Dynamic functional connectivity properties are differentially affected by anesthesia protocols and compare across species.

Gabriel Desrosiers-Gregoire[1], Gabriel A. Devenyi[2,3], Joanes Grandjean[4,5], M. Mallar Chakravarty[1,2,3,6]

1. Integrated Program in Neuroscience, McGill University, Montreal, Canada 2. Cerebral Imaging Center, Douglas Mental Health University Institute, Montreal, Canada 3. Department of Psychiatry, McGill University, Canada 4. Singapore Bioimaging Consortium, Agency for Science, Technology and Research, Singapore 5. Department of Radiology and Nuclear Medicine & Donders Institute for Brain, Cognition, and Behaviour, Donders Institute, Netherland 6. Biological & Biomedical Engineering, McGill University, Canada

Background and Methods

- fMRI has great potential to establish cross-species translation using functional connectivity (FC).
- Mice are usually anesthetized during fMRI data acquisition, which influences FC [1].
- Dynamic functional connectivity (dFC): FC correlations change over the time scale of seconds to minutes [2], and anesthesia reduces the complexity of these global dynamics [3,4]

Goals: 1- Cross-species translation of FC
2- Find markers of conserved brain dynamics during anesthesia in mice based on dFC
3- Investigate relationship between sFC and dFC

Datasets

Mouse 9.4T [1]: Iso: isoflurane 1 % (n=11), **mediso:** 0.5 % isoflurane + 0.1 mg/kg/h medetomidine (n=8), **med:** 0.1 mg/kg/h medetomidine (n=12); animals were mechanically ventilated

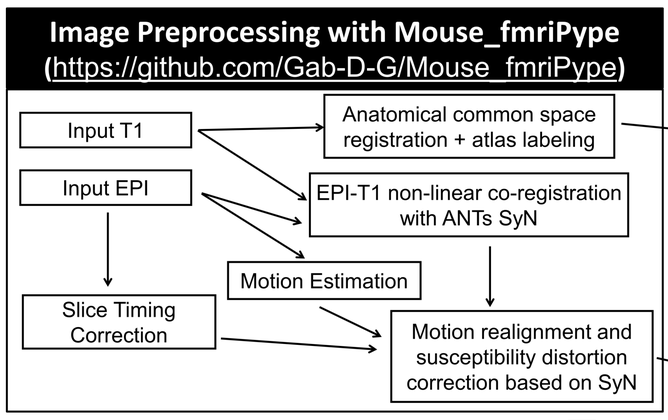
Acquisition: 1 EPI scans with 360 volumes; EPI Parameters: TR=1 sec, with voxel resolution 0.26x0.23 mm in-plane and 0.5 mm slice thickness

Mouse 11.7T: Iso: isoflurane 1% (n=5) freely-breathing, **mediso:** 0.5% isoflurane + 0.1 mg/kg/h medetomidine (n=5) mechanically ventillated, **awk:** awake mice (n=7) freely-breathing

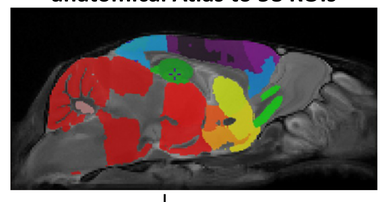
Acquisition: for each subject, 2 sessions with 3 EPI scans of 180 volumes + T2 acquired for each session; EPI Parameters: TR=1.2 sec, with voxel resolution 0.19x0.15 mm in-plane and 0.4 mm slice thickness

Human Connectome Project (HCP): 100 unrelated subjects from the HCP; used 50 ICA component timeseries; TR=0.72 sec

Image Preprocessing with Mouse_fmriPype (https://github.com/Gab-D-G/Mouse_fmriPype)



Downsampled DSURQE [5] Mouse anatomical Atlas to 58 ROIs

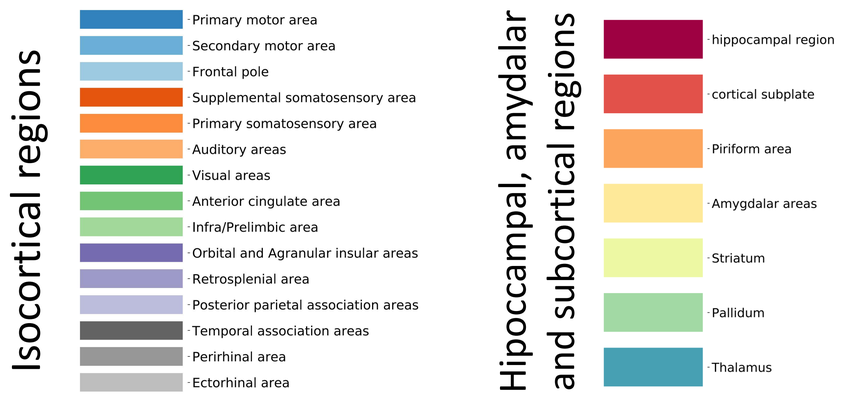


Confound regression + ROI timeseries
GSR + Friston 24 motion params + highpass filtering (0.01Hz) + scrubbing [6]

Analysis

- **Static FC (sFC) matrix:** z-transformed pearson correlation coefficient from the entire scan time.
- **Dynamic FC with sliding window correlation:** window size of 30sec and time step of 1 TR; scrubbing was also applied to mask out high motion timepoints within windows + temporal normalization across windows
- **PCA on sliding window:** extract global patterns of temporal changes in FC through principal component analysis (PCA) on the sliding windows [7,8]

Colors for Matrix Anatomical Annotations



BOLD Power Spectrum

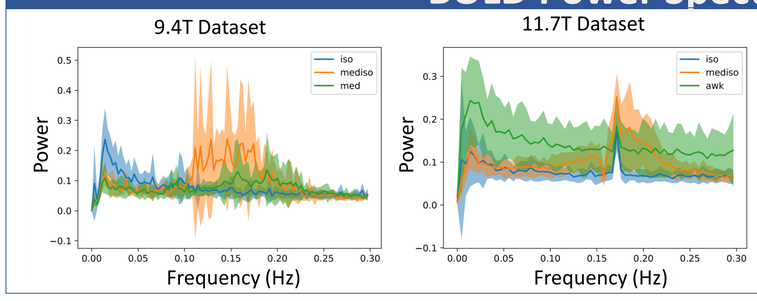


Figure 1: Average BOLD frequency power spectrum across ROIs for each group. Shaded areas represent individual variability.

Anesthesia influences the expression of global patterns of dFC measured through PCA

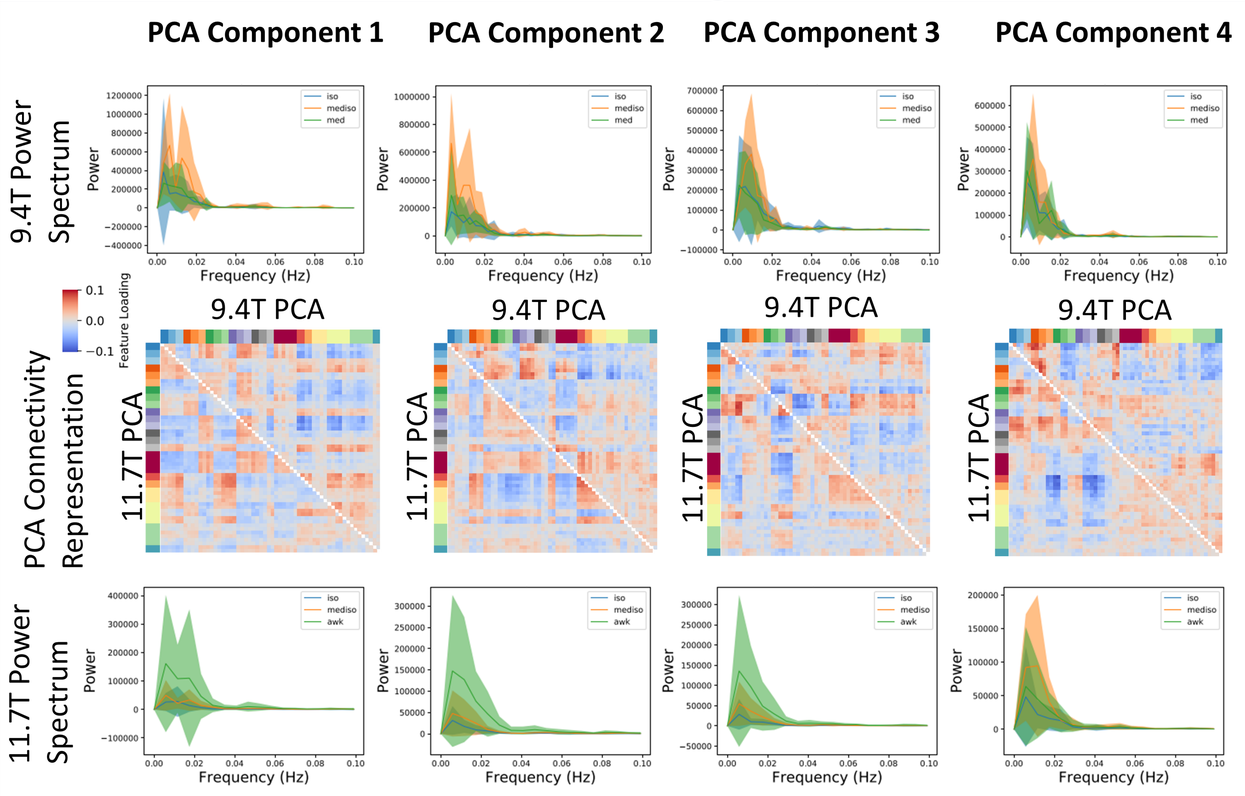


Figure 3: For each mouse dataset, all sliding windows were concatenated together and PCA was performed across all windows. The first 4 resulting components were analyzed. On the plots, the power frequency spectrum of the component timecourses within subjects' windows is compared across groups, and the connectivity representation of the components (feature loading) is compared across datasets in a connectivity matrix format.

Anesthesia influences both sFC and dFC variability

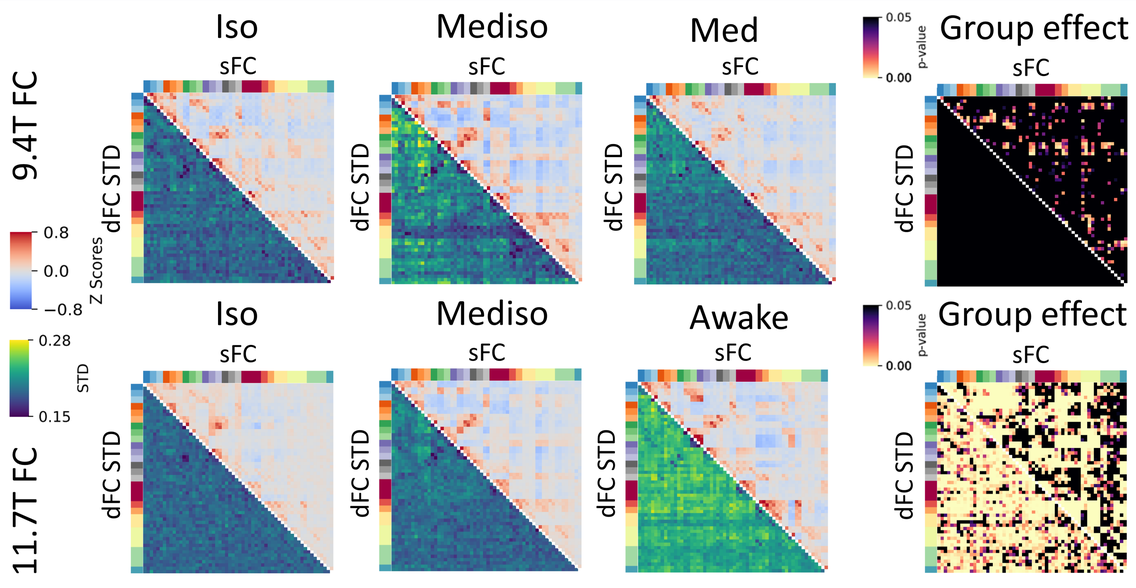
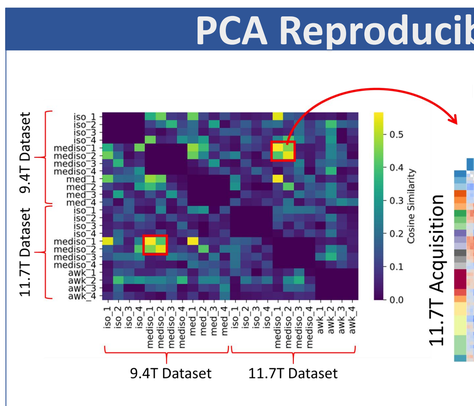


Figure 2: Comparison of sFC and the standard deviation (STD) in dFC across mouse groups and datasets. The upper half of each connectivity matrix represents sFC, and the bottom half dFC STD. On the right, the corresponding p-values for the group effects are represented after FDR correction.

PCA Reproducibility Across Dataset with Mediso



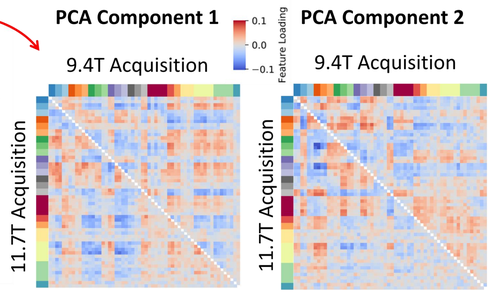


Figure 4: The cosine similarity of the connectivity profiles of the first 4 components, compared across mouse groups and datasets (left matrix). The first and second components were independently reproduced across datasets for the mediso condition (presented on the right).

Cross-species comparison of dFC variability gradient

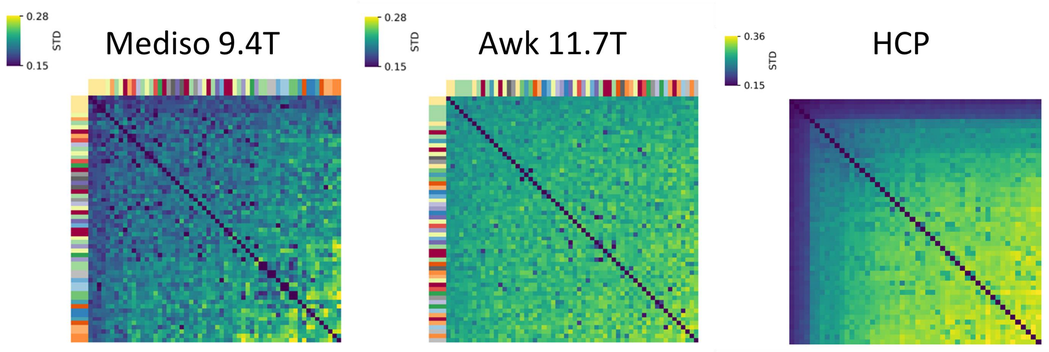


Figure 5: dFC variability matrices as in figure 2 are compared for the mediso 9.4T, awake 11.7T, and human datasets. ROIs are reordered in increasing order of node degree to reveal a gradient in dFC variability across the cortex. This gradient is most prominent in humans, which may represent a marker for the organization of global brain dynamics, and their conservation under anesthesia states in mice.

Mapping Individual Variability in sFC and dFC properties across species

sFC strength is strongly related to greater global dFC

All relationships hold in 100 human subjects, but dFC var correlations are weaker

	iso_9.4T	mediso_9.4T	med_9.4T	iso_11.7T	mediso_11.7T	awk_11.7T	HCP
Power-sFC	0.78	0.93	0.71	0.81	0.96	0.97	0.77
Power-dFC	0.2	0.63	0.68	0.46	0.63	0.65	0.32
Power-compvar	0.28	0.91	0.34	-0.17	0.7	0.87	0.89
sFC-dFC	-0.31	0.39	0.63	0.71	0.64	0.78	0.42
sFC-compvar	0.1	0.79	0.74	0.17	0.79	0.88	0.87
dFC-compvar	0.35	0.76	0.59	0.75	0.89	0.73	0.44

dFC var more organized in mediso than awk

Table 1: This table include the subject-wise pearson correlation values between 4 different FC markers, and evaluated within each groups for both species.

1. **Power:** The individual mean power spectrum across the 4 first PCA component timeseries from whole dataset PCA.
2. **sFC:** The L2-norm of the individual sFC matrix.
3. **dFC:** The L2-norm of the individual dFC variability matrix
4. **Compvar:** After conducting a single-subject level PCA, the mean variance explained by the 4 first components.

Conclusions

- Clear influence of anesthesia on dFC variability. Mediso seems to preserve more these dynamics than other anesthesia protocols.
- Robust conservation of dFC properties across different acquisitions with mediso protocol
- Demonstrated relationship between dFC properties and sFC across species

References

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