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P13

Resting breathing contribution to the BOLD- and ADC-fMRI signals

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BACKGROUND

- **BOLD-fMRI** is an **indirect measure of neuronal activity** (neurovascular coupling), but **can** also **be influenced by other components such as respiration**, as shown in breath-hold tasks[1-3].
- Spontaneous changes in depth and/or rate of breathing happening during resting breathing can also cause significant changes in the BOLD signal[1,2].
- This can be related to **variations in arterial CO_2** (vasodilator)[1,2] (as well as voluntary changes in breathing or chest motion induced B_0 inhomogeneities) and obscure true neuronal signals[4].
- **ADC-fMRI** is a **neuromorphological** contrast sensitive to transient alteration of the apparent diffusion coefficient (ADC) resulting from **changes in tissue microstructure induced by brain activity.**
- We showed that the **ADC-fMRI is less sensitive to respiratory fluctuations**, and therefore **more specific to neuronal activity.**

METHODS

Acquisition:

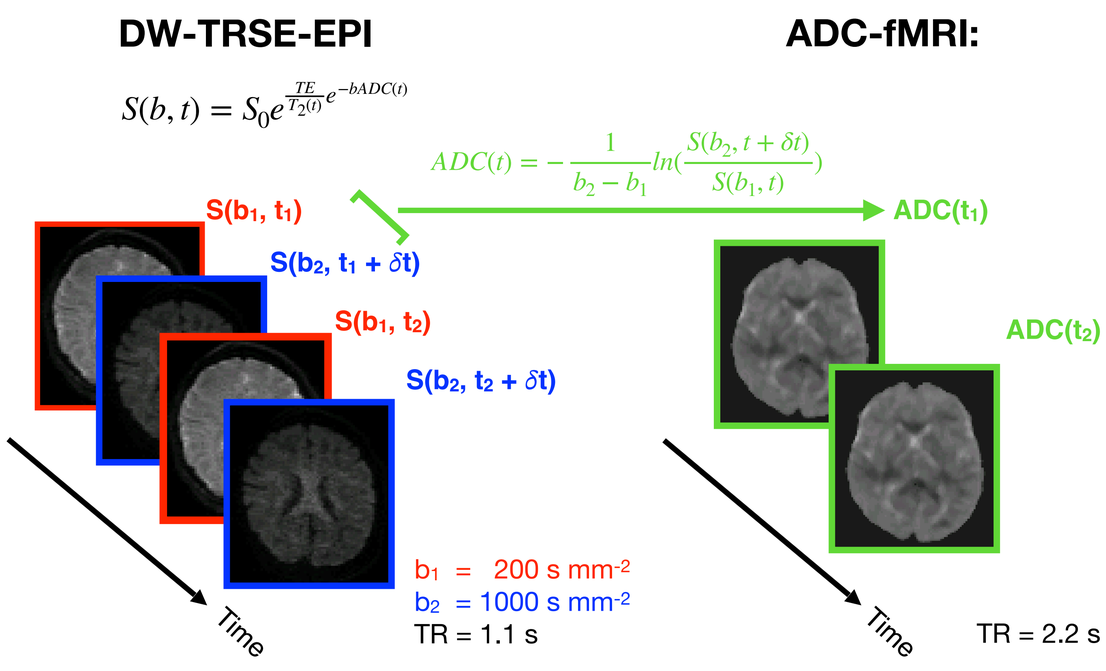
- 2 sequences:
  - Isotropic ADC-fMRI (n=8), alternating b=200 (dfMRI-200) & b=1000 s mm^{-2} (dfMRI-1000)
  - Multi-echo GE BOLD-fMRI (n=10)
- Parameters: TE=[12.6, 33.22, 53.84, 74.46] ms (BOLD)/105 ms (ADC), TR=1.1s, Matrix 82x82, 21 slices, resolution 2.8 mm isotropic, 40% slice gap, 192 s scan time
- Respiration (CO_2) recordings. End-tidal CO_2 ($P_{ET}CO_2$): interpolated signal from peaks detected at the end of exhaled breaths.

Processing :

- Pre-processing as described in ref. 5
- MRI images: spatial filtering with Gaussian kernel (4 mm), high-pass temporal filter (4th order Butterworth, cut-off=0.01Hz)
- Physio time series: polynomial detrending (up to & including 3rd order polynomials), convolving with HRF[3]

Analysis:

- Cross-correlation (Pearson) $P_{ET}CO_2$ vs fMRI, lags= -24 to 0 s (steps of 1s).
- Significance threshold determination: null distribution approximation using surrogate analysis. For all subjects, generate 5000 surrogate $P_{ET}CO_2$ traces by shuffling the phases of the Fourier transformed $P_{ET}CO_2$, and run cross-correlation analysis with 5000 randomly selected voxels from the other subjects. The final null distribution pools all the subjects together.



RESULTS

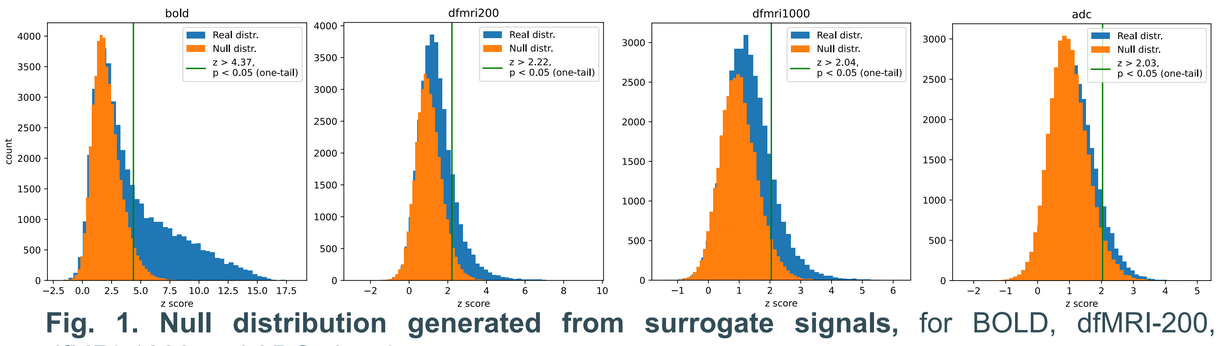


Fig. 1. Null distribution generated from surrogate signals, for BOLD, dfMRI-200, dfMRI-1000 and ADC signals.

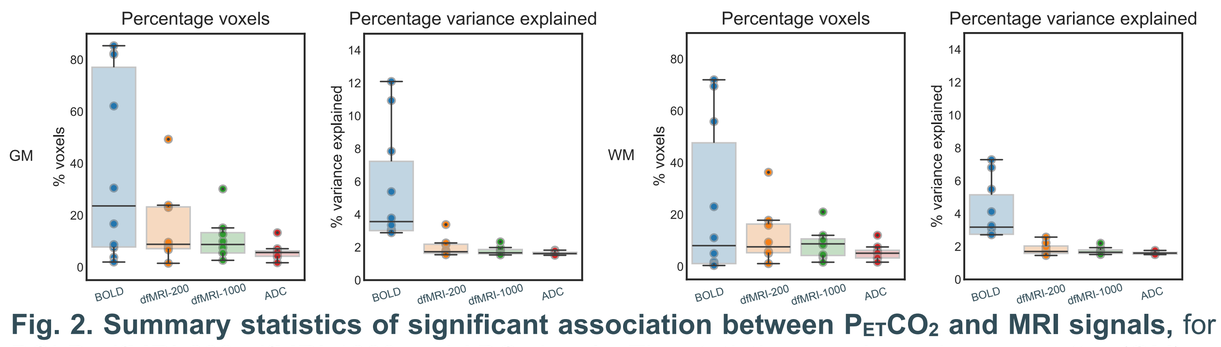


Fig. 2. Summary statistics of significant association between $P_{ET}CO_2$ and MRI signals, for BOLD, dfMRI-200, dfMRI-1000 and ADC signals. The statistics are shown in gray matter (GM) or white matter (WM) voxels which are above the significance thresholds derived in Figure 1.

- There is an increasing association between fMRI and $P_{ET}CO_2$ (Fig. 1-2):
  ADC < dfMRI-1000 < dfMRI-200 < BOLD
  - BOLD is heavily T_2*-weighted
  - dfMRI-200 suppresses blood water (small diffusion weighting) but is T_2-weighted dfMRI-1000 similar to dfMRI-200 but more heavily diffusion-weighted
  - ADC suppresses both blood contribution and attenuates T_2-weighting
- GM vs WM (Fig. 2): despite reduced vasculature (↘ blood flow & volume) in WM[6,7], $P_{ET}CO_2$ is still strongly associated with BOLD-fMRI.
- Time lag maps (Fig. 3):
  - BOLD: delayed response in the WM, as already shown in ref. 8 with breath-hold. This is consistent with the heterogeneity of BOLD response as derived in ref. 9, which prevents the simultaneous mapping of GM & WM activity.
  - Diffusion-weighted: lags are mostly non-significant (no $P_{ET}CO_2$ vs fMRI association) & no pattern is visible.

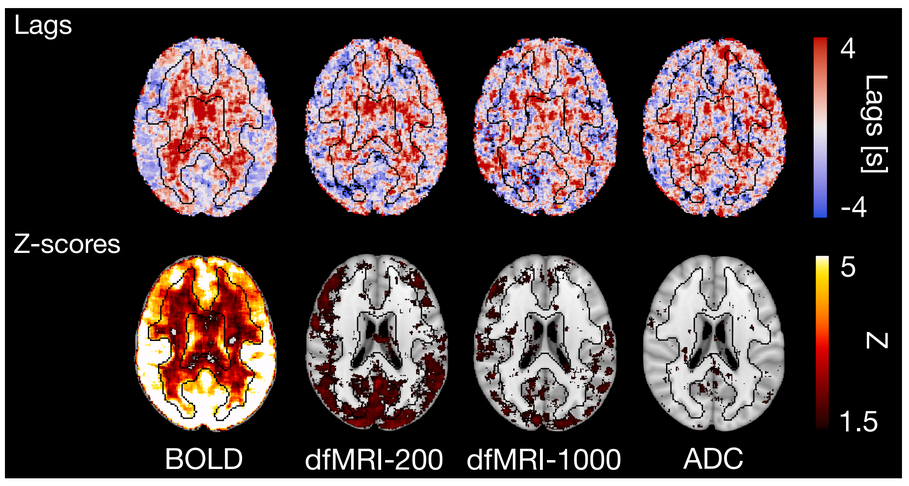


Fig. 3. Group-averaged time lag & z-score maps, for BOLD, dfMRI-200, dfMRI-1000 and ADC signals.

CONCLUSION

- A clear association is found between resting breathing & BOLD
- Using diffusion-weighted signal decreases drastically this association
  → neuromorphological contrast is closer to neuronal activity than neurovascular contrast
- ADC-fMRI is robust to respiration-induced vascular changes and is therefore a promising tool to investigate neuronal activity in task-[5,10] or rs-fMRI[11]

References:

[1]Birn et al., NeuroImage, 2008, [2]Chang and Glover, NeuroImage, 2009, [3]Murphy et al., NeuroImage, 2011, [4]Birn et al., NeuroImage, 2006, [5]Spencer et al., bioRxiv, 2024, [6]Biswal et al., Magn Reson Med, 1995, [7]Gore et al., Magn Reson Imaging, 2019, [8]Zvolanek et al., NeuroImage, 2023, [9]Li et al., Nat Commun, 2019, [10]Nguyen-Duc et al, bioRxiv, 2024, [11]de Riedmatten et al., bioRxiv, 2024

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