

# Multi-echo profiling of resting-state fMRI beyond canonical networks

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## INTRODUCTION

- Multi-echo (ME) fMRI enables identification of BOLD (TE-dependent) and non-BOLD (TE-independent) signals. This extra information in ME data has been previously exploited for automatic ICA-based denoising (e.g., tedana<sup>1</sup>), to improve deconvolution<sup>2</sup>, and to evaluate the quality of different preprocessing pipelines<sup>3</sup>.
- Most prior work has focused on improving detection of neural (BOLD) signals in the gray matter, with less emphasis on systematically characterizing non-neuronal contributions.
- We examine how ME might also aid in the characterization of non-neuronal signals in fluid compartments (CSF, vasculature).

## CENTRAL QUESTIONS

- Can ME reliably identify signals from highly vascularized regions (i.e., low  $T_2^*$ ) and CSF (i.e., high  $T_2^*$ ) regions?
- How do these signals relate to cardiac and respiratory processes?
- What are their primary TE-dependent properties?

## DATA

- 3T; 10 subjects; Four 10 min resting-state runs per subject; Full Brain; 3x3x3mm
- TR: 1.5s; 400 TRs per run; TE=10.6/28.69/46.78/64.87/82.96ms

## METHODS

- Data were preprocessed using AFNI. Unlike standard preprocessing, the mask of the brain was dilated to include the sinuses and CSF fluid beyond the pial surface. Following preprocessing, tedana is applied to each run separately to identify signals.
- Next, gRAICAR<sup>4</sup> is used to identify components that are reliable across all subjects.
- For all reliable components, we compute the power spectral density (PSD) and record their kappa ( $\kappa$ ; indicator of BOLD content), their rho ( $\rho$ ; indicator of non-BOLD content) and the rate of acceptance by tedana.
- In parallel, we compute the power spectra of the cardiac and respiratory signals, their envelopes, RVT<sup>5</sup> and RETROICOR<sup>6</sup> regressors.

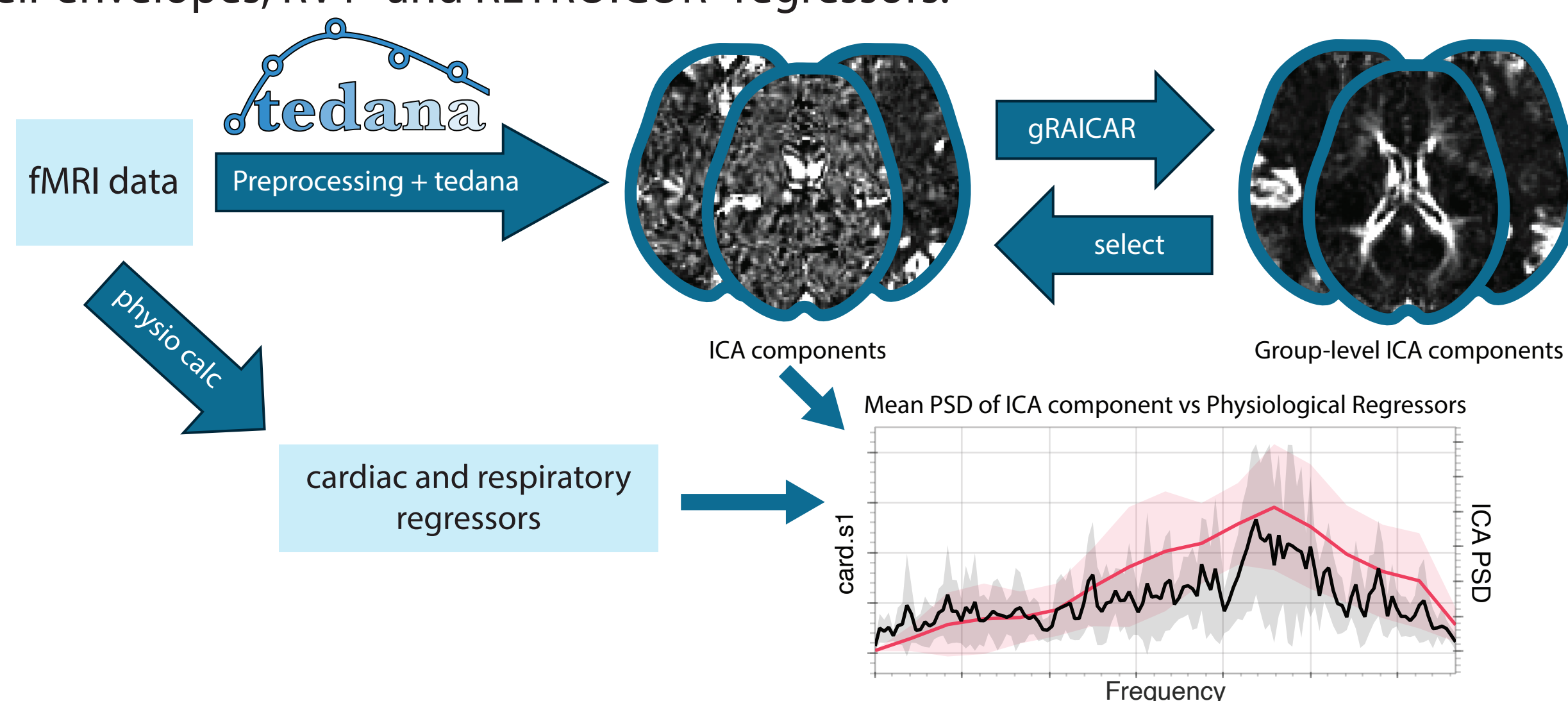
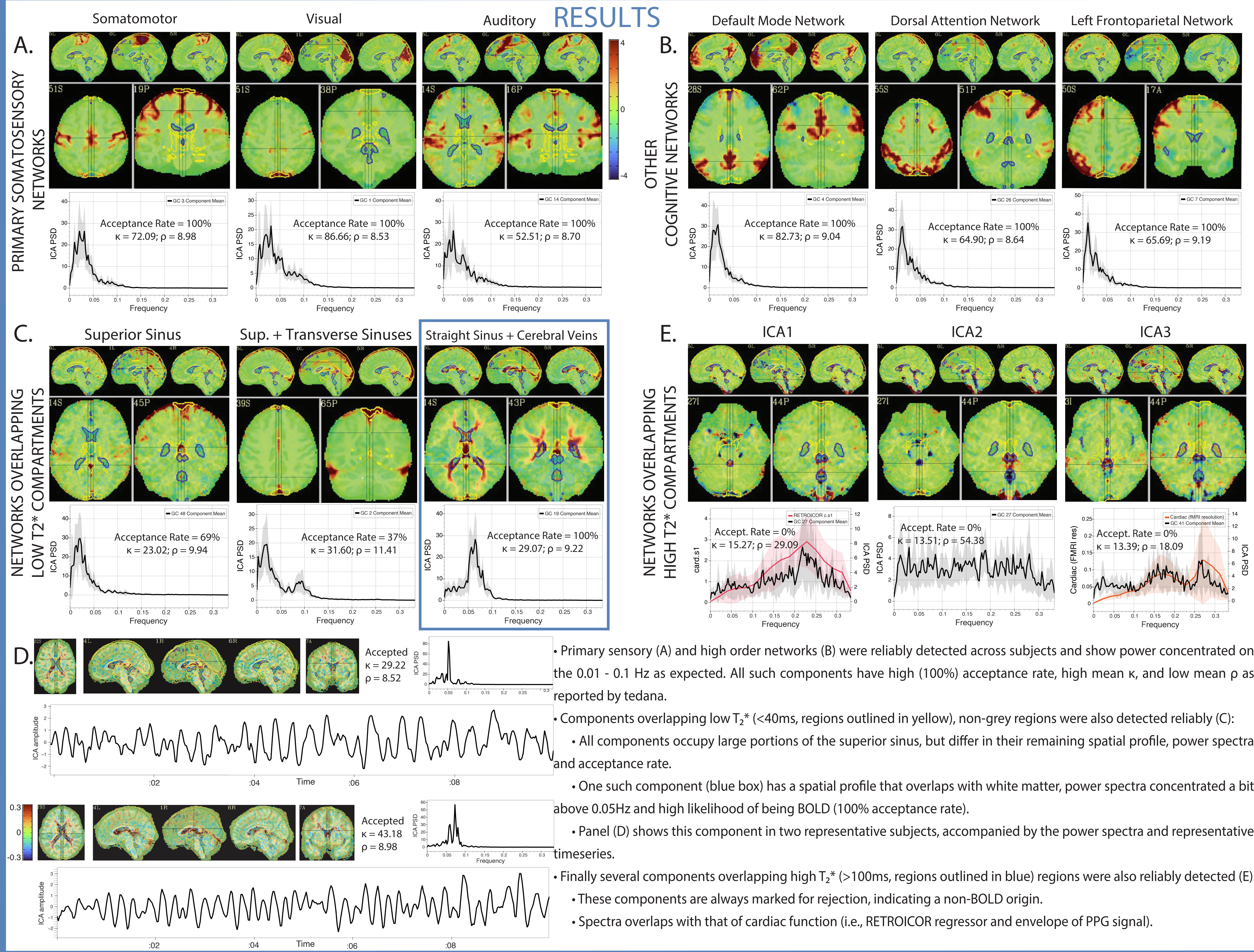


Figure 1. Data were preprocessed then decomposed using ICA via tedana. gRAICAR was then applied to identify reproducible components across subjects. Components of interest were selected qualitatively based on their spatial localization to fluid compartments (e.g., CSF and large vasculature).

## References

- DuPre et al., J Open Source Softw, 2021
- Caballero-Gaudes et al., NeuroImage, 2019
- Gonzalez-Castillo et al., bioRxiv, 2026
- Yang et al., NeuroImage, 2012
- Birn et al., NeuroImage, 2006
- Glover et al., Mag. Reson. Med., 2000
- Kolbe et al., Front. in Neurology, 2020
- Fultz et al., Science, 2019



- Primary sensory (A) and high order networks (B) were reliably detected across subjects and show power concentrated on the 0.01 - 0.1 Hz as expected. All such components have high (100%) acceptance rate, high mean  $\kappa$ , and low mean  $\rho$  as reported by tedana.
- Components overlapping low  $T_2^*$  (<40ms, regions outlined in yellow), non-grey regions were also detected reliably (C):
  - All components occupy large portions of the superior sinus, but differ in their remaining spatial profile, power spectra and acceptance rate.
  - One such component (blue box) has a spatial profile that overlaps with white matter, power spectra concentrated a bit above 0.05Hz and high likelihood of being BOLD (100% acceptance rate).
- Panel (D) shows this component in two representative subjects, accompanied by the power spectra and representative timeseries.
- Finally several components overlapping high  $T_2^*$  (>100ms, regions outlined in blue) regions were also reliably detected (E).
  - These components are always marked for rejection, indicating a non-BOLD origin.
  - Spectra overlaps with that of cardiac function (i.e., RETROICOR regressor and envelope of PPG signal).

## CONCLUSIONS & FUTURE DIRECTIONS

- ME-fMRI can reliably detect and help characterize signal contributions in non-grey matter tissue compartments, extending its utility beyond grey matter tissue.
- BOLD signals overlapping larger sinuses were segregated according to their spatial extent and frequency profile.
  - One component overlapping WM venous vasculature is of particular interest, as prior work<sup>7</sup> has shown that its power spectra is related to levels of neuroinflammatory activity linked to venous damage in multiple sclerosis. Future work should evaluate if ME can improve the detection of this clinically relevant component over single-echo methods.
- Non-BOLD signals were found overlapping in CSF regions. All such signals were reliably marked as non-BOLD, with power spectra overlapping different aspects of cardiac function.
  - No CSF signal showed power concentrated at 0.05Hz (a signature recently linked to low vigilance/sleep states<sup>8</sup>), despite the above-mentioned WM signal having such signature.

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