FSL advanced analysis for animal studies

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Why study the brain across species?

• What is self? Perhaps, humans may be only species that want to know and understand yourself.

• Among many, one approach is to compare our brain with those of other species.

Brodmann 1909, Sherrington et al., 1890, Leyton & Sherrington 1917

• Animals are also becoming important to increase the predictability of human disease and develop treatments

Brodmann 1909
Brain and Neurons

Herculano-Houzel et al., *Brain Beh Evol* 2015
Van Essen et al., *PNAS* 2019

Beaulieu-Laroche et al., *Nature* 2021
• Highly myelinated areas including ‘early areas’ of somatosensorimotor, auditory, visual function
• Lightly myelinated areas implicated in ‘higher cognitive’ functions.
• T1w/T2w myelin is comparable with histologically-proven distribution - Flechsig 1921, Hopf 1956
Data acquisitions - general principle

• Use high-quality MRI acquisition system
  • high-field MRI – but note that ultra high field scanner often suffer from B1 homogeneity

• Acquire multi-modal MRI scans
  • Structure: T1w and T2w volumes
  • Functional MRI: resting-state & task fMRI
  • diffusion MRI: neurite mapping & tractography

• Spatial resolution
  • *Neuroanatomical* resolution – **histogram of cortical thickness**
    Structural MRI (<minimum thickness): Human: 0.7mm, Macaque: 0.5mm, Marmoset: 0.36mm
    Functional MRI (<5%ile thickness): Human: 2.0mm, Macaque: 1.25mm, Marmoset: 1.0 mm

• Temporal resolution
  • *Neurophysiological* resolution - **frequency of resting-state network**
    TR < 1sec

• Anesthesia for resting-state fMRI
  • Dexmedetomidine 4.5 ug/kg/hr + 0.5% isoflurane (see protocol at [https://brainminds-beyond.riken.jp/](https://brainminds-beyond.riken.jp/))

Hayashi et al., *NeuroImage* 2021
High-quality MRI system

- High quality multi-modal MRI data is collected by 3T scanner, sequence and NHP RF receive coil
- 3T system is balanced in term of B0, B1 and gradient strength
- Ultra-high field is promising in future, but B1 homogeneity needs to be improved
## Tools specific to animal’s data

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Configuration of FSL for animal studies

• Scaling by brain size
  • Field-of-view & spatial resolution of templates
  • Spatial resolution of the non-linear registration (FNIRT, TOPUP)
  • Biasfield smoothness
    • B1(−) : related to Rx coil element size * head size
    • B1(+) : related to Tx coil size * head size
Bet4animal

Scaling → BET → Rescaling
Bet4animal

- Accepts chimp, macaque, marmoset, night monkey, rat, mouse, mini pig
- Use ‘–c’ option and specify posterior part of the thalamus to make it more successful.

Hayashi & Smith 2023
ICA-FIX for macaque

- Distortion & motion correction is effective but not perfect for motion-related noise
- Denoising with machine learning (ICA-FIX) remove motion-related noise
- Noise classification training file for macaque is implemented in the ICA-FIX

Hayashi, Glasser, Smith
sphynx2reorient

MRI in sphinx position with a scanner setting of Head-First-Prone (HFP)

Correct labeling of orientation
HCP pipeline

- **HCP pipeline** - Glasser et al., 2016
  - Allows surface-based analysis
  - Multi-modal analysis – structure, function and diffusion MRI
  - A large amount and modality of data, high spatial and temporal resolution, respect spatial fidelity, accurate registration, parcellation, minimize blurring & smoothing
  - CIFTI ‘grayordinate’ coordinates
  - FSL, FreeSurfer, Workbench

- **NHP version** - Donahue et al. 2016, Hayashi et al. 2021
  - Adapts to chimp, macaque, marmoset, night monkey
Myelin evolution

- Example of convergent evolution - commonly functions for ‘fast’ transmission of neural activity
  - Mount and Monje, *Neuron* 2017
- But myelin can inhibit branching of the axons and plastic changes of neurons in the brain tissue.
- Cerebral cortical myelination during development is related to functional organization from rodents to primates
  - Van Essen et al., *PNAS* 2019

Mount and Monje, *Neuron* 2017

Hartline and Colman., *Curr Biol* 2007
Surface-based analysis and myelin map

- Cortical folding & T1w/T2w myelin across five genus
- Inflation uncovers homologous ‘early areas’ across genus
- Light myelin (blue) ‘higher cognitive cortex’ expands from marmoset to human
Take home messages

1. FSL provides a set of tools useful for neurobiology across humans and animals.

2. **Cortical surface area, folding, the number of cortical areas** are large in human, so that these factors need to be taken into account in the analysis of human and NHP data to achieve fair comparison between species.

3. Apply **high-quality MRI and cortical-surface based preprocessing**.

4. Use **T1w/T2w myelin map** for capturing homologous cortical areas across species.

5. Brain connectomics across species is underway in **NHP_NNP (NHP neuroimaging & neuroanatomy project)** to establish the brain atlas of non-human primates.

6. Future studies across species allow to investigate animal disease model, aberrant connectome, rewiring and intervention of the disease.

Hayashi et al., *Neuroimage* 2021