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# Can physiological signals estimation improve fMRI connectivity assessment in anesthetized rats?

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## Background


Resting-state functional magnetic resonance imaging (fMRI) is a common translational method to evaluate brain functional connectivity (FC) in preclinical neurologic applications. However, unlike human studies, preclinical fMRI studies are usually performed under anesthetic condition. The confounding effect of the anesthesia on fMRI measurements is not clear. Indeed, a controversy exists between those who claim that anesthesia change FC (Paasonen et al., 2018) and other who maintain that FC is preserved (Becq et al., 2020). Our hypothesis is that physiological changes induced by anesthesia could explain this discrepancy. While in human studies, fMRI analysis generally includes cleaning of physiological-noise (Glover et al., 2000; Kassinosopoulos & Mitsis, 2019), preclinical study processing is rather often limited to a low-pass temporal filtering. We aimed first to demonstrate that the global MRI signal of animal brain includes, like in human, a physiological component. Second, that a normalization of this component based on global signal can reduce variability of FC assessment.

## Results

## Methods




Wistar rats



70/18 BioSpec 7T Scanner (Bruker)

High temporal sampling rate fMRI  
TR=100ms, TE=13ms, flip-angle=20°,  
voxels-size=400x400microns<sup>2</sup>, FOV  
25.6x25.6cm<sup>2</sup>, slice-thickness=2mm



BIOPAC MP150

Physiological records  
Respiration: pillow and CO2 sensors,  
Cardiac: ECG and PPG sensors

Induction : isoflurane 5%  
then Isoflurane 3%  
**15 minutes**

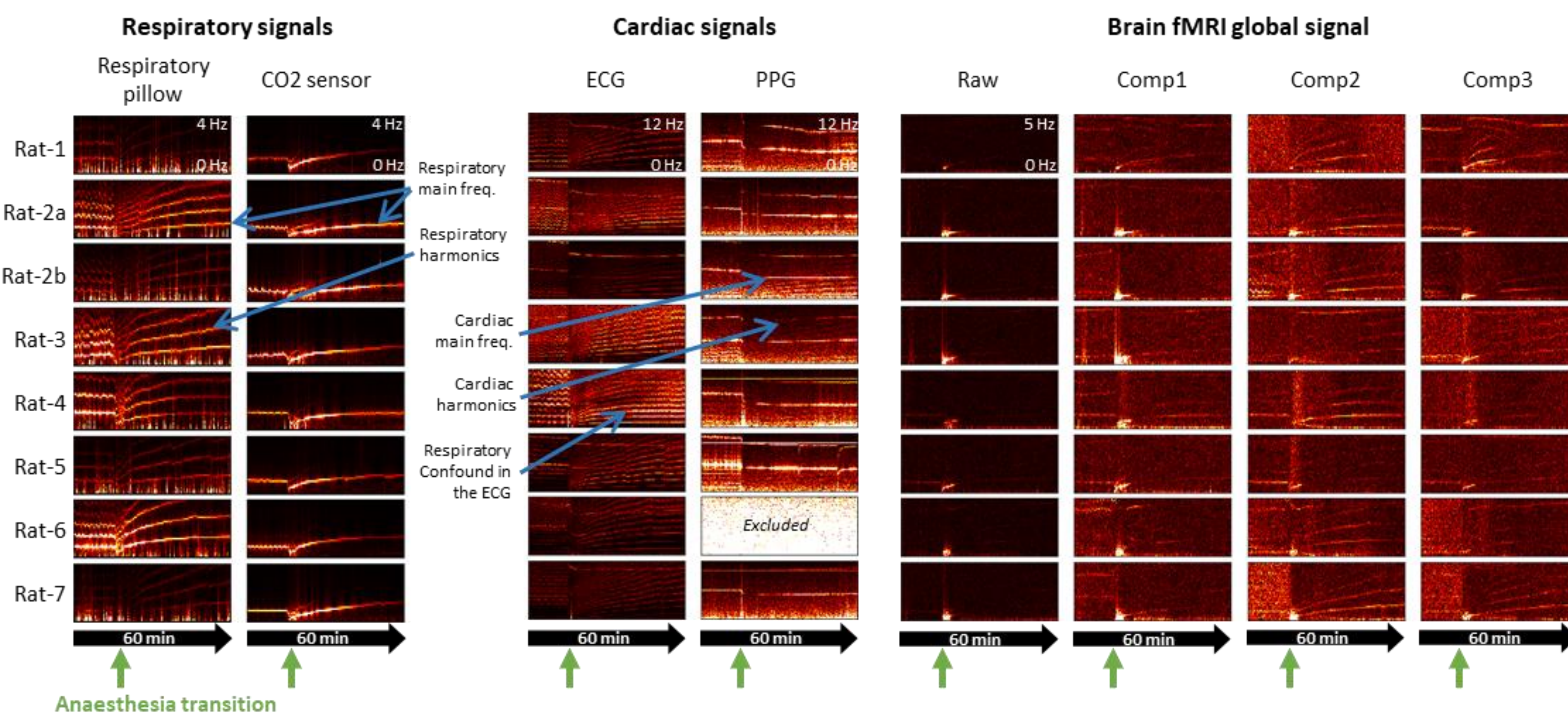
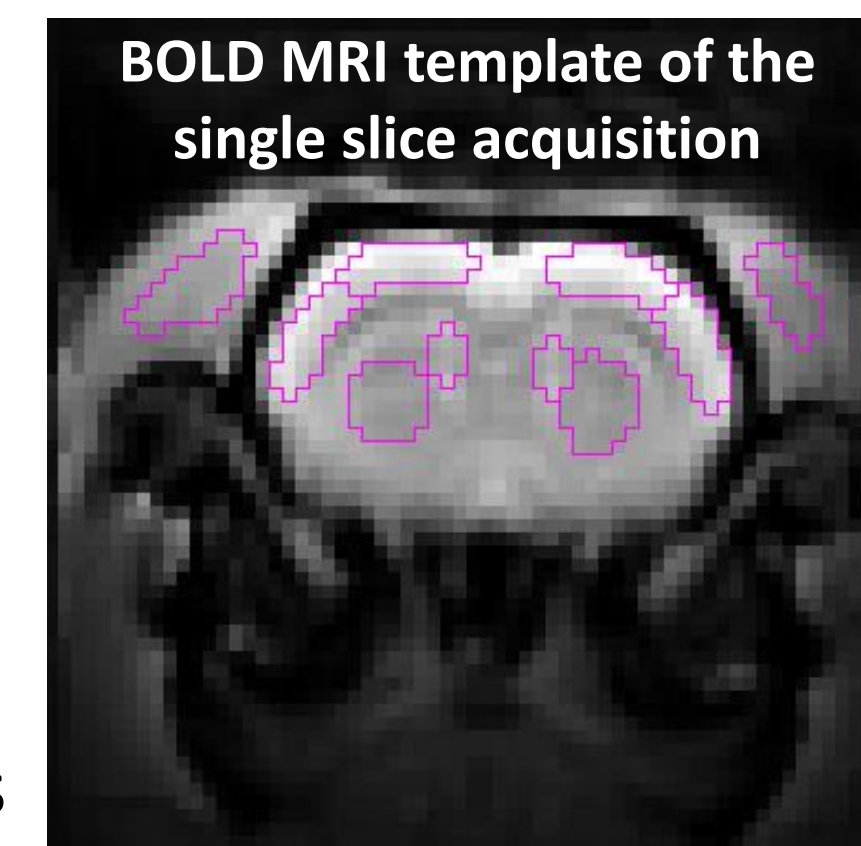
Medetomidine IV Bolus: 0.05mg/Kg  
then 0.1mg/Kg/h  
**45 minutes**

### Time frequency analysis of the 60 minutes record:

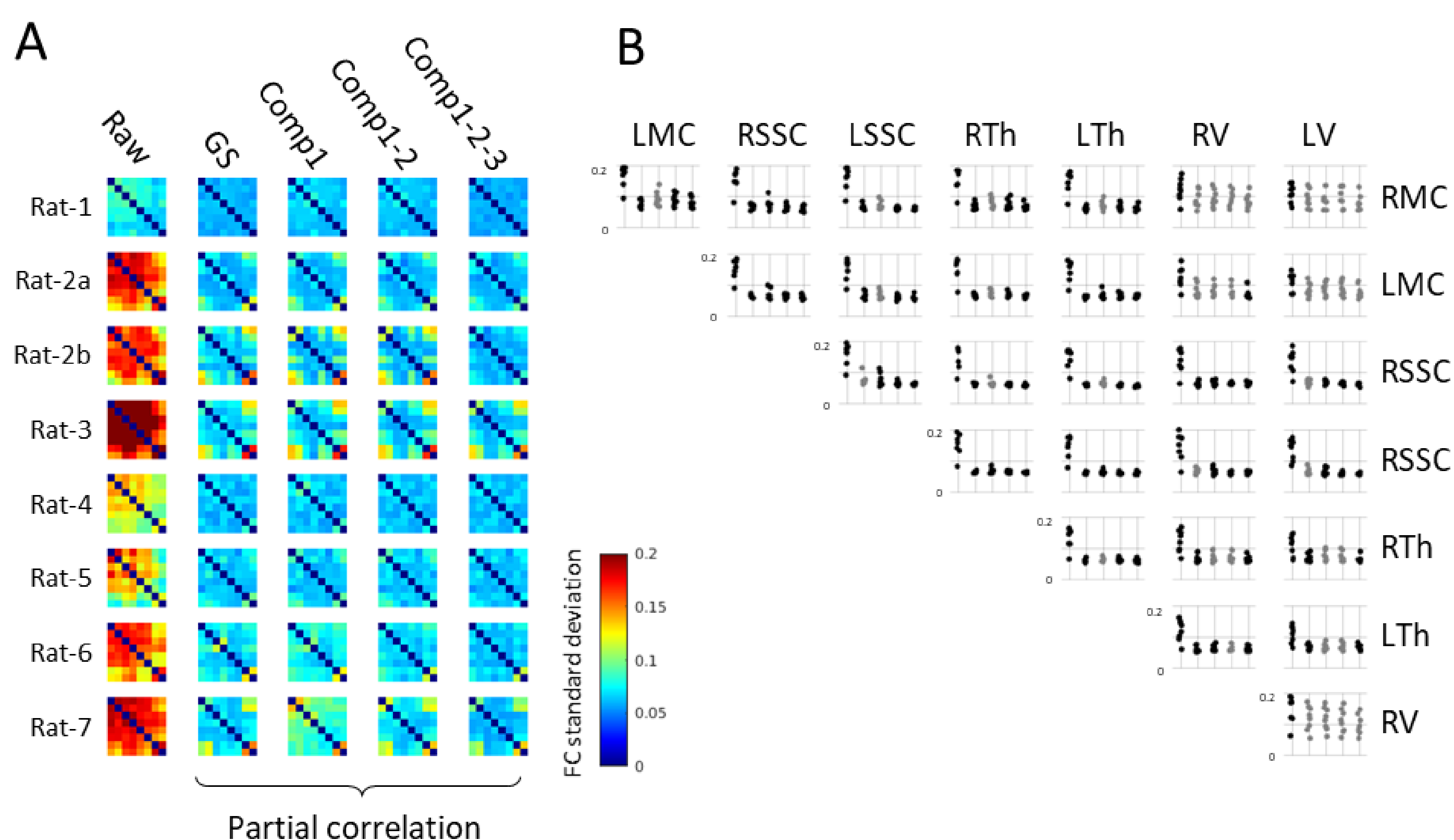
- Physiological signals
- Global MRI signal of the brain and its 3 principal components

### Sliding window functional connectivity analysis:

- Bilateral ROIs: Motor Cortex (MC), Somatosensory Cortex (SSC), Thalamus (Th) and Ventricle (V)
- FC with and without correction of the global signal and its principal components (Behzadi et al., 2007)



**Figure 1: Time-frequency analysis of the physiological and MRI signals.** Fourier transforms are computed on a 10s time window with a 5s overlap over the 60min fMRI experiment. Photoplethysmogram (PPG) of the rat-6 is excluded due to sensor failure. Colormap of the power spectrum are the same across animals but scaled independently for each signal type. Blue arrows show some examples of the main frequencies, harmonics and confounds of each physiological signal.



**Figure 2: A** Symmetric matrices of the standard deviation of the Functional Connectivity (FC) over time for each animal (in rows). Regions of interest are ordered this way : Right Motor Cortex (RMC), Left Motor Cortex (LMC), Right Somatosensory Cortex (RSSC), Left Somatosensory Cortex (LSSC), Right Thalamus (RTh), Left Thalamus (LTh), Right Ventricle (RV), Left Ventricle (LV). **B** Distribution comparison of the standard deviation of the FC across animals (Kruskall-Wallis). For each pair of regions, the five jittered plots correspond to (1) Raw FC, (2) partial-FC with the Global Signal (GS), (3) partial-FC with comp1 of GS, (4) partial-FC with comp1-2 of the GS, (5) partial-FC with comp1-2-3 of the GS. Gray dot means that the distribution of the FC does not differ statistically of the Raw FC distribution ( $\alpha=0.05$ , Tukey-HSD corrected for multiple comparisons).

## Conclusion

We showed that the physiological variability of both respiratory and cardiac cycles is captured by the global brain fMRI signal. When the global signal was used as a confounding factor to compute the FC, the variability across the different stages of the anesthesia is reduced, even if there were strong physiological modifications.

We now have to investigate the best way to correct the fMRI signal for the physiological variation. Our best bet is to use the methods developed for human brain fMRI preprocessing and adapt them for preclinical imaging.

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