

Now that I have Multi-echo data, what else can I do with it?

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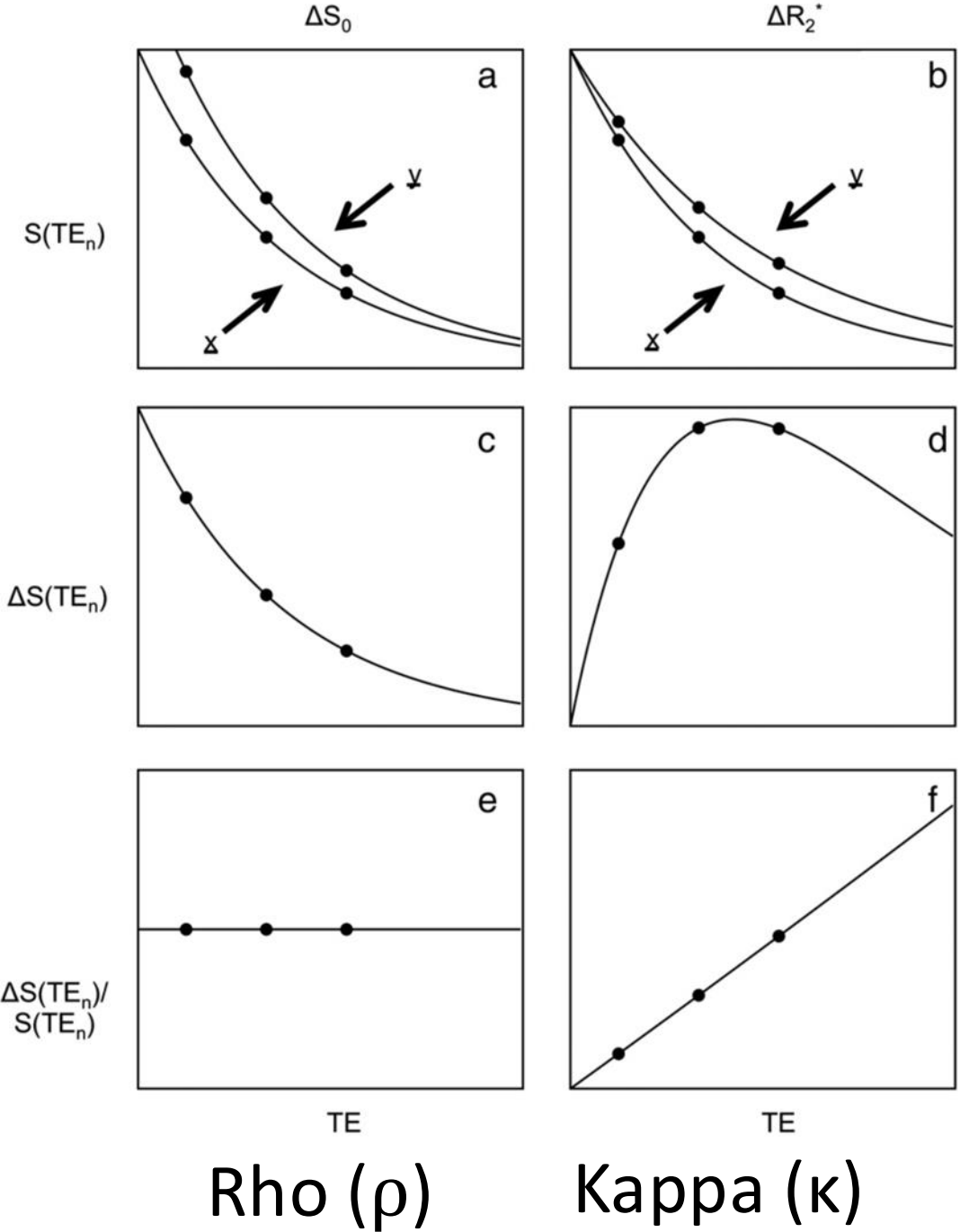


OHBM 2026 DISCLOSURES

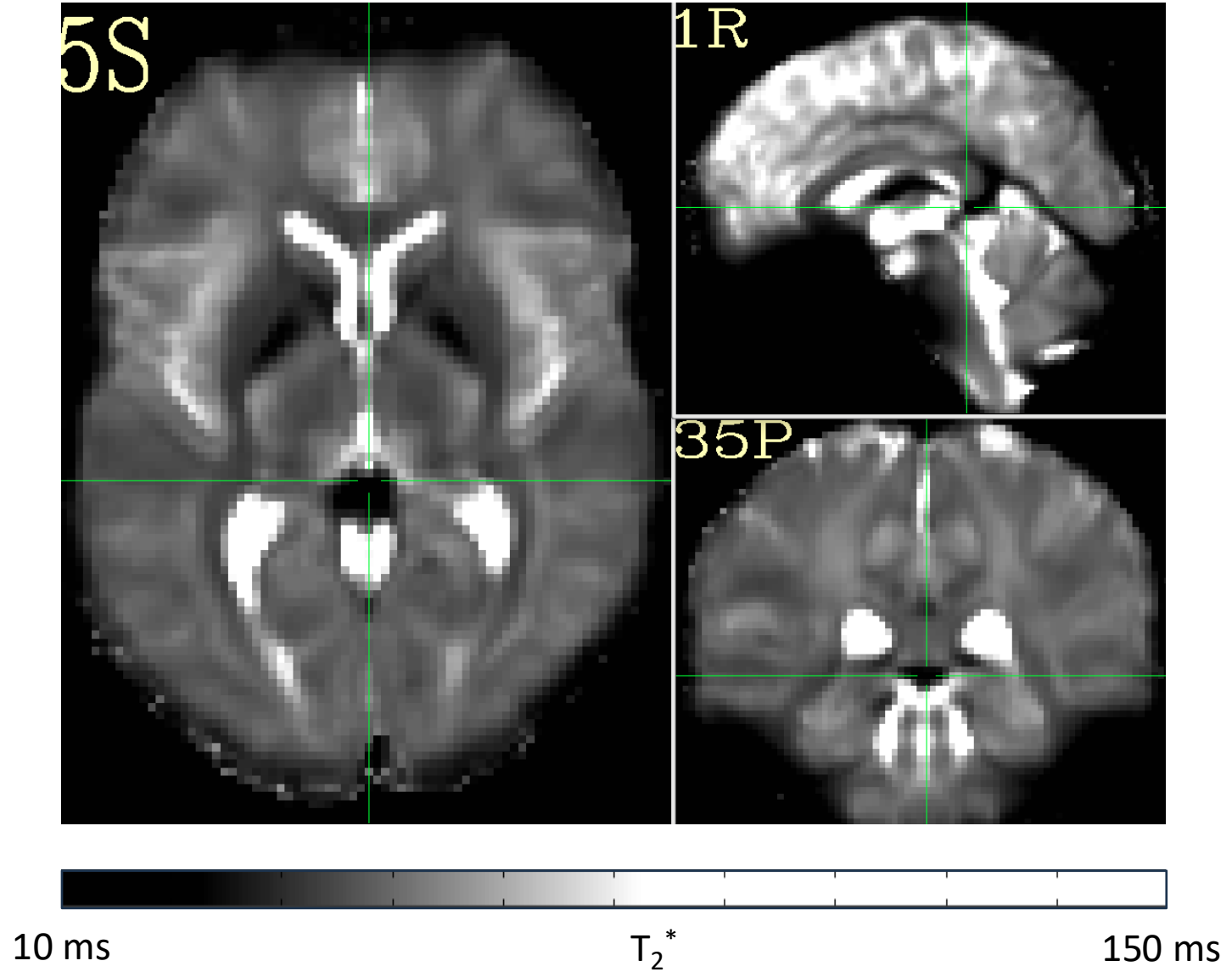
I have no conflicts of interest in relation to this presentation to disclose.

Multi-Echo Information

Differential Behavior for BOLD and non-BOLD Fluctuations



Spatial T_2^* Map



How to take advantage of all this extra info

Automatic Denoising (tedana, ME-ICA, tedana + NN)

ME Hemodynamic
Deconvolution

ME Quality
Assurance (p_{BOLD})

Study signals from
non-GM
compartments

How to take advantage of all this extra info

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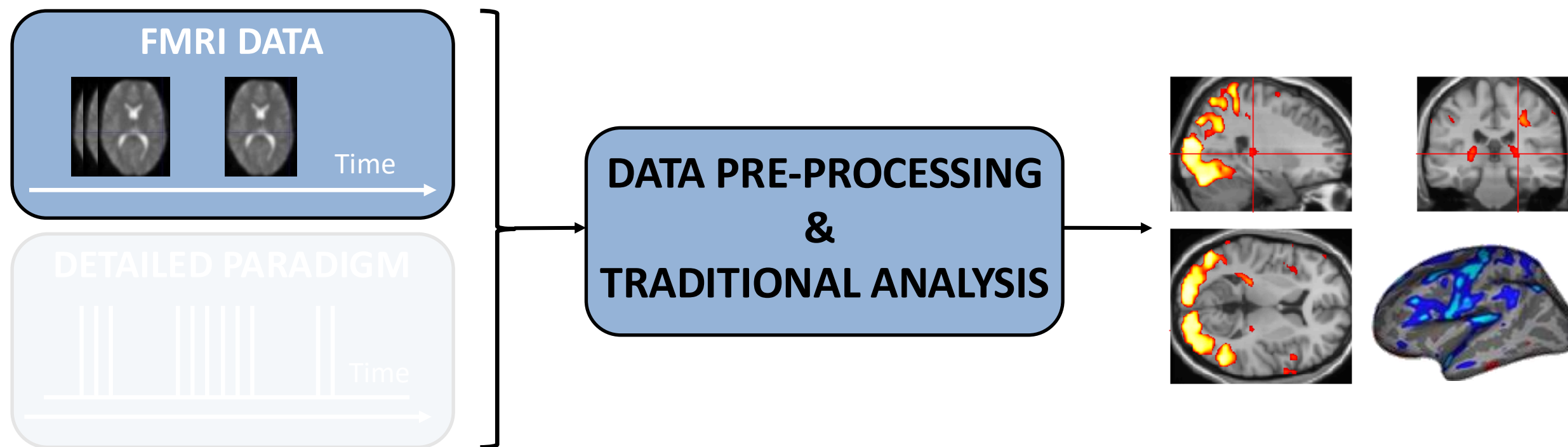
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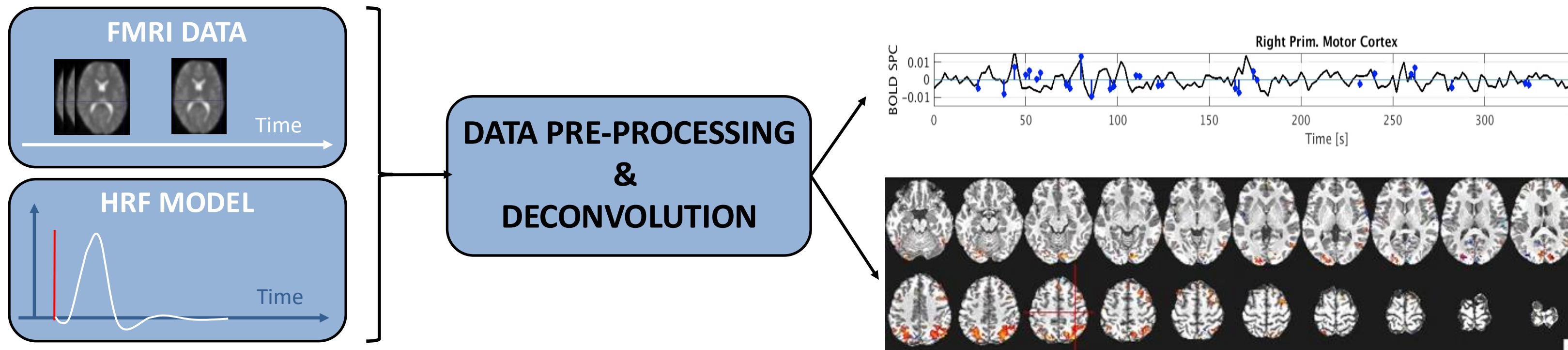
When to use deconvolution analysis?



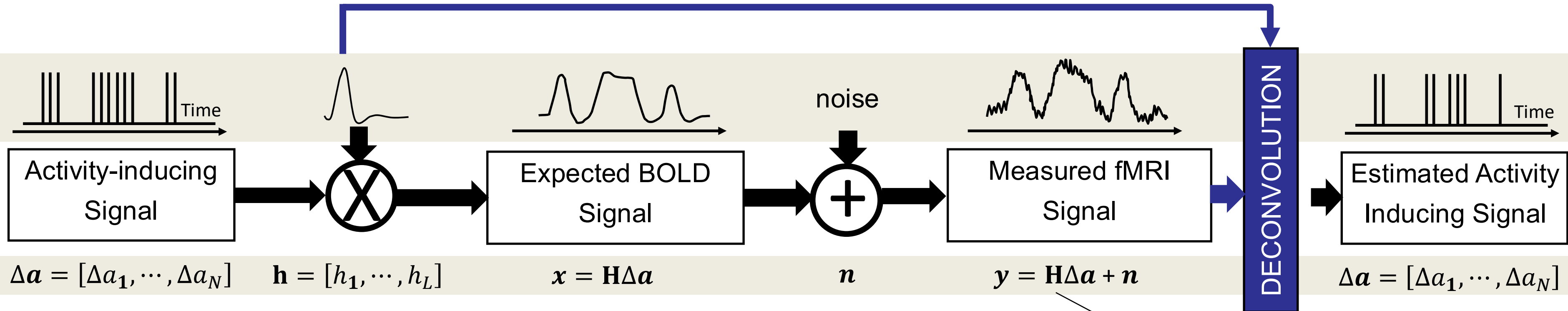
There are experimental scenarios where event timing might be missing:

- Naturalistic paradigms
- Clinical studies (e.g., interictal events)
- Resting State

Deconvolution methods are an alternative in such scenarios:



Single-Echo Deconvolution



If one assumes the underlying activity-inducing signal to consist of brief, sparse events, then the formulated deconvolution problem can be solved using LASSO regularization:

$$\Delta \hat{\mathbf{a}} = \arg \min_{\Delta \mathbf{a}} \underbrace{\frac{1}{2} \|\mathbf{y} - \mathbf{H}\Delta \mathbf{a}\|_2^2}_{\text{Error Minimization Term}} + \underbrace{\lambda \|\Delta \mathbf{a}\|_1}_{\text{L1-Norm Regularization (Sparseness)}}$$

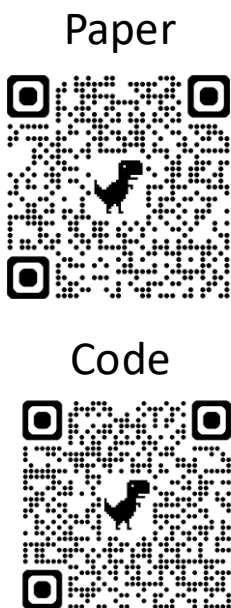
Single-Echo Sparse Free Paradigm Mapping Algorithm



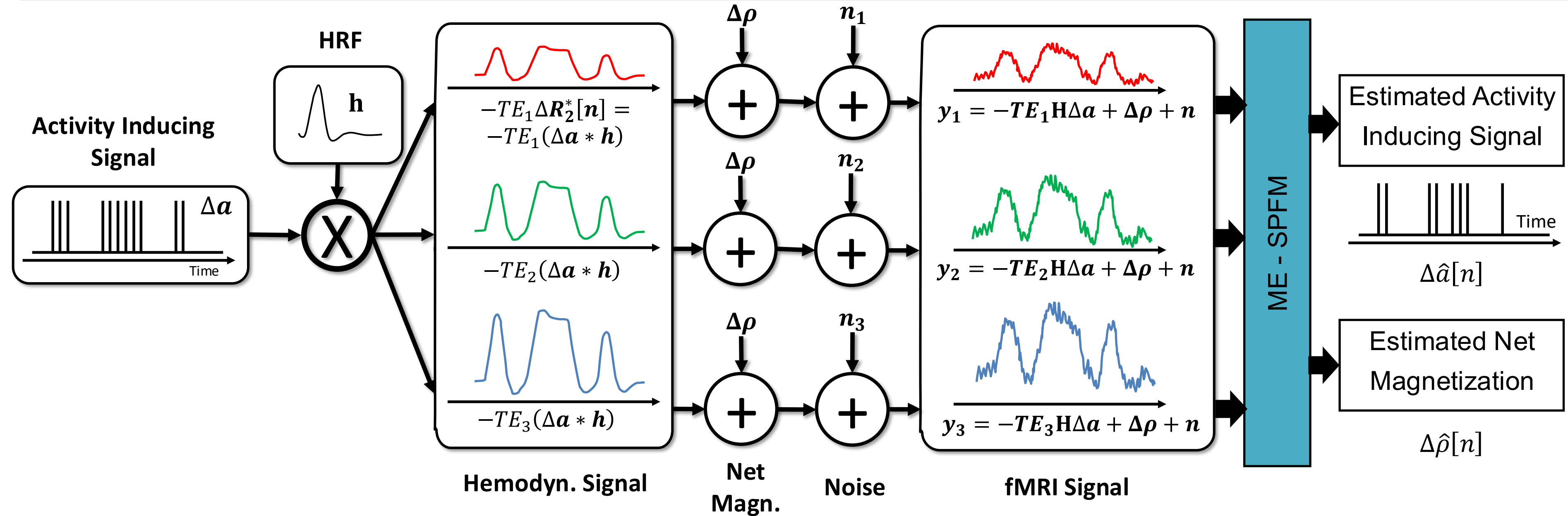
3dPFM



Caballero-Gaudes et al. HBM (2011)



Multi-Echo Deconvolution

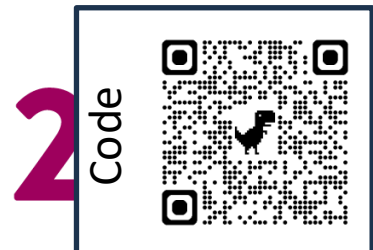


$$\bar{\mathbf{y}} \stackrel{\text{def}}{=} \begin{bmatrix} \mathbf{y}_1 \\ \vdots \\ \mathbf{y}_K \end{bmatrix} = \begin{bmatrix} \mathbf{I} \\ \vdots \\ \mathbf{I} \end{bmatrix} \Delta \boldsymbol{\rho} - \begin{bmatrix} TE_1 \mathbf{H} \\ \vdots \\ TE_K \mathbf{H} \end{bmatrix} \Delta \mathbf{a}$$

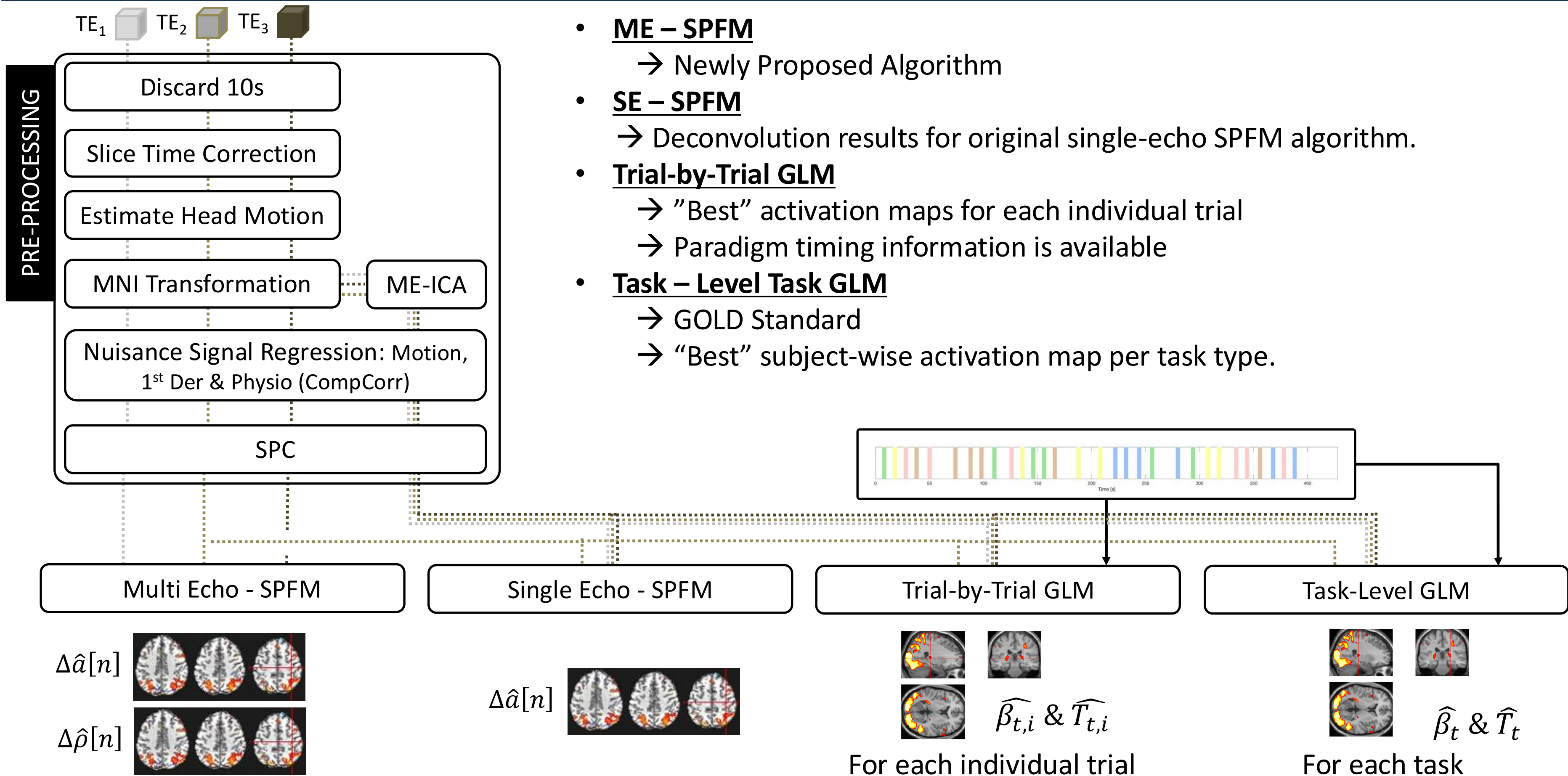
Assuming sparsity in both unknowns, we can solve using LASSO regularization

$$\Delta \hat{\mathbf{a}}, \Delta \hat{\boldsymbol{\rho}} = \arg \min_{\Delta \mathbf{a}, \Delta \boldsymbol{\rho}} \frac{1}{2} \|\bar{\mathbf{y}} - \bar{\mathbf{H}} \Delta \mathbf{a} - \bar{\mathbf{I}} \Delta \boldsymbol{\rho}\|_2^2 + \lambda_1 \|\Delta \mathbf{a}\|_1 + \lambda_2 \|\Delta \boldsymbol{\rho}\|_1$$

Caballero-Gaudes et al. NeuroImage (2019)



Single-Echo vs. Multi-Echo Deconvolution

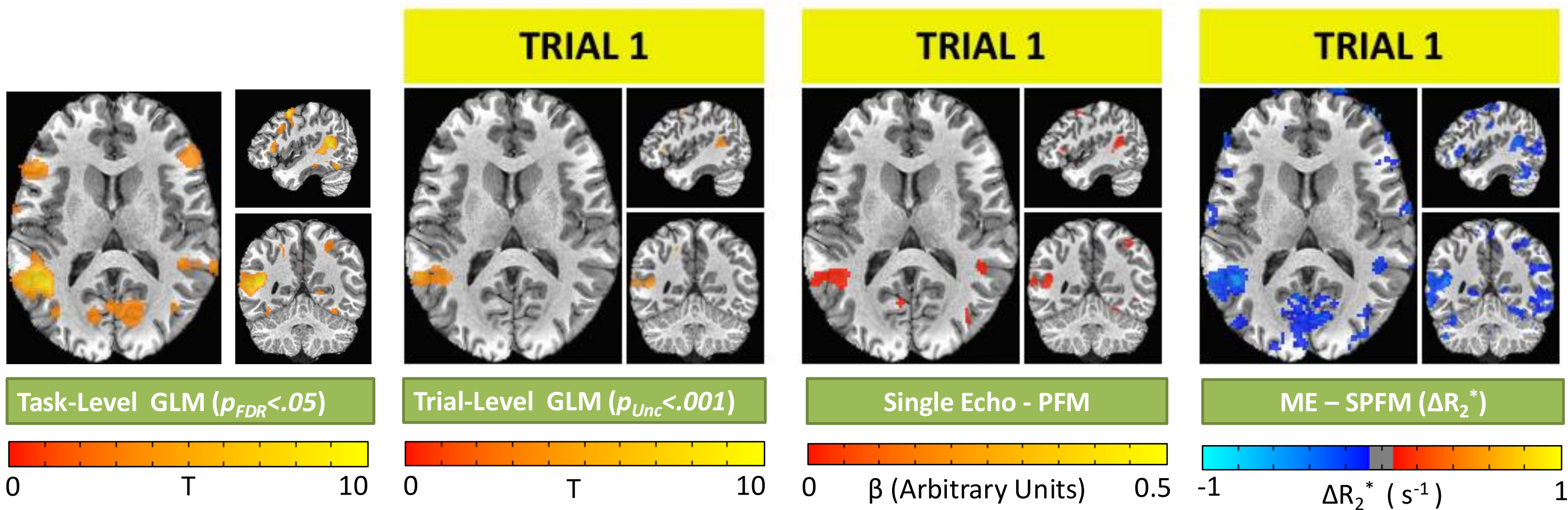
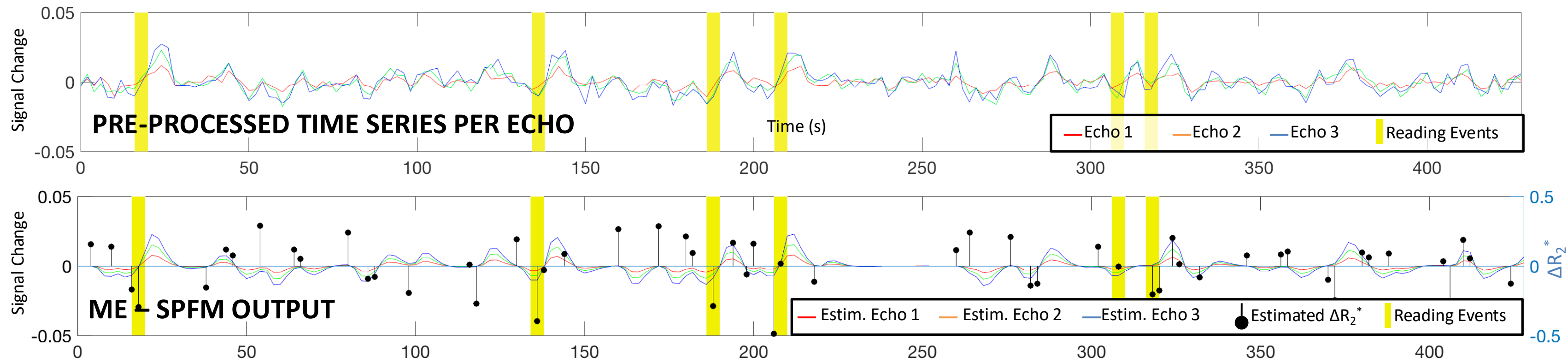


- **ME – SPFM**
→ Newly Proposed Algorithm
- **SE – SPFM**
→ Deconvolution results for original single-echo SPFM algorithm.
- **Trial-by-Trial GLM**
→ "Best" activation maps for each individual trial
→ Paradigm timing information is available
- **Task – Level Task GLM**
→ GOLD Standard
→ "Best" subject-wise activation map per task type.

Single-Echo vs. Multi-Echo Deconvolution



READ THIS

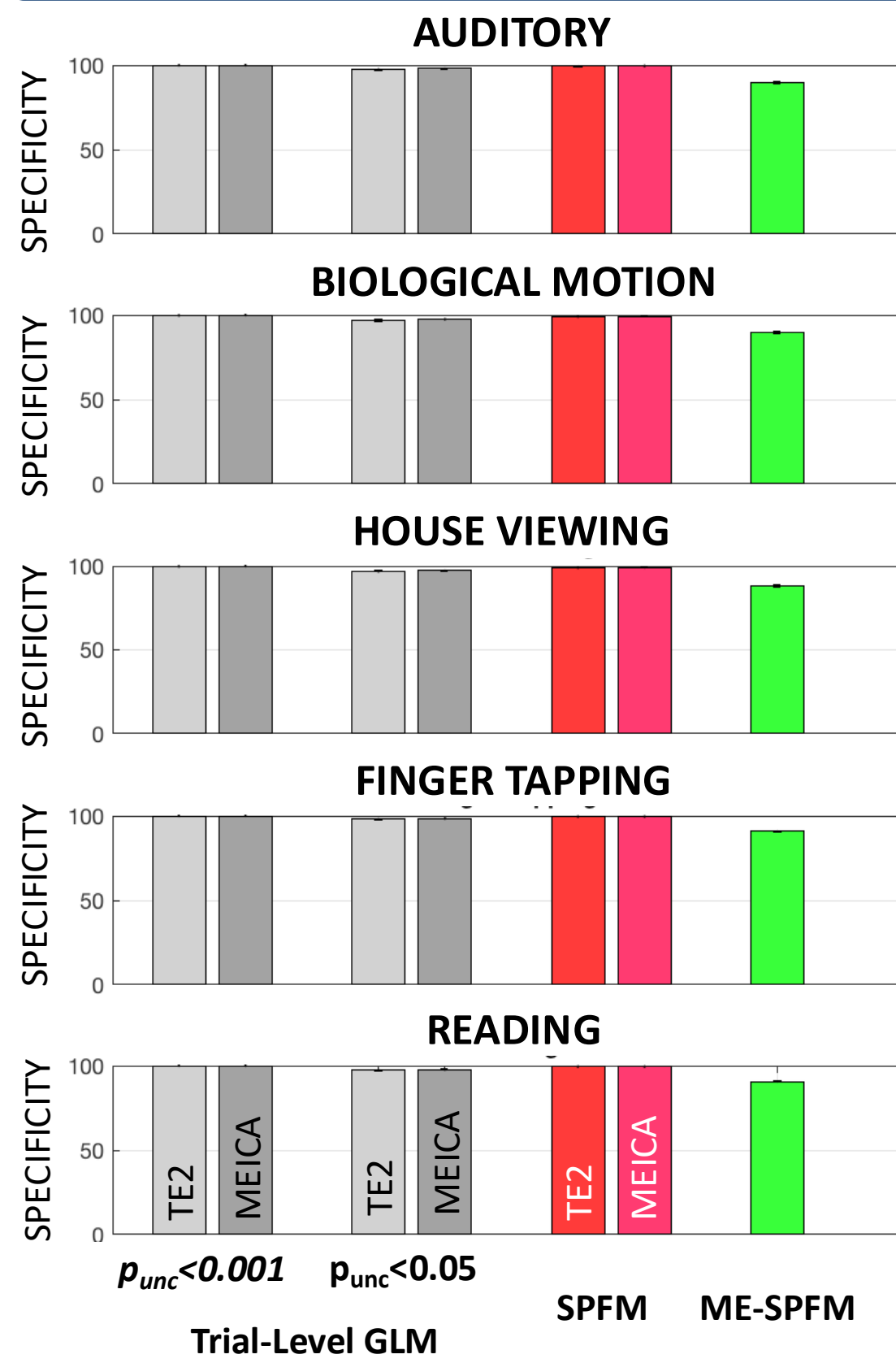
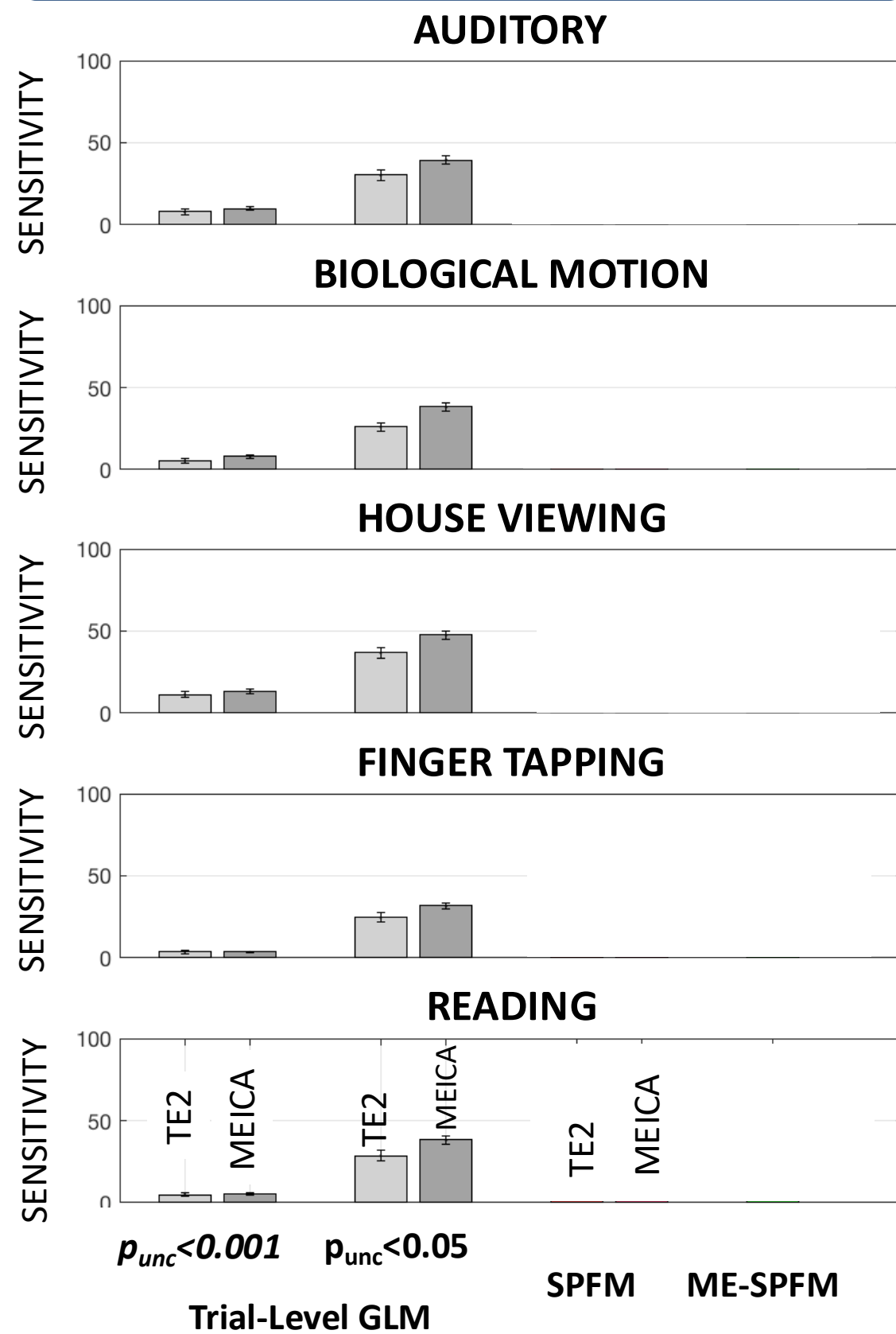


Single-Echo vs. Multi-Echo Deconvolution

SENSITIVITY vs. TASK-LEVEL GLM

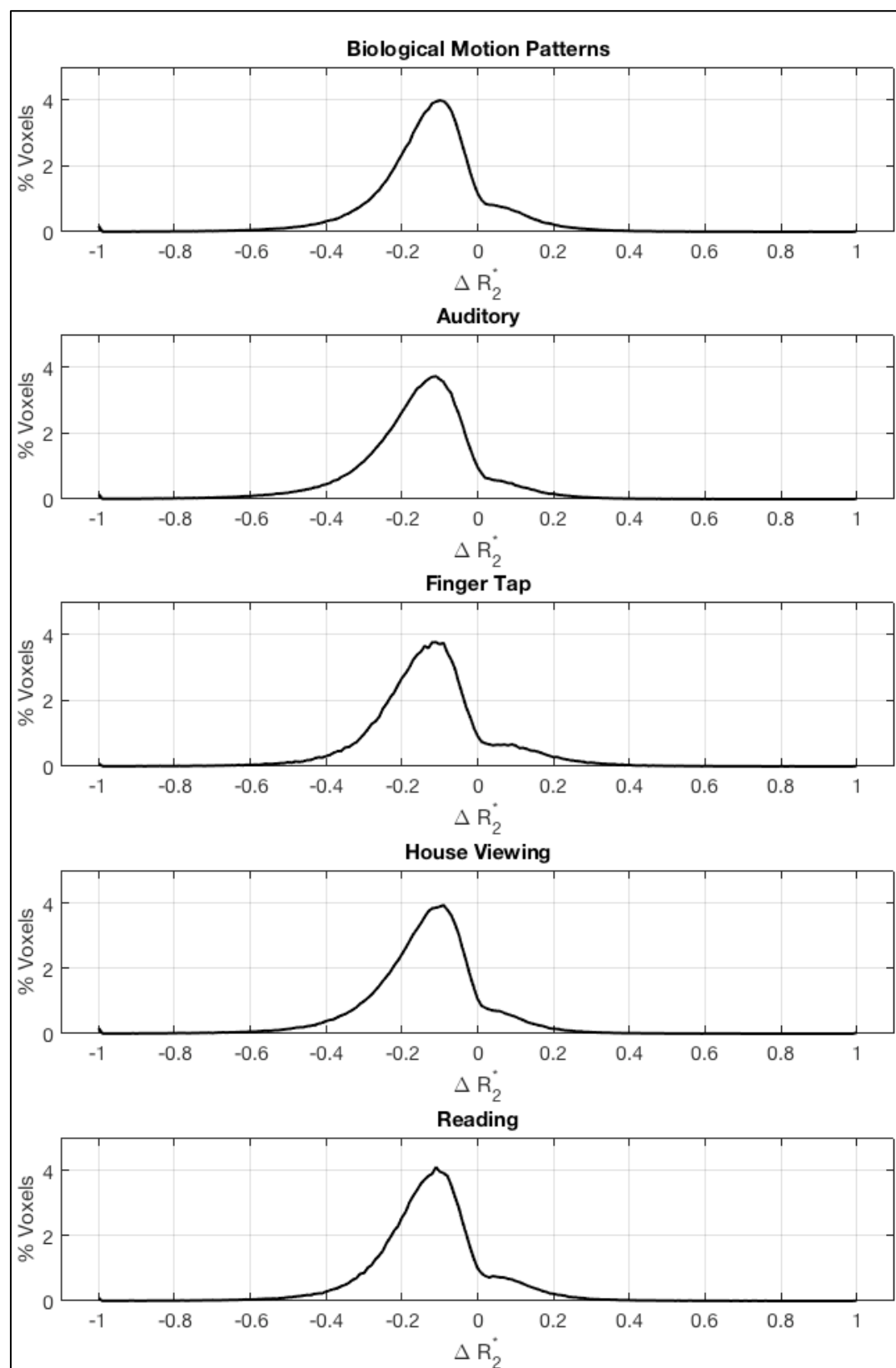
SPECIFICITY vs. TASK-LEVEL GLM

DICE COEFFICIENT

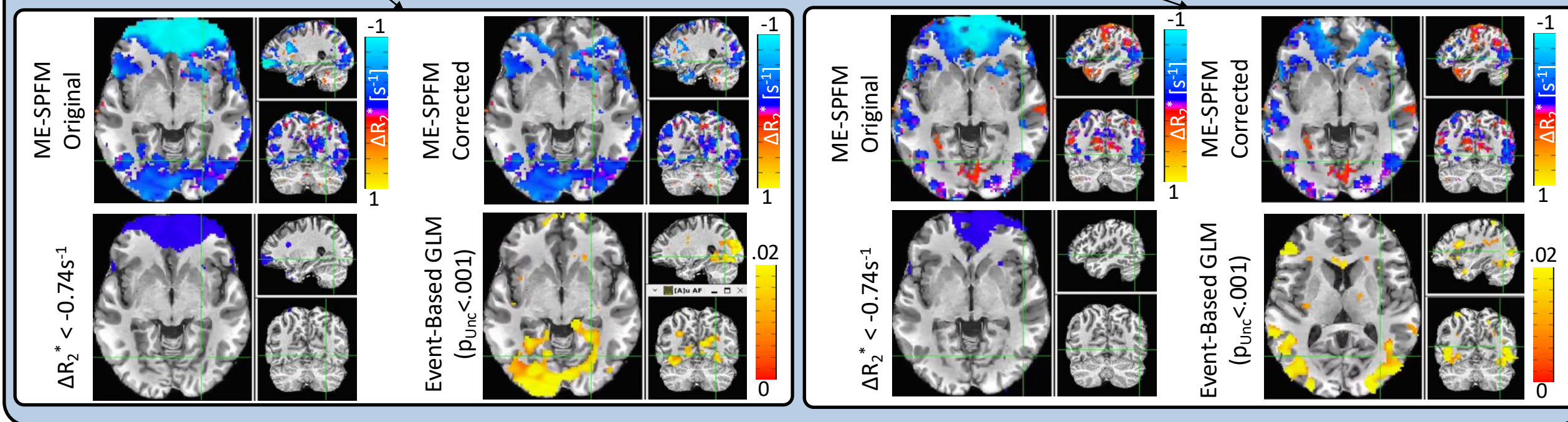
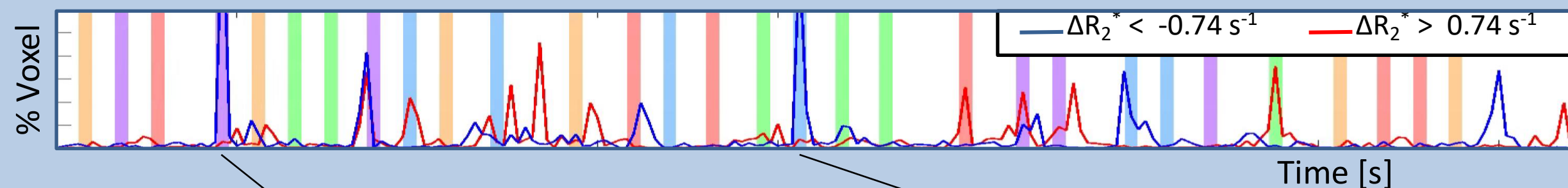


Multi-Echo Deconvolution: Interpretable Units

Distribution of ΔR_2^* in GLM task-level active voxels for each task

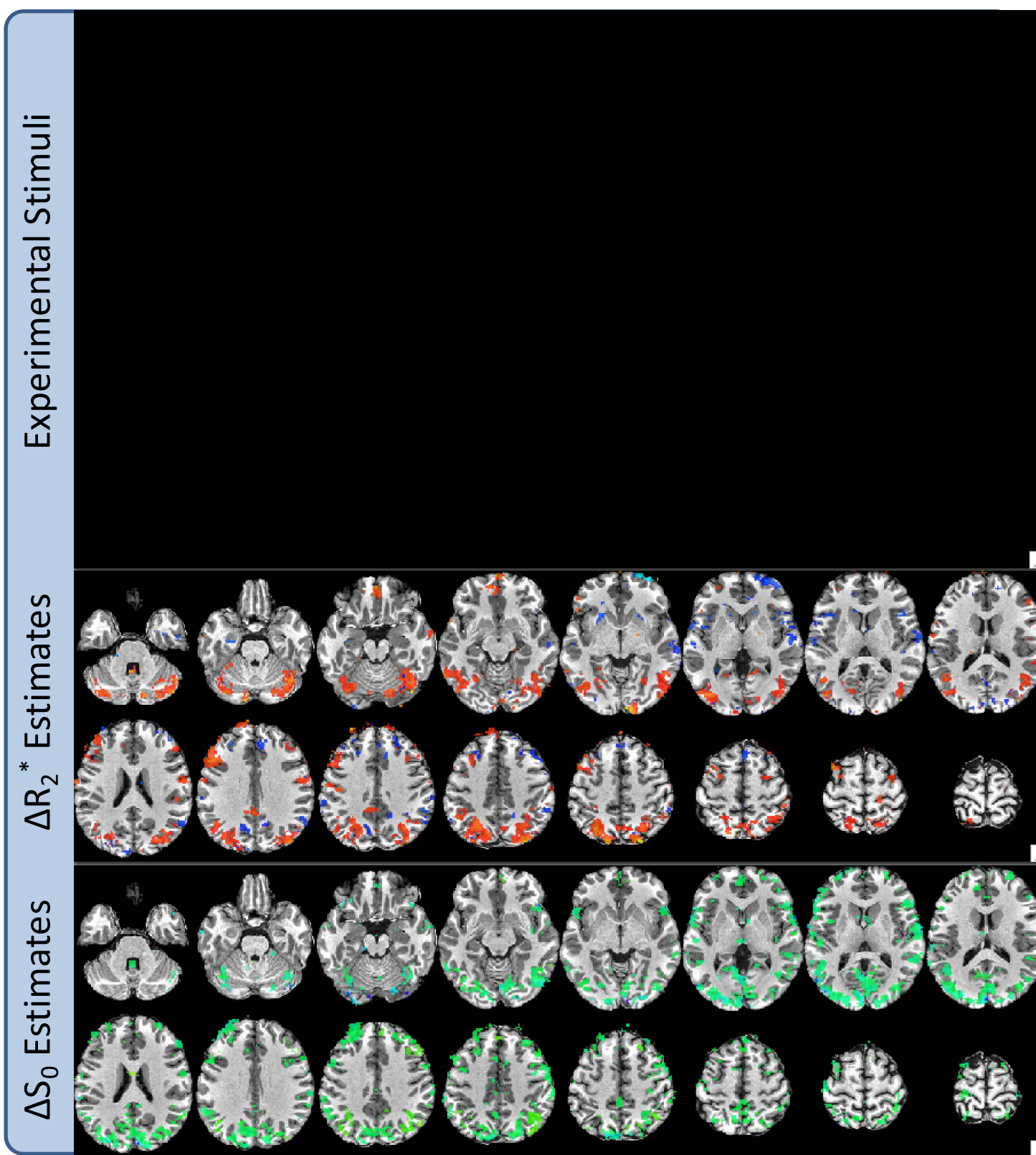


Distribution of ΔR_2^* across all voxels on a volume-by-volume basis



Reference	Region	ROI / Compartment	$\Delta R_2^* [\text{s}^{-1}]$
W. Van der Zaag et al, NeuroImage, 2009	Motor Cortex	Voxels active across all echoes	-0.98 ± 0.08
		Voxels active at any echo	-0.54 ± 0.03
Donahue et al, NMR in Biomedicine, 2011	Visual Cortex	Total	-0.74 ± 0.05
		Extravascular	-0.52 ± 0.07

ME-Deconvolution: Conclusions



- ME-SPFM is a deconvolution algorithm specifically formulated for multi-echo data.
- ME-SPFM can reliably detect individual events without a priori information about their timing.
- ME-SPFM outperforms its single-echo counterpart in terms of sensitivity and nearly matches GLM-based results at the single-trial level.
- ME-SPFM estimates ΔR_2^* with interpretable units [s^{-1}], which fell within physiologically plausible limits.
- ME-SPFM can help us decipher the dynamic nature of brain activity in naturalistic paradigms, resting-state or clinical applications with unknown event-timing.

Caballero-Gaudes et al. NeuroImage (2019)

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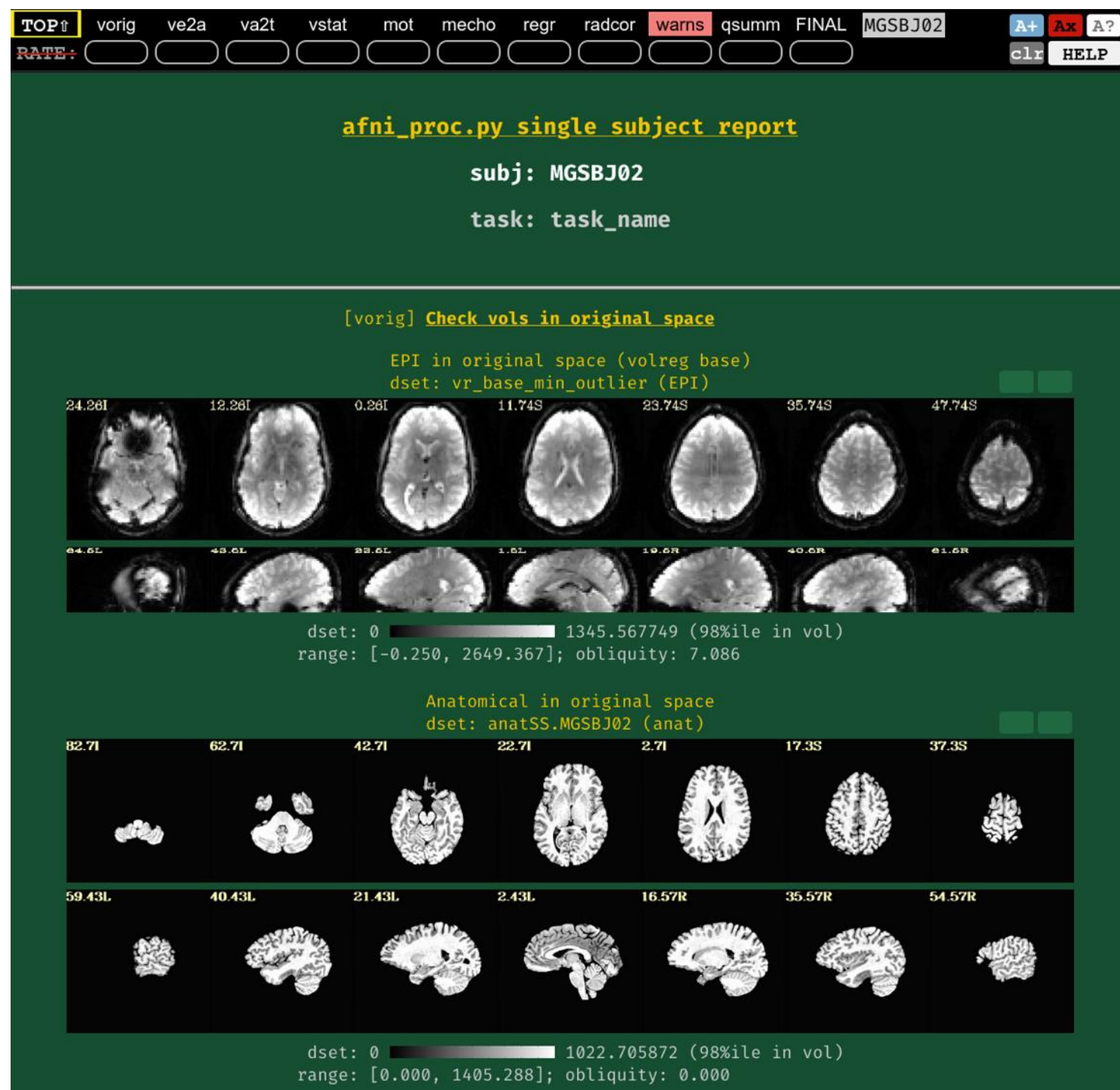
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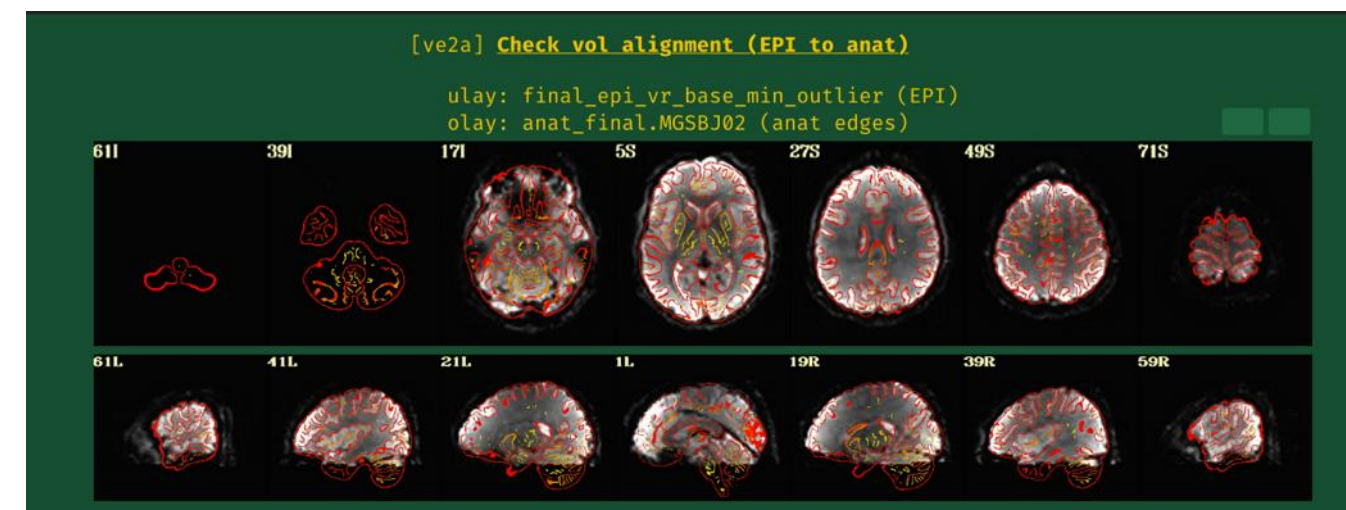


QA for ME-data: Why? (I)

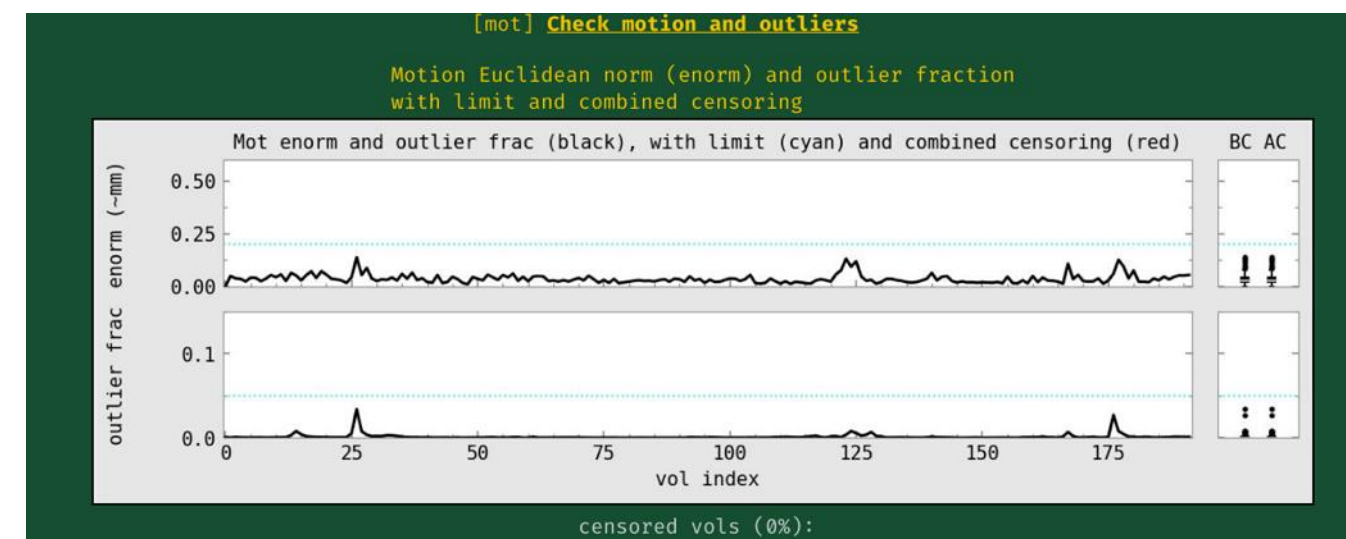
AFNI QC Reports



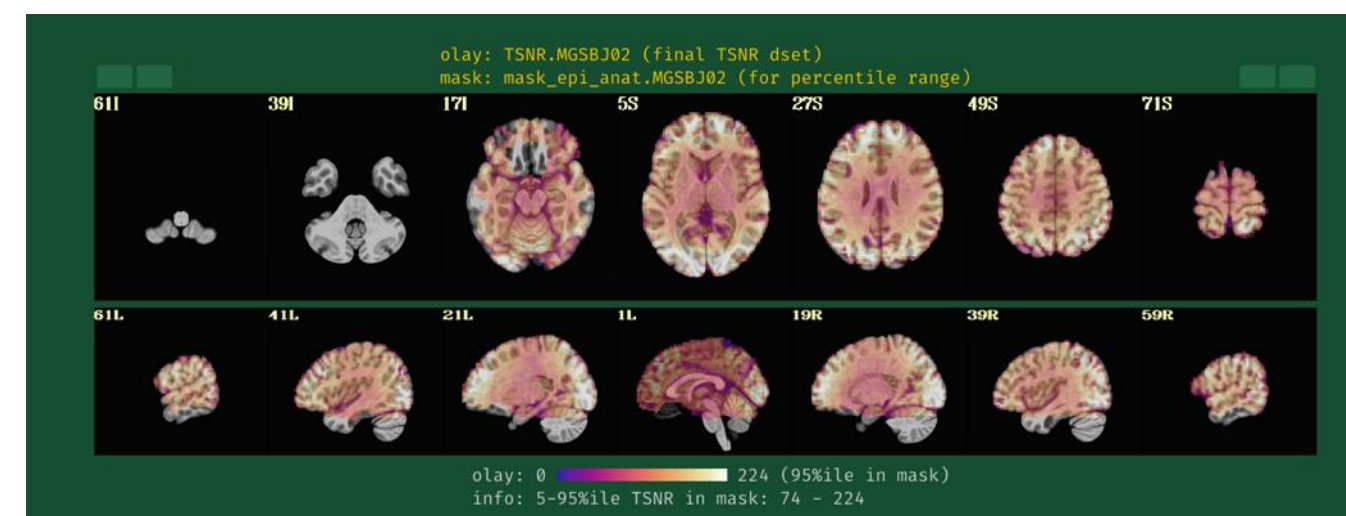
Alignment



Head Motion

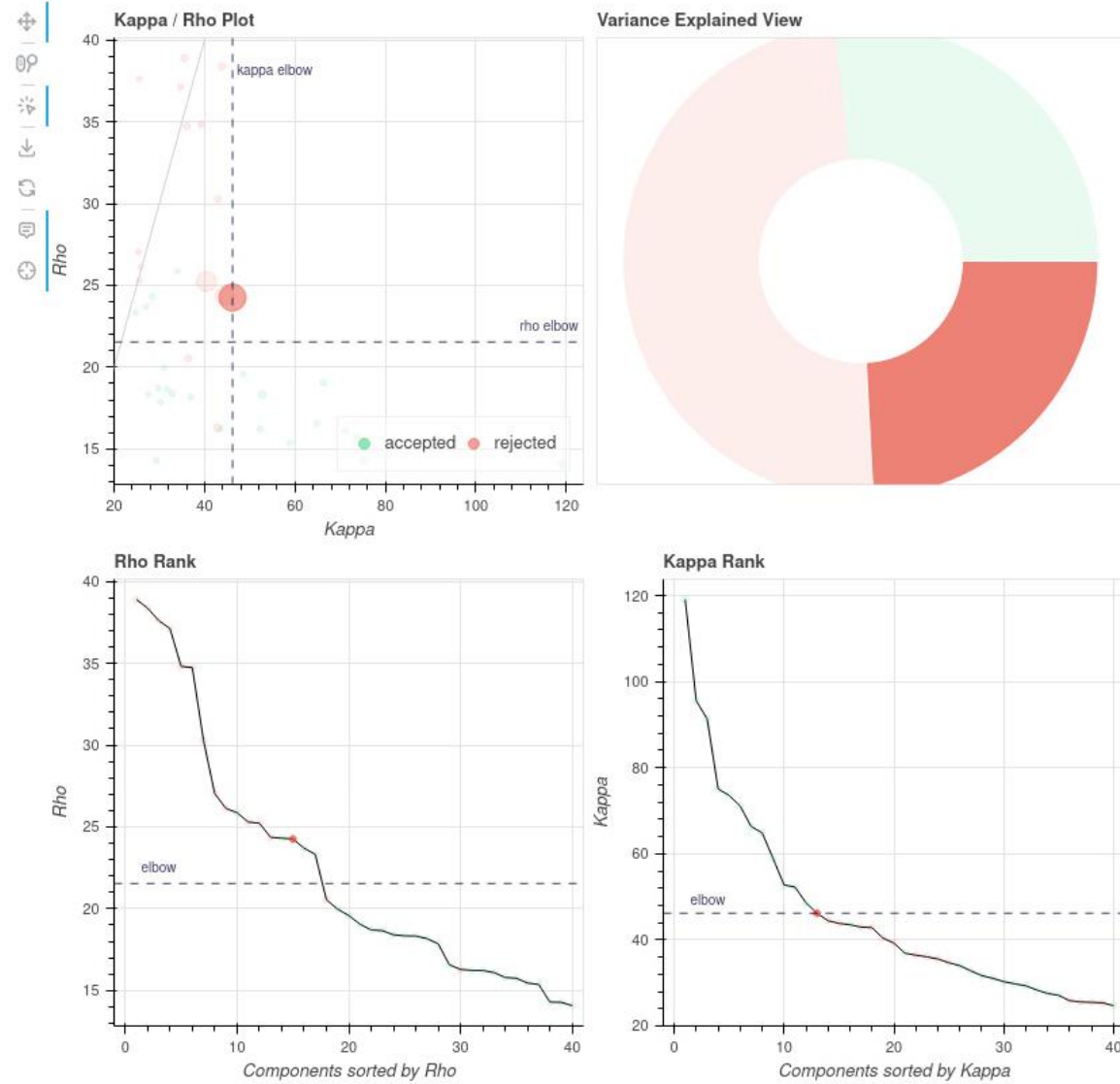


TSNR

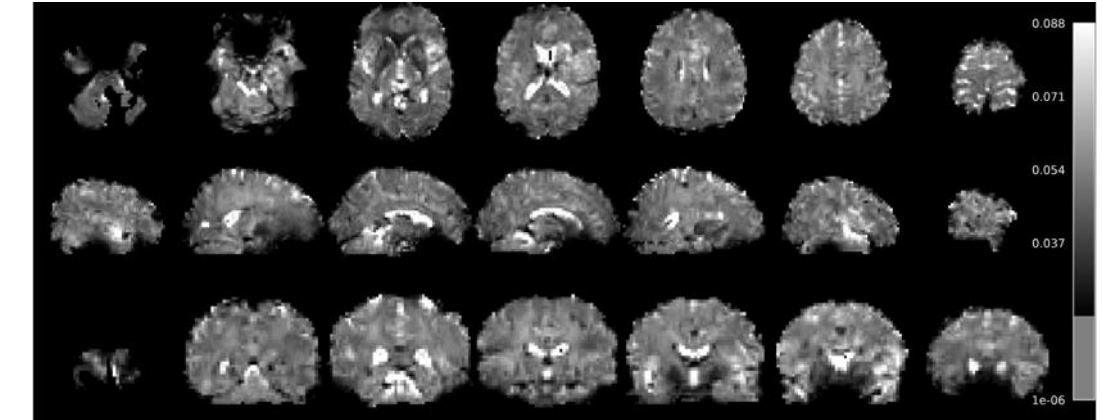
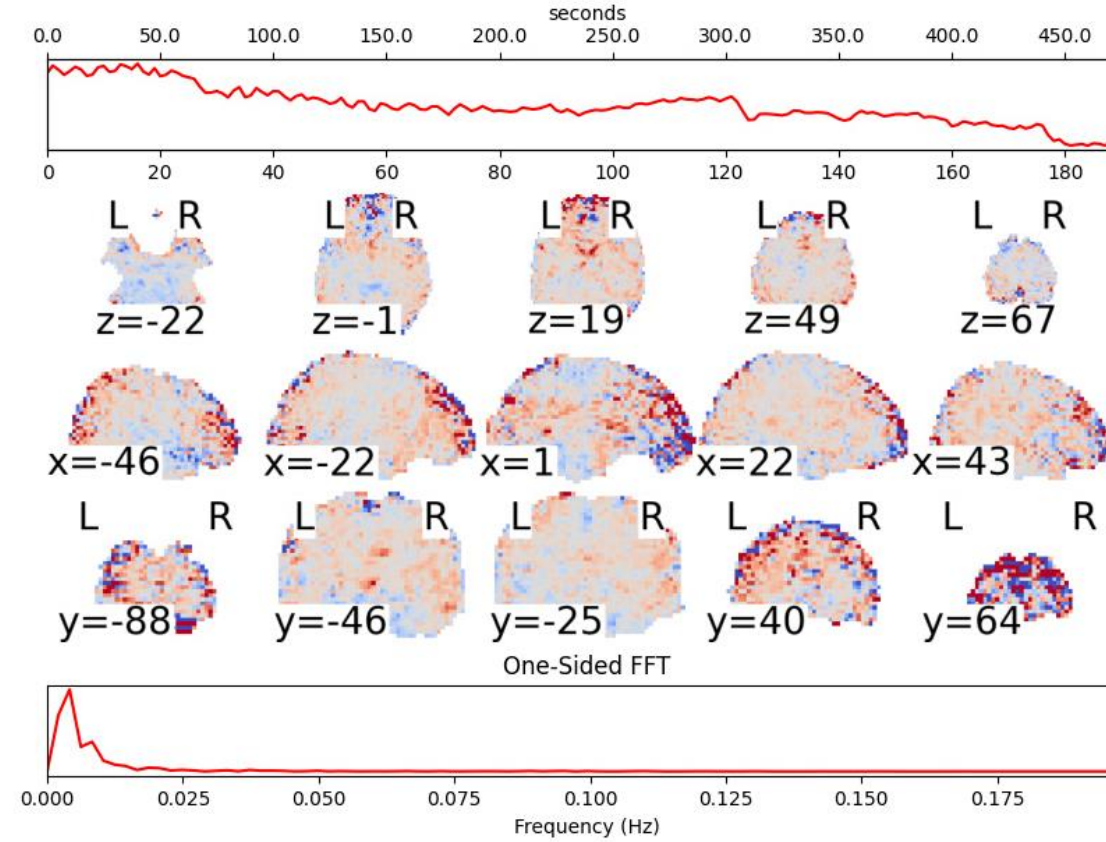


QA for ME-data: Why? (II)

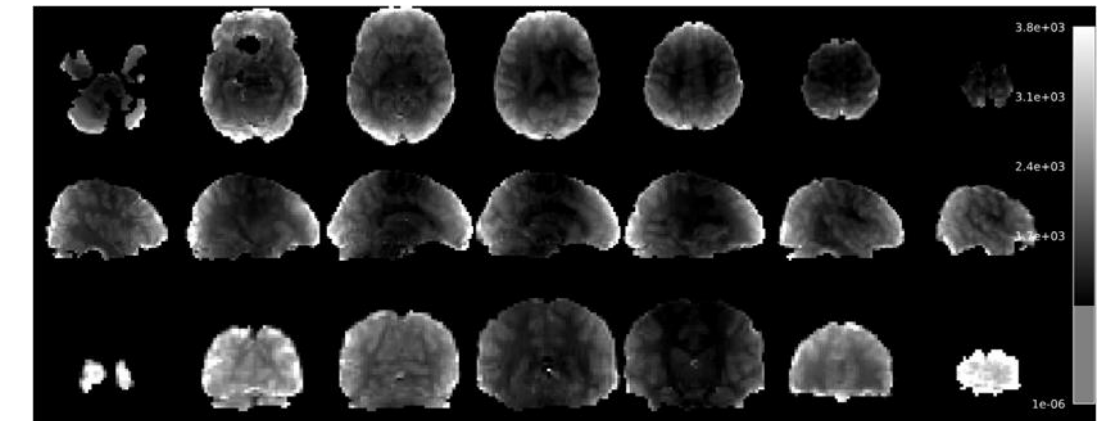
ICA components



Comp. 29: variance: 24.16%, kappa: 46.18, rho: 24.26, rejected reason(s): Unlikely BOLD



T2* Estimation



S0 Estimation

Component Selection

QA for ME-data: Why? (III)

- Higher Temporal Signal-to-Noise Ratio

👍 As we remove noise-related variance, TSNR increases

👎 Yet, as we remove variance of interest, TSNR also increases

- Higher Test-Retest Reliability

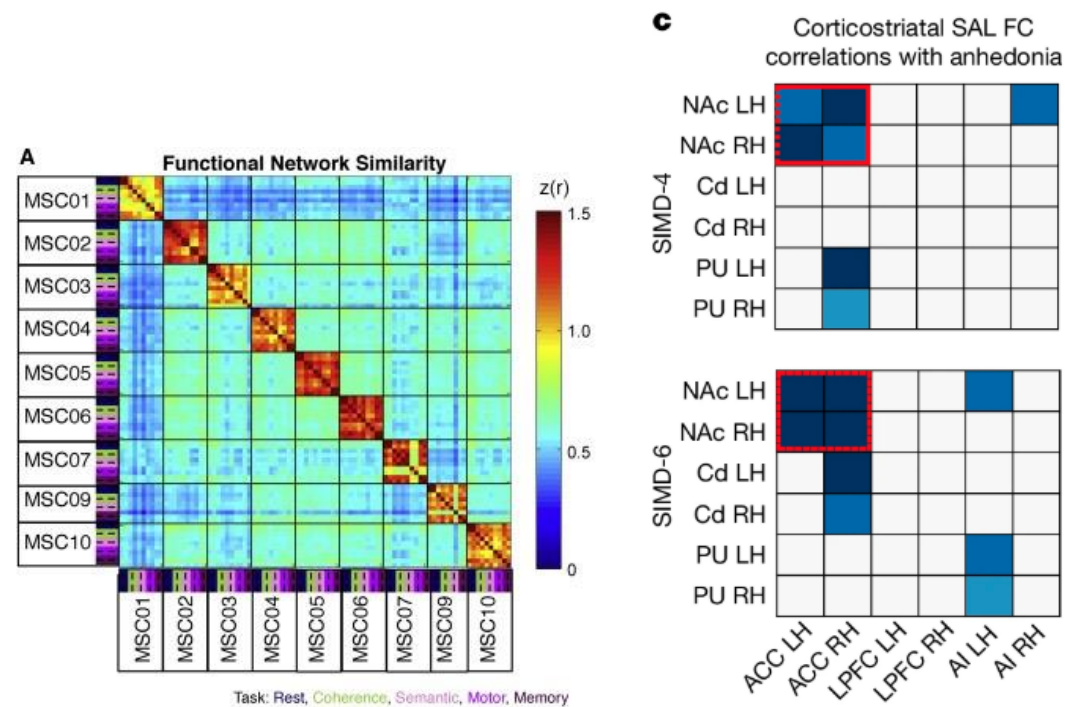
👍 Functional patterns of interest should be stable in time

👎 Yet, some changes are clinically relevant

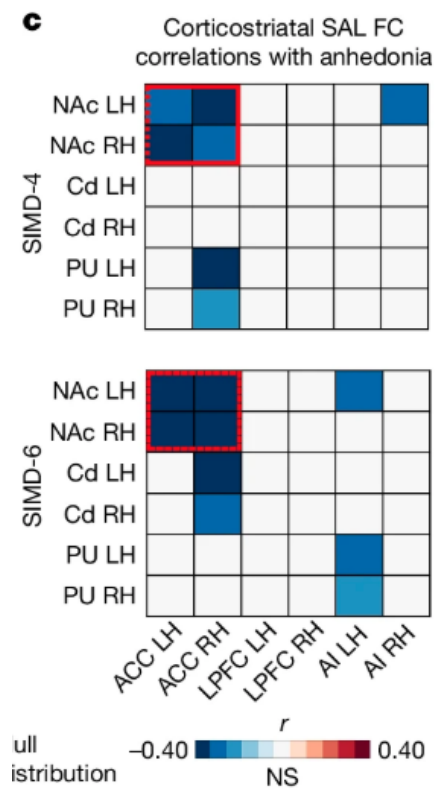
- Higher Correlation with an external phenotype

👍 Stronger brain-behavior relationships signal better data

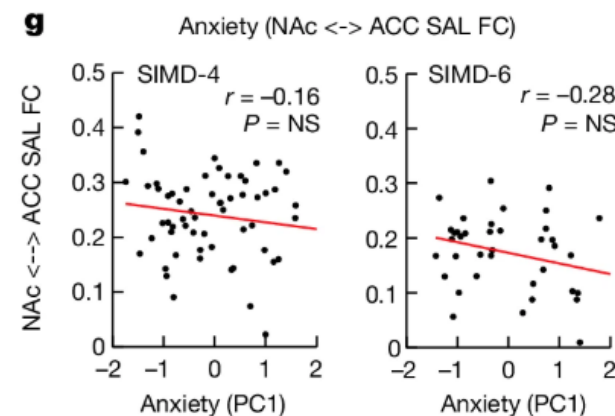
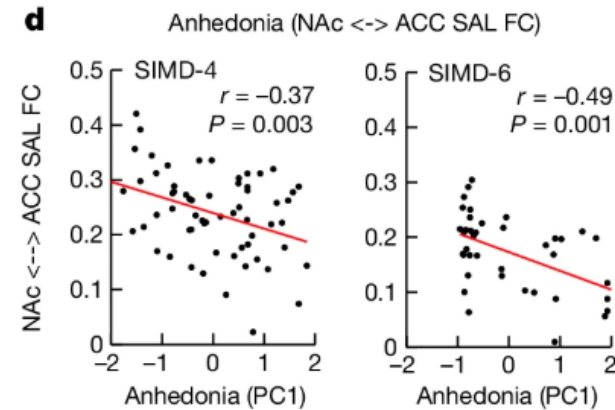
👎 Yet, systematic differences in nuisance factors can alter this relation



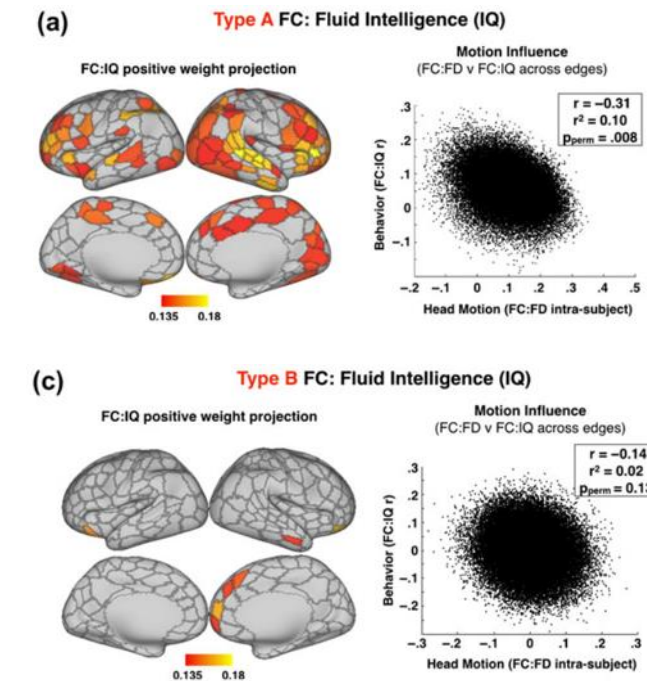
Gratton et al. (2018)



Lynch et al. (2024)



Subject measures	Pearson r
ReadEng (AgeAdj)	-0.23
ReadEng (Unadj)	-0.23
Vocabulary (AgeAdj)	-0.19
Dexterity (Unadj)	-0.18
CardSort (Unadj)	-0.18
Dexterity (AgeAdj)	-0.18
CardSort (AgeAdj)	-0.18
Education	-0.17
Fluid intelligence	-0.17
Spatial orientation	-0.17
Vocabulary (unadj)	-0.17
Emotion recognition	-0.16
DSM somatic problems (pct)	0.16
DSM antisocial (raw)	0.16
ASR externalizing (raw)	0.16
DSM somatic problems (raw)	0.16
Tobacco use 7 day	0.18
Diastolic blood pressure	0.18
ASR externalizing	0.18
Tobacco use today	0.2
Systolic blood pressure	0.23
Weight	0.52
Body mass index (BMI)	0.66



Siegel et al. (2017)

- More significant voxels are better

👉 Not always

QA for ME-data: How?

Signal at voxel/ROI 'x',
timepoint 't' and echo 'k'

BOLD fluctuations

$$S(x, t, TE_k) = S_o(x, t) \cdot e^{-R_2^*(x, t) \cdot TE_k} + n(x, t)$$

Fluctuations in net
magnetization

Thermal Noise

Data free of fluctuations in net magnetization and thermal noise is better data

$p_{BOLD} \sim$ probability of data being dominated by BOLD fluctuations

QA for ME-data: Correlation across TEs | Theory

$s_{x,i} \approx \Delta\rho_x - \Delta R_x \cdot TE_i$ ← Signals at two ROIs [x and y] acquired at two different TEs [i and j] → $s_{y,j} \approx \Delta\rho_y - \Delta R_y \cdot TE_j$

$$R(s_{x,i}, s_{y,j}) = R_{xi,yj} = \frac{\sum (s_{x,i} - \overline{s_{x,i}}) \cdot (s_{y,j} - \overline{s_{y,j}})}{\sqrt{\sum (s_{x,i} - \overline{s_{x,i}})^2 \cdot \sum (s_{y,j} - \overline{s_{y,j}})^2}} \xrightarrow{\overline{s_{x,i}} = \overline{s_{y,j}} = 0} \frac{\sum s_{x,i} \cdot s_{y,j}}{\sqrt{\sum (s_{x,i})^2 \cdot \sum (s_{y,j})^2}}$$

$$R_{xi,yj} = \frac{\sum (\Delta\rho_x - \Delta R_x \cdot TE_i) \cdot (\Delta\rho_y - \Delta R_y \cdot TE_j)}{\sqrt{\sum (\Delta\rho_x - \Delta R_x \cdot TE_i)^2} \cdot \sqrt{\sum (\Delta\rho_y - \Delta R_y \cdot TE_j)^2}}$$

BOLD-DOMINATED REGIME

$$\Delta\rho_x \ll \Delta R_x \text{ \& \ } \Delta\rho_y \ll \Delta R_y$$

$$R_{xi,yj} = \frac{\cancel{TE_i} \cdot \cancel{TE_j} \cdot \sum (\Delta R_x \cdot \Delta R_y)}{\cancel{TE_i} \cdot \cancel{TE_j} \cdot \sqrt{\sum (-\Delta R_x)^2} \cdot \sqrt{\sum (-\Delta R_y)^2}}$$

R is TE-independent

S₀-DOMINATED REGIME

$$\Delta\rho_x \gg \Delta R_x \text{ \& \ } \Delta\rho_y \gg \Delta R_y$$

$$R_{xi,yj} = \frac{\sum \Delta\rho_x \cdot \Delta\rho_y}{\sqrt{\sum (\Delta\rho_x)^2} \cdot \sqrt{\sum (\Delta\rho_y)^2}}$$

R is TE-independent

Gonzalez-Castillo et al. BioRxiv (2026)

QA for ME-data: Covariance across TEs | Theory

$s_{x,i} \approx \Delta\rho_x - \Delta R_x \cdot TE_i$ ← Signals at two ROIs [x and y] acquired at two different TEs [i and j] → $s_{y,j} \approx \Delta\rho_y - \Delta R_y \cdot TE_j$

$$C_{xi,yj} = \frac{1}{N_t - 1} \cdot \sum (s_{x,i} - \overline{s_{x,i}}) \cdot (s_{y,j} - \overline{s_{y,j}}) \xrightarrow{\overline{s_{x,i}} = \overline{s_{y,j}} = 0} \frac{1}{N_t - 1} \cdot \sum s_{x,i} \cdot s_{y,j}$$

$$C_{xi,yj} = \frac{1}{N_t - 1} \cdot \sum (\Delta\rho_x - \Delta R_x \cdot TE_i) \cdot (\Delta\rho_y - \Delta R_y \cdot TE_j)$$

BOLD-DOMINATED REGIME

$$\Delta\rho_x \ll \Delta R_x \text{ \& } \Delta\rho_y \ll \Delta R_y$$

$$C_{xi,yj} = \frac{TE_i \cdot TE_j}{N_t - 1} \cdot \sum \Delta R_x \cdot \Delta R_y$$

C is a function of contributing echoes

S₀-DOMINATED REGIME

$$\Delta\rho_x \gg \Delta R_x \text{ \& } \Delta\rho_y \gg \Delta R_y$$

$$C_{xi,yj} = \frac{1}{N_t - 1} \cdot \sum \Delta\rho_x \cdot \Delta\rho_y$$

C is TE-independent

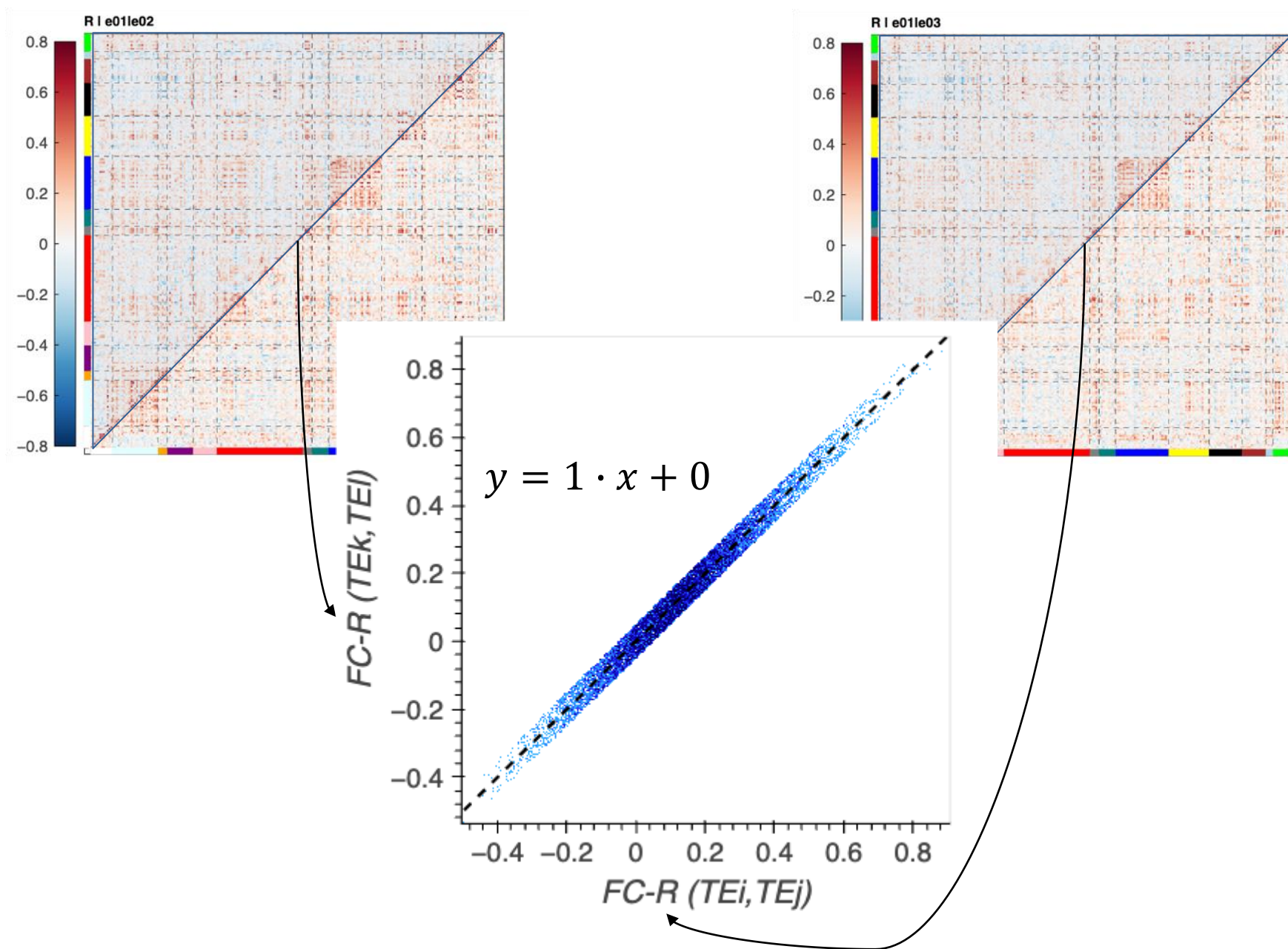
Gonzalez-Castillo et al. BioRxiv (2026)

QA for ME-data: R and Cov across TEs | Theory

FC as Pearson's Correlation

FC-R is TE-independent for both BOLD and So dominated data

$$R_{xk,yl} = R_{xi,yj} \forall i, j, k, l$$



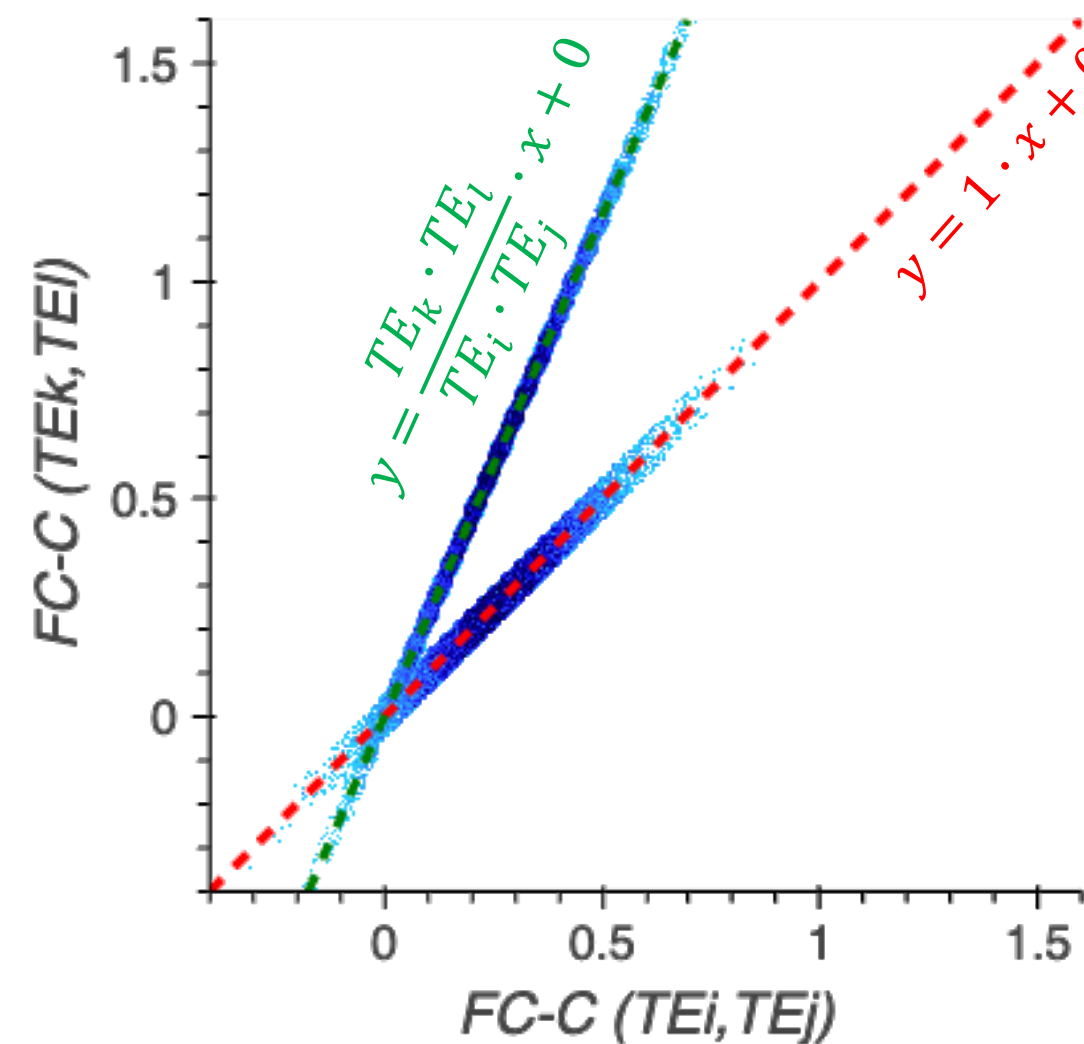
FC as Covariance

FC-C is TE-independent for So dominated data

$$C_{xk,yl} = C_{xi,yj} \forall i, j, k, l$$

FC-C is TE-dependent for BOLD dominated data

$$C_{xk,yl} = \frac{TE_k \cdot TE_l}{TE_i \cdot TE_j} \cdot C_{xi,yj}$$



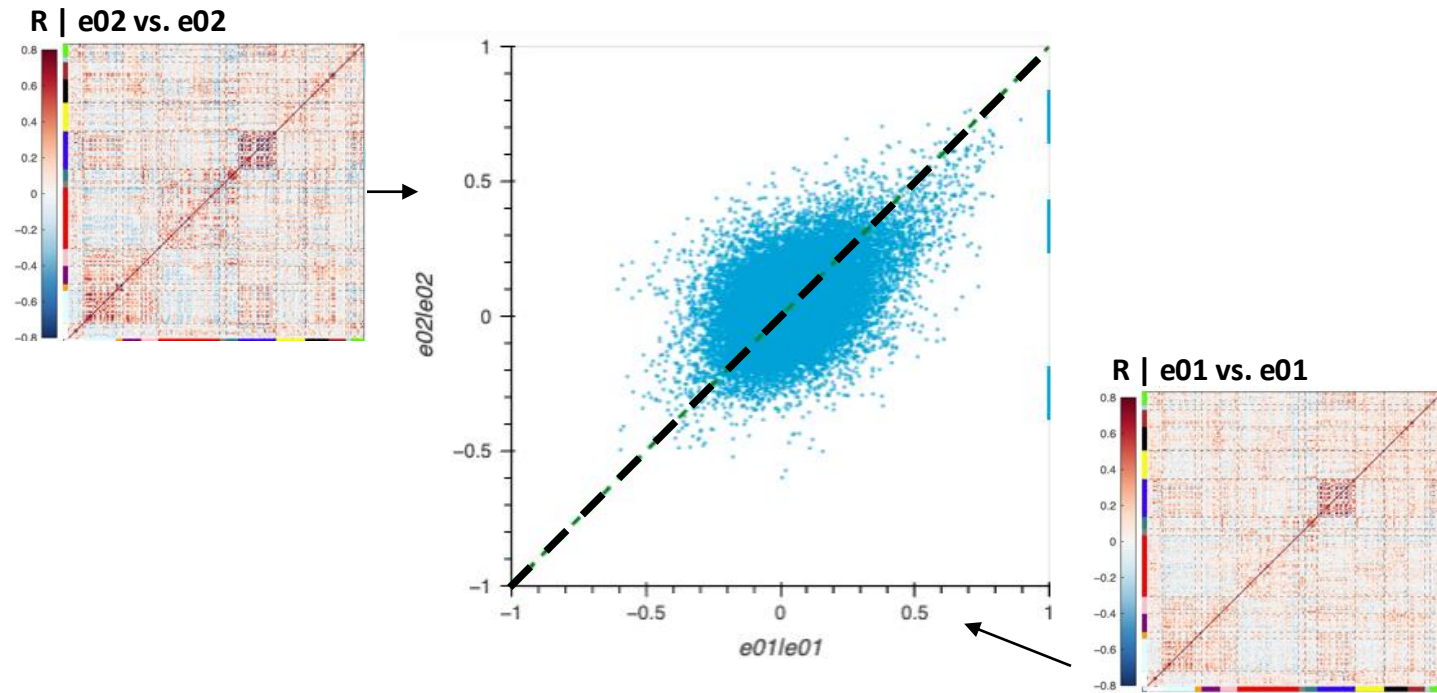
Gonzalez-Castillo et al. BioRxiv (2026)

R and Cov across TEs – Empirical Data

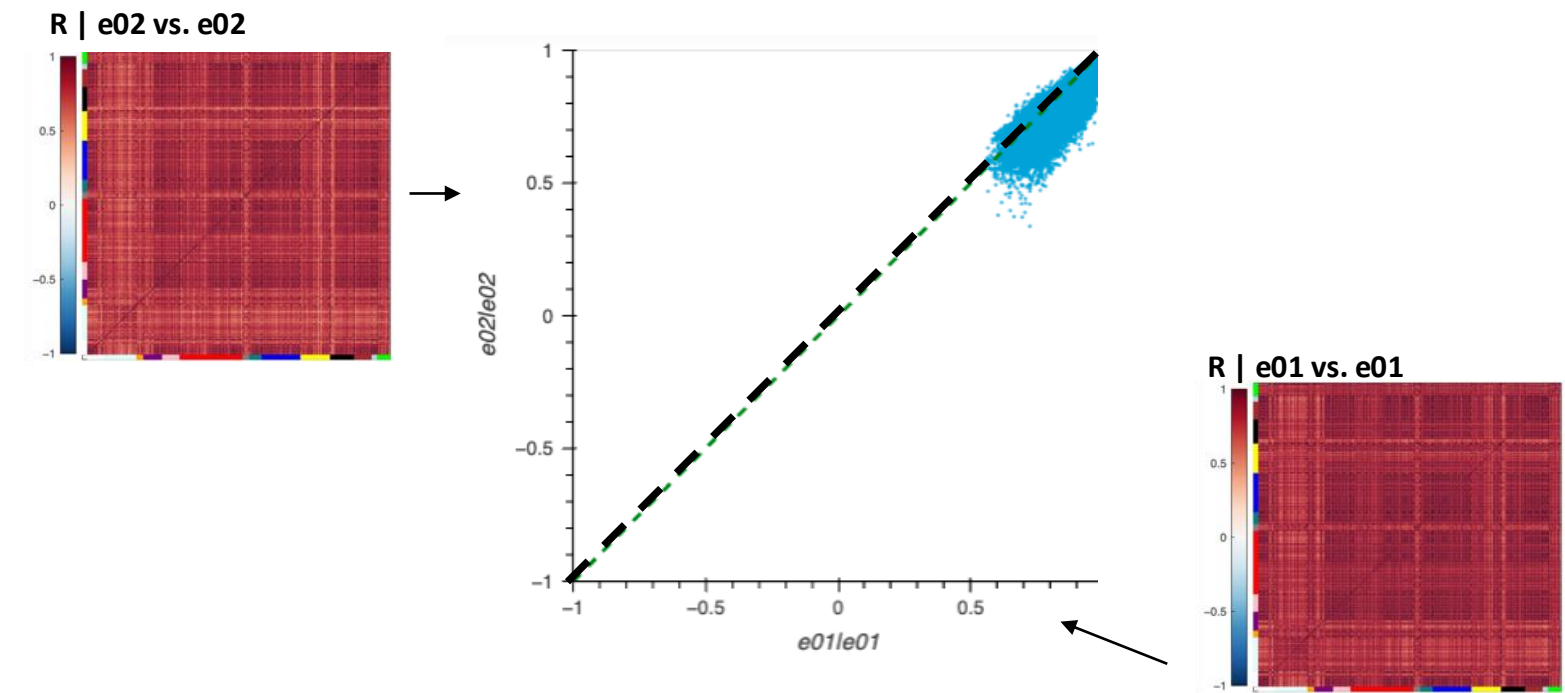
BOLD Dominated Data:
Constant TR + Low Motion + Tedana Denoising

Non-BOLD Dominated Data:
Variable TR + Basic Denoising

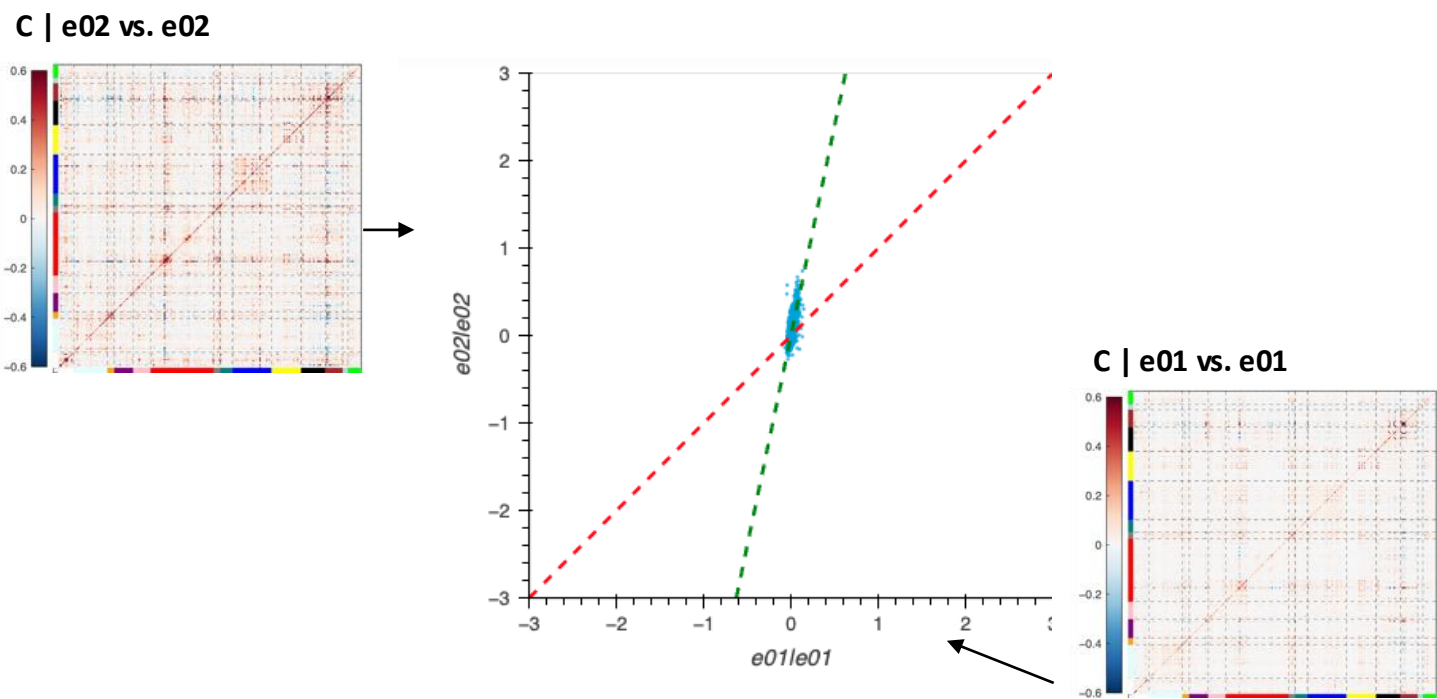
FC as Pearson's Correlation



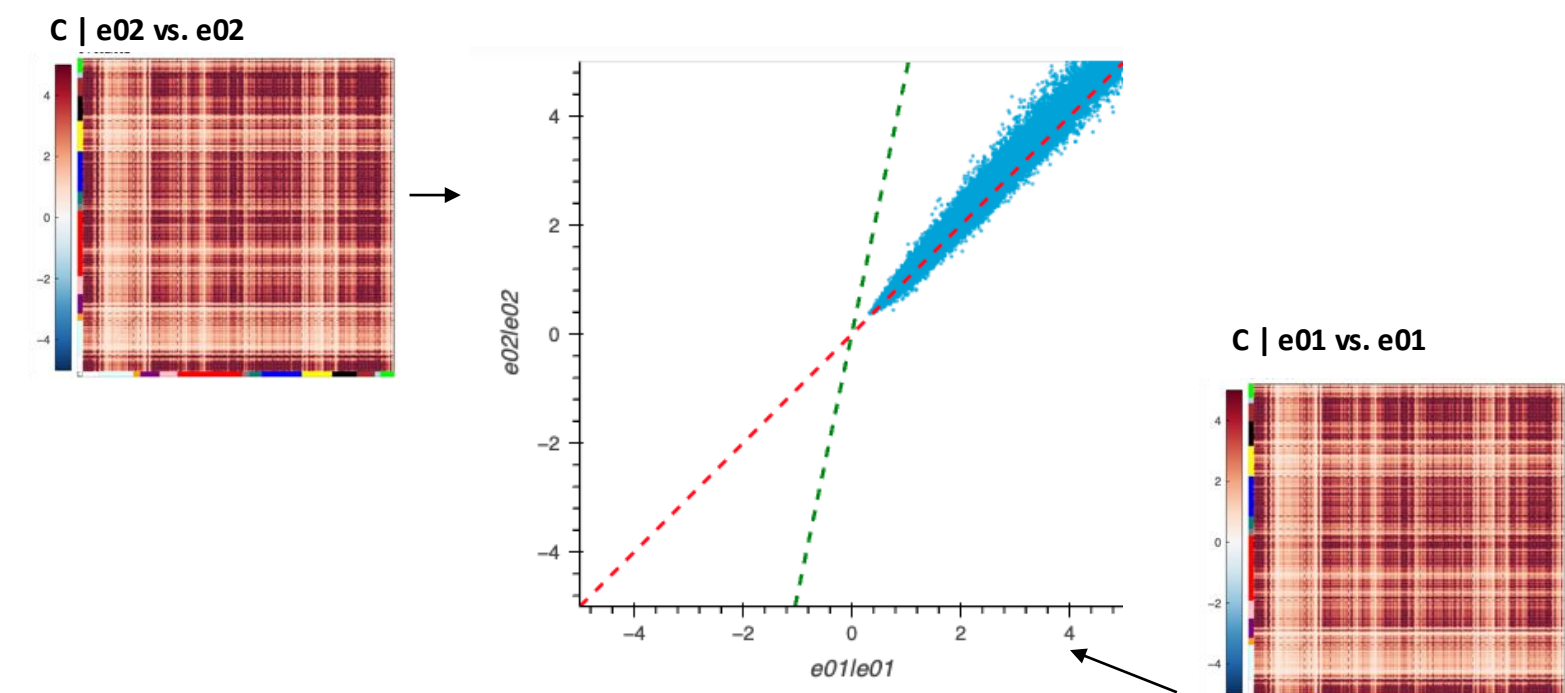
Same Behavior



FC as Covariance



Differential Behavior



Gonzalez-Castillo et al. BioRxiv (2026)

How to quantify this: p_{BOLD}

- 1) Compute $FC_C[(x, y), TE_i, TE_j]$
- 2) Compute $FC_C[(x, y), TE_k, TE_l]$
- 3) Create scatter plot
- 4) Estimate $d_{So} \forall edges$
- 5) Estimate $d_{BOLD} \forall edges$

6) Given d_{So} , d_{BOLD} & $\delta = 10^{-3}$, compute pref. towards BOLD line:

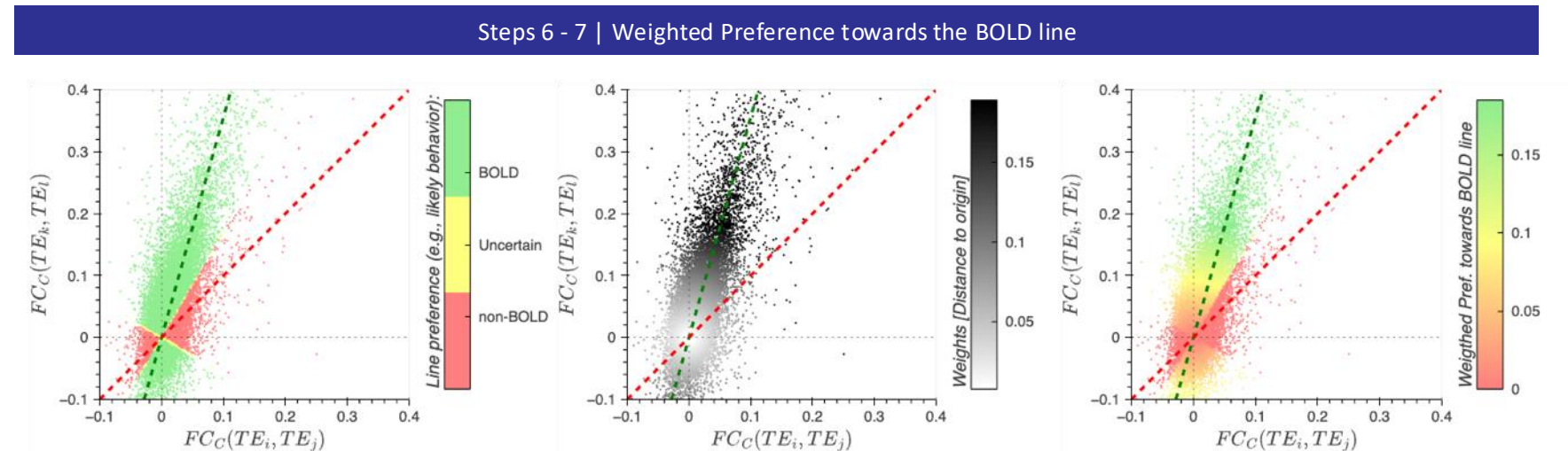
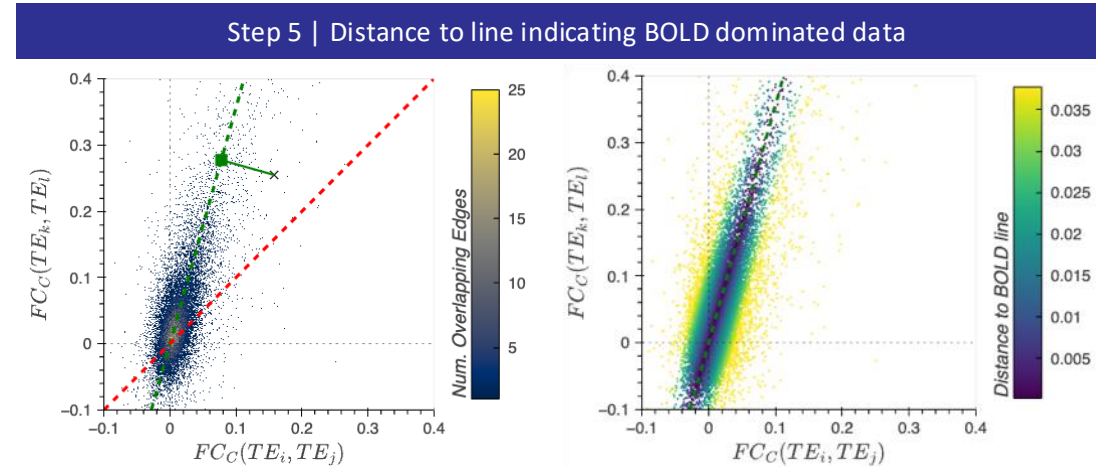
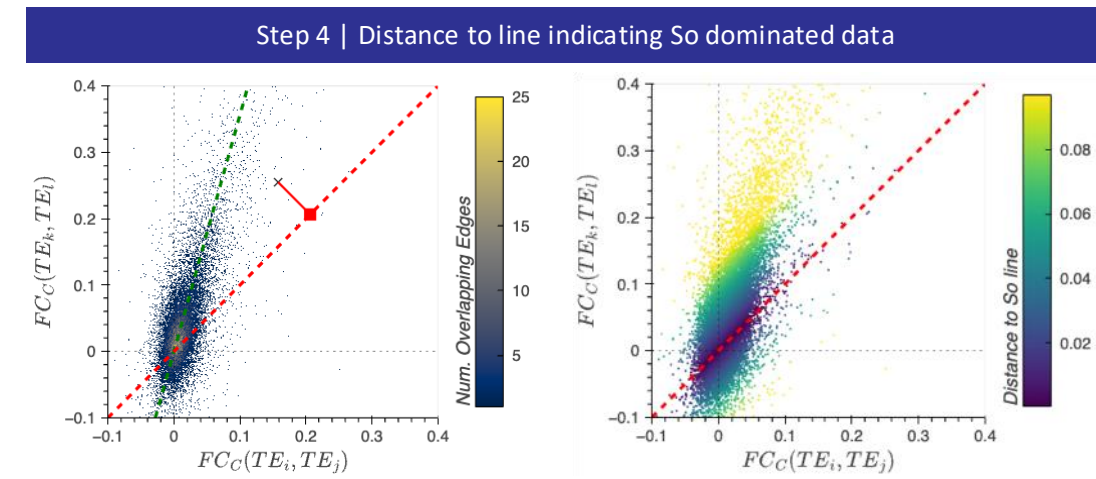
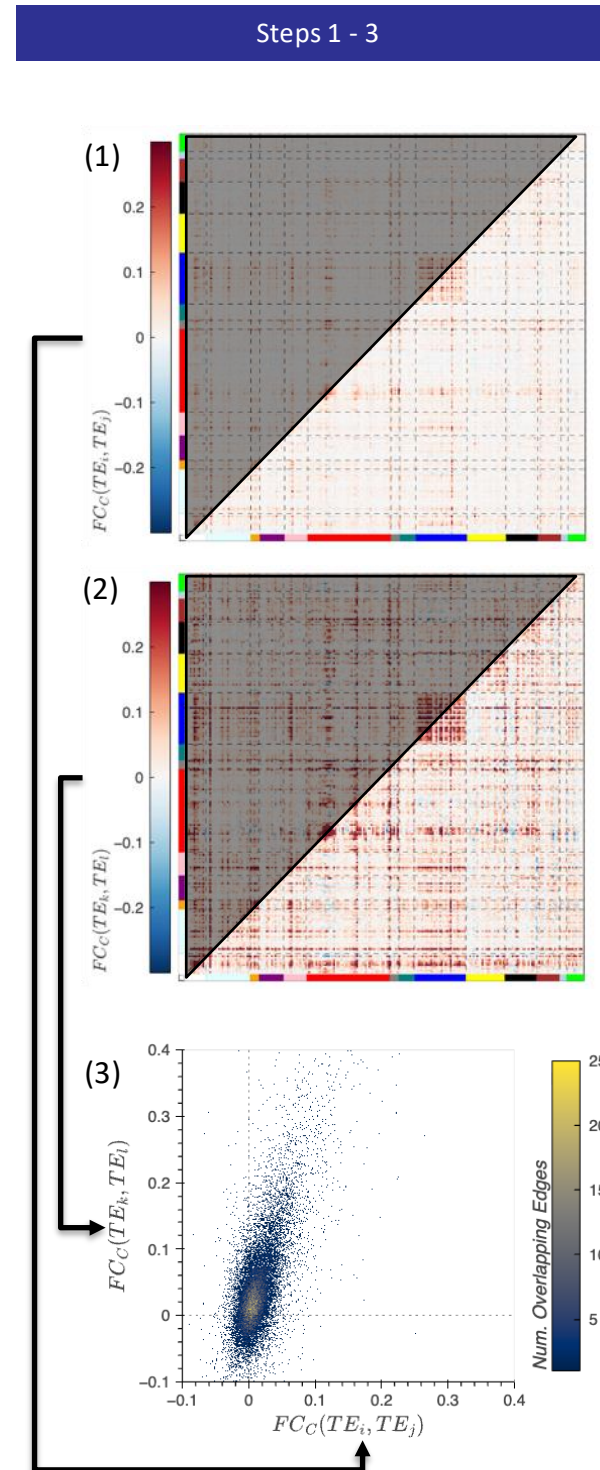
$$pref_to_BOLD_{(x,y)} = \begin{cases} 1 & \text{if } dBOLD_{(x,y)} > dSo_{(x,y)} + \delta \\ 0 & \text{if } dBOLD_{(x,y)} < dSo_{(x,y)} + \delta \\ 0.5 & \text{otherwise} \end{cases}$$

7) To minimize the influence of edges near the origin, we weight BOLD preference by distance to the origin ($w_{(x,y)}$).

$$W_{pref_to_BOLD_{(x,y)}} = w_{(x,y)} \cdot pref_to_BOLD_{(x,y)}$$

8) Average across all edges

$$p_{BOLD}^{(TE_i, TE_j), (TE_k, TE_l)} = \frac{\sum_{(x,y)} W_{(x,y)} \cdot pref_to_BOLD_{(x,y)}}{\sum_{(x,y)} W_{(x,y)}}$$



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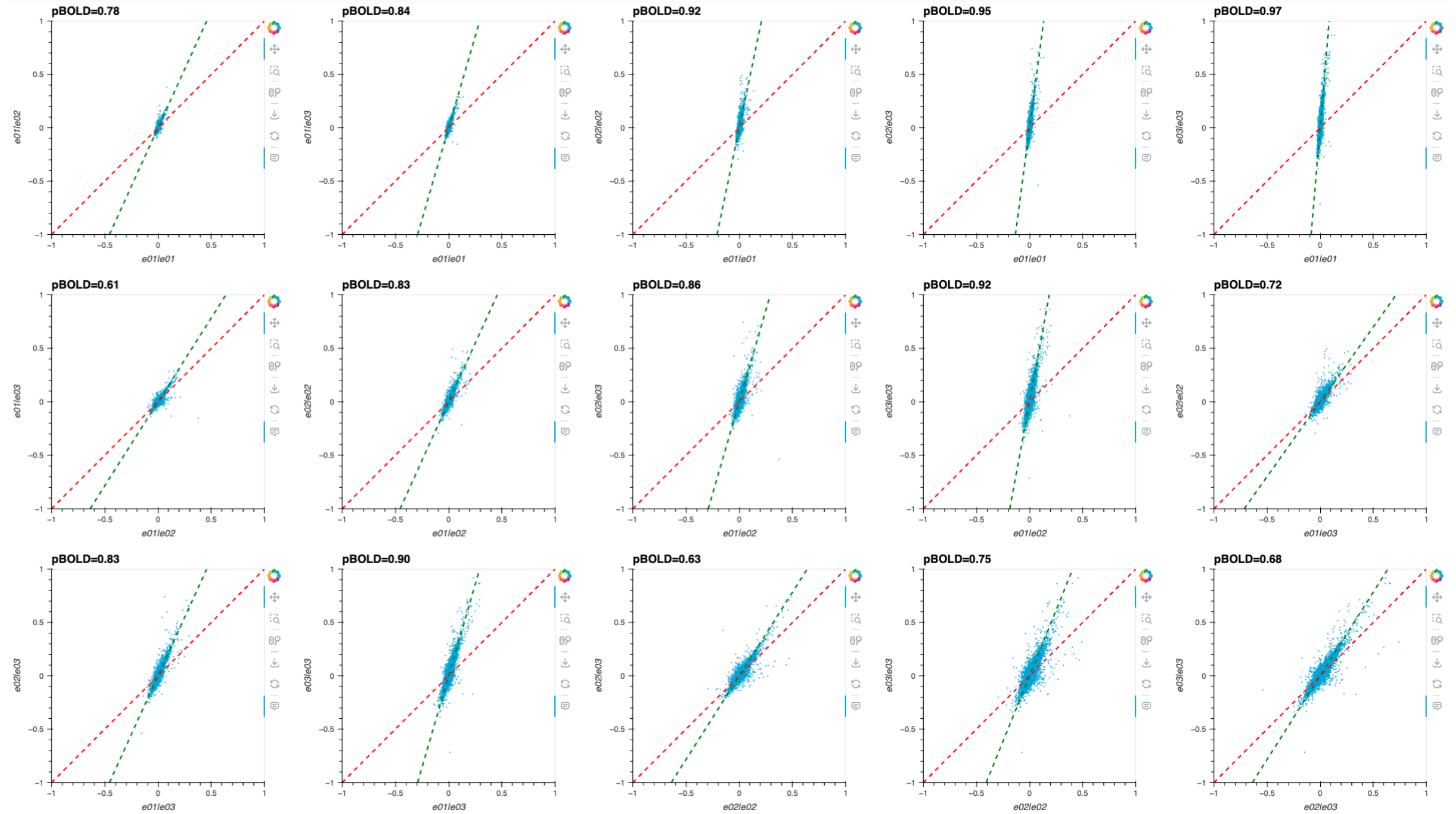
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Gonzalez-Castillo et al. BioRxiv (2026)

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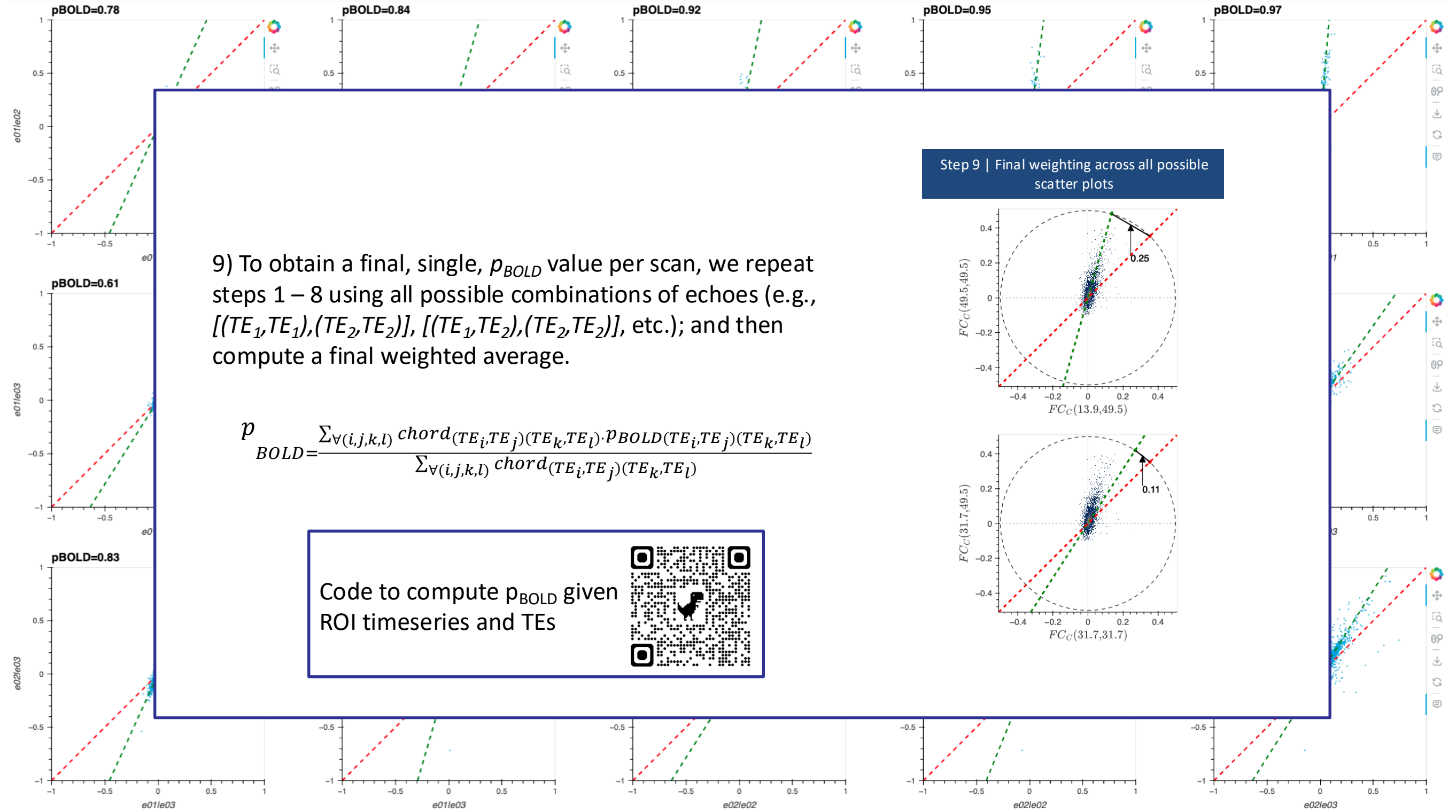
$$pref_to_BOLD_{(x,y)} = \begin{cases} 1 & \text{if } dBOLD_{(x,y)} > dSo_{(x,y)} + \delta \\ 0 & \text{if } dBOLD_{(x,y)} < dSo_{(x,y)} + \delta \\ 0.5 & \text{otherwise} \end{cases}$$

- 7) To minimize the influence of edges near the origin, we weight BOLD preference by distance to the origin ($w_{(x,y)}$).

$$W_{pref_to_BOLD_{(x,y)}} = w_{(x,y)} \cdot pref_to_BOLD_{(x,y)}$$

- 8) Average across all edges

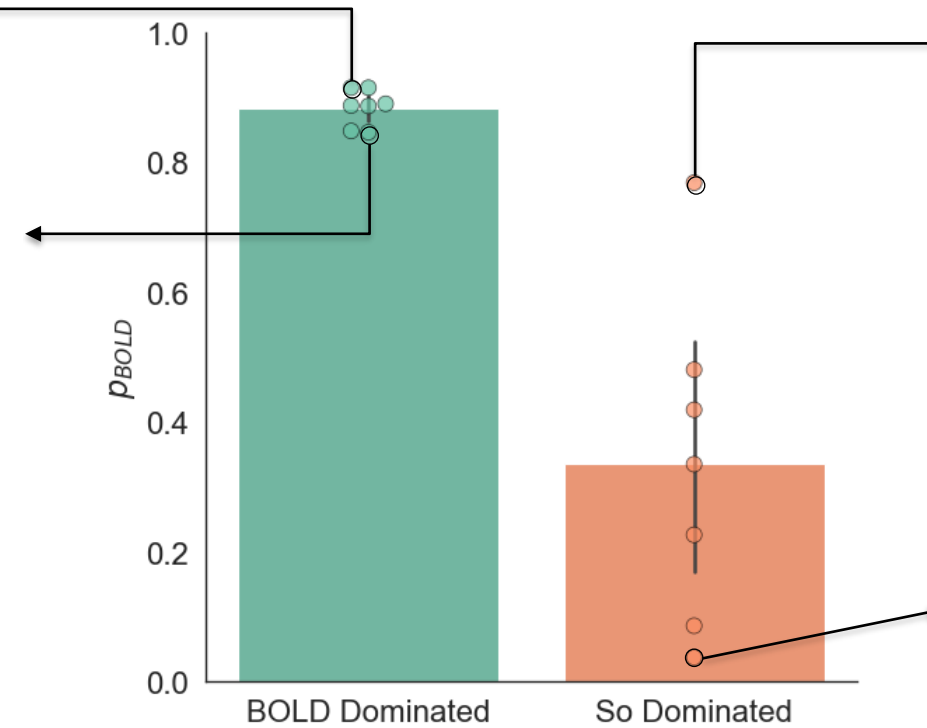
$$p_{BOLD}^{(TE_i, TE_j), (TE_k, TE_l)} = \frac{\sum_{(x,y)} W_{(x,y)} \cdot pref_to_BOLD_{(x,y)}}{\sum_{(x,y)} W_{(x,y)}}$$



R and Cov across TEs – Empirical Data

Constant-gated scans + Tedana Pre-processing

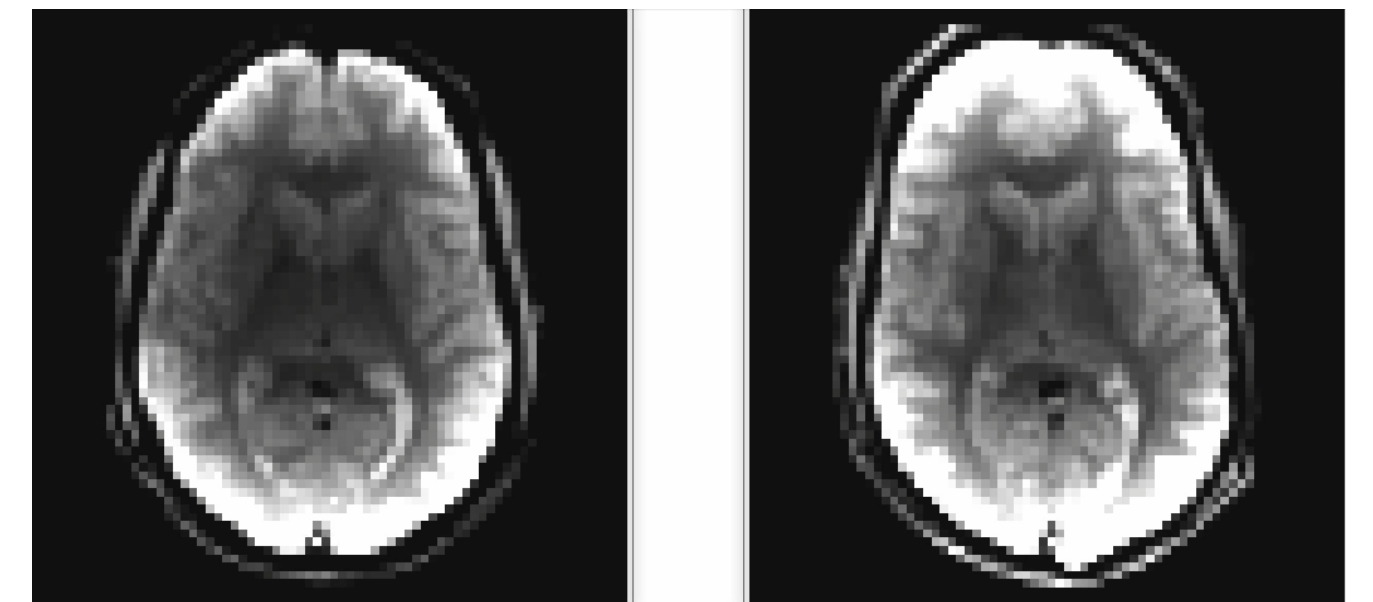
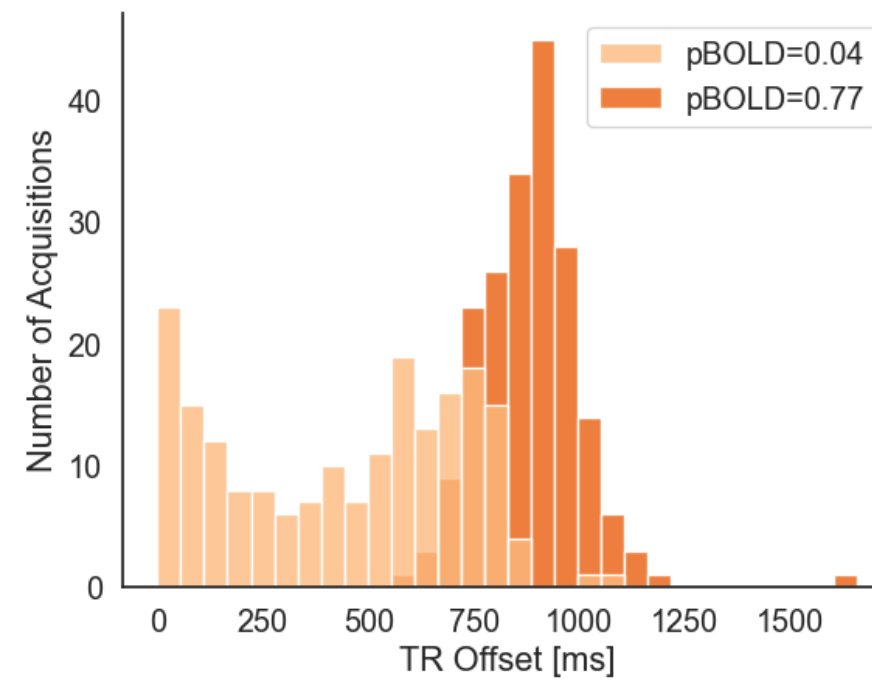
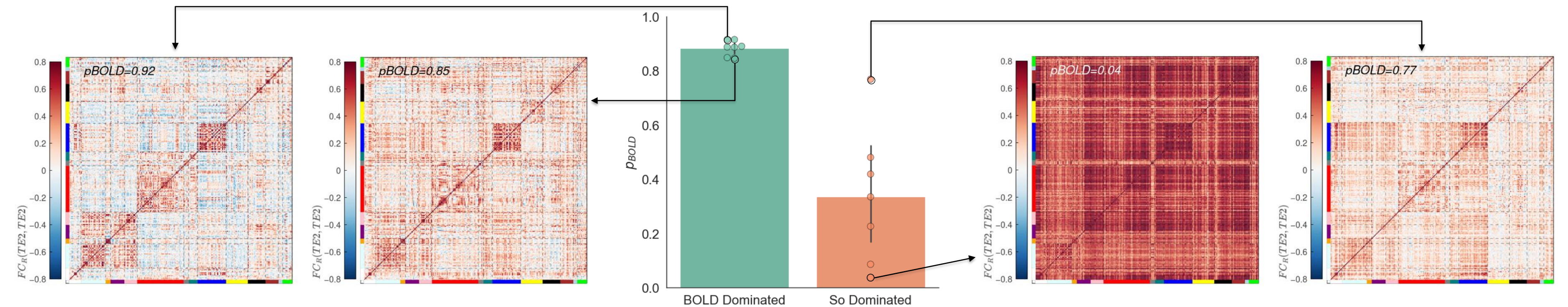
Cardiac-gated scans + Basic Pre-processing



R and Cov across TEs – Empirical Data

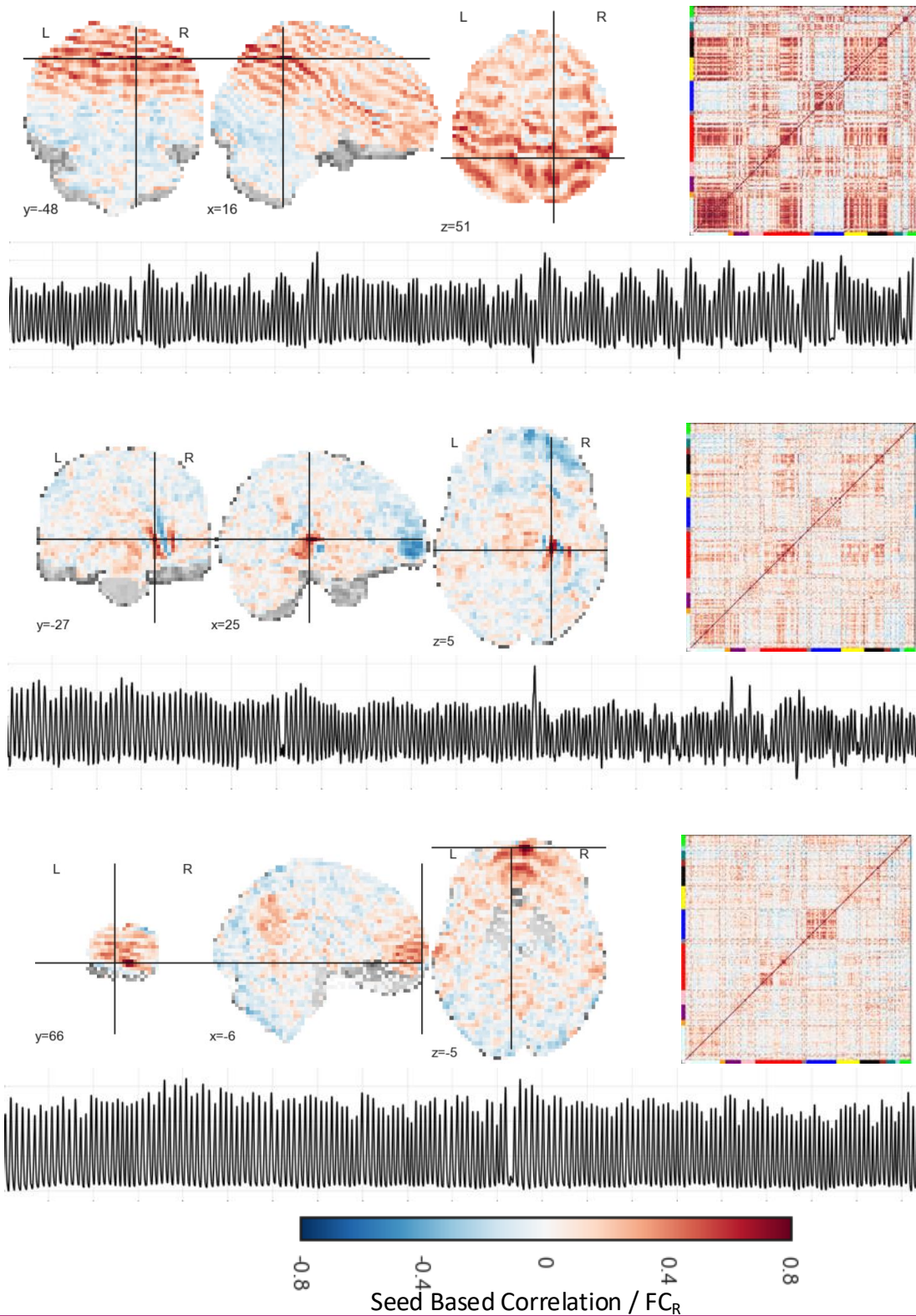
Constant-gated scans + Tedana Pre-processing

Cardiac-gated scans + Basic Pre-processing

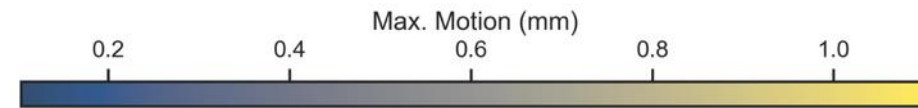


ρ_{BOLD} Applications: Evaluate Individual Scans

Scans deemed problematic only by ρ_{BOLD}



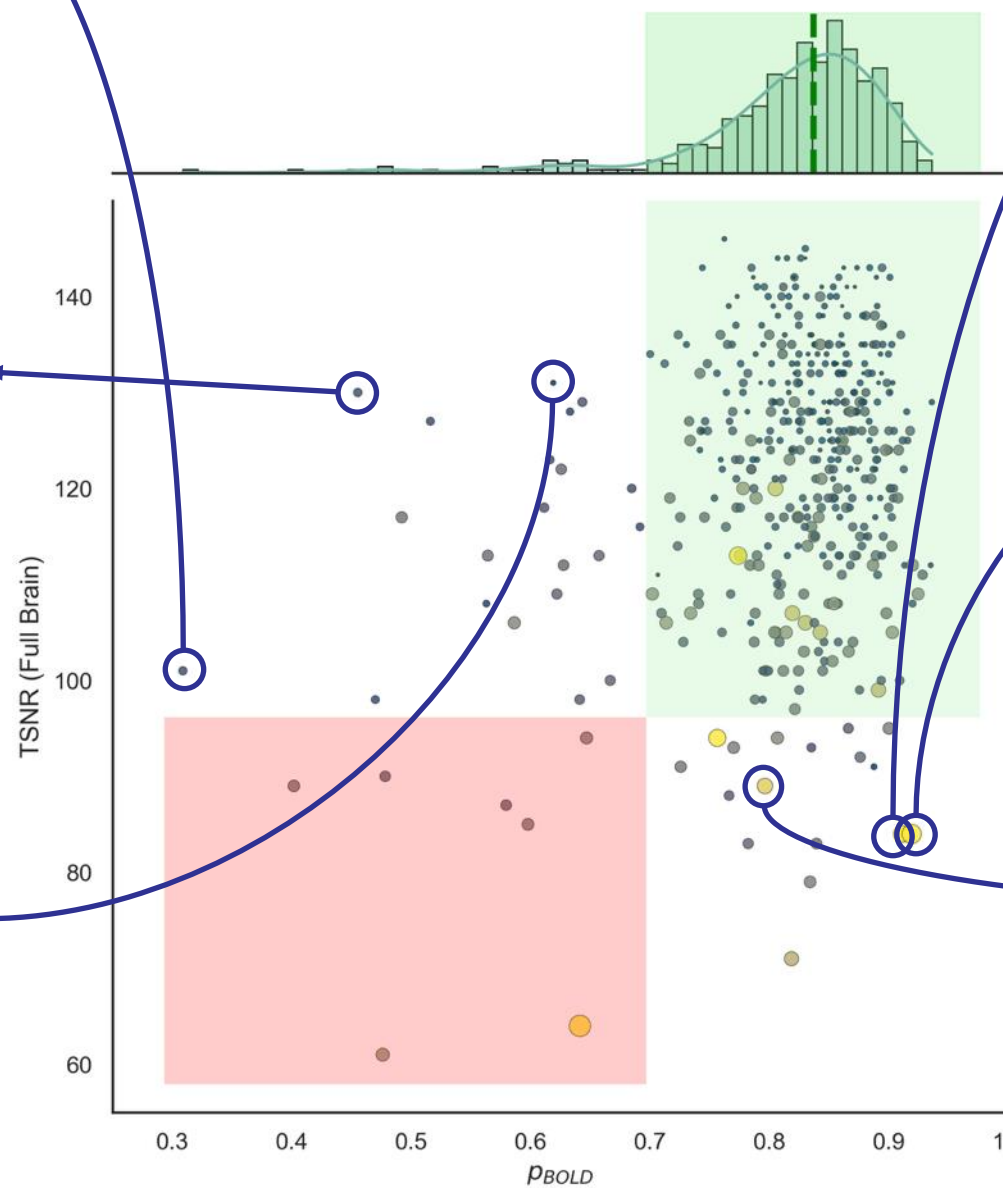
- Site 1 from Spreng et al.: 3T GE MR750 | 32-Channels Coil
- 436 rs-fMRI scans from 221 subjects
- Scan Duration = 10m6s | TR = 3s | # Acqs = 201
- TEs = 13.7 / 30 / 47 ms | Spatial Resolution = 3x3x3 mm³
- Includes behavioral assessments (IQ, personality, etc.)



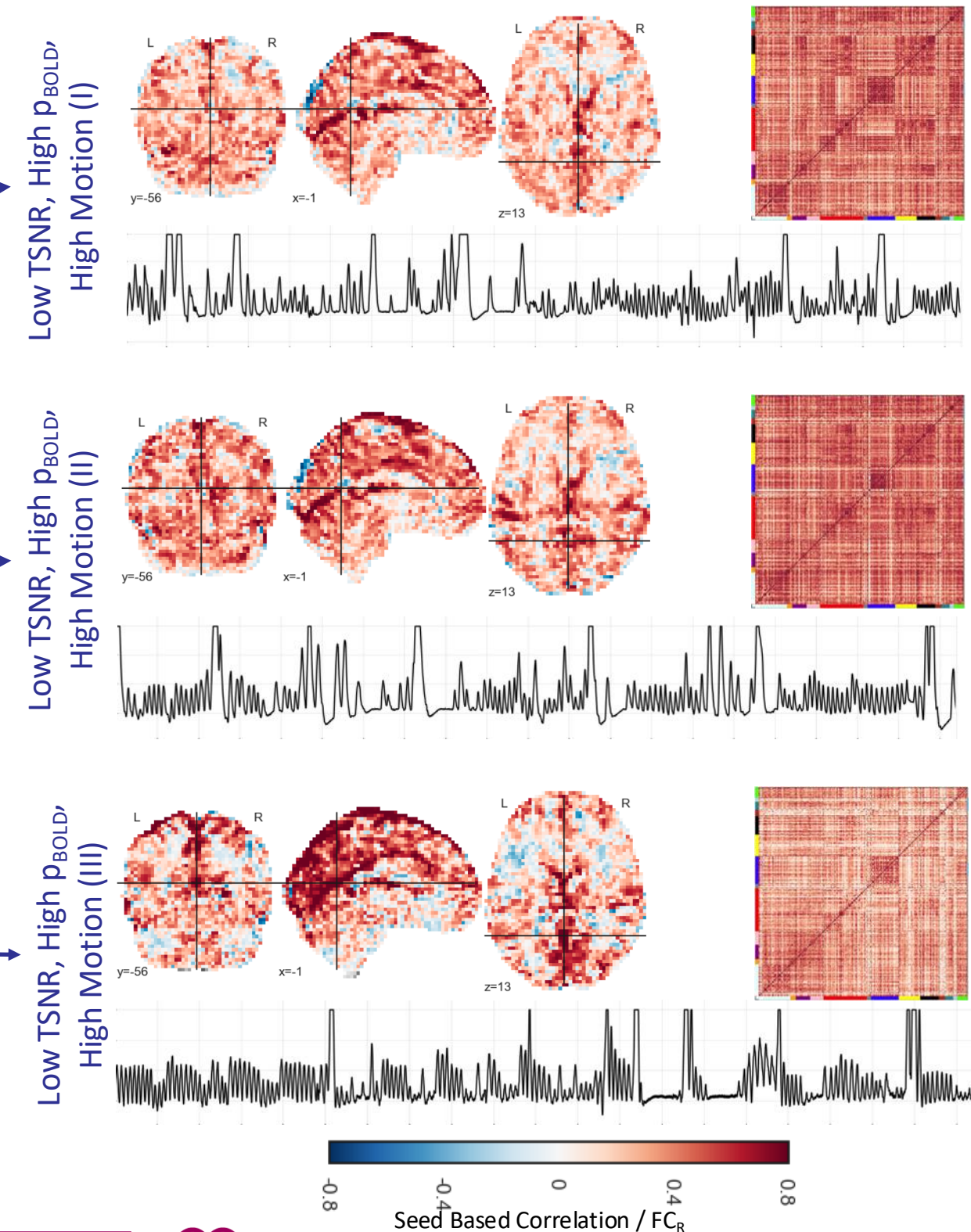
Low ρ_{BOLD} / Medium TSNR

Low ρ_{BOLD} / High TSNR

Med. ρ_{BOLD} / High TSNR



Scans deemed problematic only by TSNR

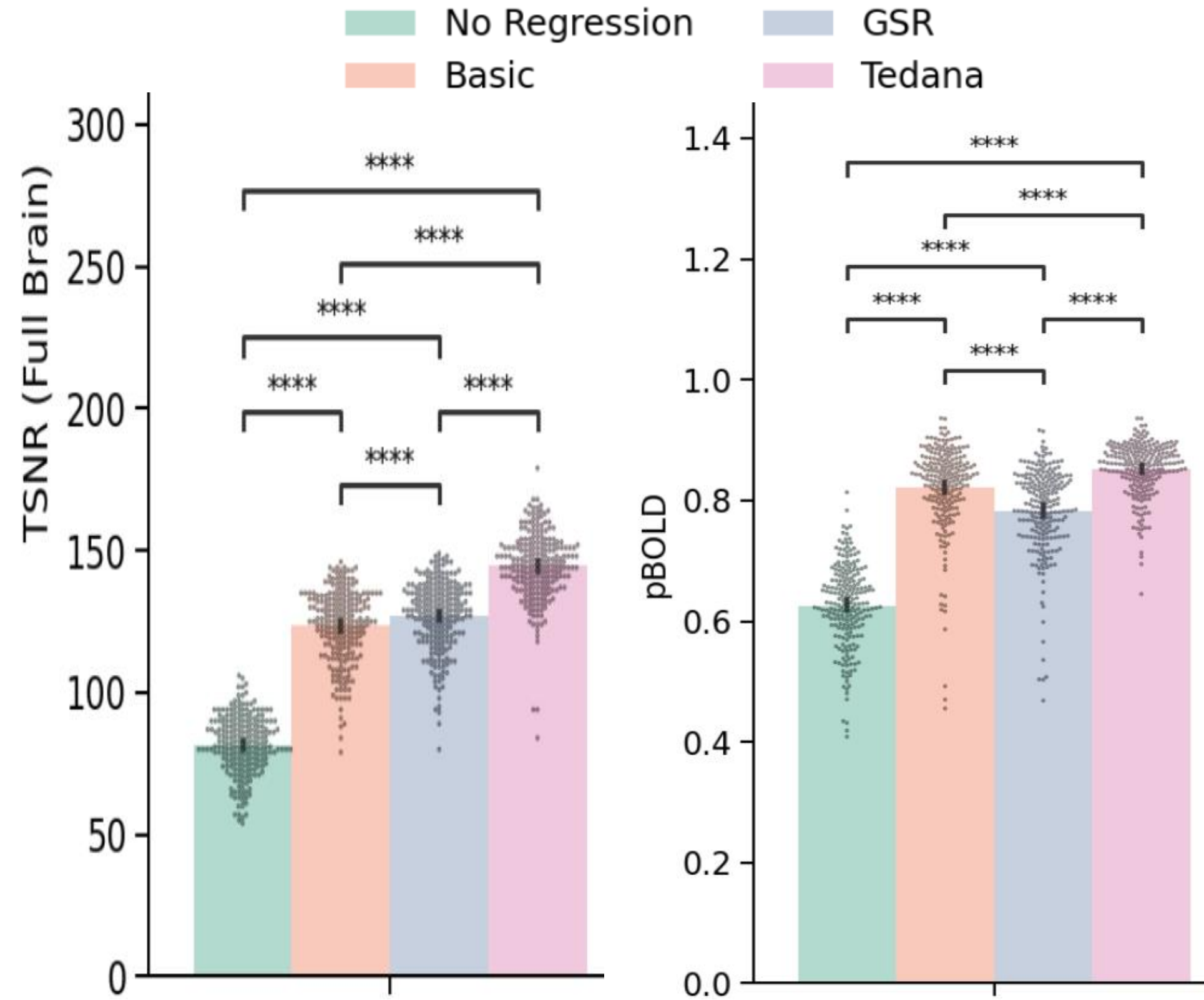


Low TSNR, High ρ_{BOLD} / High Motion (I)

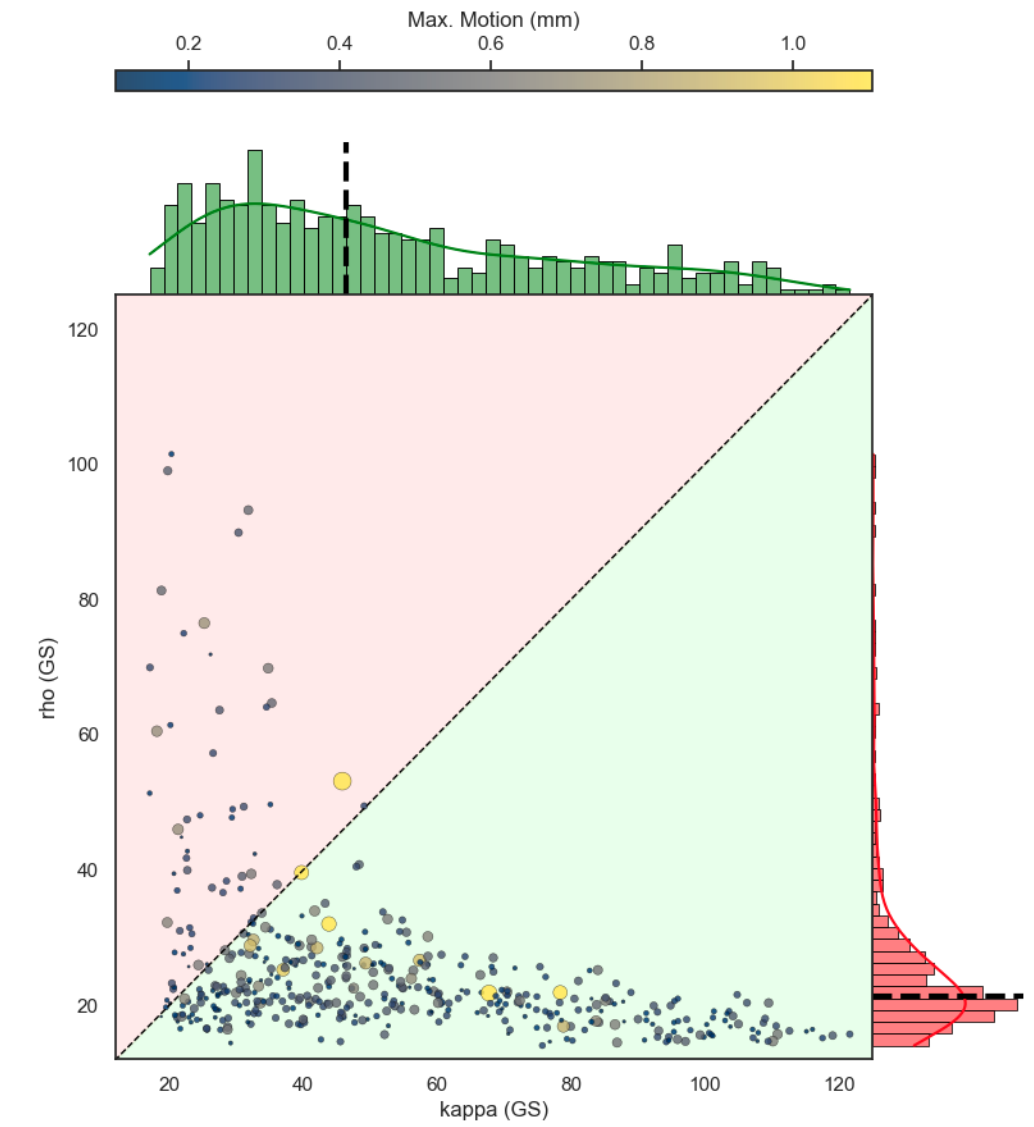
Low TSNR, High ρ_{BOLD} / High Motion (II)

Low TSNR, High ρ_{BOLD} / High Motion (III)

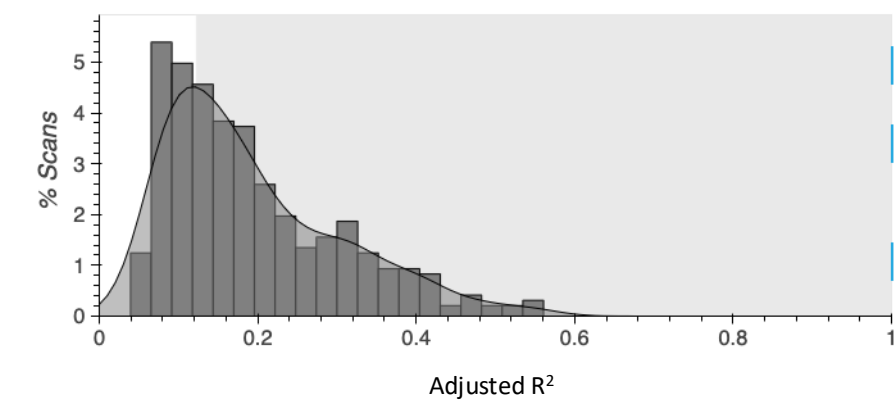
ρ_{BOLD} Applications: Evaluate Pipelines



"BOLDness" of the Global Signal



Relationship to Physiological Regressors



Gonzalez-Castillo et al. BioRxiv (2026)

QA for ME-data: Conclusions

- We can leverage the additional information present in ME data to better assess the quality of our data.
- The proposed metric (p_{BOLD}) provides complementary information to TSNR.
- Demonstrated p_{BOLD} applications in two scenarios:
 - Detection of problematic scans.
 - Comparison of pre-processing pipelines.
- Because not all BOLD is good BOLD, p_{BOLD} ought to be interpreted cautiously.
- The same principle applies to voxel-wise covariance \rightarrow working on an alternative metric at the voxel level.

Preprint



Code to compute p_{BOLD} given ROI timeseries and TEs



How to take advantage of all this extra info

Automatic Denoising (tedana, ME-ICA, tedana + NN)

ME Hemodynamic
Deconvolution

ME Quality
Assurance (p_{BOLD})

Study signals from
non-GM
compartments



How to take advantage of all this extra info

Automatic Denoising (tedana, ME-ICA, tedana + NN)

ME Hemodynamic
Deconvolution

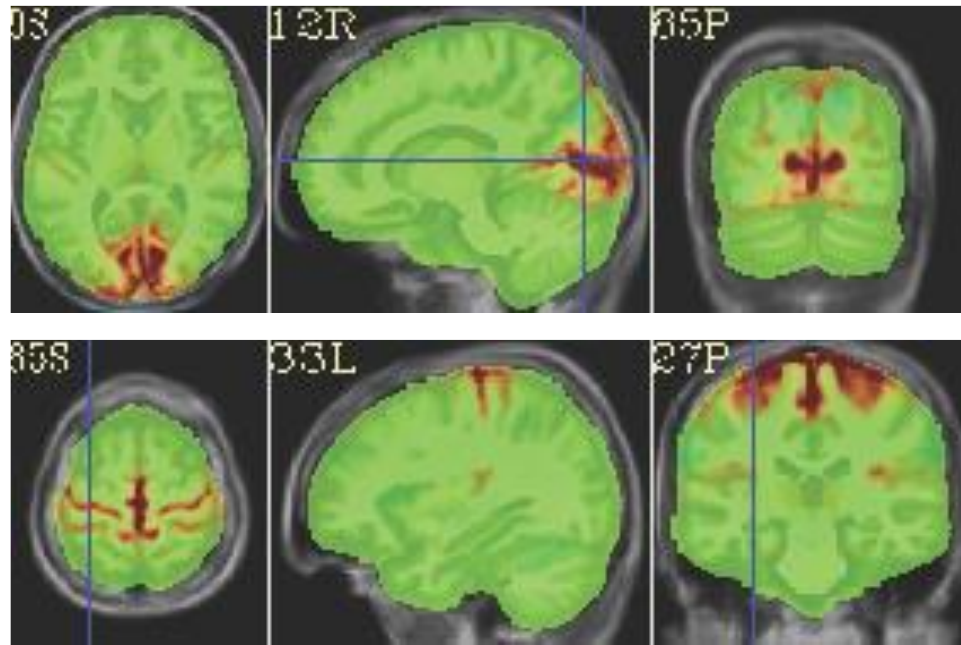
ME Quality
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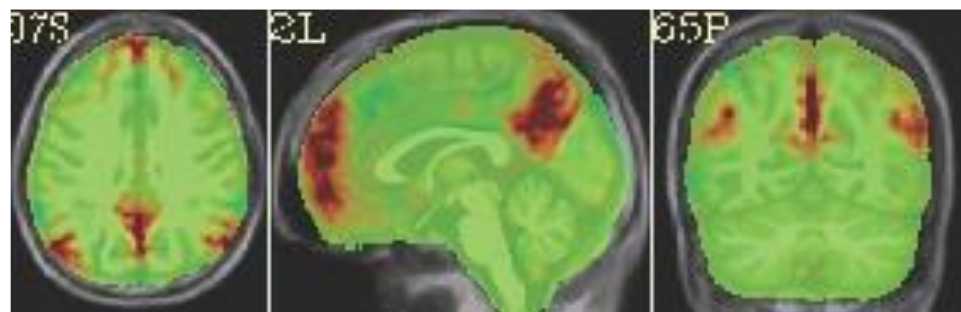


ME Components Exploration

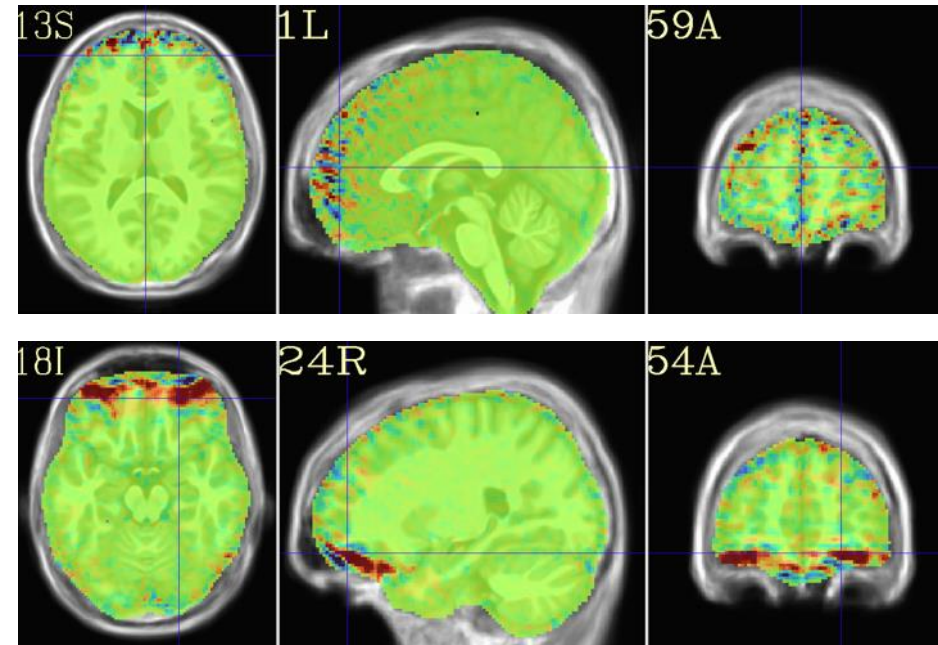
Components of interest



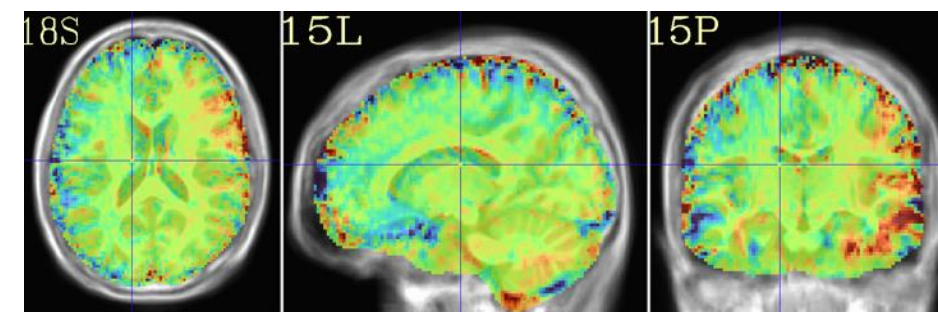
⋮



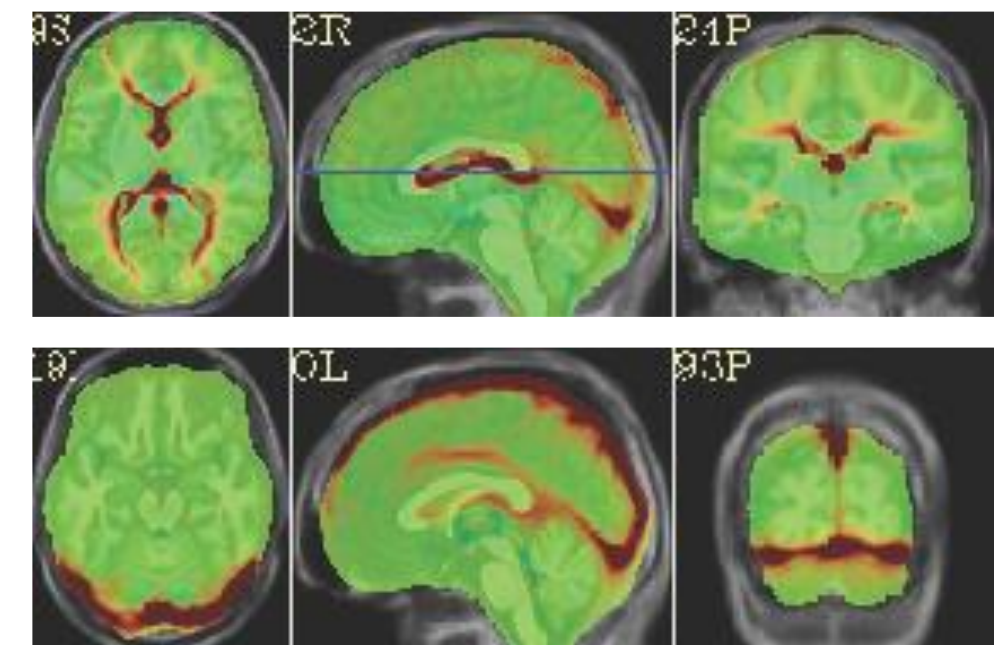
Components to remove



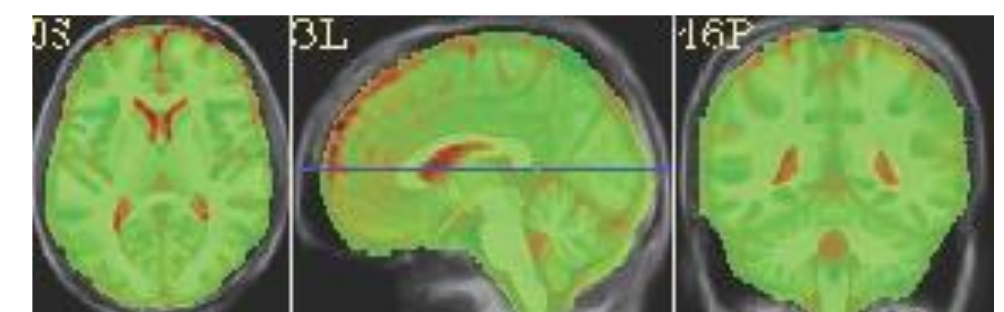
⋮



Other Components

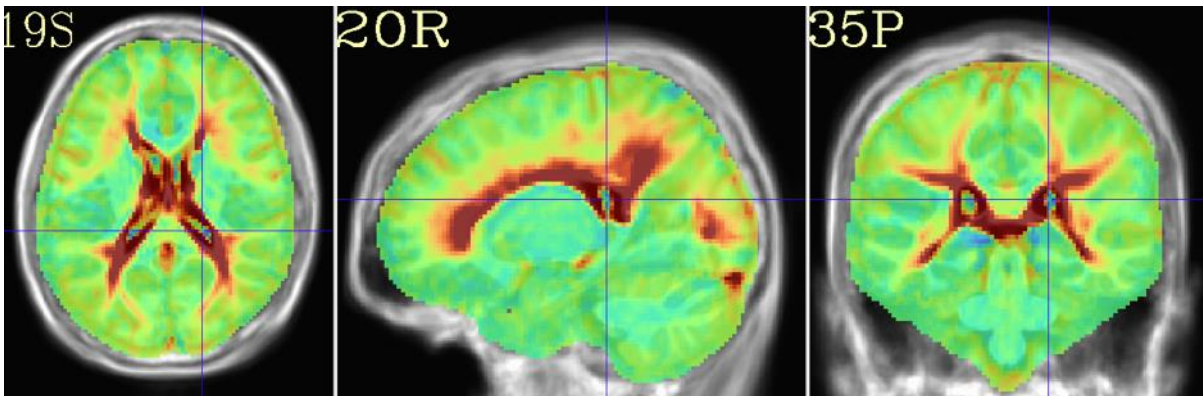


⋮

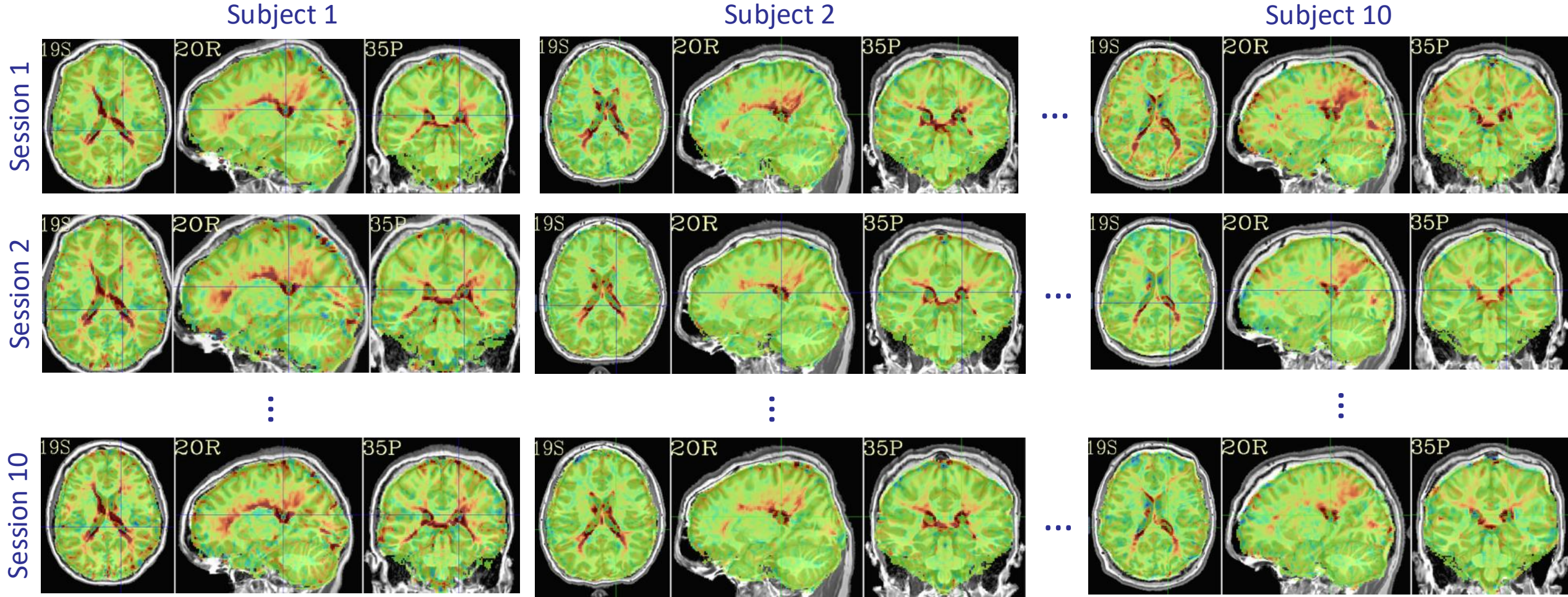


Example: Periventricular + WM Component

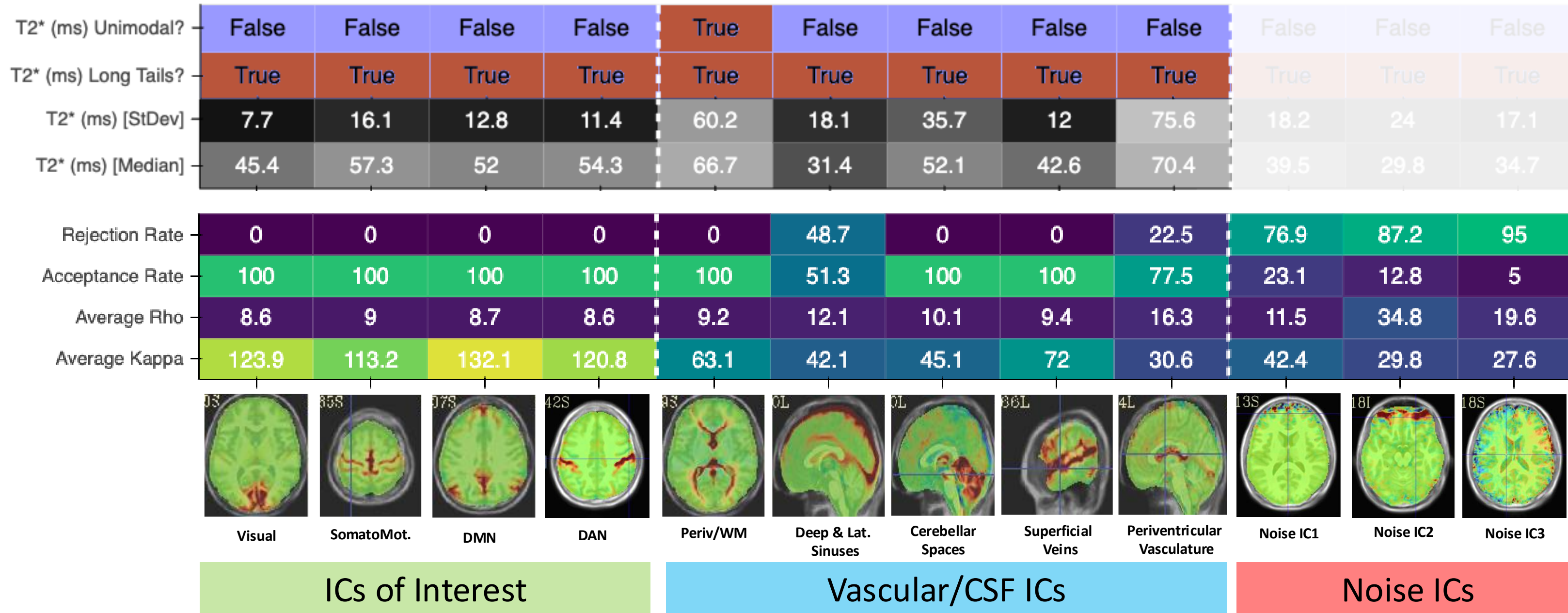
Group-Level (gRAICAR)



Reproducible across subjects and sessions? ✓



Other components of interest...



Poster #2481 (Wednesday / Thursday)

Deconvolution

ME-QC

Non-GM Compartments

Now that I have ME data, what can I do?

Automatic Denoising (tedana, ME-ICA, tedana + NN)

Improve data quality, increase sensitivity, scan less...

ME Hemodynamic Deconvolution

Reliably detect individual events without a priori information about their timing

Estimates have interpretable units [s^{-1}] that proved to be within physiologically plausible limits



ME Specific QA

Inter-regional covariance as a way to quantify how much BOLD dominates over other fluctuations (p_{BOLD})

Provides complementary information to TSNR

Scenarios: problematic scan detection, pipeline evaluation



Characterize Non-GM components with ME

Kappa, Rho, etc. provide information about BOLD content

T2* map provide information about contributing tissue compartments

Reliably detect components for WM vasculature, deep and lateral sinuses, and superficial veins

Poster #2481
(Wednesday / Thursday)

Thank You



Peter
Bandettini



Daniel
Handwerker



Marly
Rubin



Puja
Panwar



BASQUE CENTER
ON COGNITION, BRAIN
AND LANGUAGE



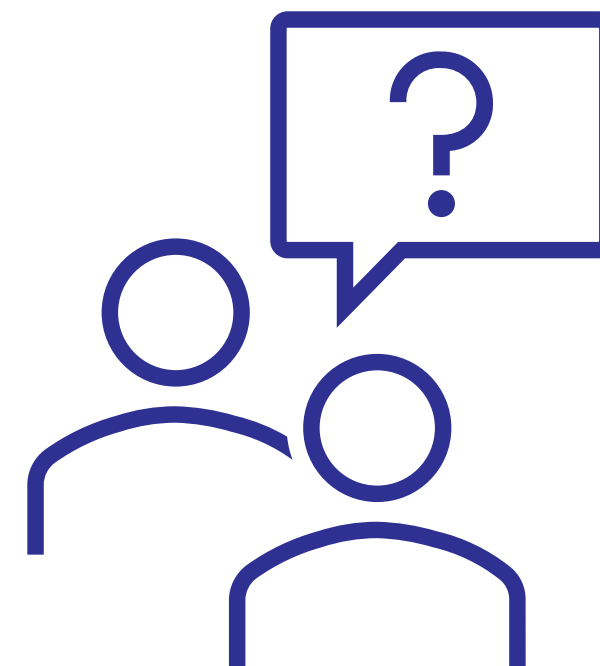
Cesar
Caballero-Gaudes



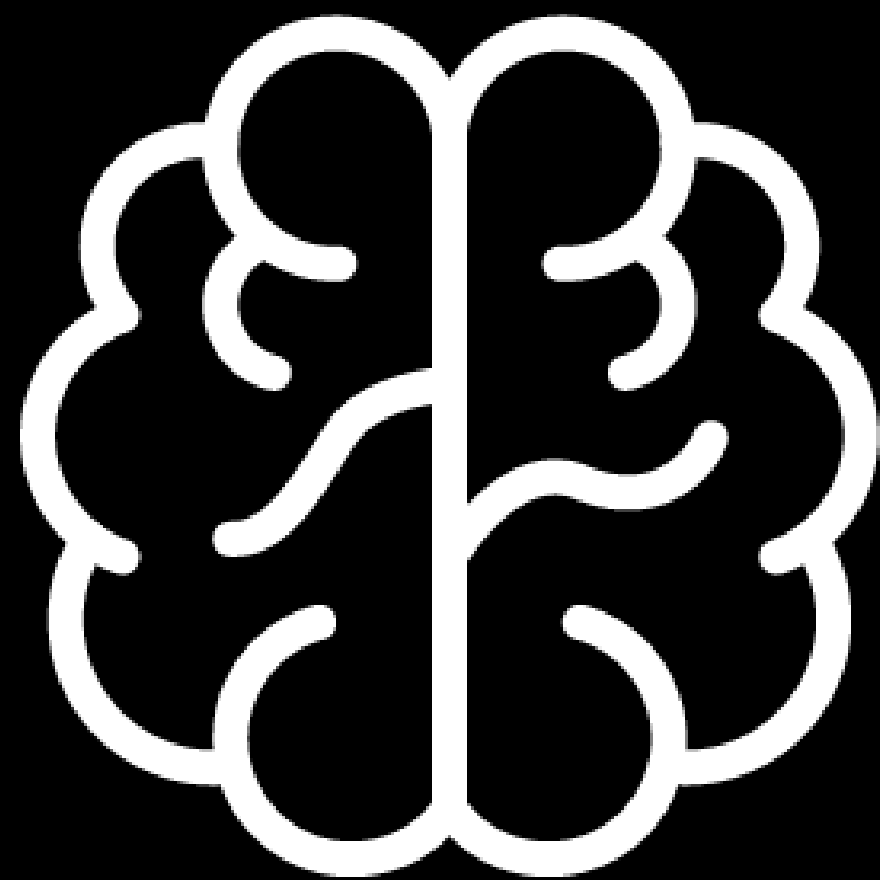
Stefano
Moia
(now @ Maastricht University)



Eneko
Uruñuela
(now @ Univ. of Calgary)



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