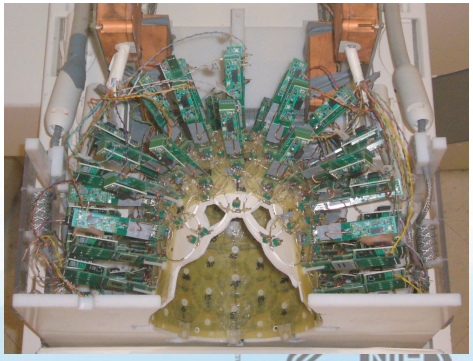
- Higher Magnetic Field
  - Animal: 21T 11cm @ UFL 2014
  - Human: 10.5T 88cm @ UMN 2014
  - SNR α B_0^1.7

- Stronger Gradients
  - Animal: 1500mT/m 6cm @ UFL 2015 & others
  - Human: 300mT/m 56cm @ Harvard 2013
  - Spatial resolution, diffusion, echo time



- Higher Coil Sensitivity
  - Animal: 15ch 2.4cm @ UWO 2017
  - Human: 96ch 5cm @ Harvard 2009
  - Better SNR for smaller brain
  - Cryogenic coils, 2 times SNR gain

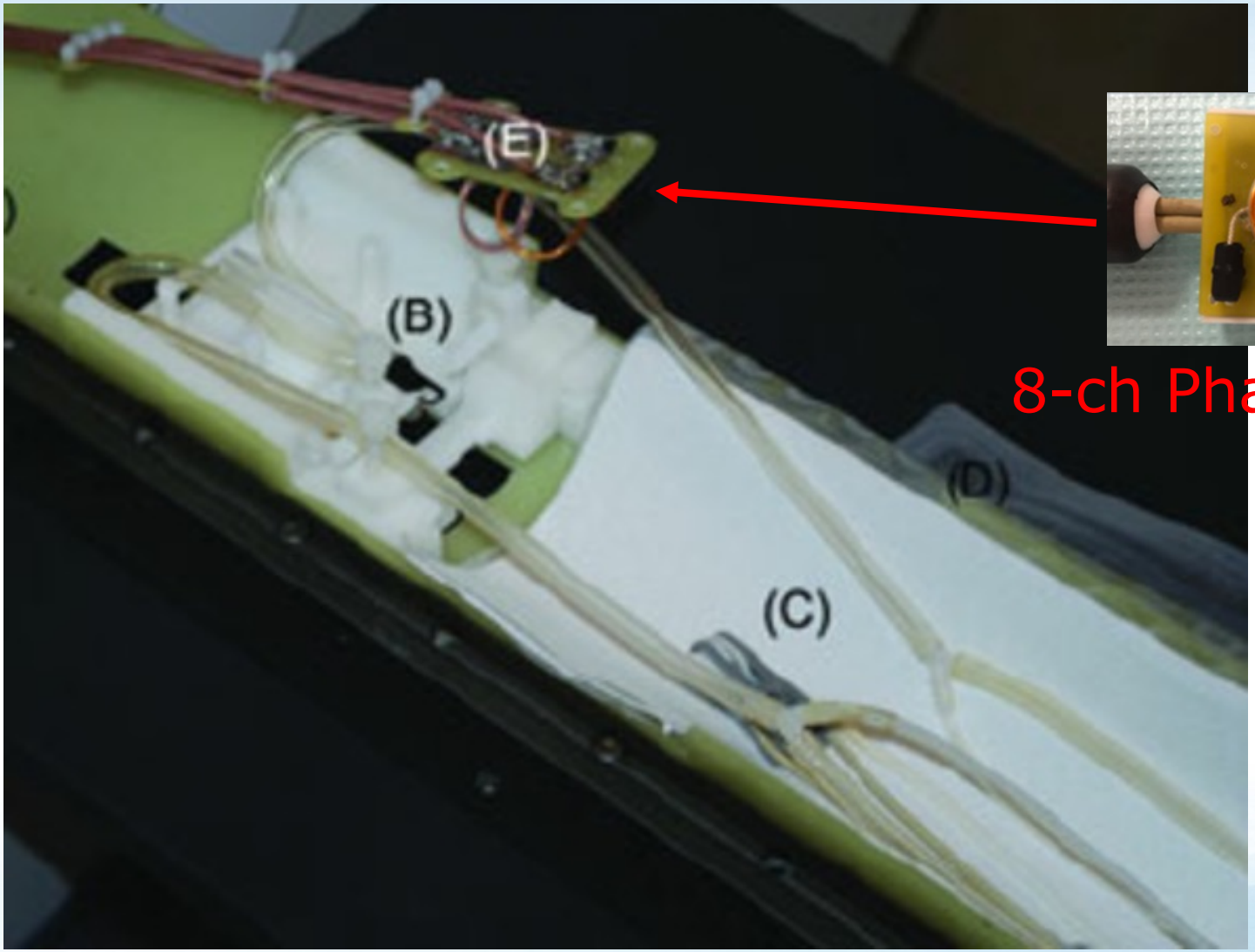


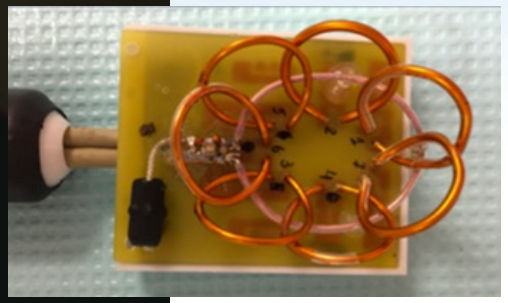


MRI Setup of Marmosets

- 7T 30cm, 450mT/m 15cm
- Two types of setup
  - Anatomical MRI
    - Isoflurane anesthetized
  - Functional MRI
    - Awake/ Conscious
- Physiological Monitoring
  - Temperature
  - Heart rate and pulse oximetry
  - Reparation rate and ET-CO_2

Setup for Anesthetized Marmosets



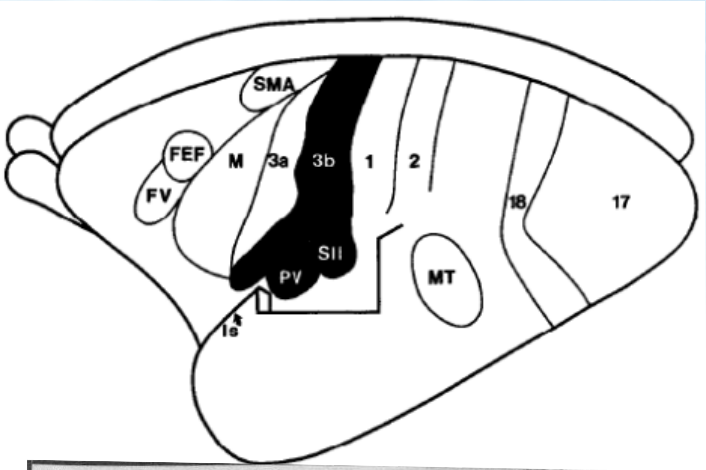


8-ch Phase Array

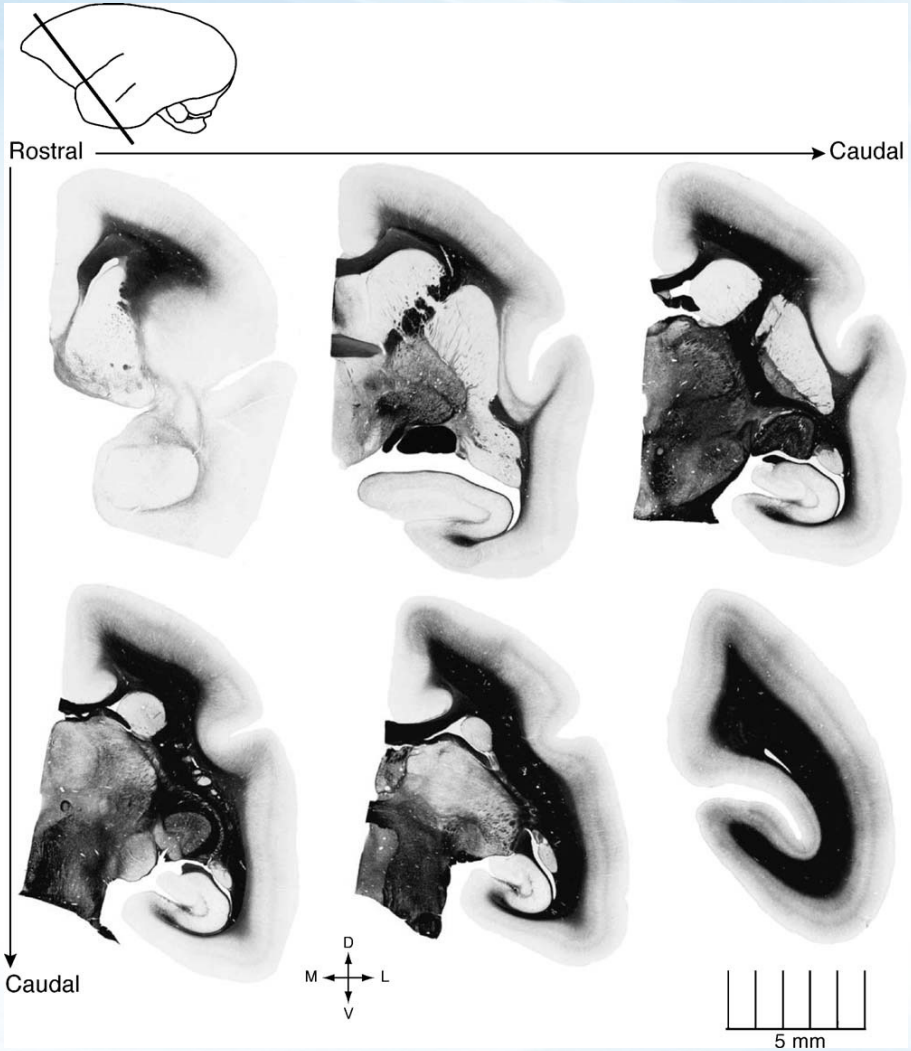
Papoti et al. MRM 2017

Silva et al. Methods in Molecular Biology 2010 pp281-302

Myelination of the Marmoset Cortex

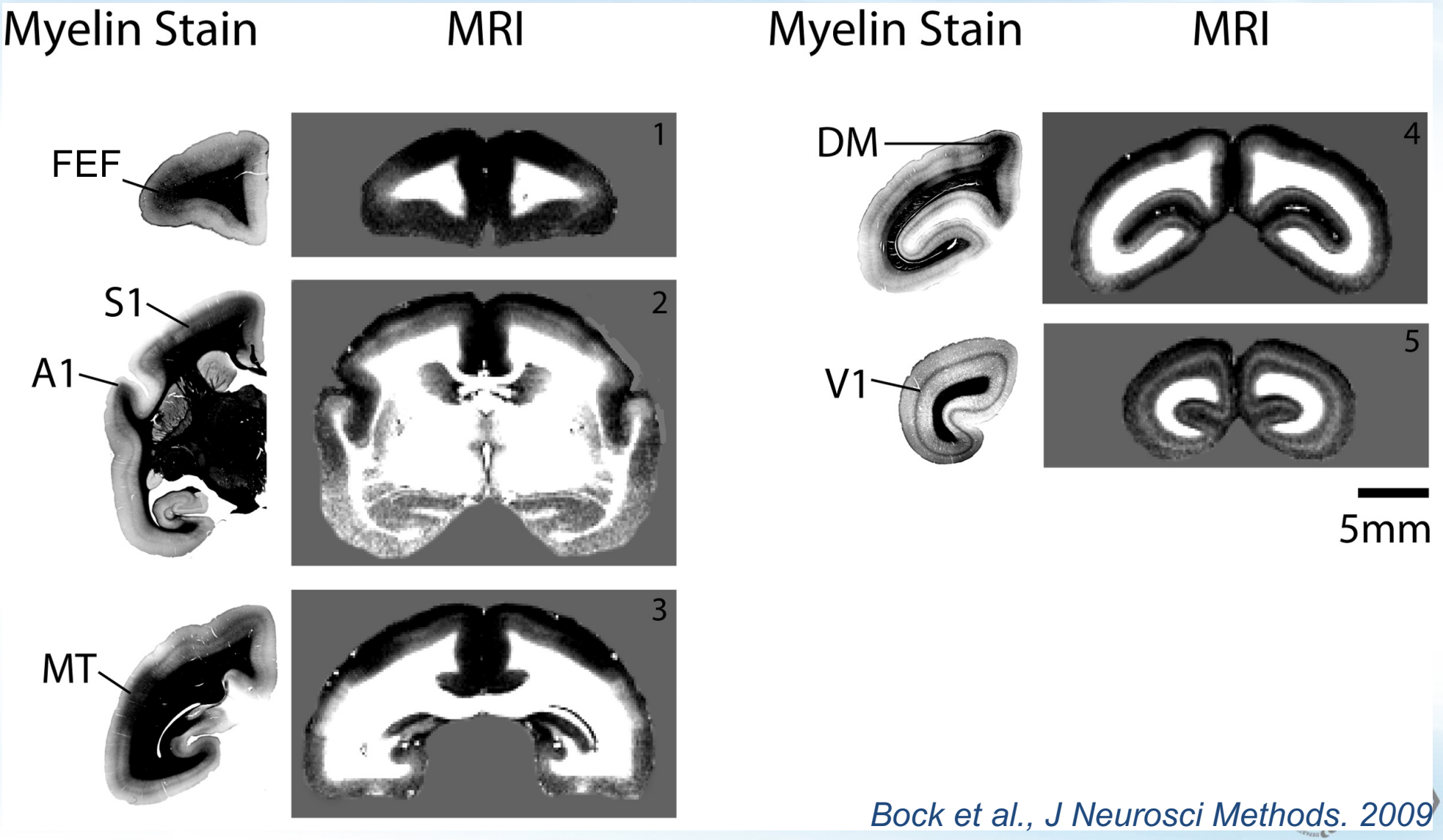


Krubitzer and Kaas J Neurosci..



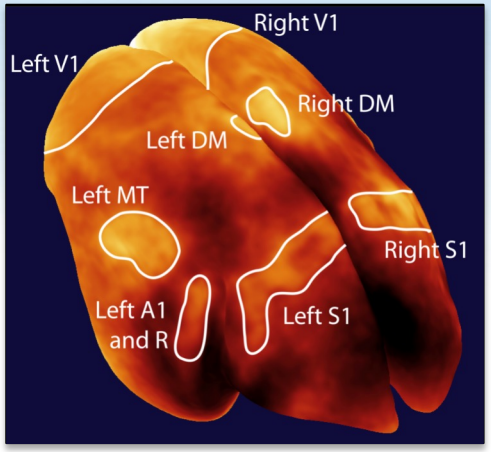
Pistorio et al., J Neurosci Methods 2006

T1-Weighted MRI Reveals Cortical Myeloarchitecture



Bock et al., J Neurosci Methods. 2009

Reproducible and Quantitative Myeloarchitecture

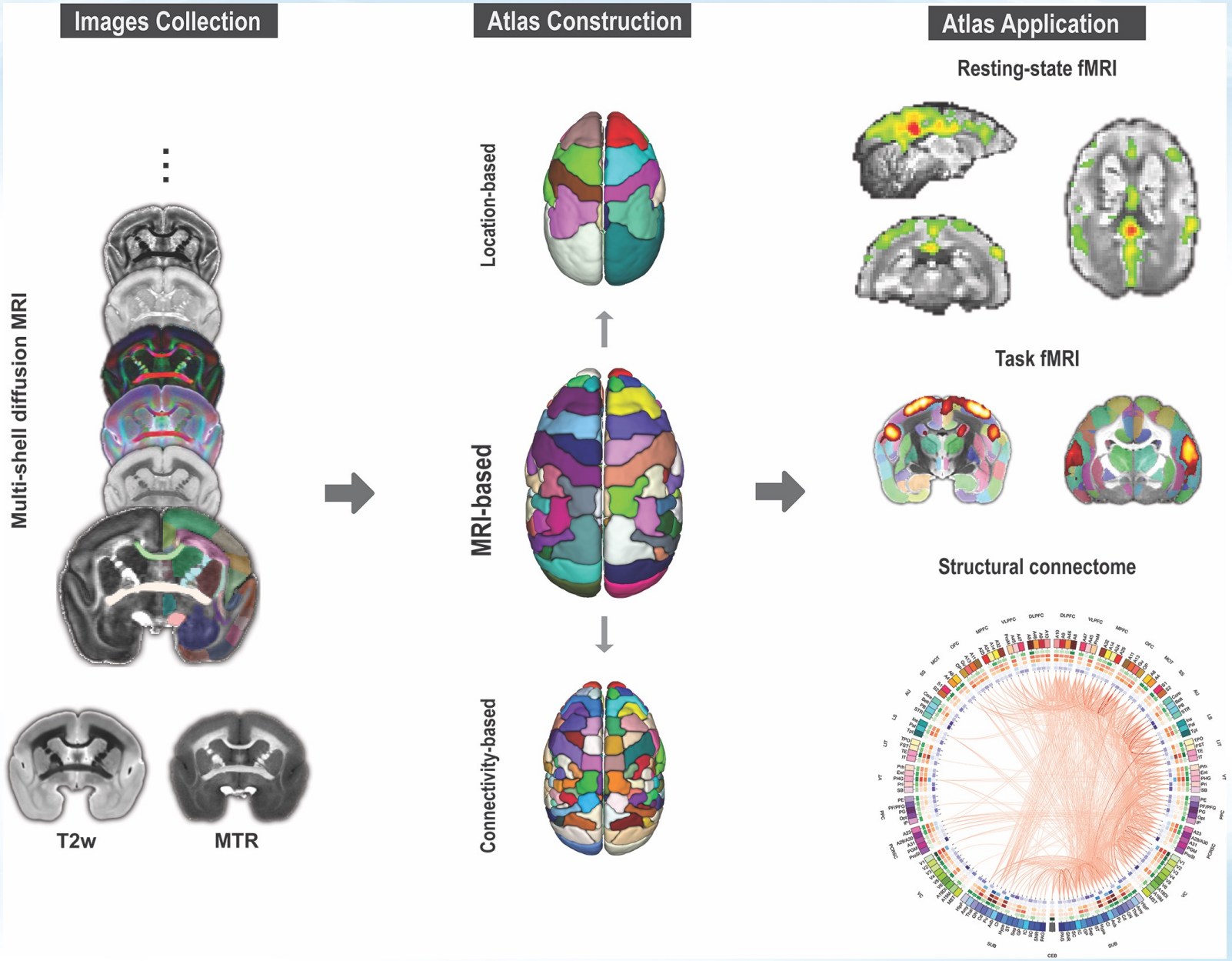


Region	Surface Area (mm²)		Surface Area (%)
	Left	Right	
Cortex	1005 ± 21	1007 ± 34	100
V1	219 ± 12	222 ± 3	22
S1	28 ± 4	30 ± 4	3
MT (V6)	17 ± 3	19 ± 2	2
A1 and R	11 ± 3	11 ± 3	1
DM (V4)	8 ± 1	7 ± 1	1

- Agrees well with histological measures of areas:
  - V1: 200-205 mm^2: *Fritsches and Rosa 1996 JCN 372:264-82; Missler, Wolff 1993 JCN 333:53-67*
  - MT: 14 mm^2: *Pessoa et al. 1992 Exp. Brain Res. 2: 459–462.*
- More than ¼ of the marmoset cortex dedicated to processing of visual information

Bock *Ann N Y Acad Sci. 2011 1225 Suppl 1:E171-81*

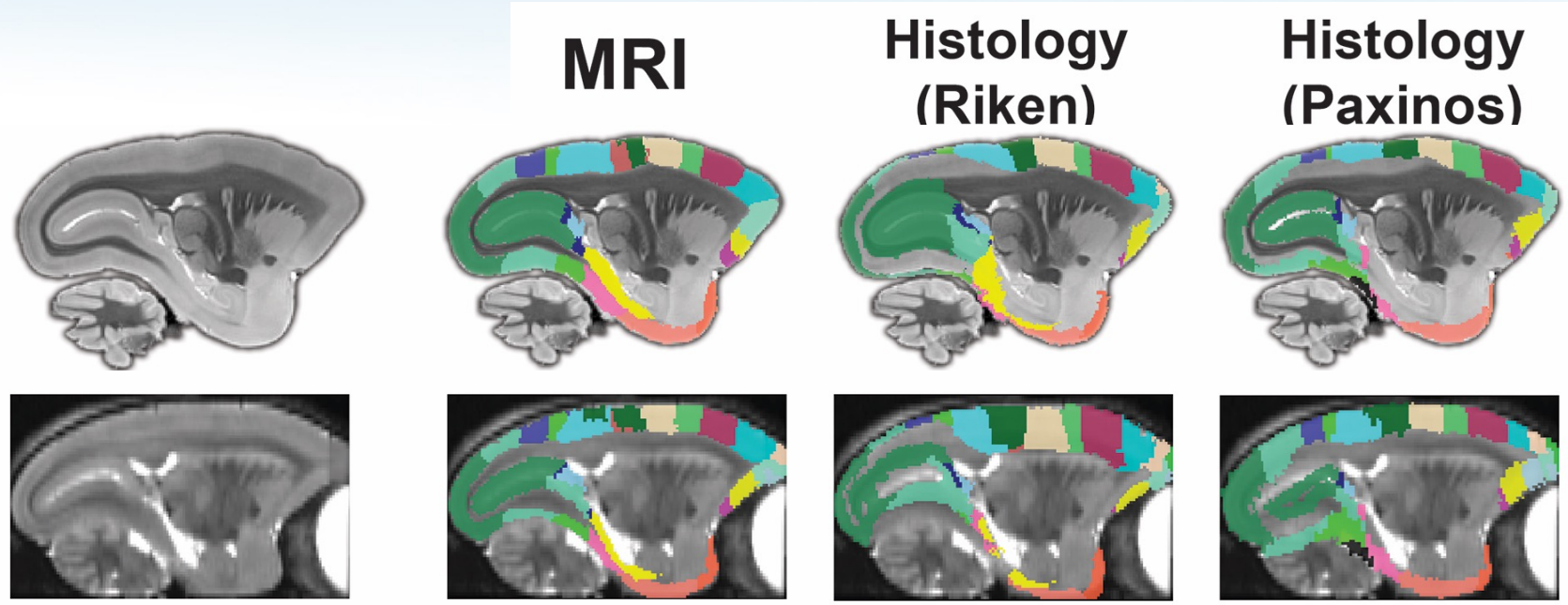
Marmoset MRI Atlas



Cerebral Microcirculation Section, LFMI, NINDS, NIH

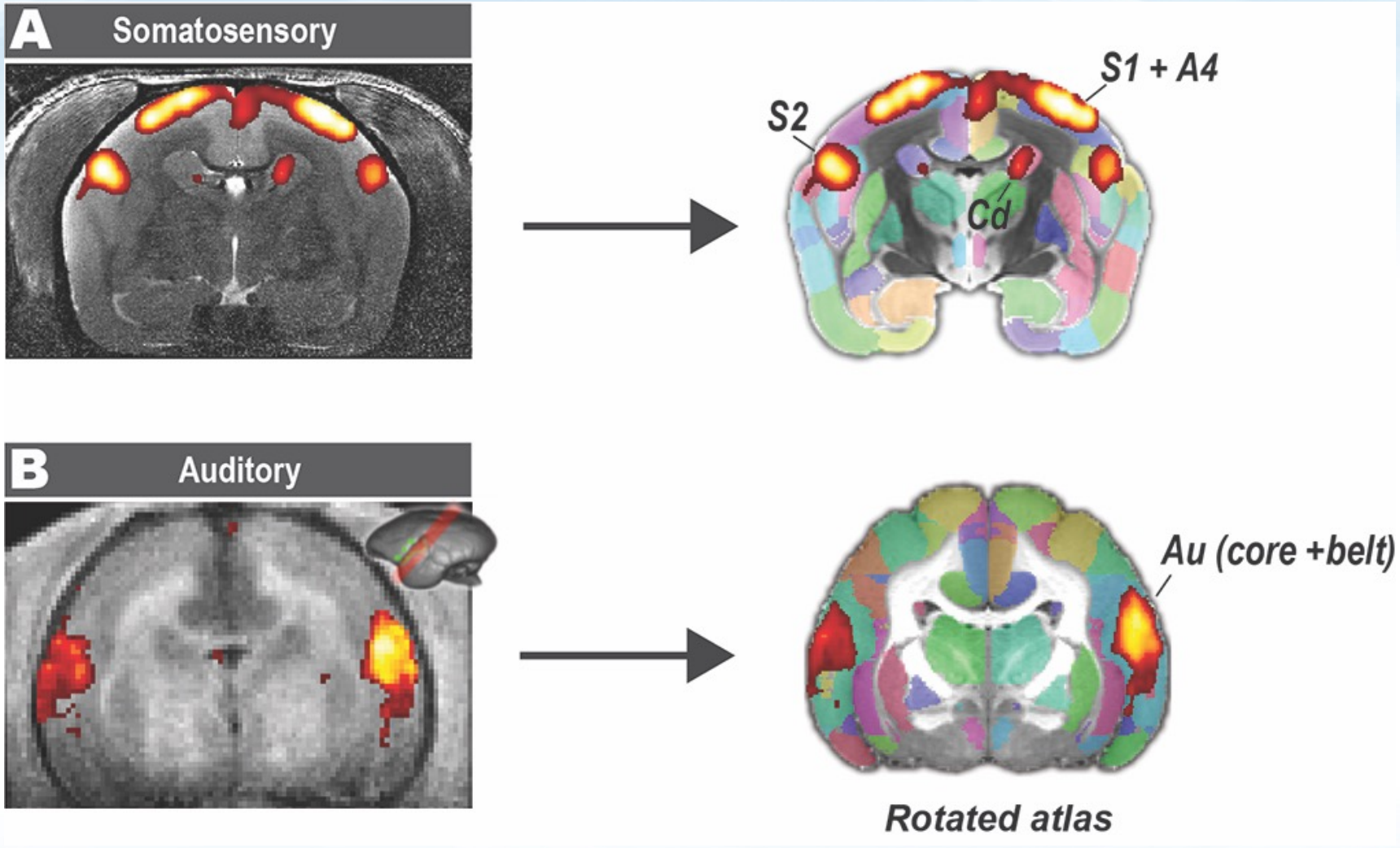
Liu et al. NeuroImage under review

Comparison of Atlas Registration



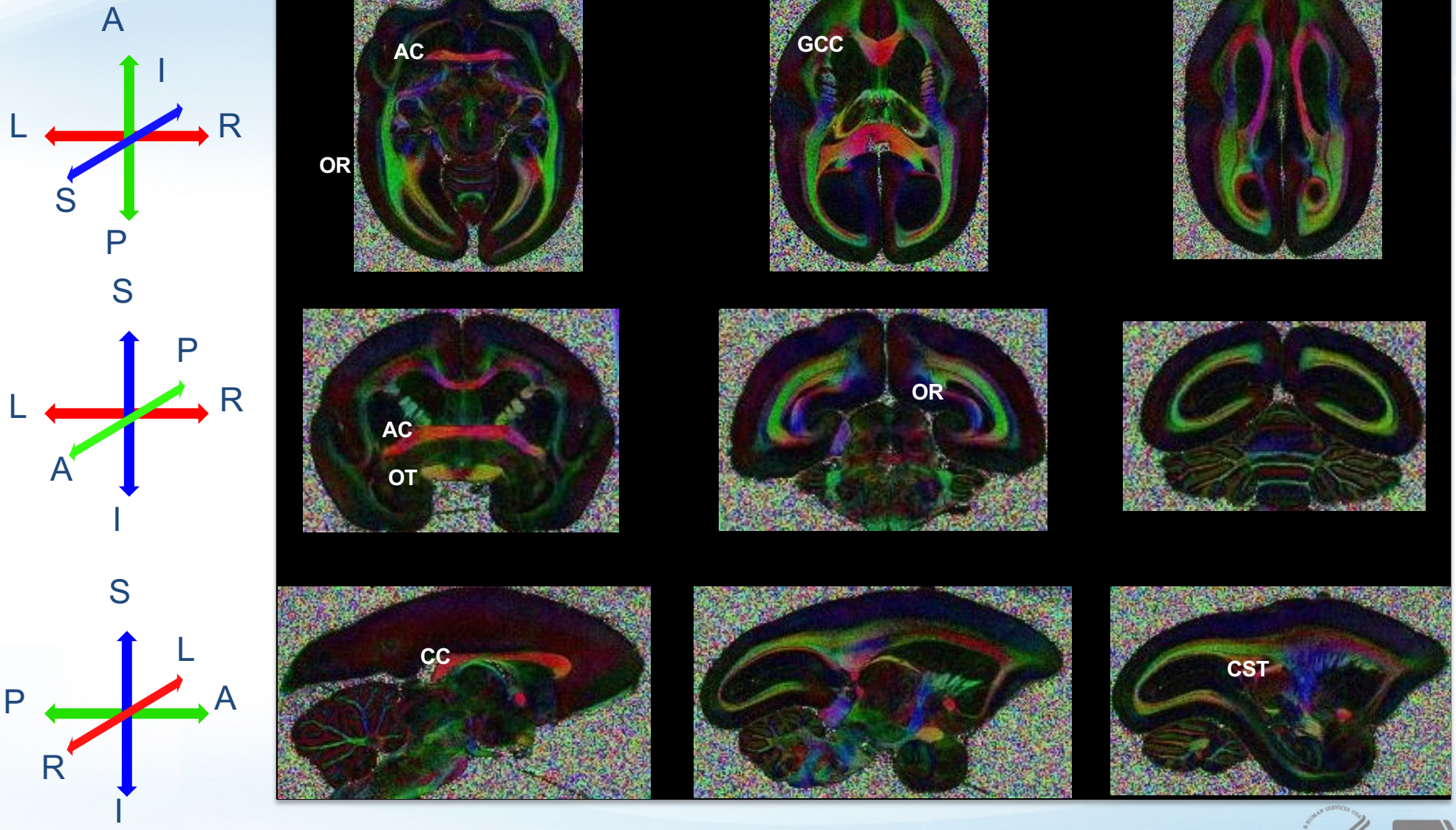
Liu et al. NeuroImage under review

Mapping fMRI Response on to Atlas



Liu et al. NeuroImage under review

DTI: Fractional Anisotropy Maps

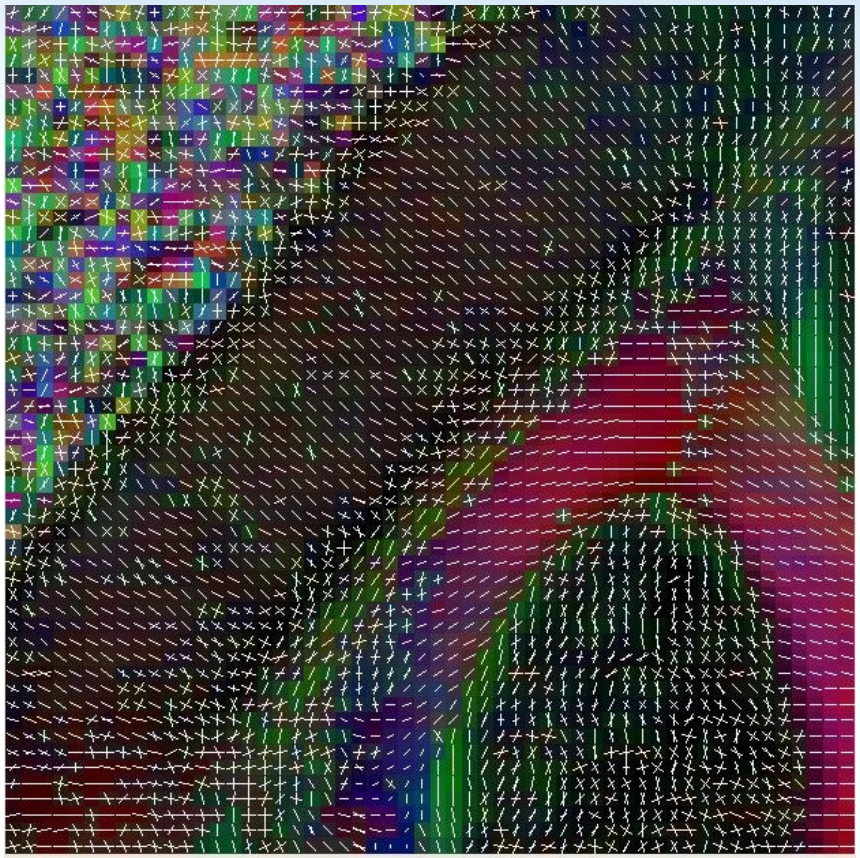


Maximum b-value: 4000 s/mm^2, 30 directions Spatial resolution: 150μm^3

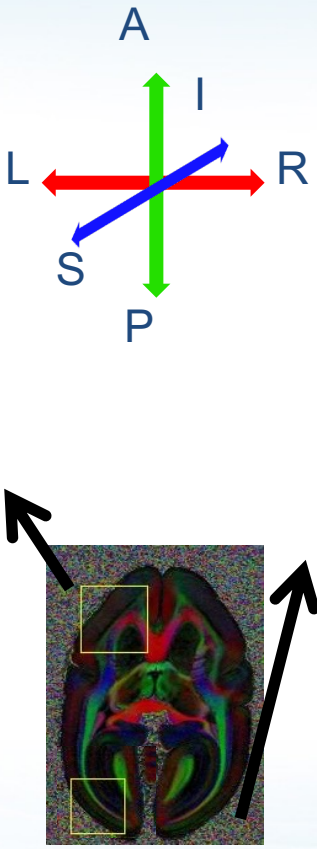
Pascal Sati , Frank Ye

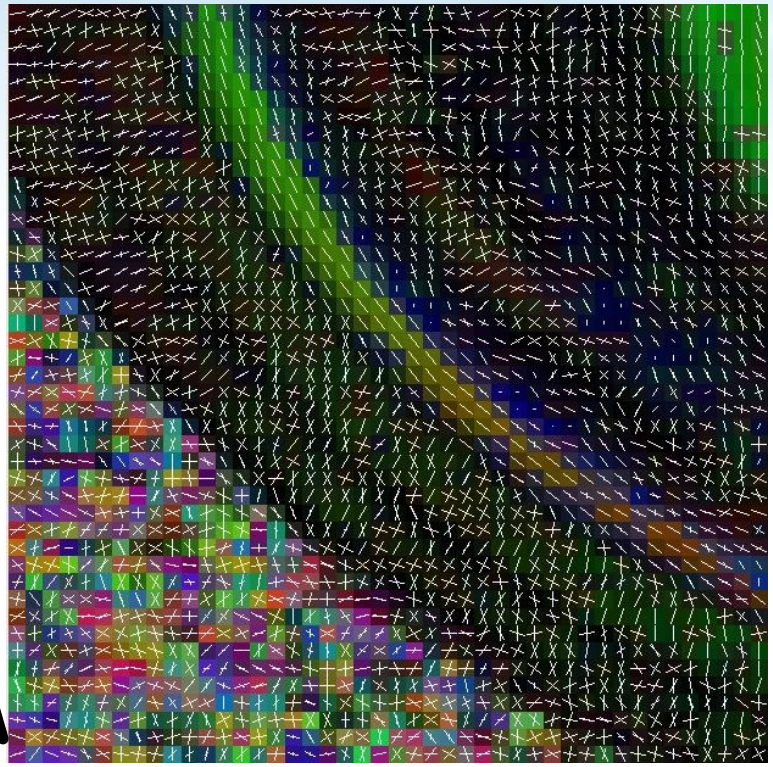
Cerebral Microcirculation Section, LFMI, NINDS, NIH

DTI: Microstructure of the Marmoset White Matter



GCC





OR

Maximum b-value: 4800 s/mm^2, 126 directions Spatial resolution: 150μm^3

Frank Q. Ye, David A. Leopold, Mustafa Irfanoglu, Carlo Pierpaoli, Afonso C. Silva

Cerebral Microcirculation Section, LFMI, NINDS, NIH

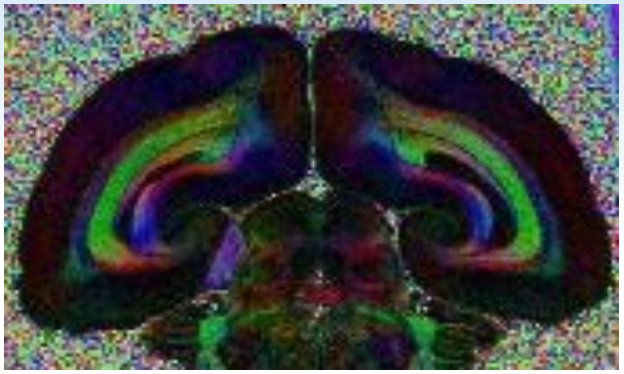
T_2^* vs. Brain Orientation

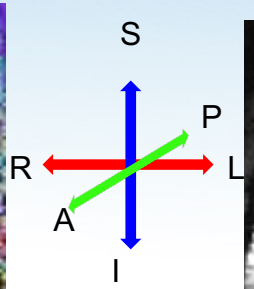
Sphinx Position

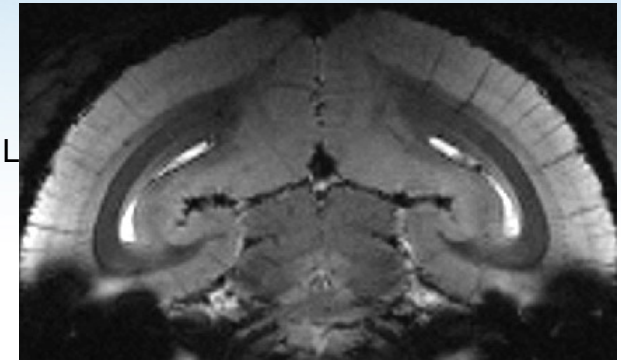
Supine Position

FA Map

T_2 weighted

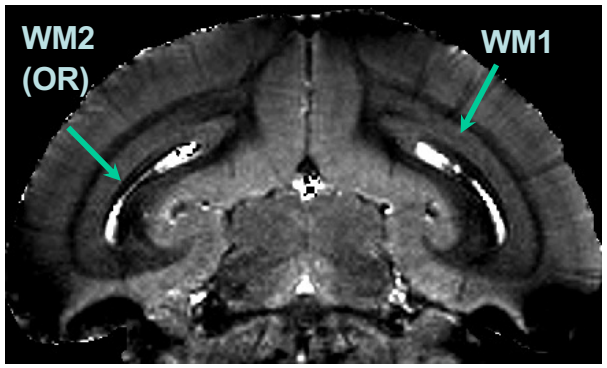


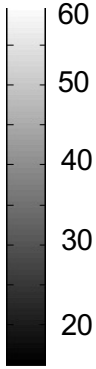


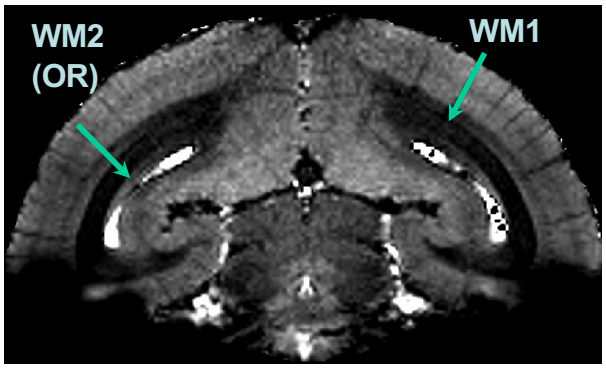


B_0

T_2^* map





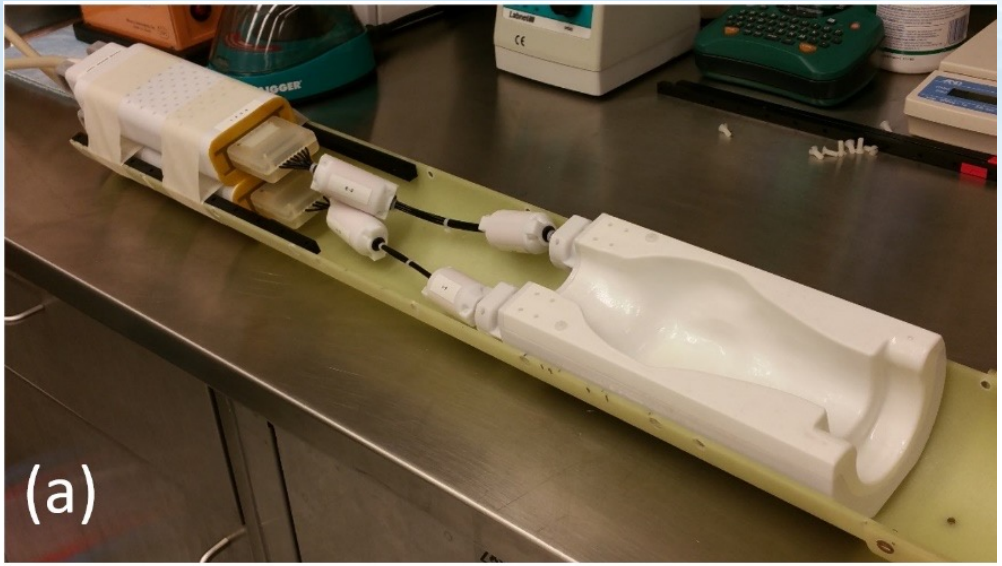


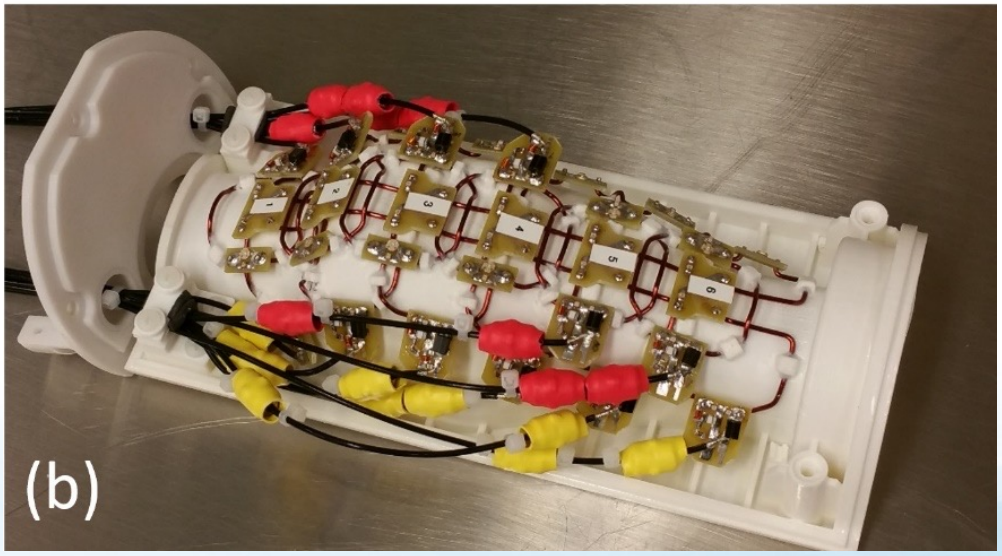
B_0

Animal Position	WM1	WM2 (OR)
Sphinx	25.4 ± 3.1	32.4 ± 3.0
Supine	29.2 ± 5.2	22.5 ± 2.8

Pascal Sati et al., Neuroimage 2011

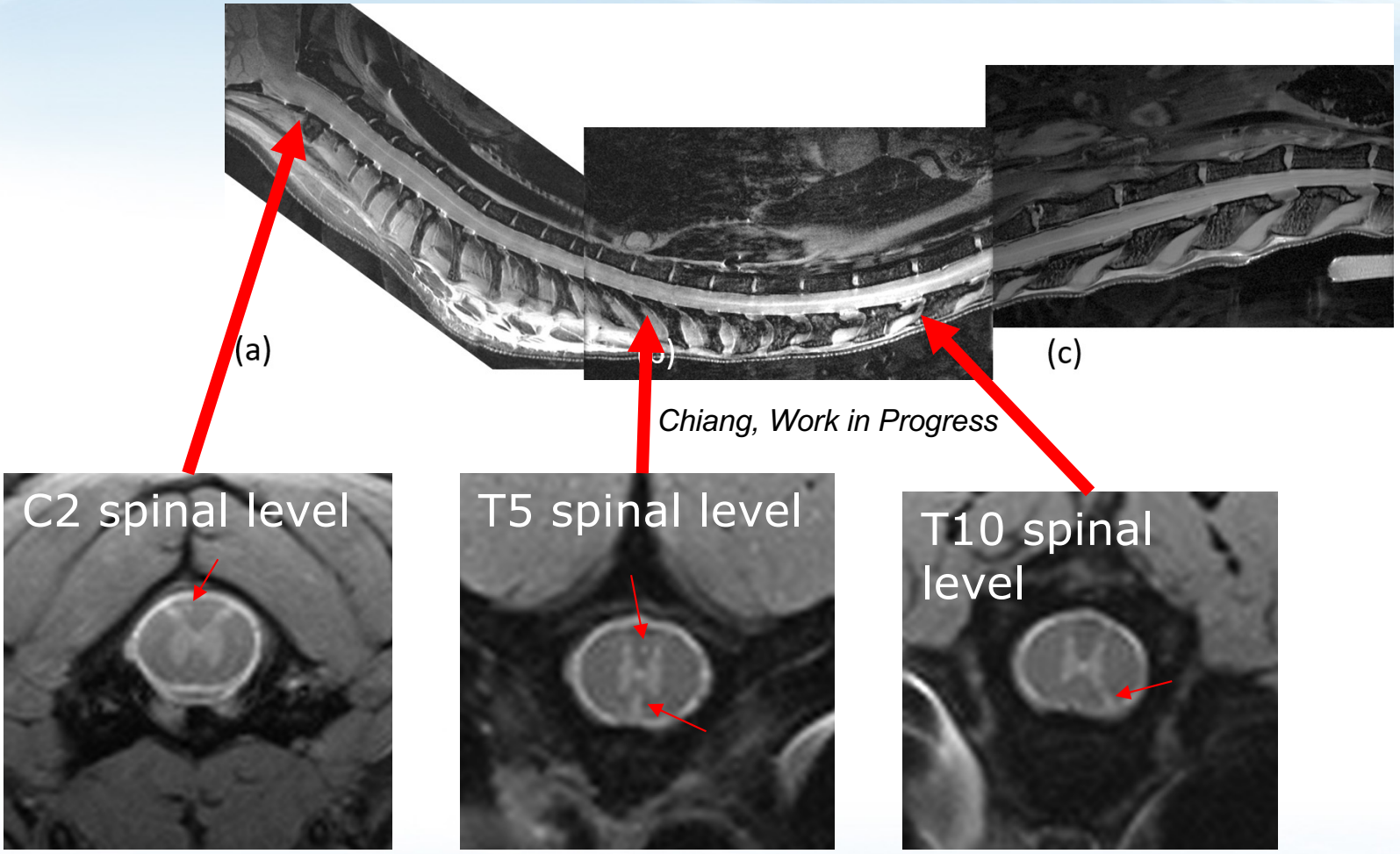
Setup for Spinal Cord Imaging





Chiang, Work in Progress

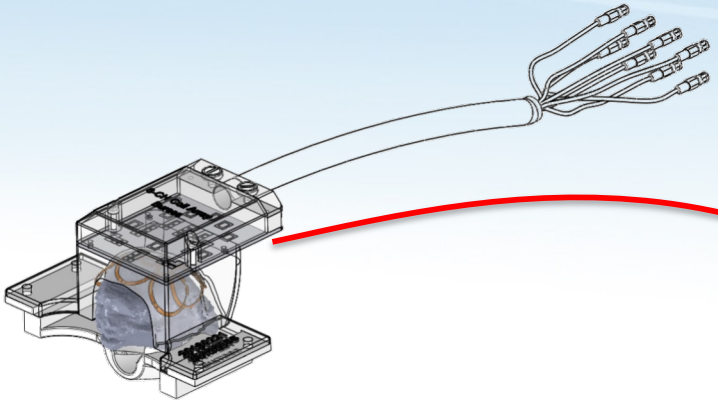
Detecting EAE Lesions in Marmoset's Spine Using MRI

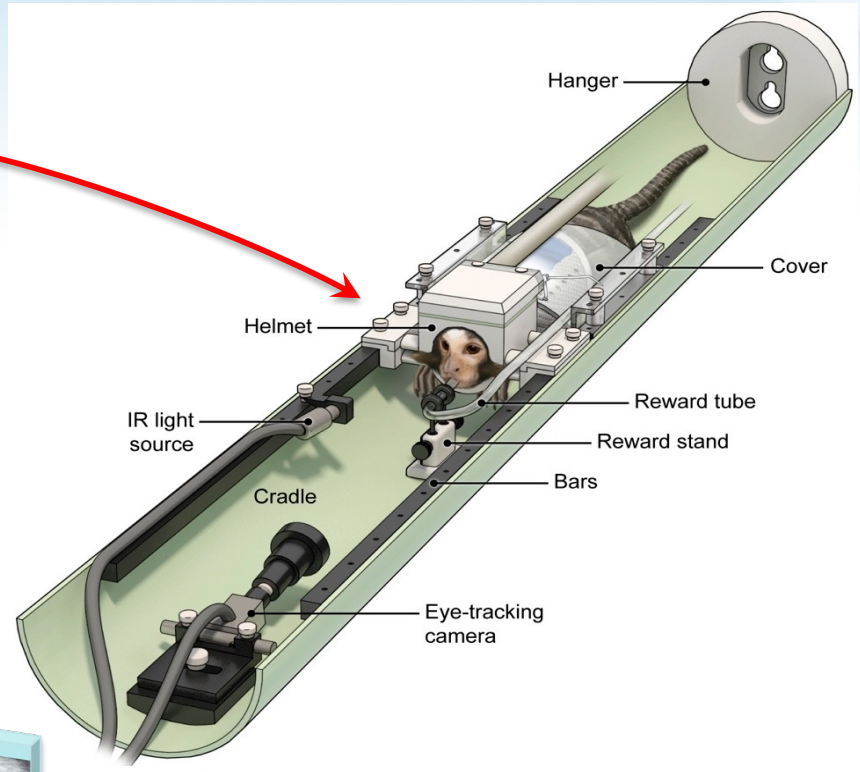


Chiang, Work in Progress

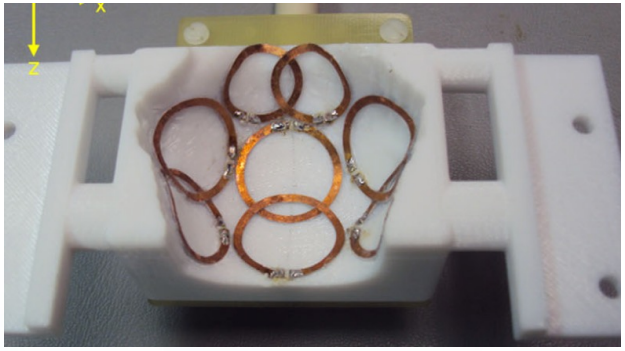
Lefeuvre, Work in Progress

Setup for Awake Marmosets



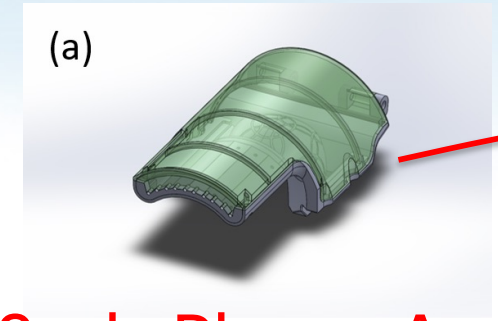


8-ch Phase Array

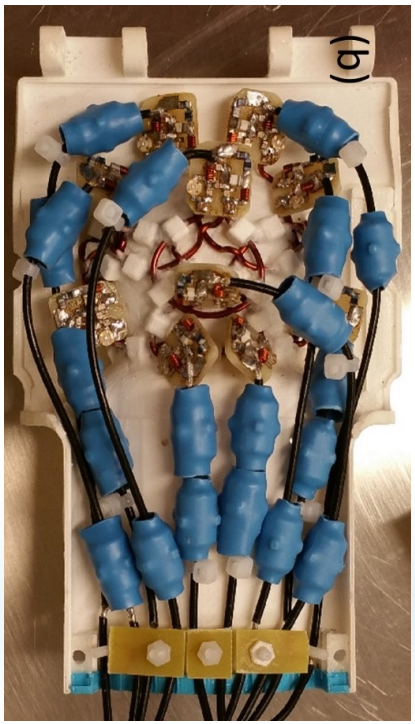


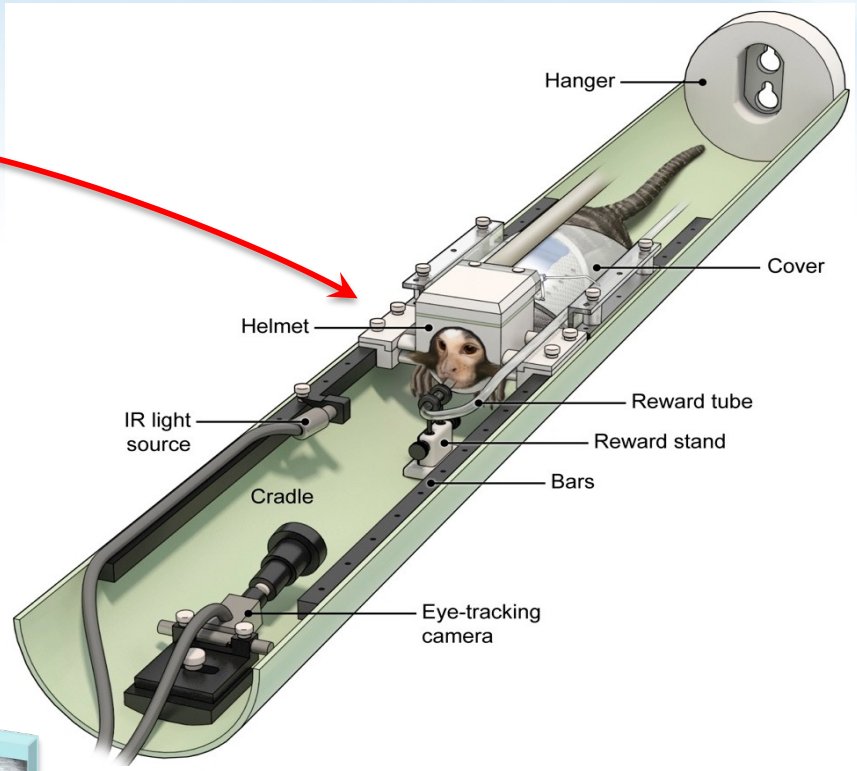
Papoti et al. MRM 2017

Setup for Awake Marmosets



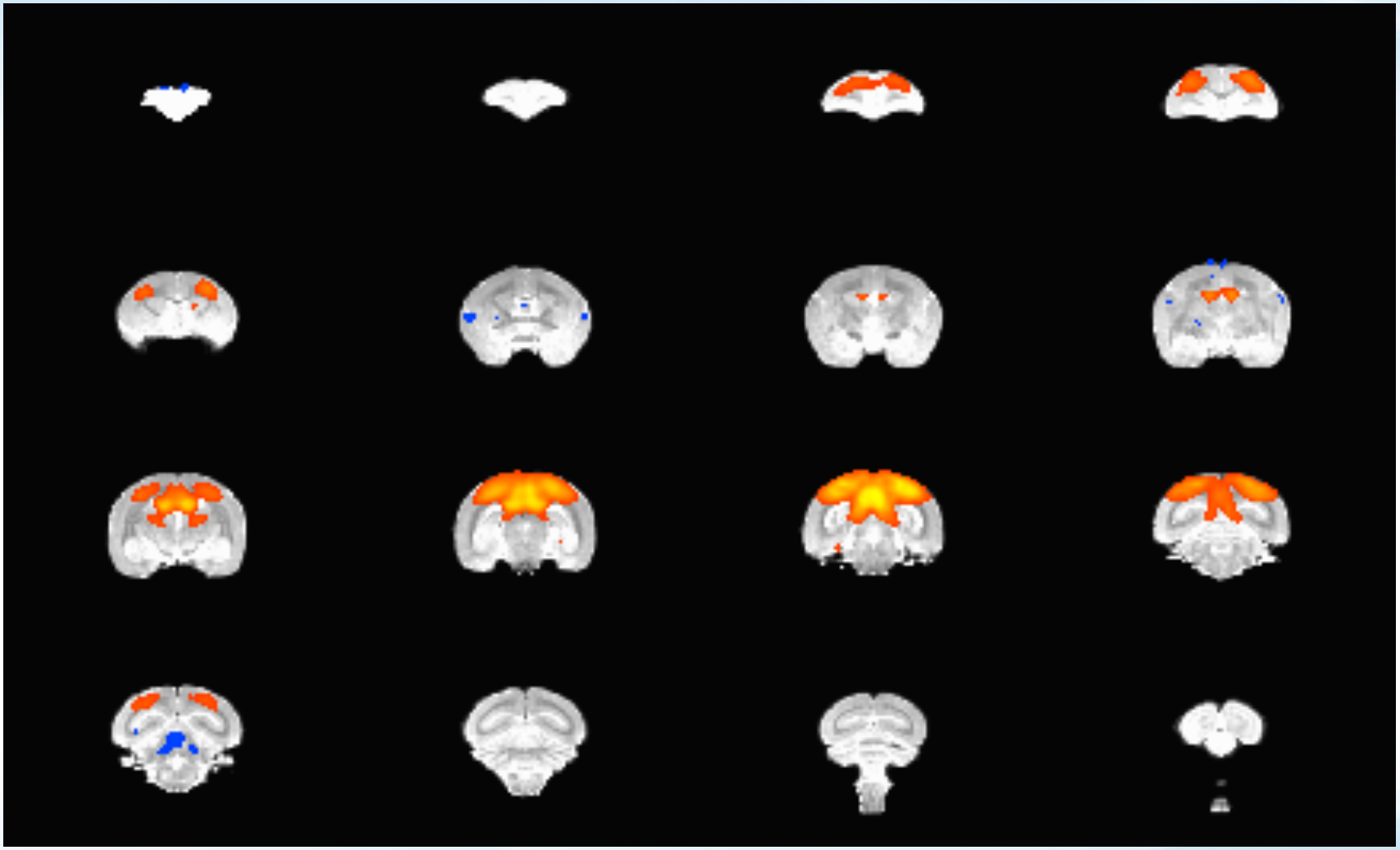
10-ch Phase Array





Chiang, Work in Progress

Resting-state fMRI: Default Mode Network

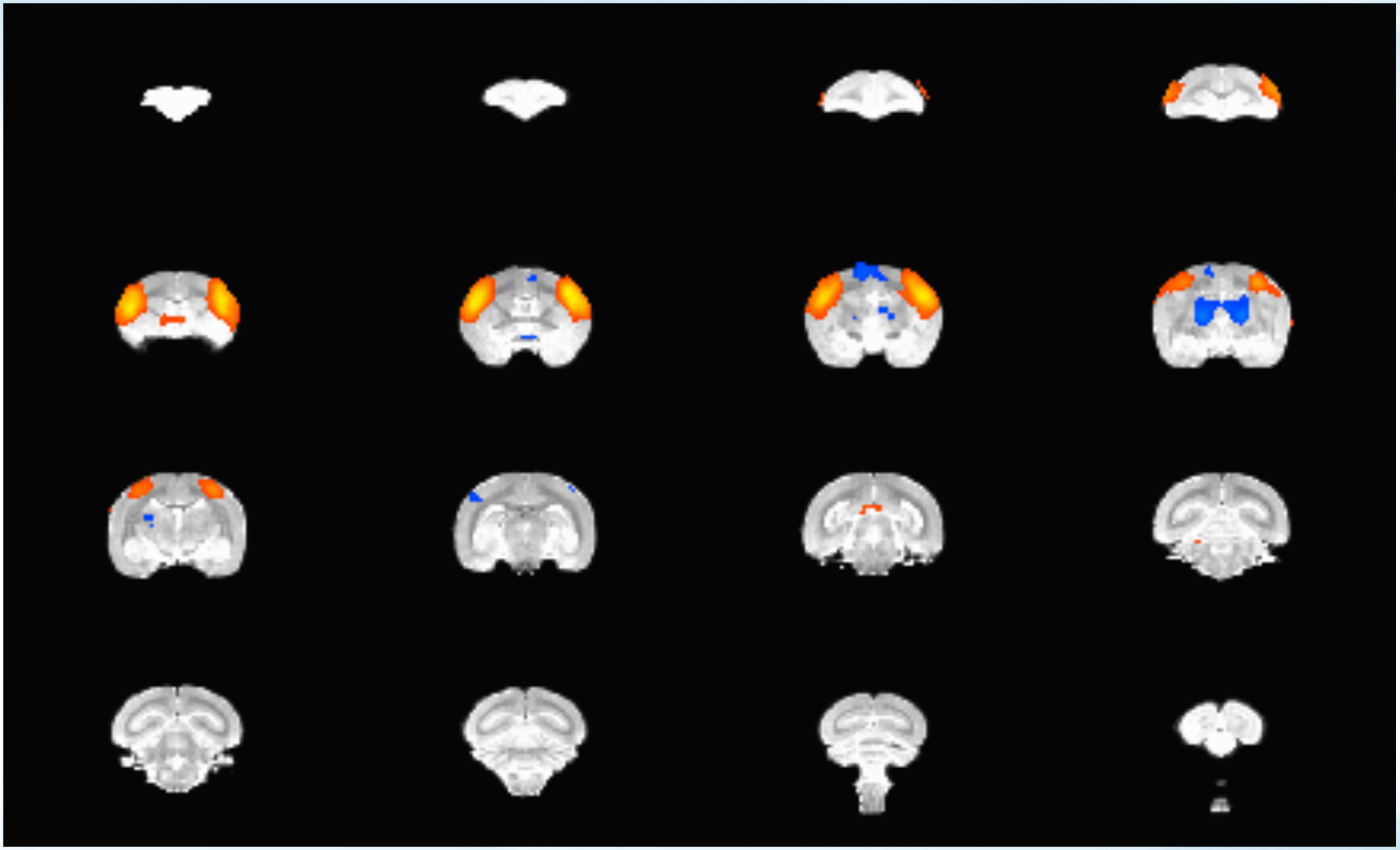


Belcher J Neurosci. 2013 33(42):16796 –16804

6 marmoset averaged

ICA, Z> 7

Resting-state fMRI: Somatosensory Network

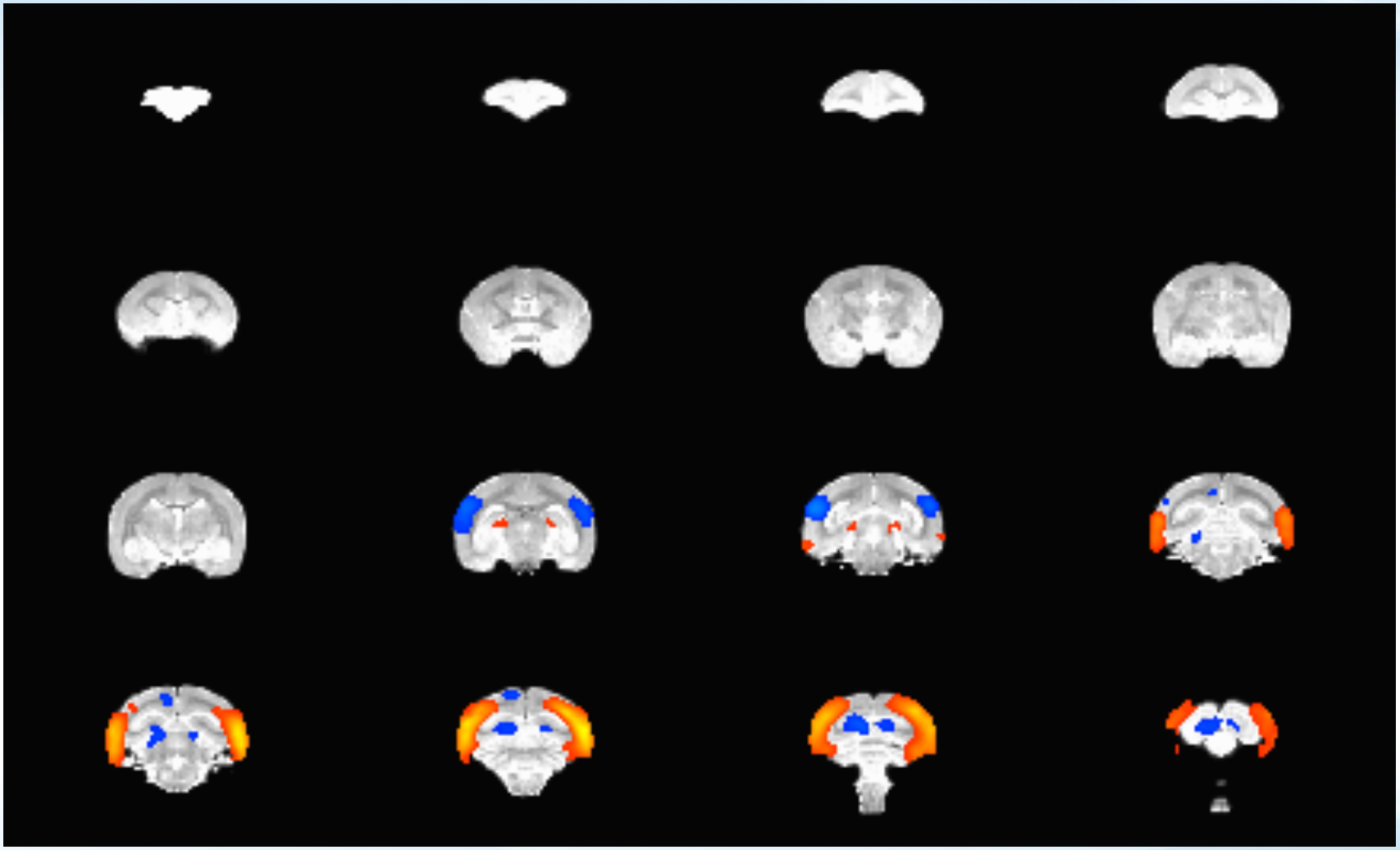


Belcher J Neurosci. 2013 33(42):16796 –16804

6 marmoset averaged

ICA, Z> 7

Resting-state fMRI: Higher-order Visual Network



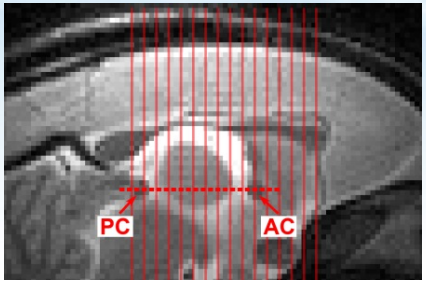
Belcher J Neurosci. 2013 33(42):16796 –16804

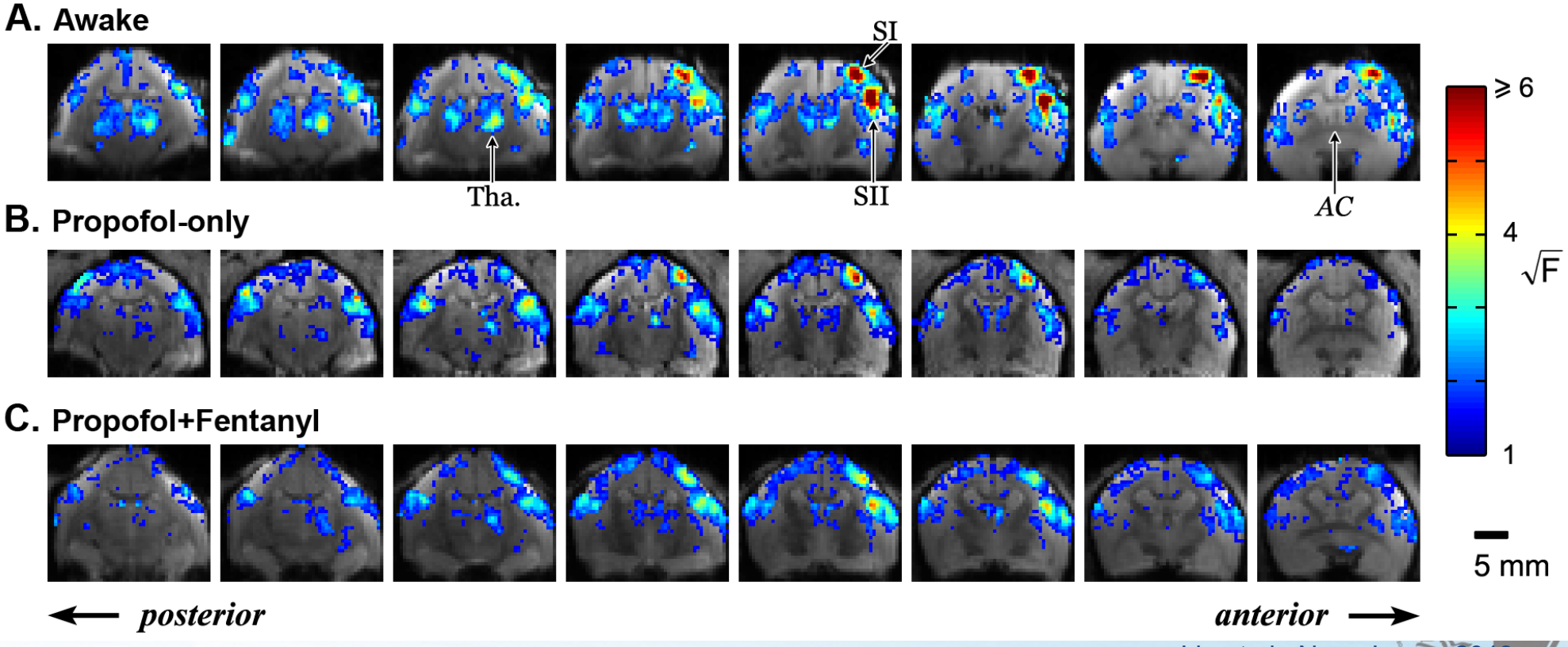
6 marmoset averaged

ICA, Z> 7

More Widespread Spatial Extent of Functional Regions in Awake Marmosets

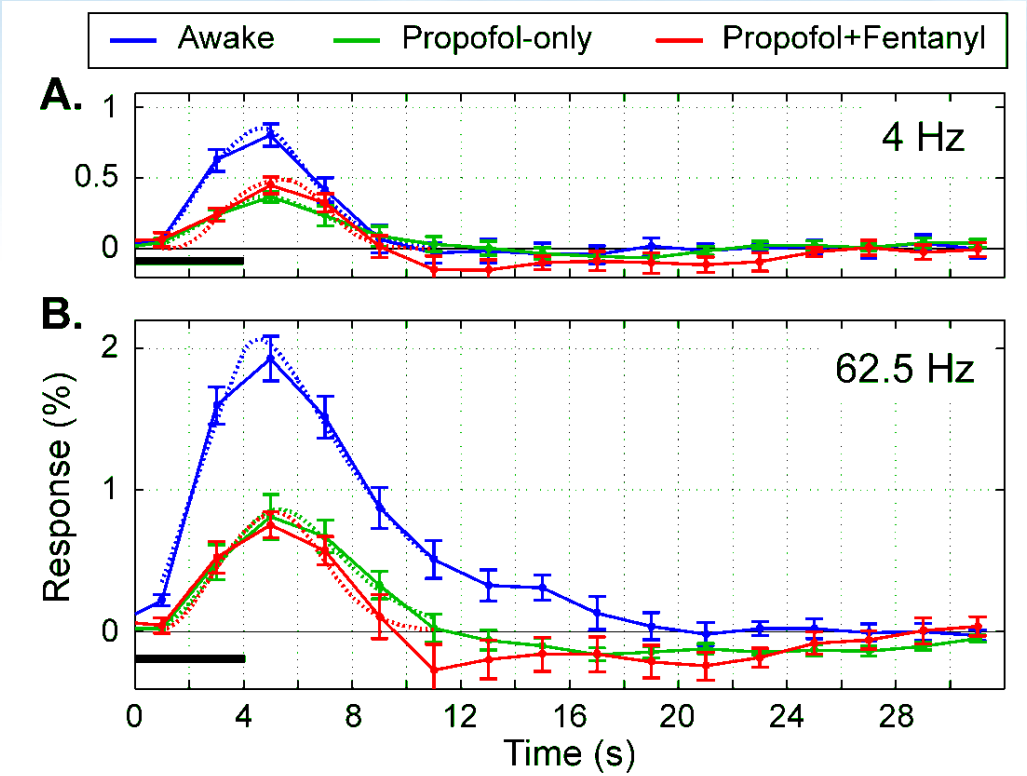
Responses throughout the somatosensory pathway significantly enhanced when compared to anesthetized subjects





Liu et al., NeuroImage 2013

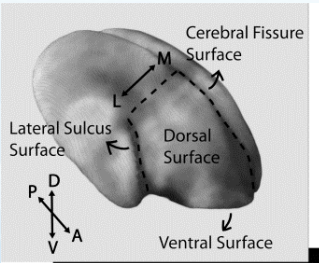
BOLD HRF in Awake Marmosets Has Faster Times-to-Peak

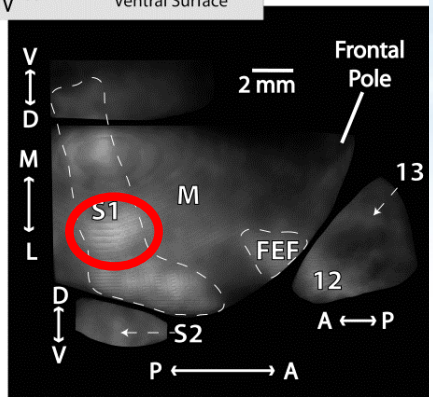


TTP shorter by ~0.5 s

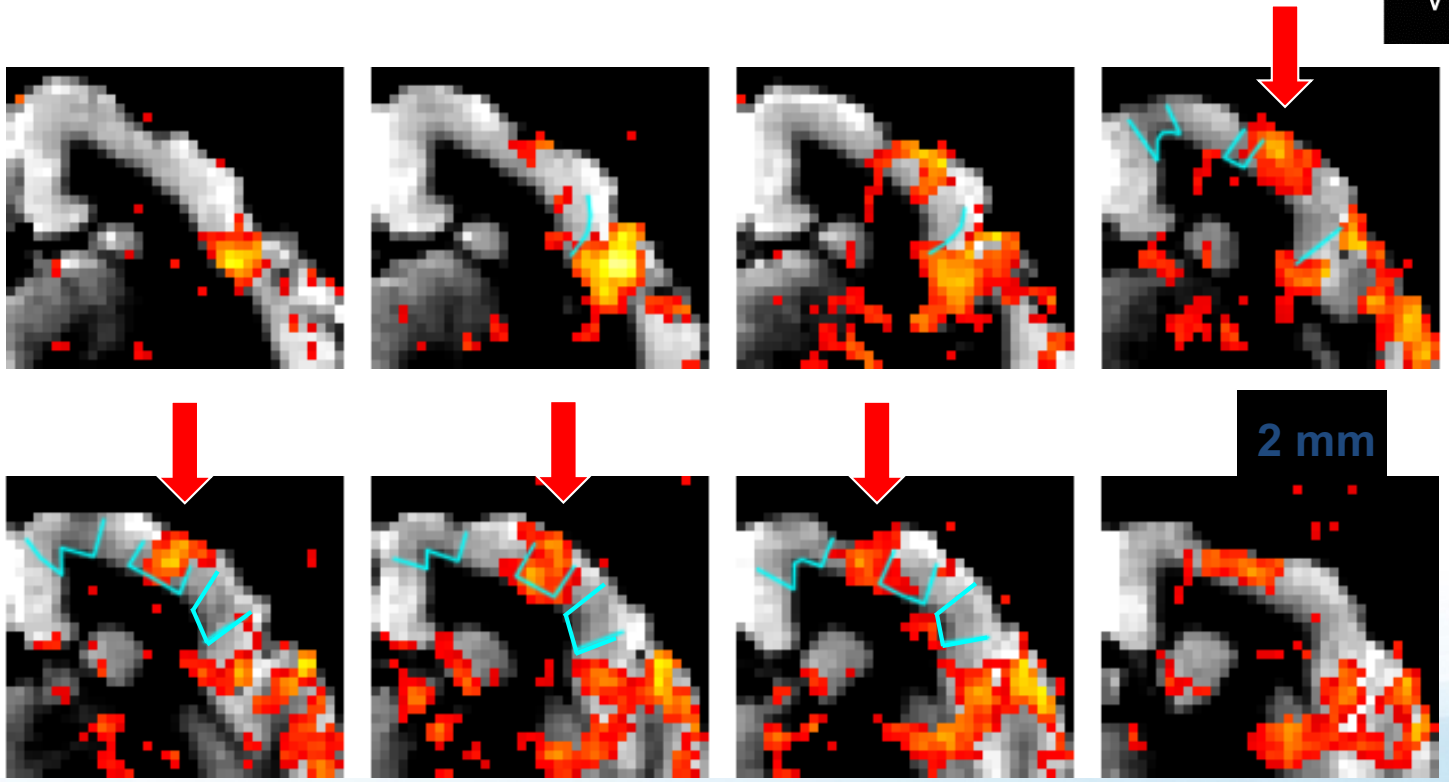
Liu et al., NeuroImage 2013

fMRI Activation Regions Map Well onto Myeloarchitectonic Maps





Forearm/Wrist Stimulation: 1.5 mA, 0.3ms, 50 Hz



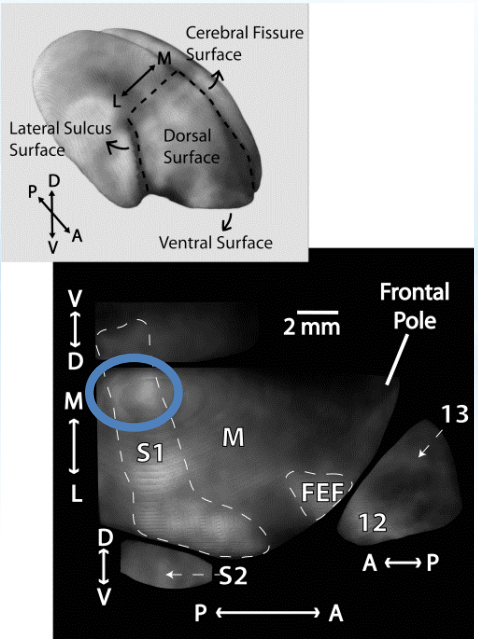
0.60

Correlation Coefficient

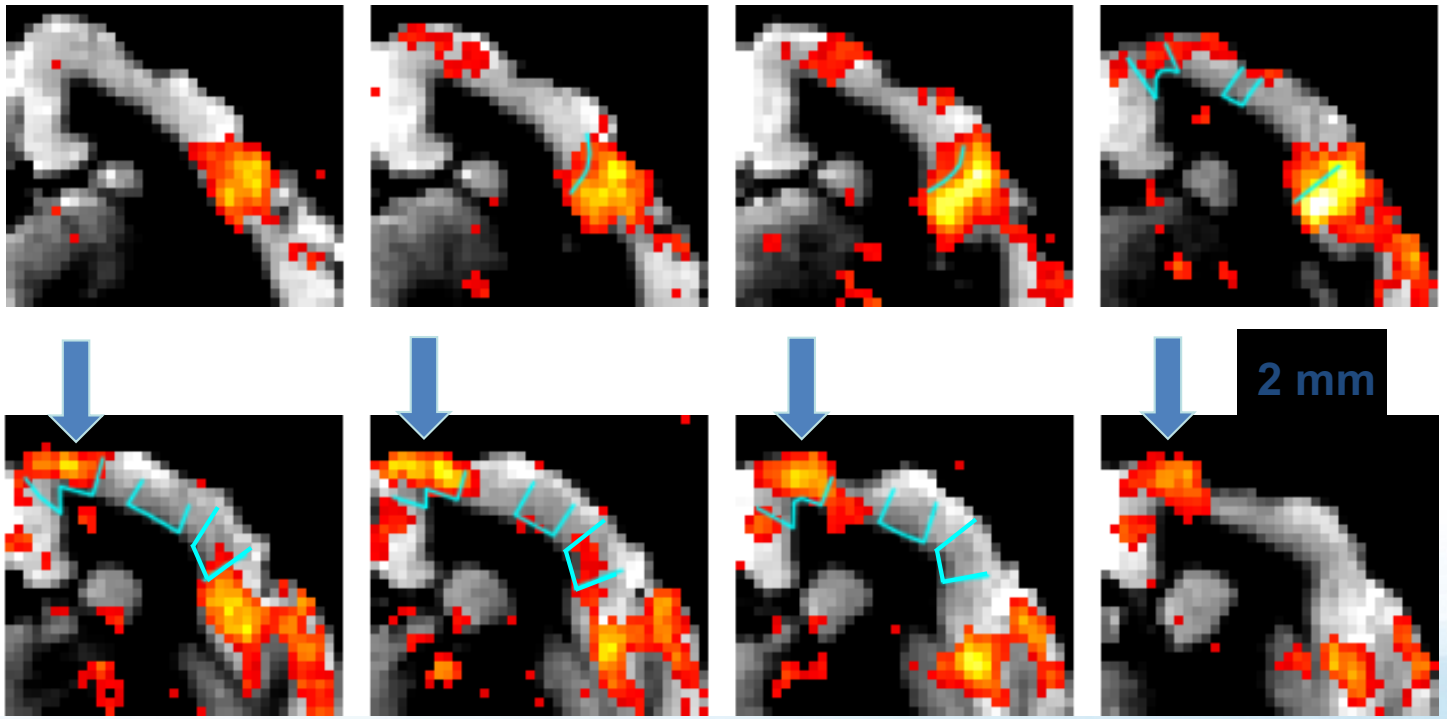
0.20

Junjie Liu, Neuroimage. 2011; 56(3):1154-63.

fMRI Activation Regions Map Well onto Myeloarchitectonic Maps



Leg Stimulation: 1.5 mA, 0.3ms, 50 Hz



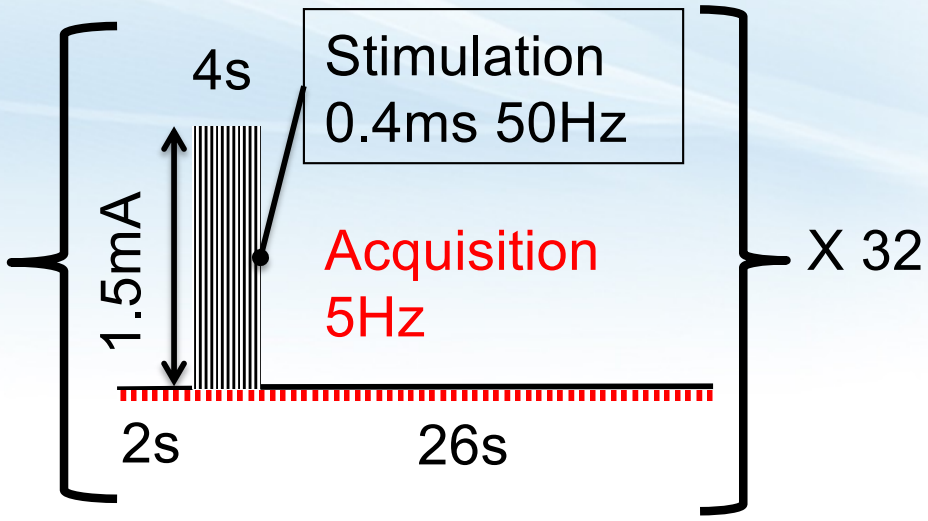
Correlation Coefficient

Junjie Liu, Neuroimage. 2011; 56(3):1154-63.

Protocol

- **Somatosensory Stimuli Paradigm**

0.4ms, 1.5mA, 50Hz electrical pulses for 4s



- **MRI Parameters**

Custom-built 4-channels phase array

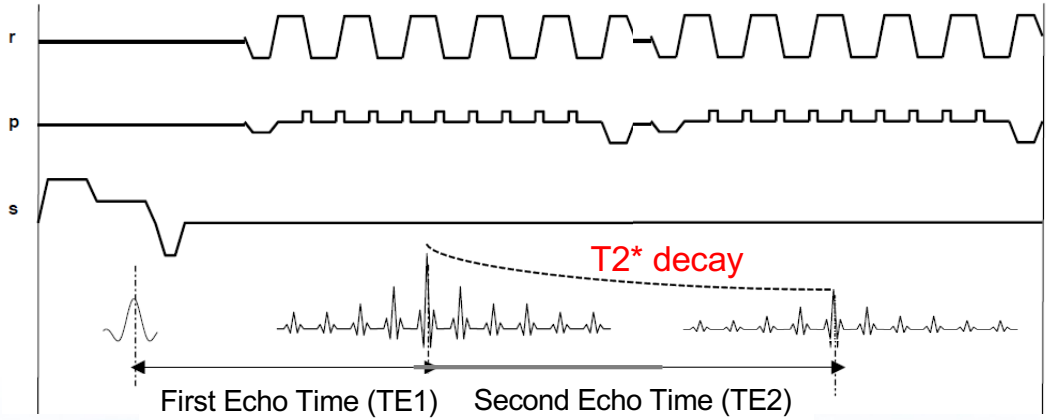
Dual gradient-recalled EPI

Matrix = 128 x 48

TE1/TE2/TR = 13.5/40.5/200 ms

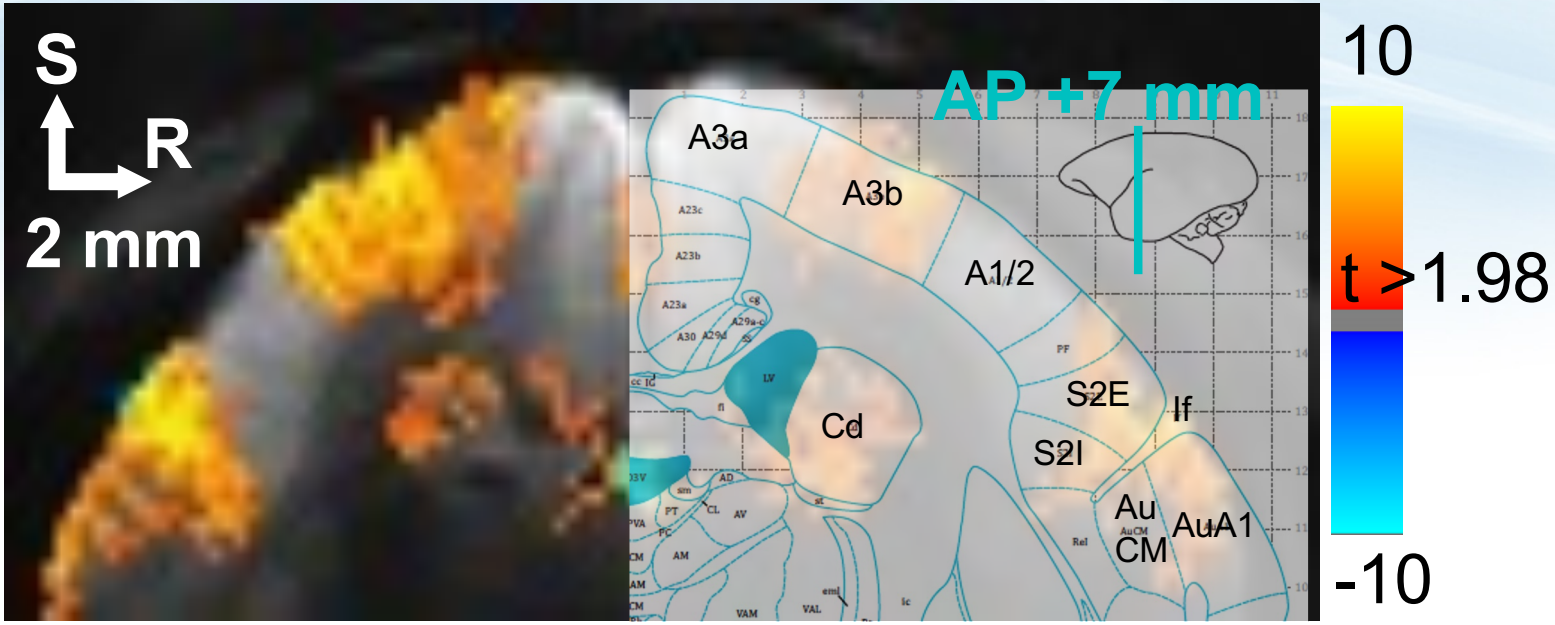
Resolution = 0.25 x 0.25 x 1 mm^3

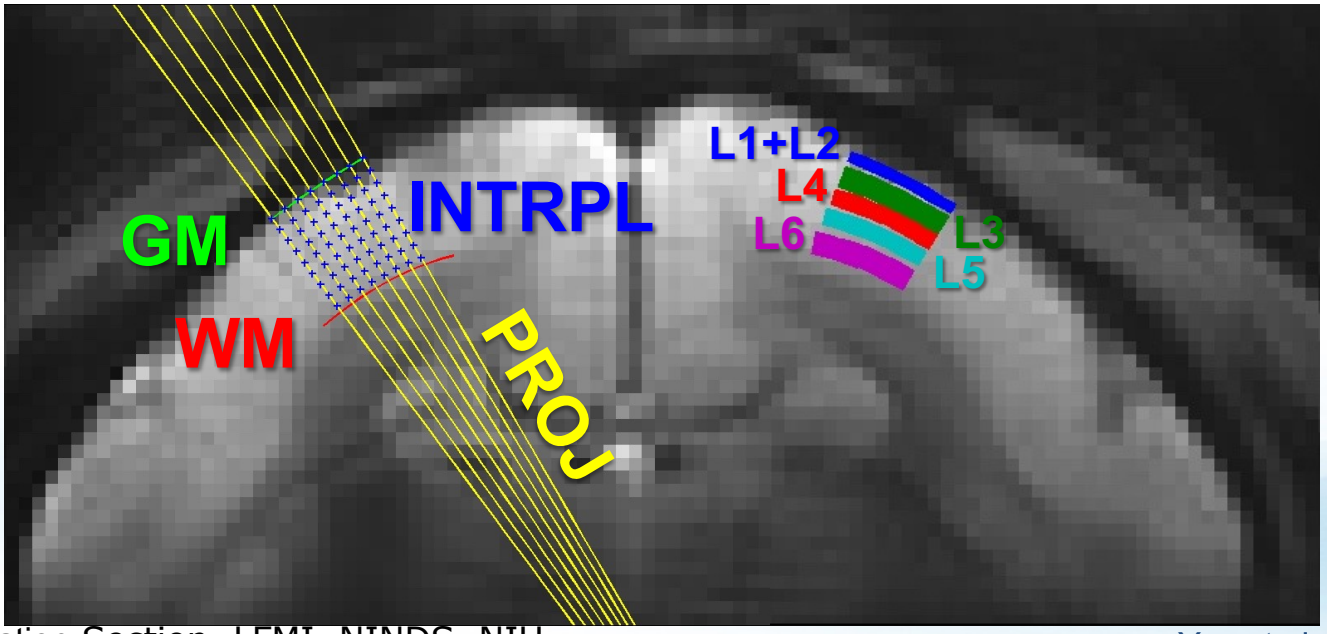
1 coronal slice w/ saturation band



Dual gradient-recall EPI

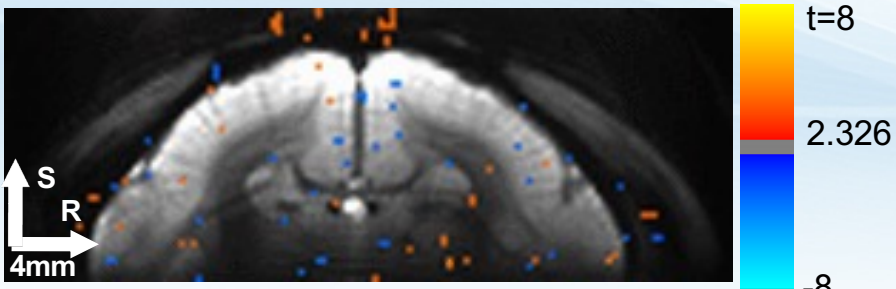
T2* Activation Map and Layer Profile





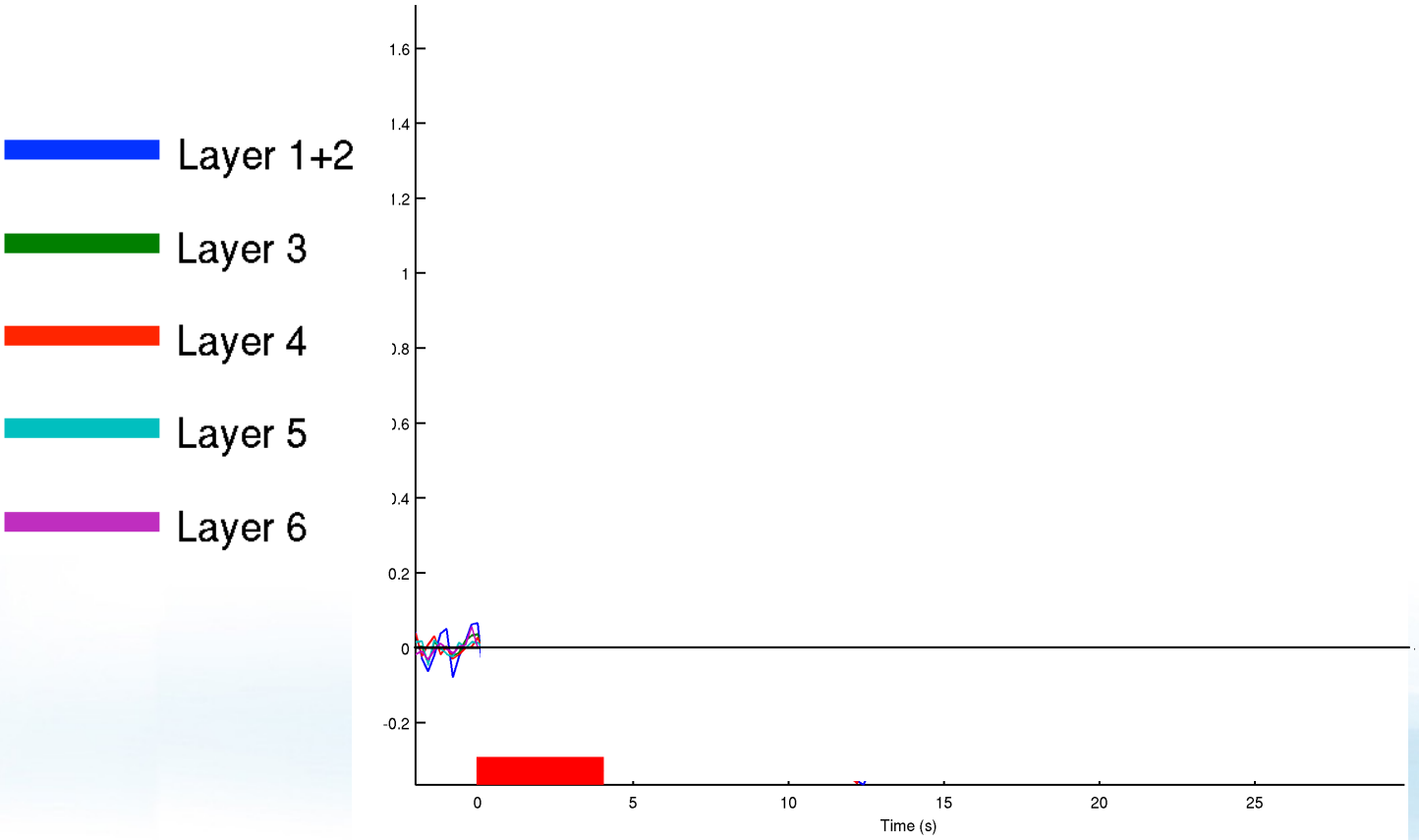
Yen et al., NeuroImage 2017

Time-lapse BOLD Activation Map



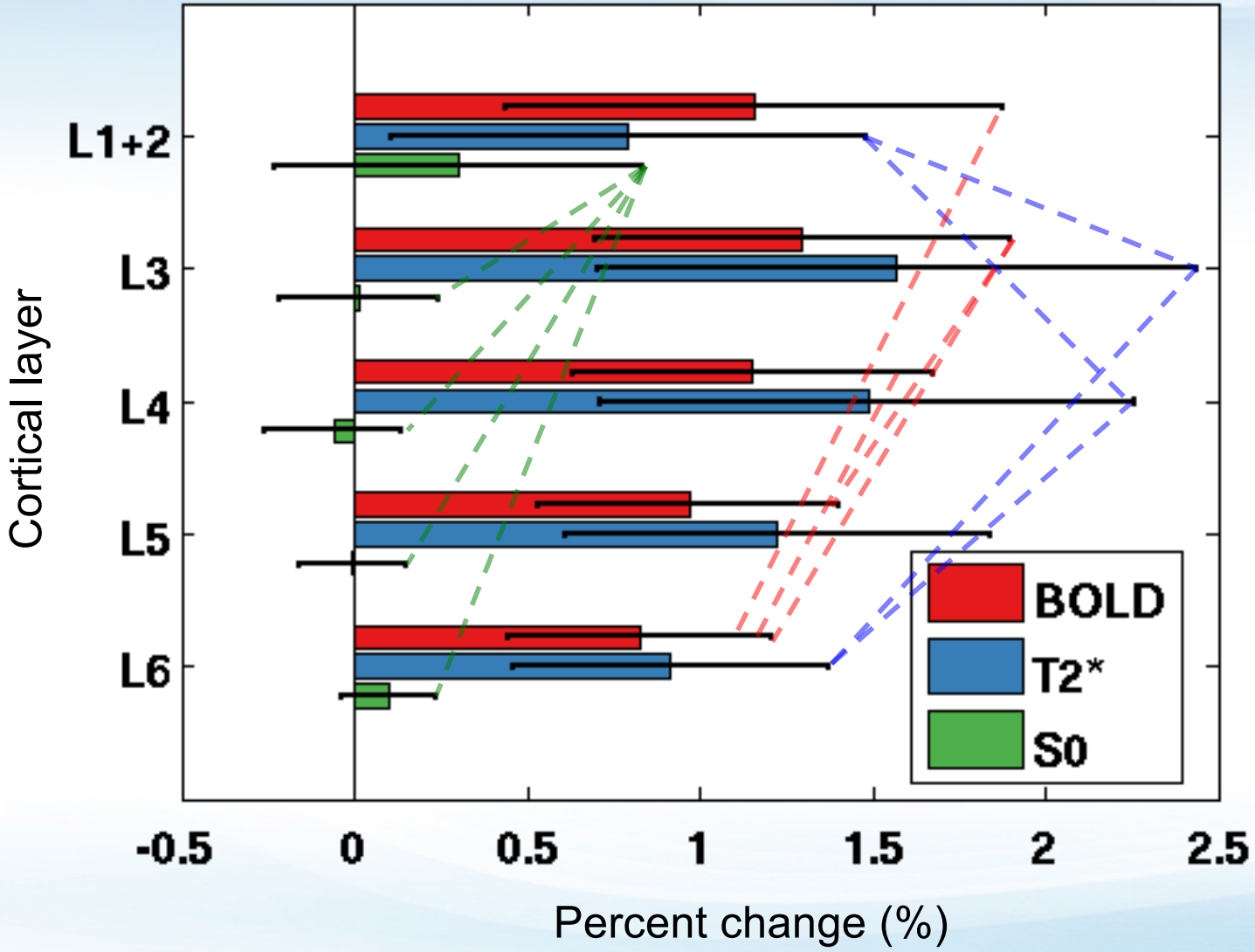
Chronological T Map of BOLD TE=27ms & TR=200ms

+00.0 second



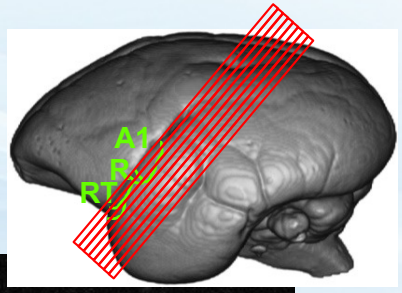
Yen et al., NeuroImage 2017

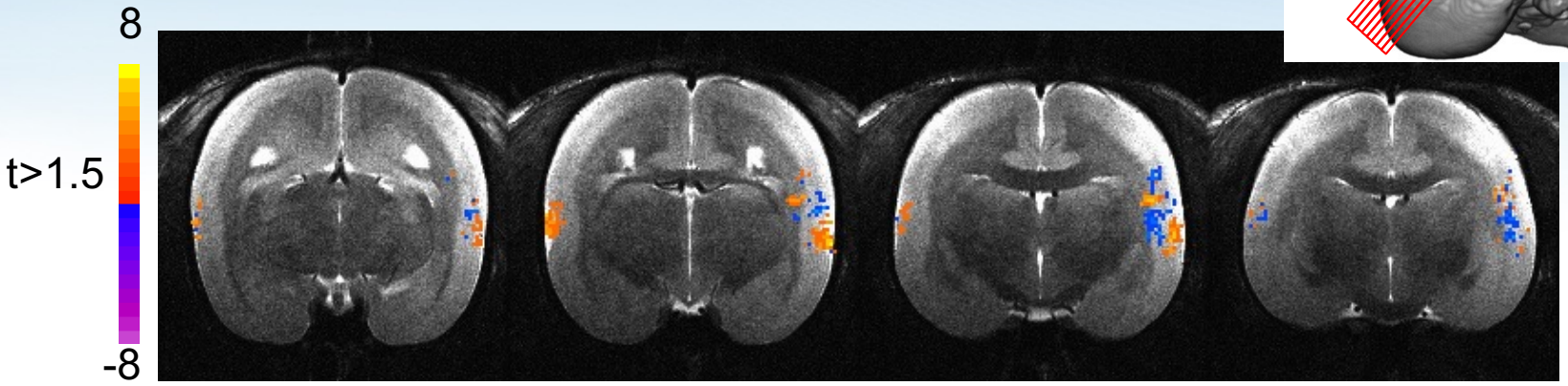
Averaged Laminar Responses

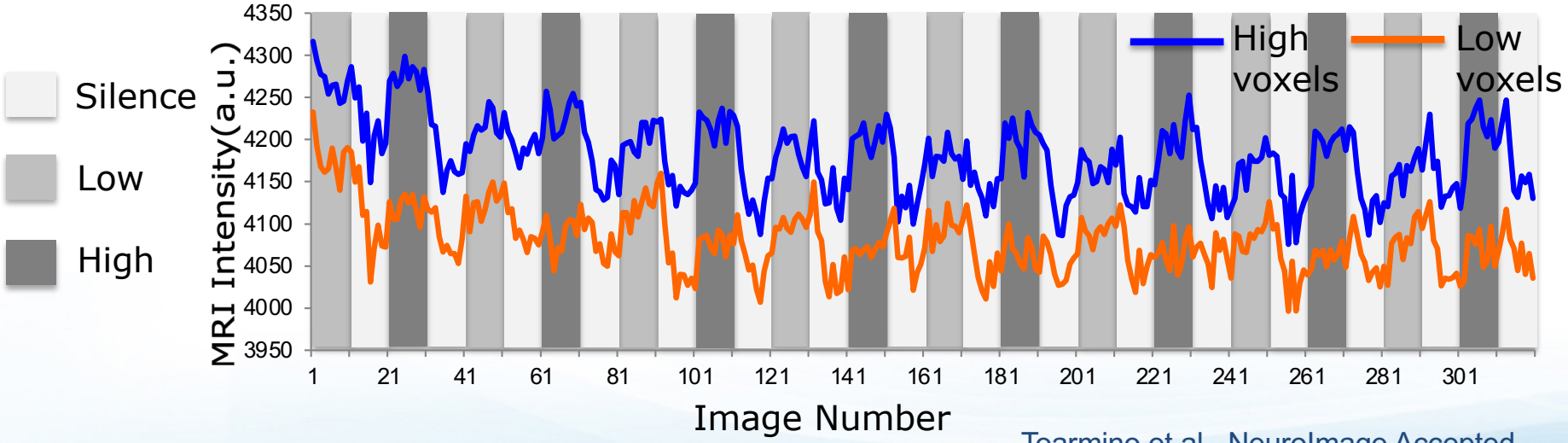


Yen et al., NeuroImage 2017

Tonotopic Mapping in Marmoset Auditory Cortex

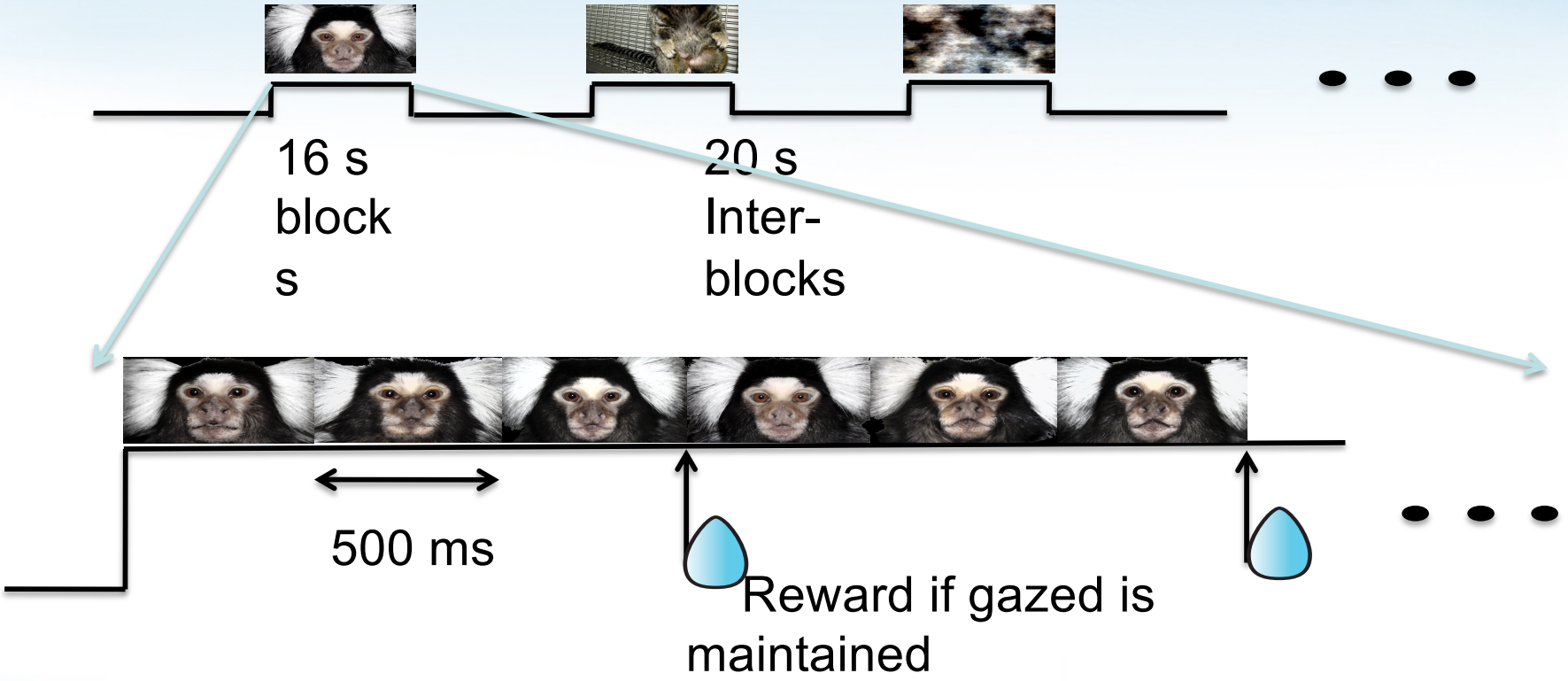






Toarmino et al., NeuroImage Accepted

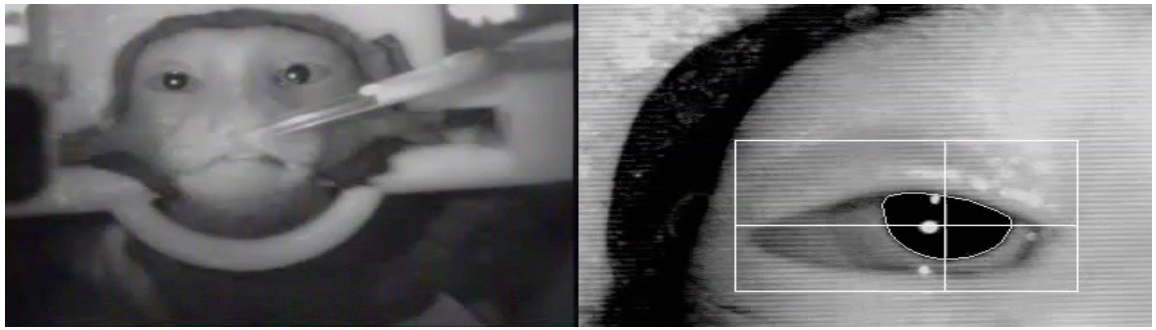
Experimental paradigm for fMRI of Visual System



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

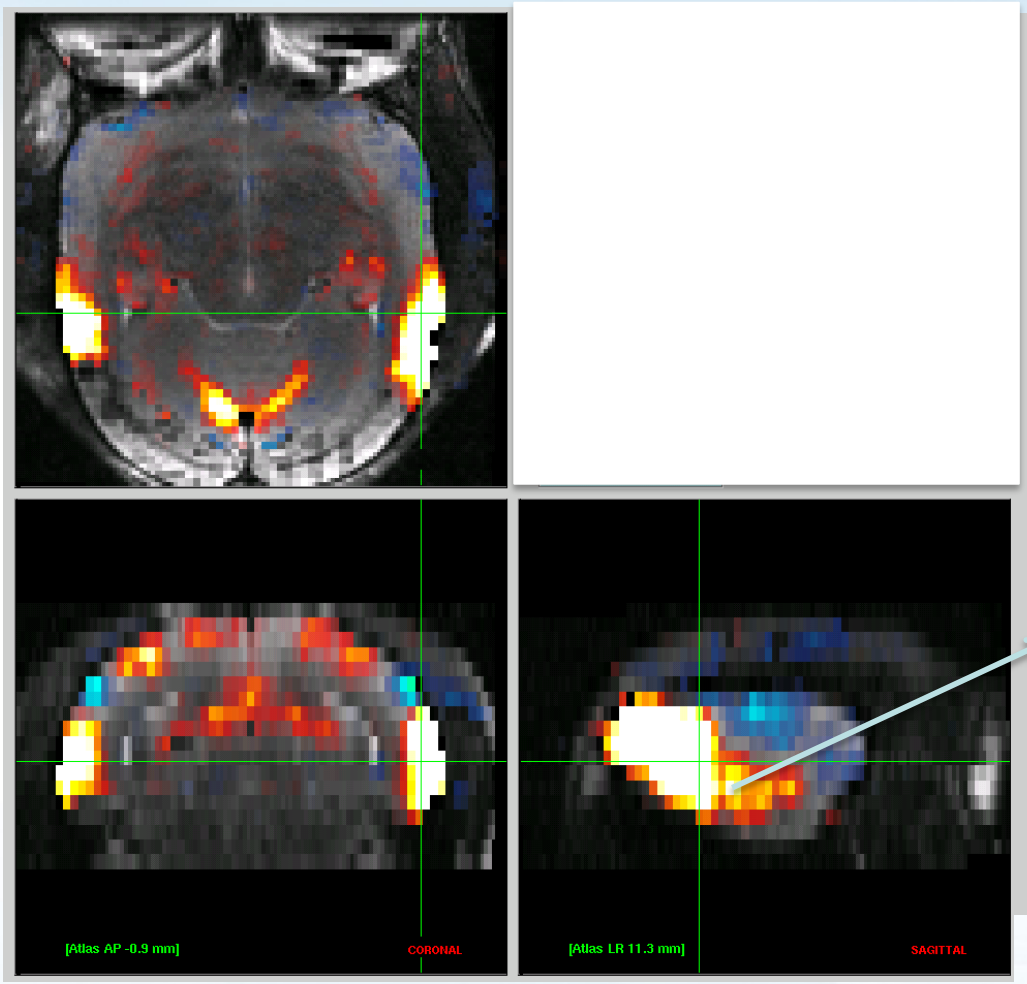
Typical behavior of awake marmoset to a stimulus block

Positive reinforcement Infra-red eye-tracking Visual Stimulus

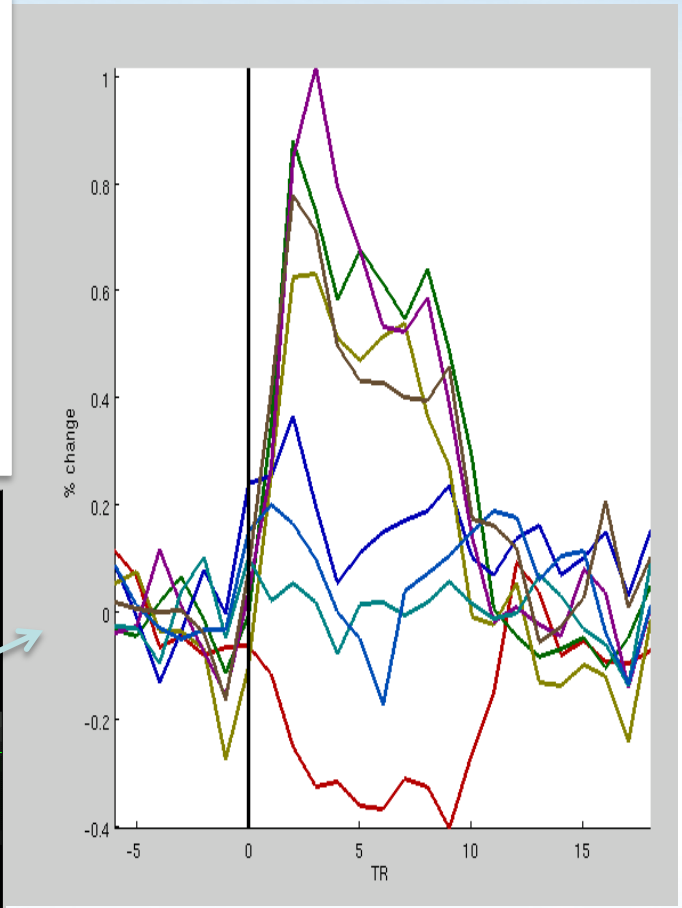


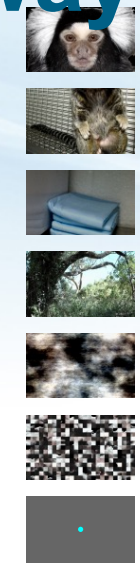
C.-C. Hung et al J Neurosci 2015 35(3):1160-72.

Visual fMRI: Object Recognition Pathway



Occipital Temporal Area





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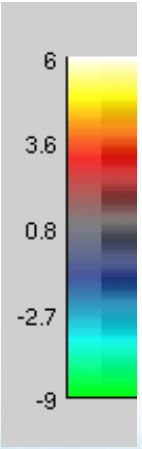
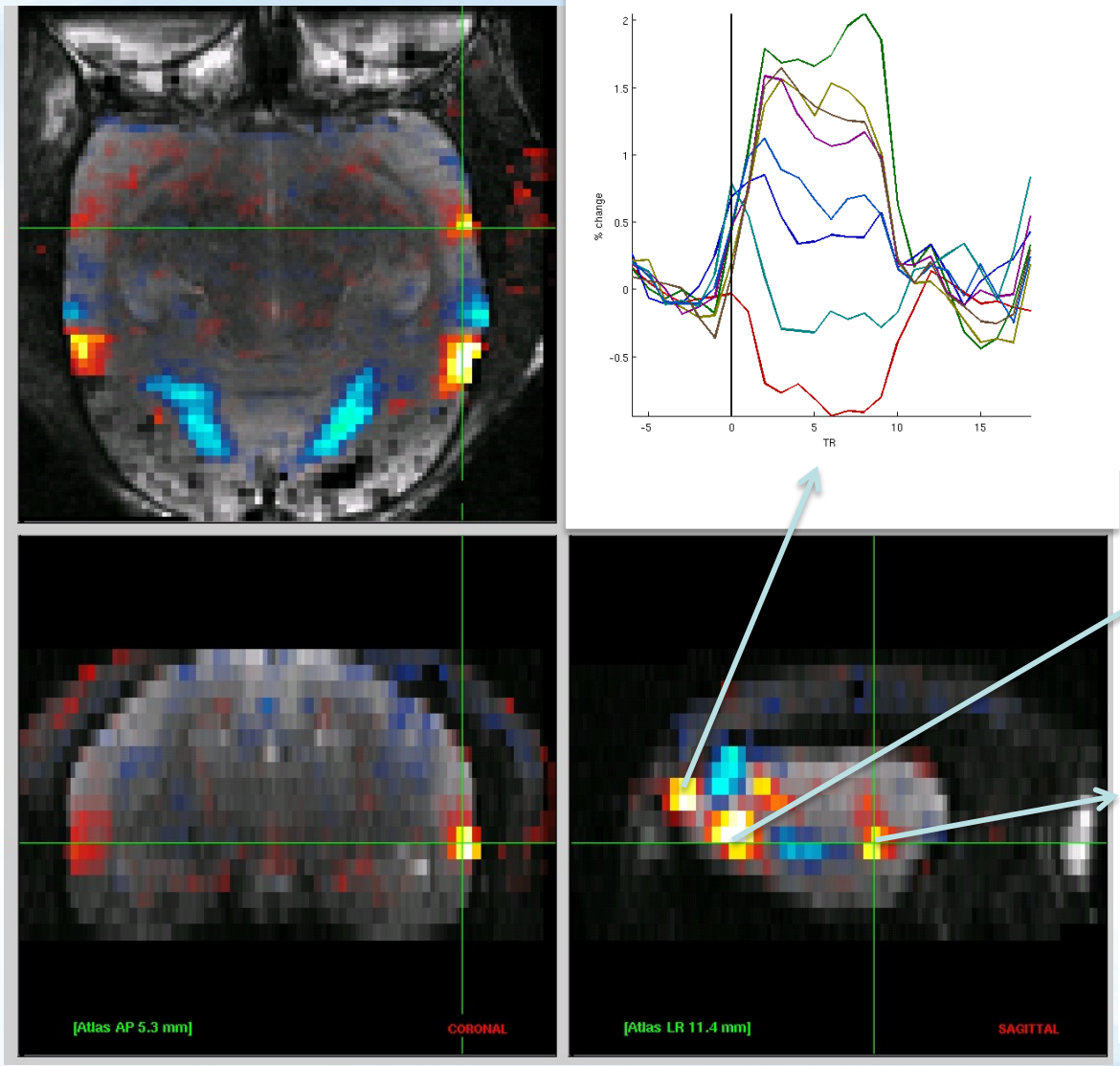


Work in progress

Cecil C. Yen, Chiah-Chun Hung, Jennifer Ciuchta, David Leopold, Afonso Silva, NIH, USA

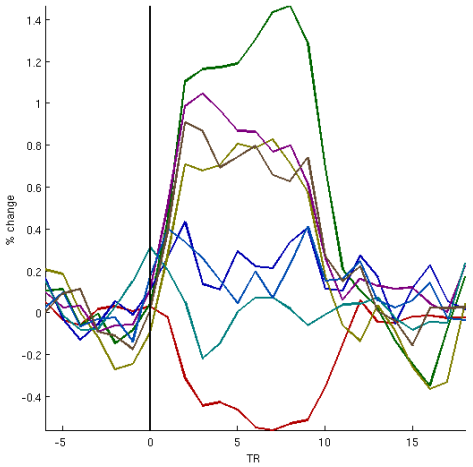
Cerebral Microcirculation Section, LFMI, NINDS, NIH

Visual fMRI: Face Selective Areas

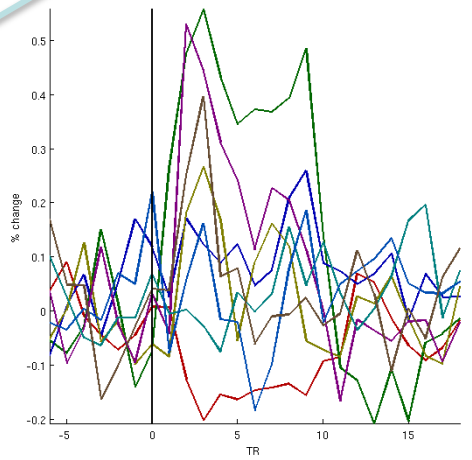


V3

V4



Temporal Area



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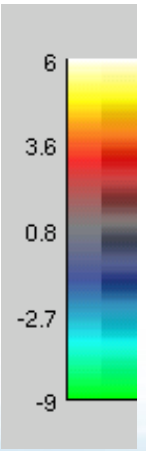
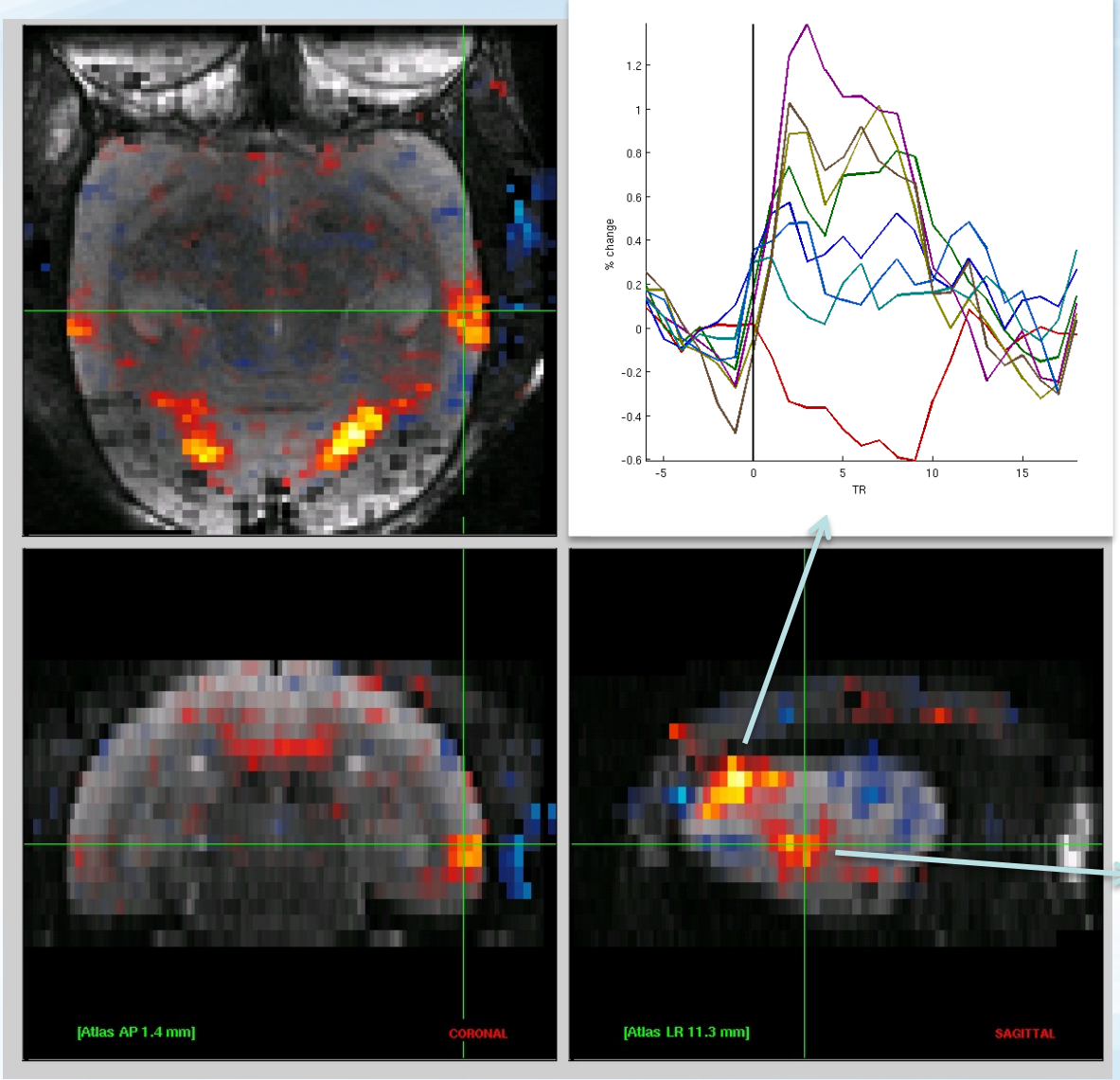


t-value

Visual fMRI: Body Selective Areas

V4



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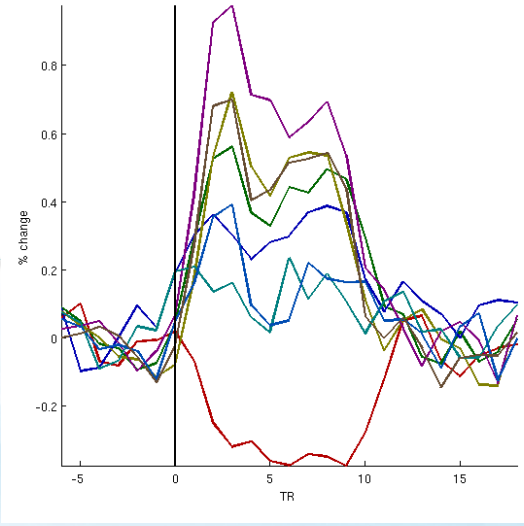
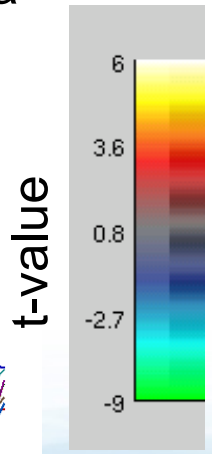
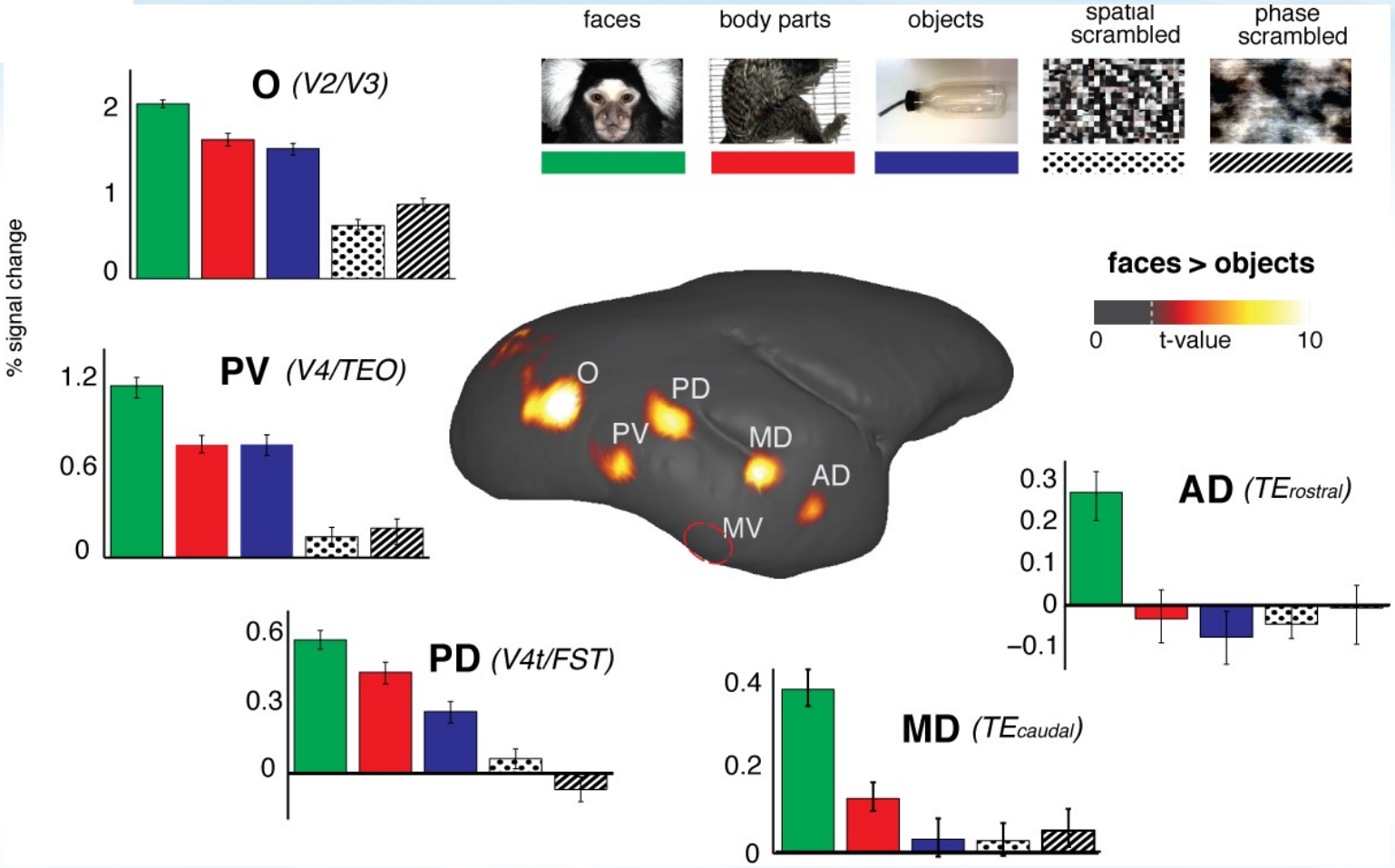
Occipital Temporal Area





Face-selective patches along ventral visual pathway



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

Recap

- Advantages of Animal Models
  - Allow multi-modal investigations
  - Dedicated hardware permit higher spatiotemporal resolution
- Marmoset is an important experimental animal model for translational research.
- Anatomical MRI of the marmoset brain and spine can be obtained with remarkable cytoarchitectonic detail.
- Functional MRI can be used to study functional connectivity and various sensory system including somatosensory, auditory and visual areas.

Cerebral Microcirculation Section

- Chief:
  - **Afonso Silva**
- Research Fellows:
  - ***Sang-Ho Choi***
- Postdoctoral Fellows:
  - ***Jungeun Park***
  - ***Cirong Liu***
- Predoctoral Fellow:
  - ***Diego Szczupak***
- Post-bac IRTAS:
  - ***Madeline Marcelle***
  - ***Kathy Crystal Young***
- Lab Technician
  - ***Lisa Zhang***

Thank You!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