

Practical multi-echo fMRI:
Underlying principles, challenges,
potential, & applications

Introduction to
multi-echo fMRI & tedana

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Section on Functional Imaging Methods

Laboratory of Brain and Cognition

Intramural Research Program

National Institute of Mental Health

OHBM 2026 DISCLOSURES

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

COURSE OVERVIEW

INTRODUCTION & CONCEPTS

9:00	Dan Handwerker (+ Sarah Goodale): Introduction to multi-echo fMRI and tedana
9:50	Mélanie Garcia: Multi-echo fMRI data quality control
10:25	Javier Gonzalez-Castillo: Now that I have multi-echo data, what else can I do with it?
11:00	Discussion and Q&A: Best practices for collecting and validating multi-echo fMRI data
11:20	Break

RESEARCH & CLINICAL APPLICATIONS

11:30	Eric Pierre: Multi-echo fMRI in a large clinical study — insights from the Australian Epilepsy Project
12:05	Eui-Jin Jung: Enhancing predictive modeling using multi-echo fMRI in pain
12:40	Lunch break 🥪🧀🍇 with informal Q&A for the final 20 minutes of the break
13:40	Julia Moser: Multi-echo fMRI in developmental neuroimaging
14:15	Discussion and Q&A: Advice & challenges for using multi-echo fMRI in clinical studies

PUSHING METHODS

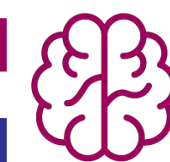
14:35	Kathryn Lamar-Bruno: Benefits and challenges of Echo Planar Time-Resolved Imaging (EPTI) for multi-echo fMRI
15:10	Nathan Spreng + Prantik Kundu: Subcortical connectivity at 3T & 7T with ME fMRI
15:45	Break
15:55	Logan Dowdle: The higher the field, the faster it falls — challenges and opportunities of multi-echo fMRI at 7T
16:40	Eneko Uruñuela: Is generative AI the next step in multi-echo fMRI denoising?
17:05	Panel Discussion and Q&A: Unmet needs, future goals and challenges

This schedule & other resources including a fast OHBM abstract browser



TALK OVERVIEW

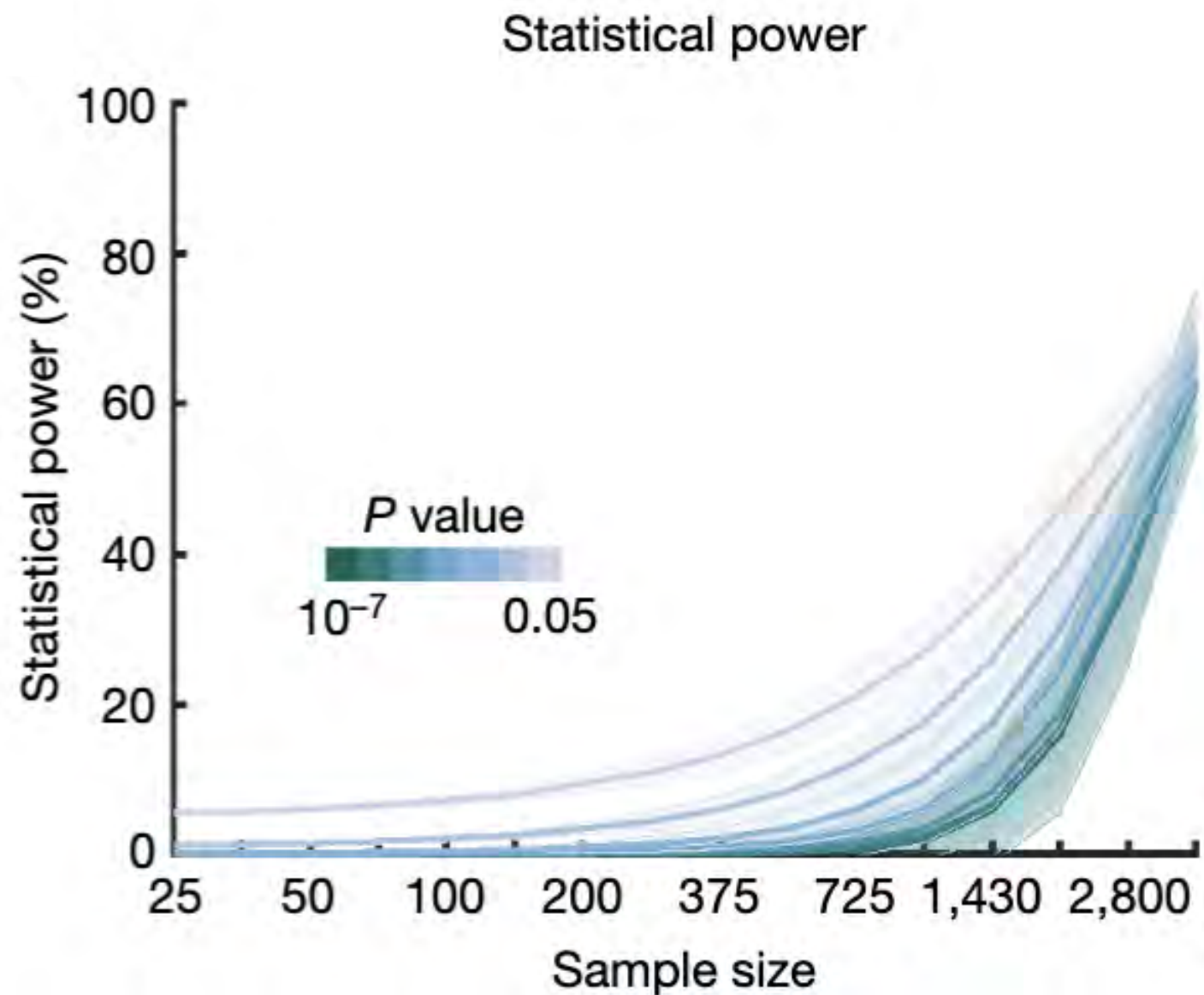
- General Intro
 - Why care about multi-echo fMRI?
 - A bit of history
 - What is multi-echo fMRI?
- Multi-echo denoising
 - General concepts
 - ICA-based denoising (ME-ICA & tedana)
 - Multi-echo and external regressors for ICA (Sarah Goodale)
- Resources for learning more
- What to expect across the day



WHY CARE ABOUT MULTI-ECHO FMRI?

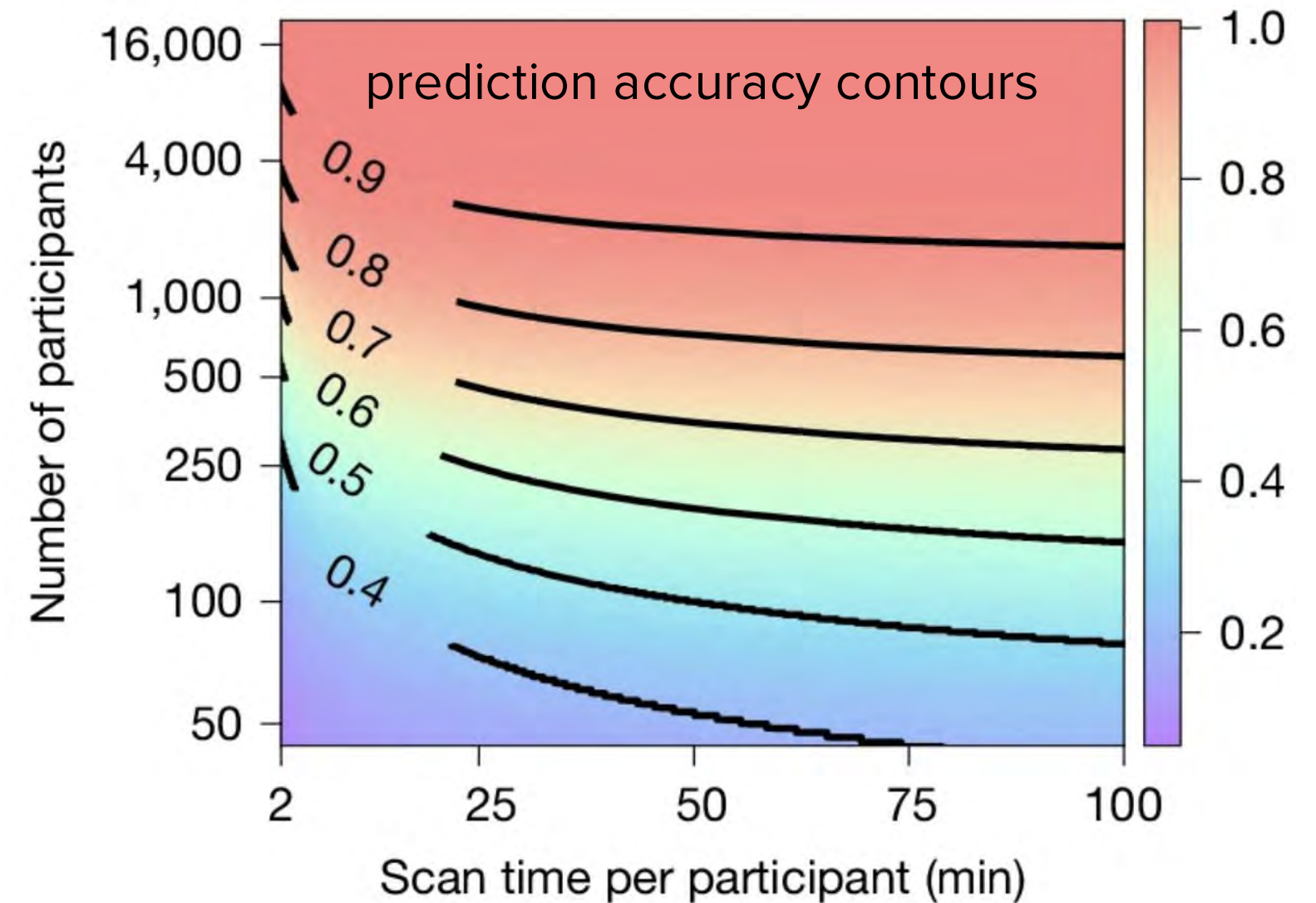
Designing a good fMRI study

How many participants?



Marek, Tervo-Clemmens, et. al. *Nature* 2022
Reproducible brain-wide association studies require thousands of individuals

Scan time per participant?

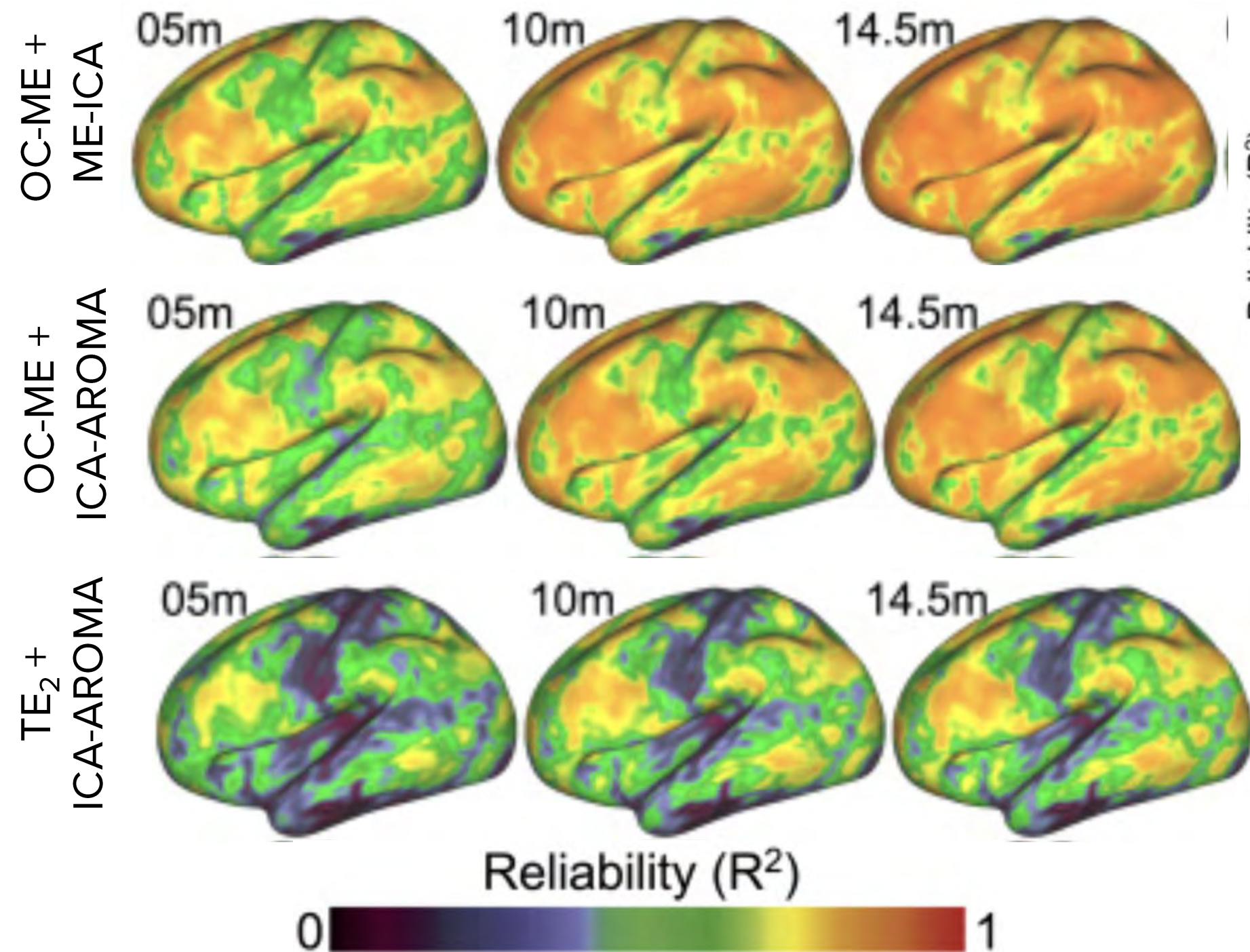


Ooi, Orban, et. al. *Nature* 2024
Longer scans boost prediction and cut costs in brain-wide association studies

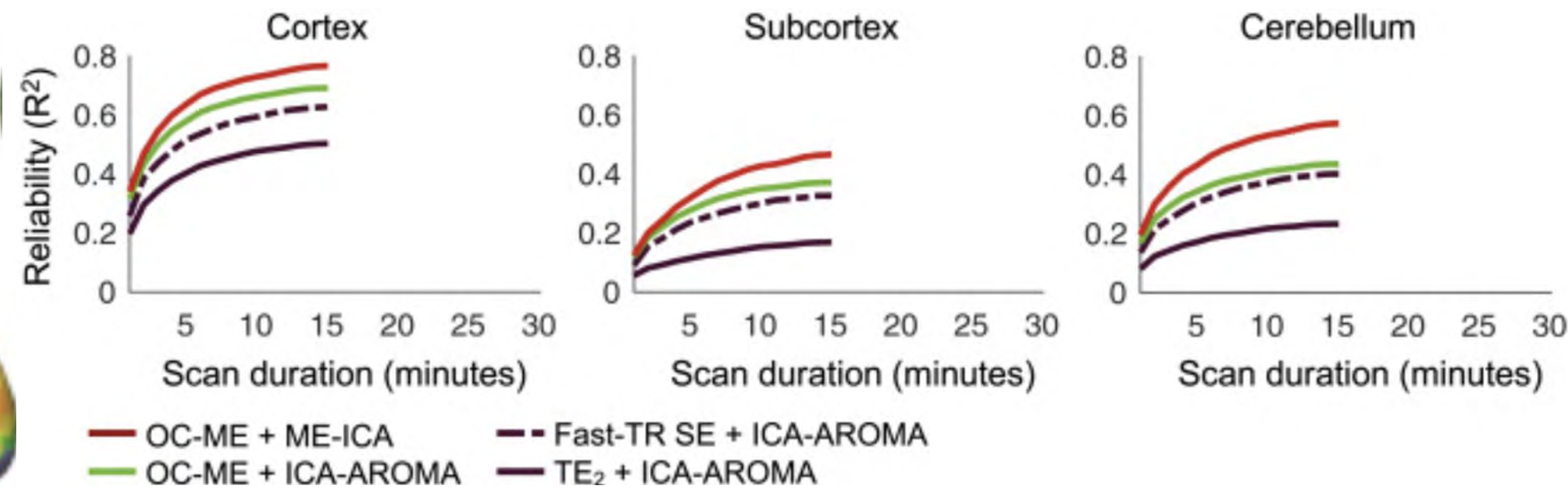
Scan duration is one of multiple ways to improve intra-subject data quality

MULTI-ECHO FMRI IMPROVES DATA

Reliability map, sbj ME01



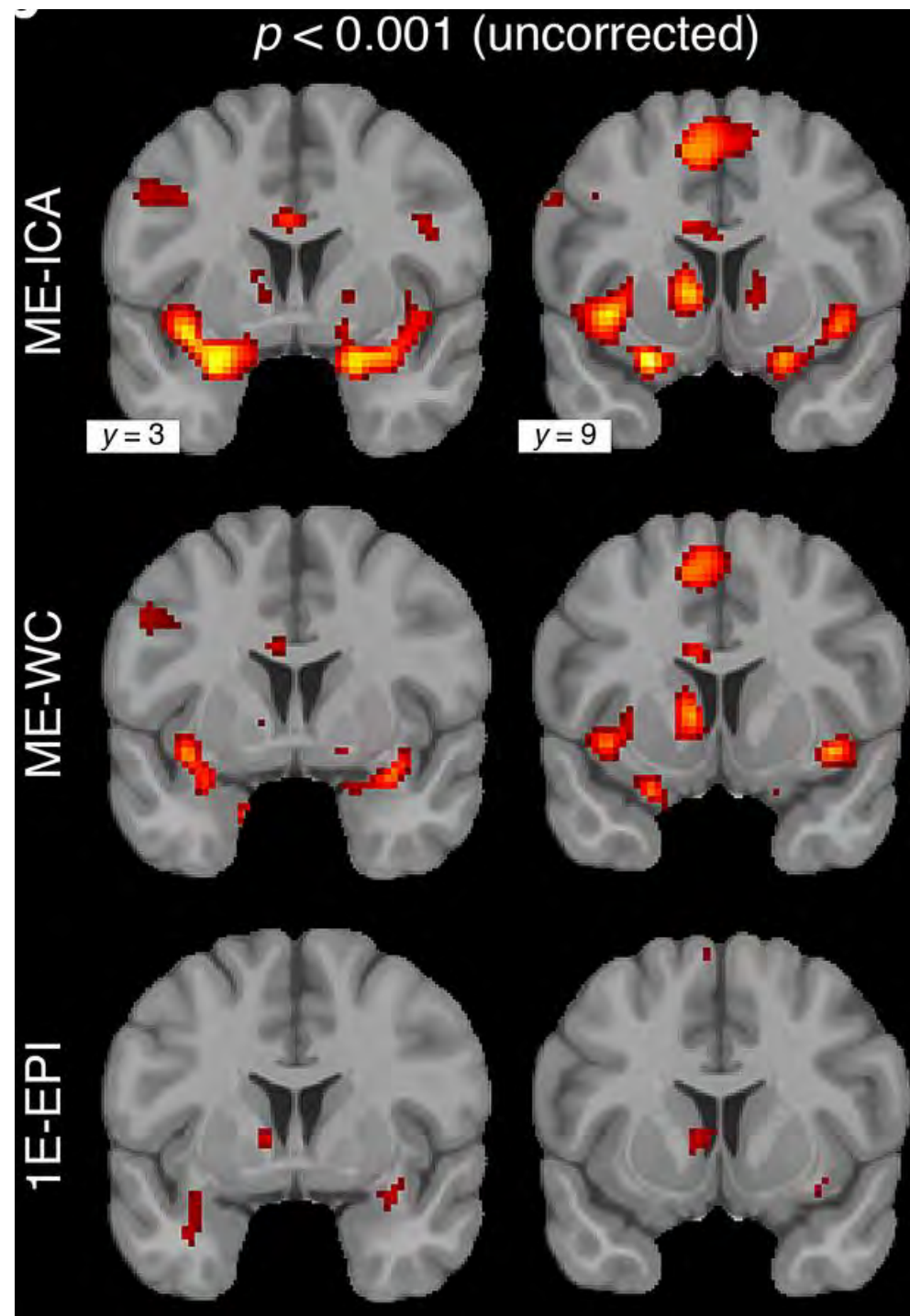
Time x reliability, sbj ME01



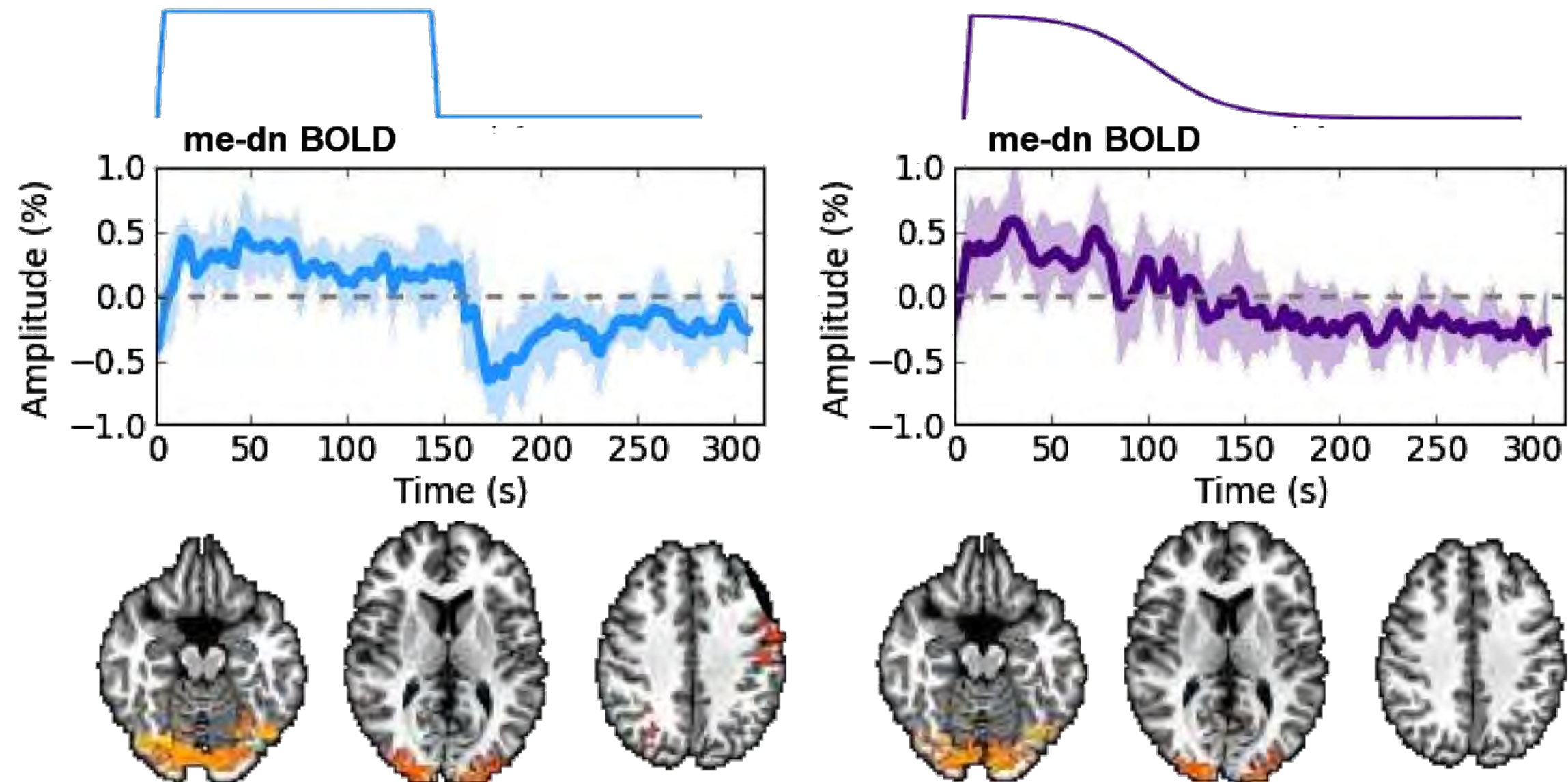
Collecting Multi-echo data + multi-echo denoising is better than multi-echo data without denoising and single-echo data with a shorter-TR

MULTI-ECHO FMRI IMPROVES DATA

Regions with high dropout



Temporally slow changes

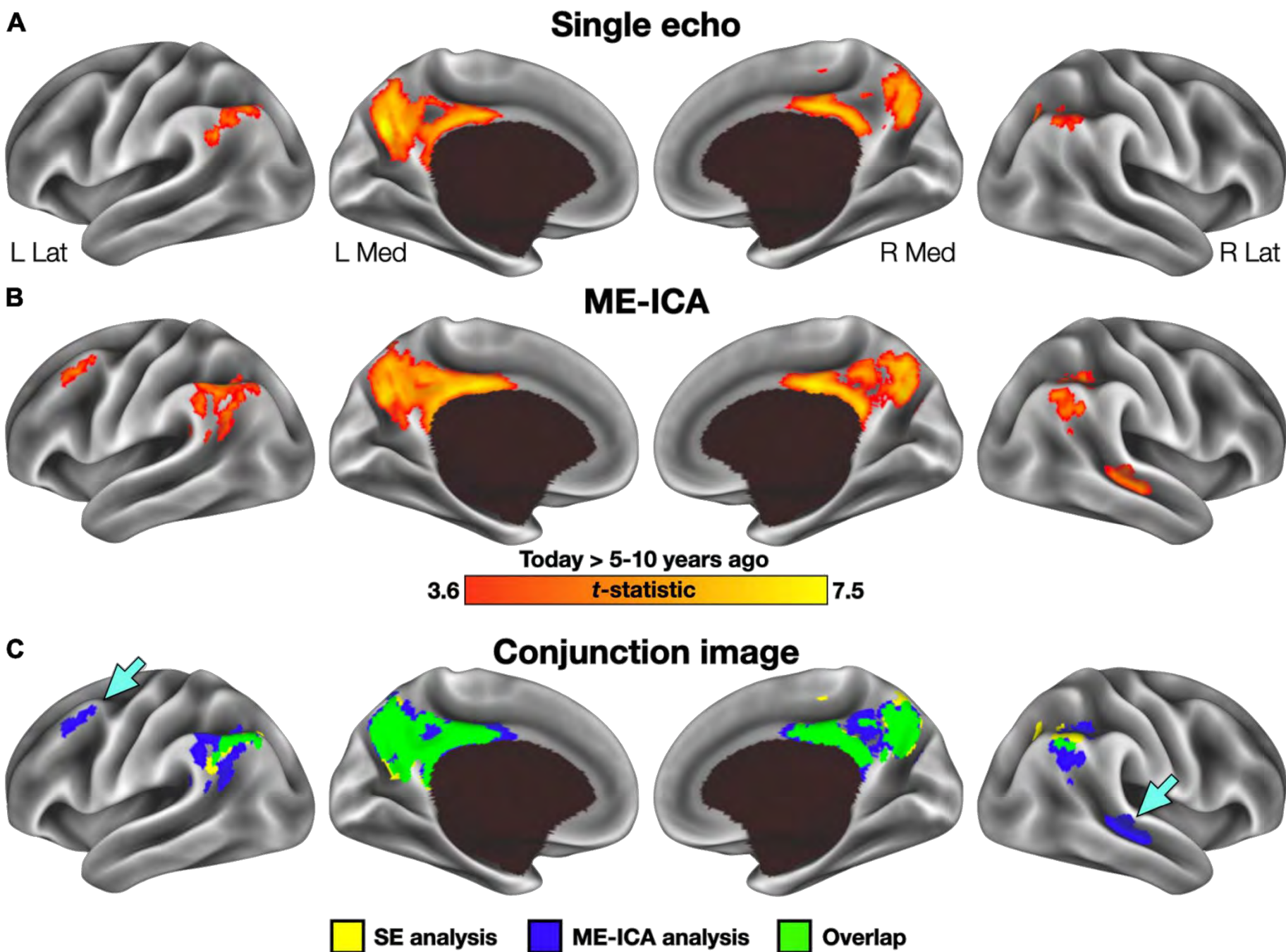


Evans et al. "Separating Slow BOLD from non-BOLD baseline..." NeuroImage 2015

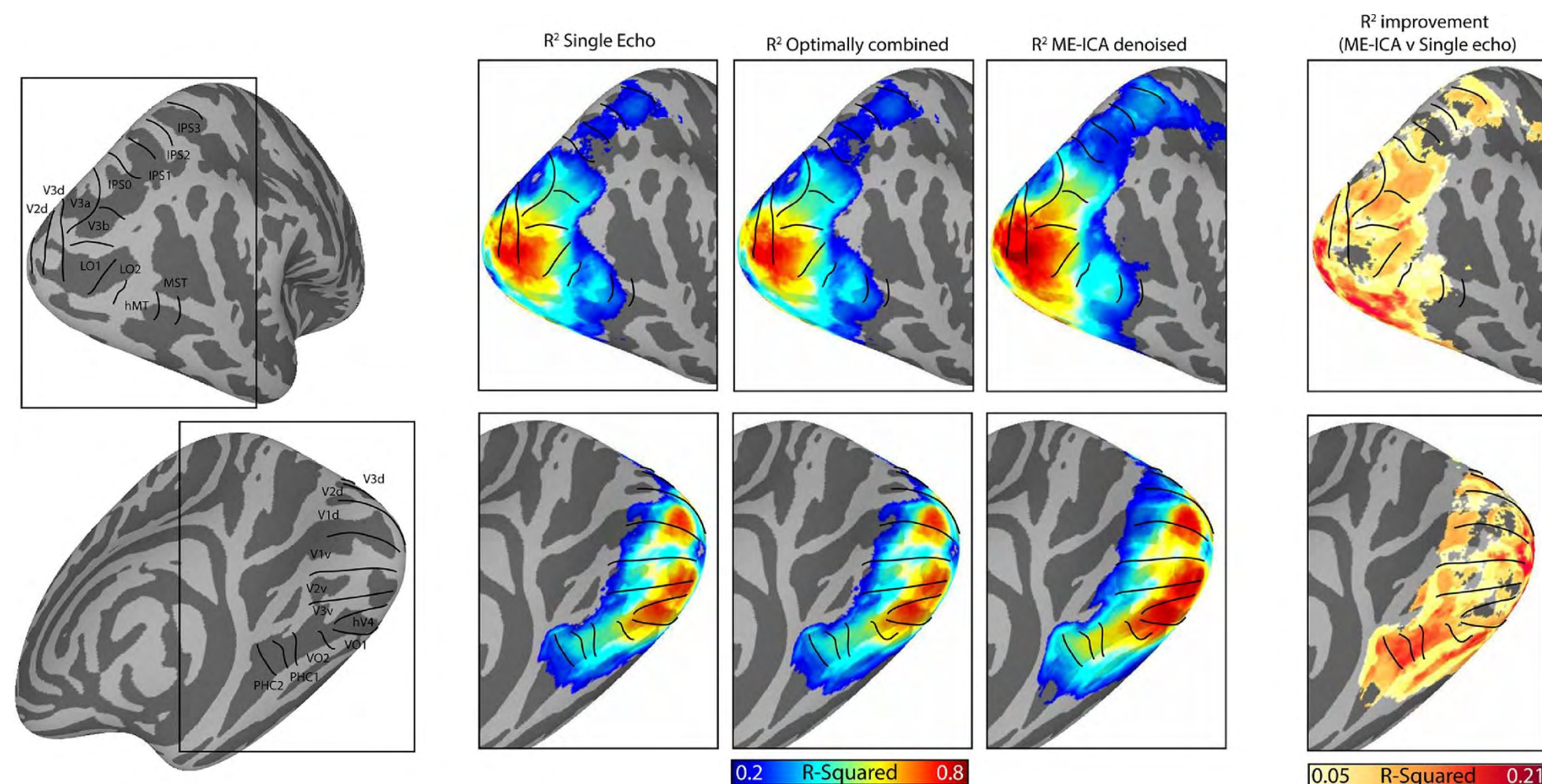
Zhao, Raithel et al olfactory fMRI. Imaging Neuro 2024

MULTI-ECHO FMRI IMPROVES DATA

Overt Speech



Better retinotopy



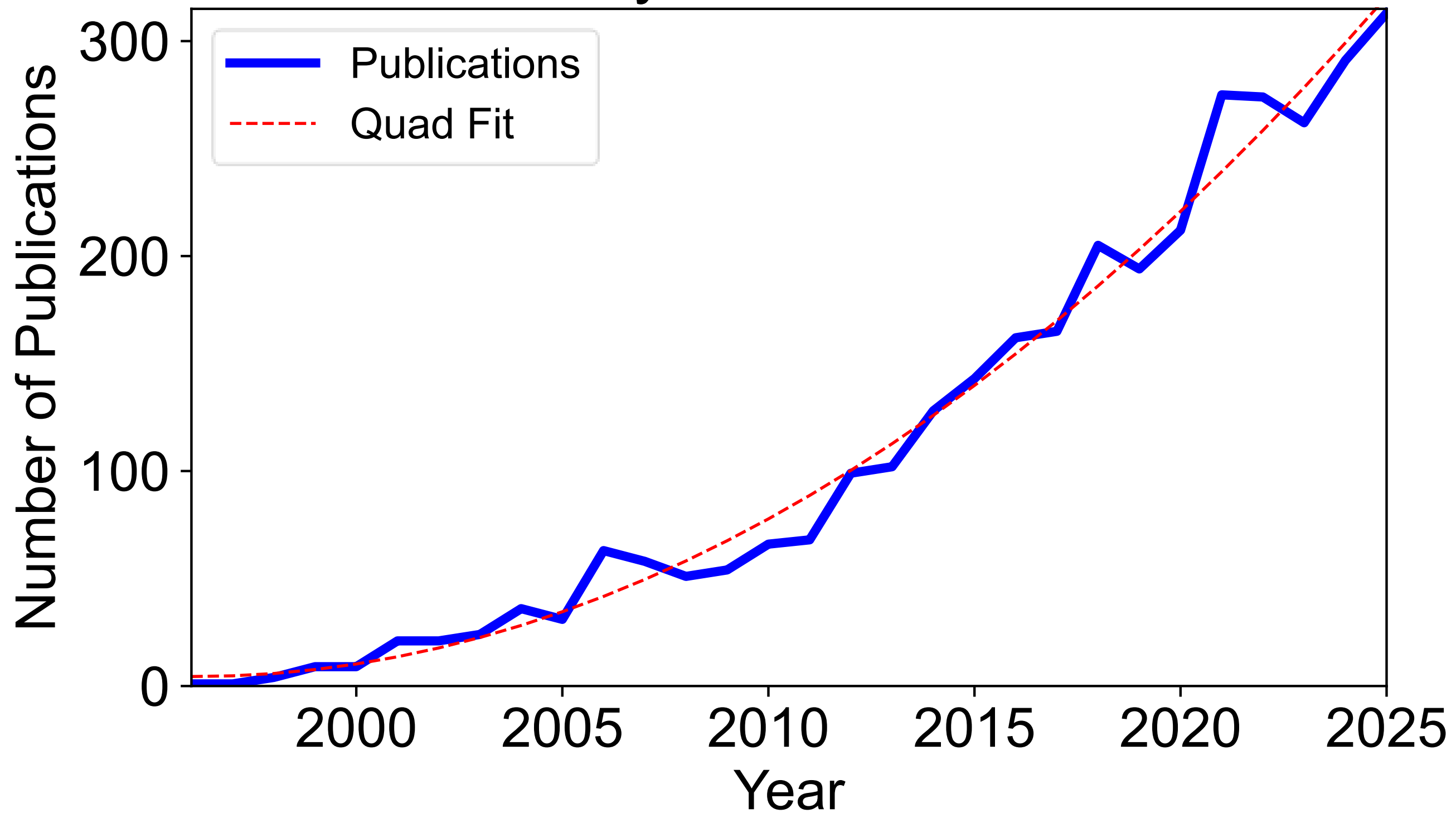
Up to 21% Improvement in population receptive field mapping model fit

Steel A. et al. "Evaluating the efficacy of multi-echo ICA denoising on model-based fMRI" NeuroImage 2022

Gilmore et al. "A comparison of single- and multi-echo processing of fMRI Data during autobiographical recall" Front. Neurosc. 2022

HISTORY: GROWTH OF MULTI-ECHO FMRI

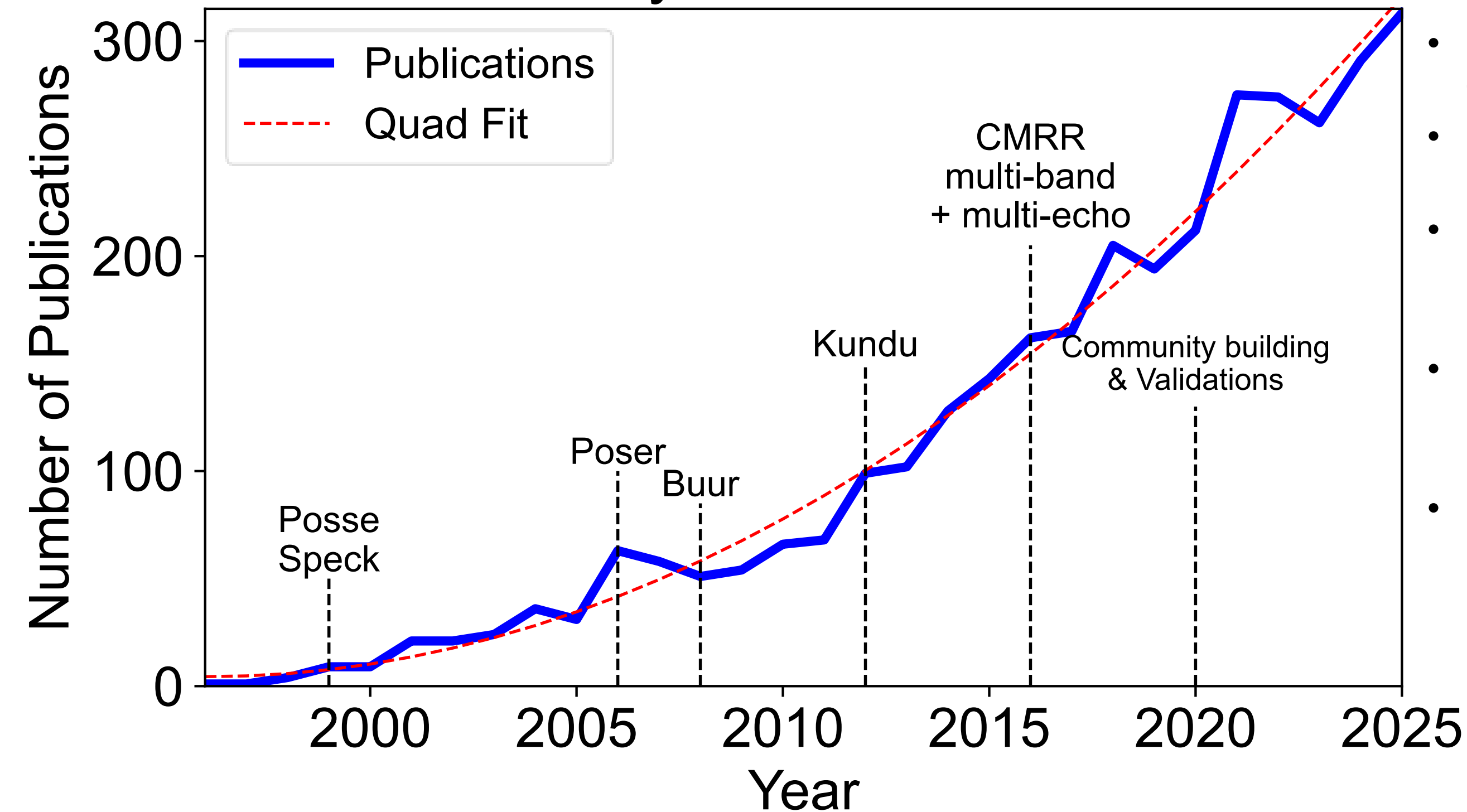
Publication History of Multi-echo fMRI Studies



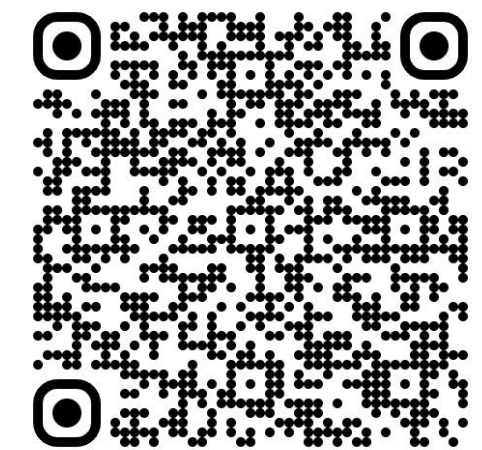
Scopus query: ((ALL(multi-echo) OR ALL(multiecho)) AND ALL(FMRI) AND PUBYEAR > 1991 AND PUBYEAR < 2027)

HISTORY: GROWTH OF MULTI-ECHO FMRI

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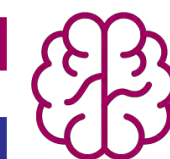


- 1999-2008: Development of key theory and noise reduction methods
- 2008-2015: MRI Hardware & pulse sequences limited practical ME usage
- 2012-3: Kundu developed ME-ICA, showing practical benefits that generated wider interest
- 2016: First widely available multi-band + ME sequence made ME possible with minimal compromises
- 2020: Validations of ME benefits started to get published



Reading list & more history

Scopus query: ((ALL(multi-echo) OR ALL(multiecho)) AND ALL(FMRI) AND PUBYEAR > 1991 AND PUBYEAR < 2027)

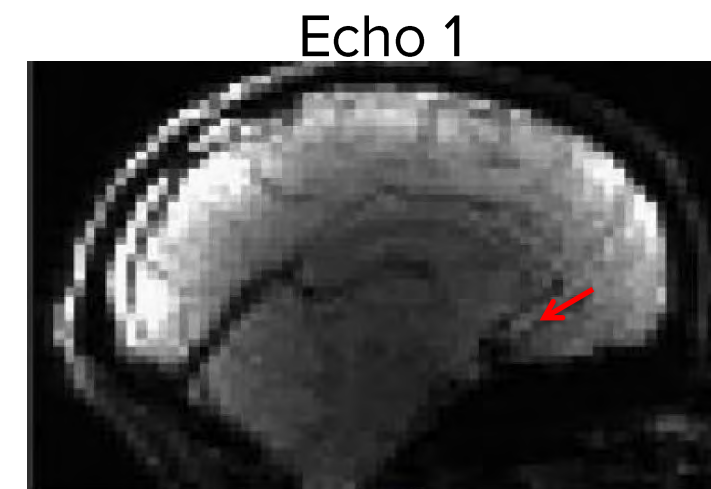
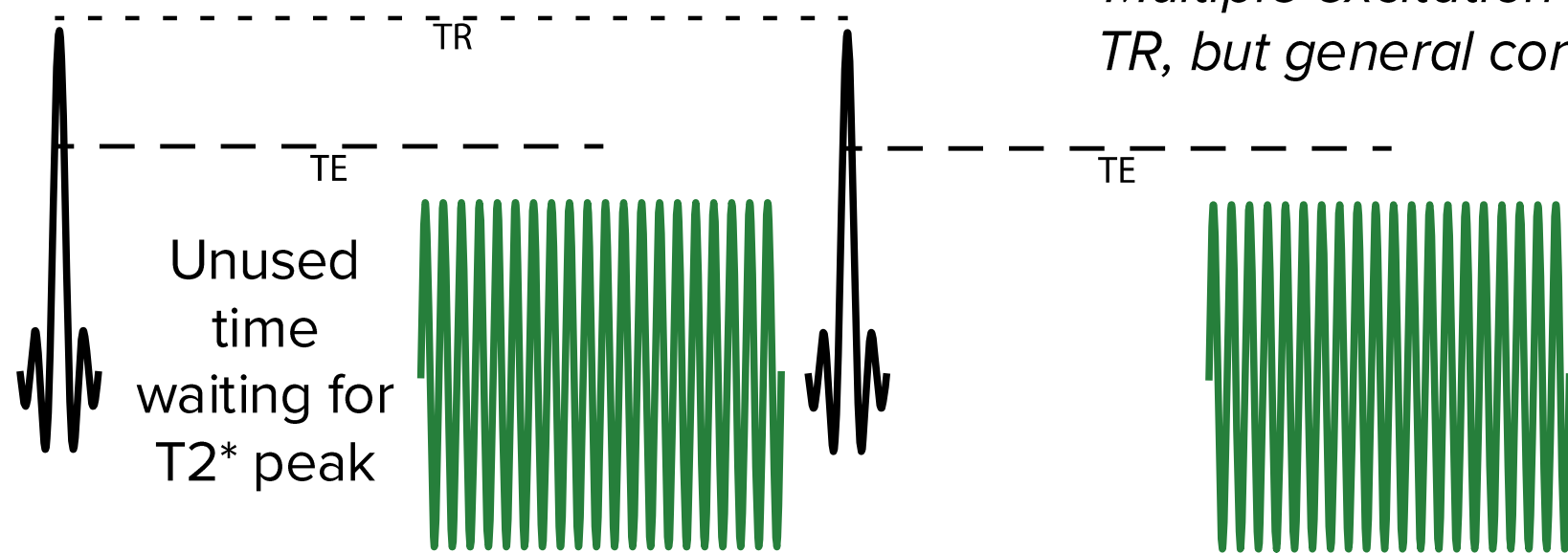


OHBM 2026

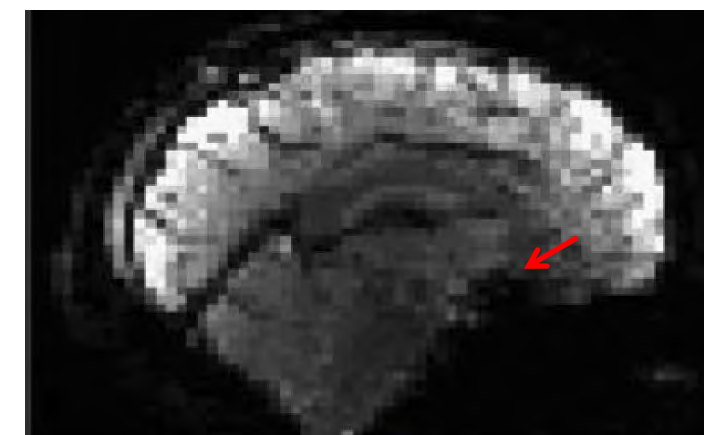
WHAT IS MULTI-ECHO FMRI?

Single Echo

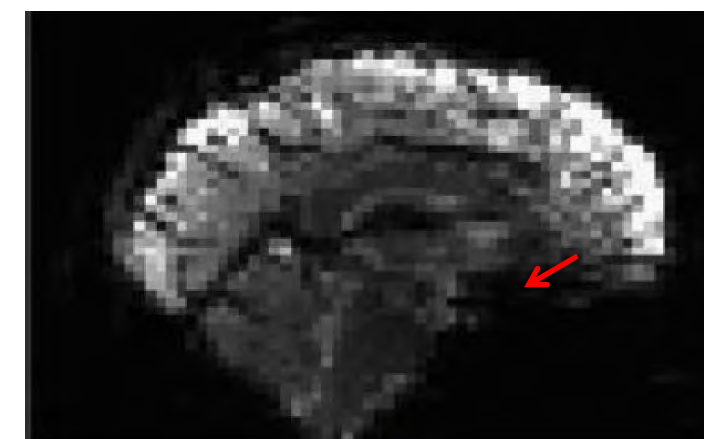
Multiple excitation pulses per TR, but general concept holds



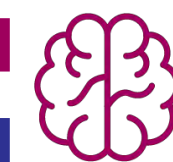
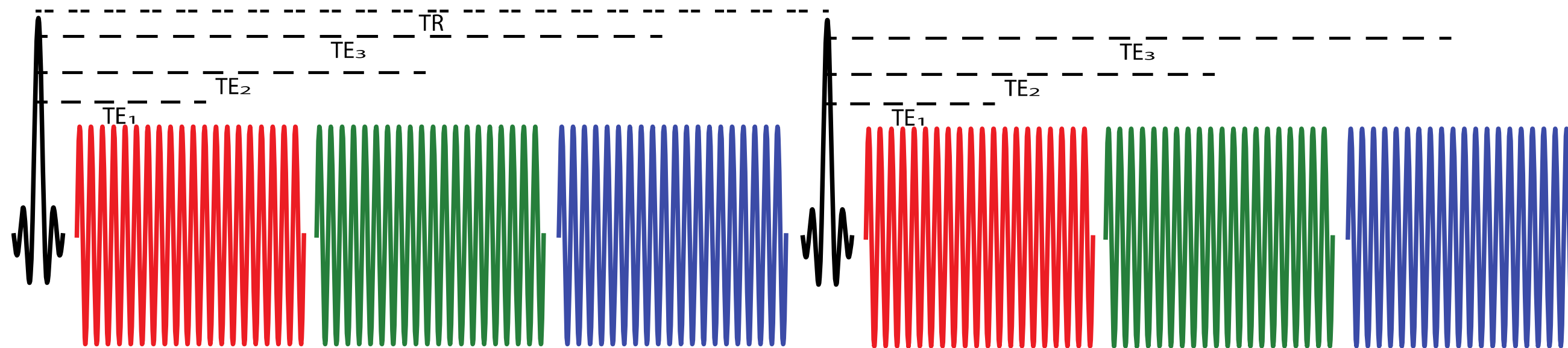
Echo 2



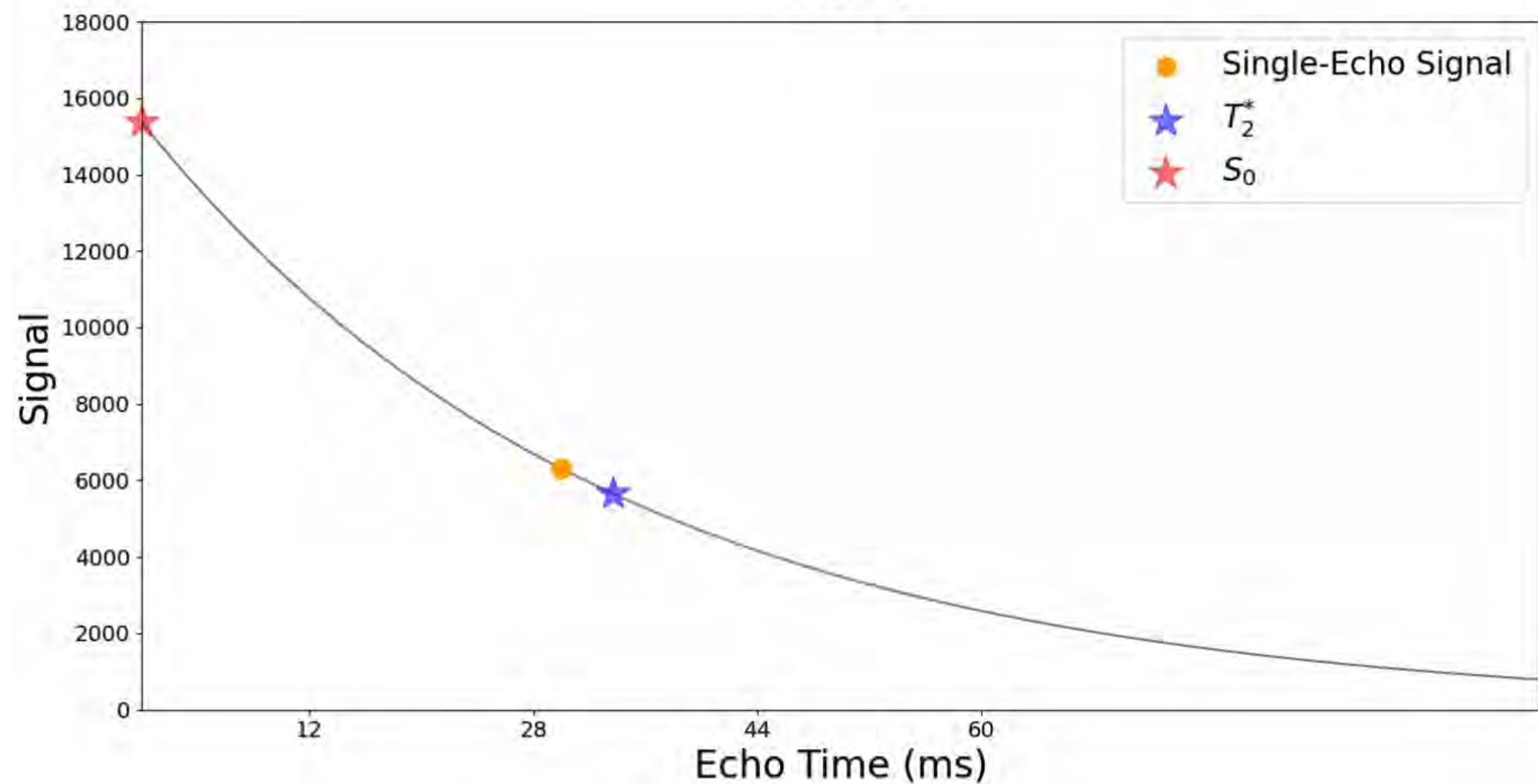
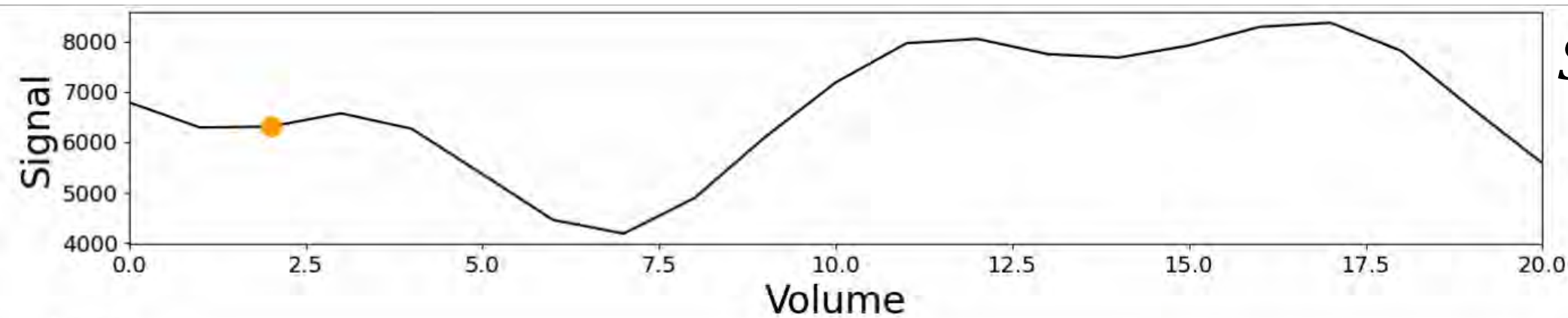
Echo 3



3 Echo



USING MULTI-ECHO INFORMATION



$$S(x, t, TE_k) = S_0(x, t) \cdot e^{-R_2^*(x, t) \cdot TE_k} + n(x, t)$$

The signal decays with echo time

S_0

- The y-intercept at TE=0
- Non-neural signals including head motion & scanner artifacts

$$R_2^* = 1/T_2^*$$

- The rate of decay
- Altered by several factors including changes in blood oxygenation (BOLD)

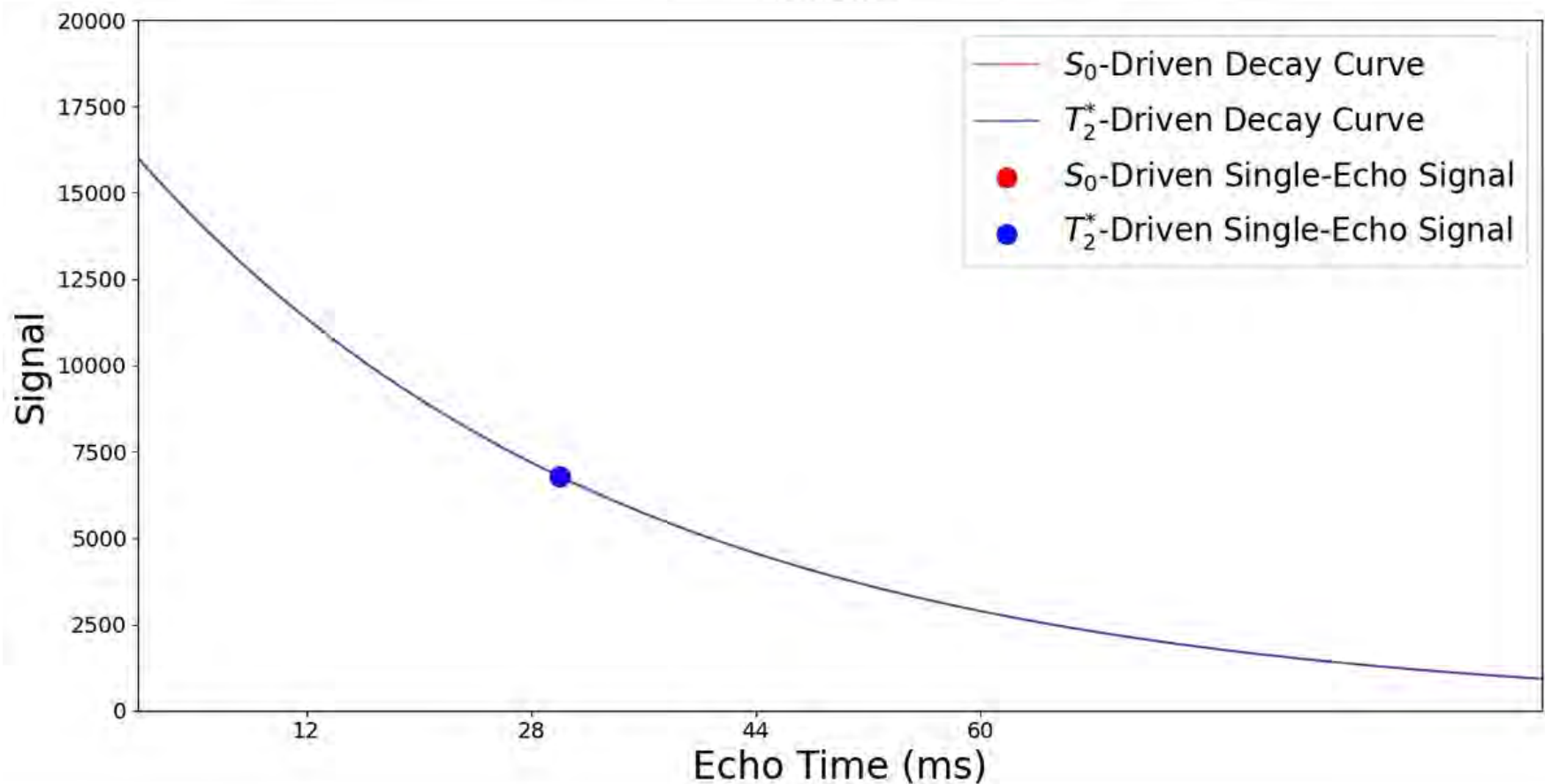
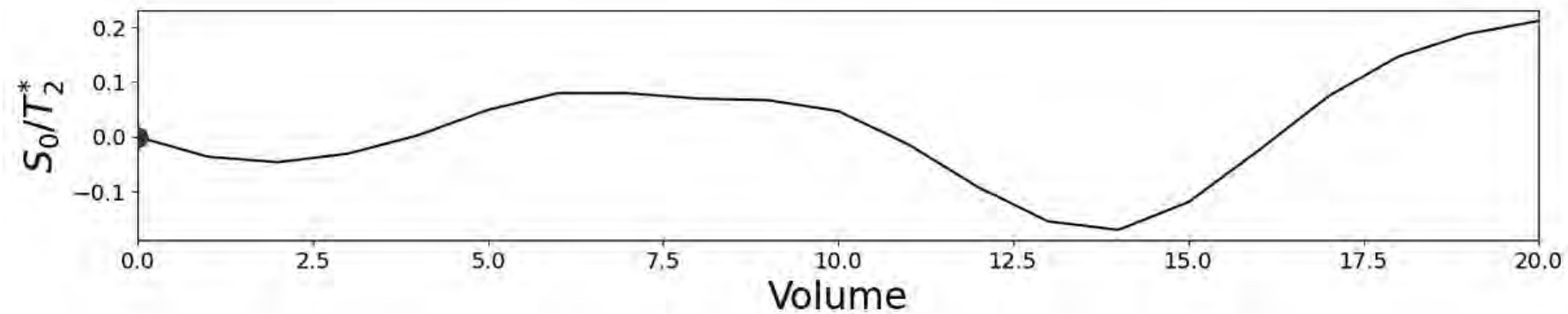
n = thermal noise

- Rician for magnitude only data
- Gaussian for complex data
- Echo time independent

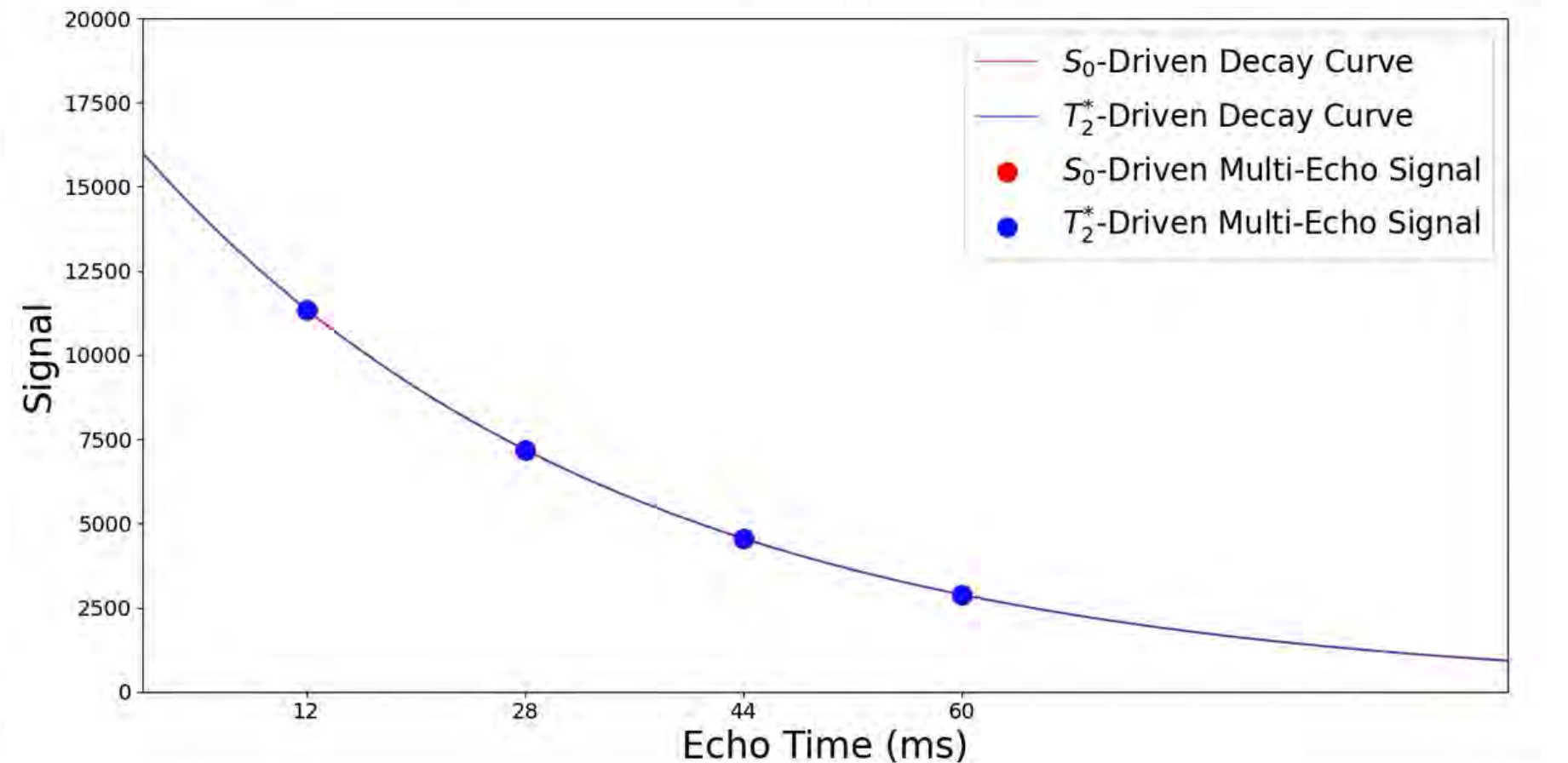
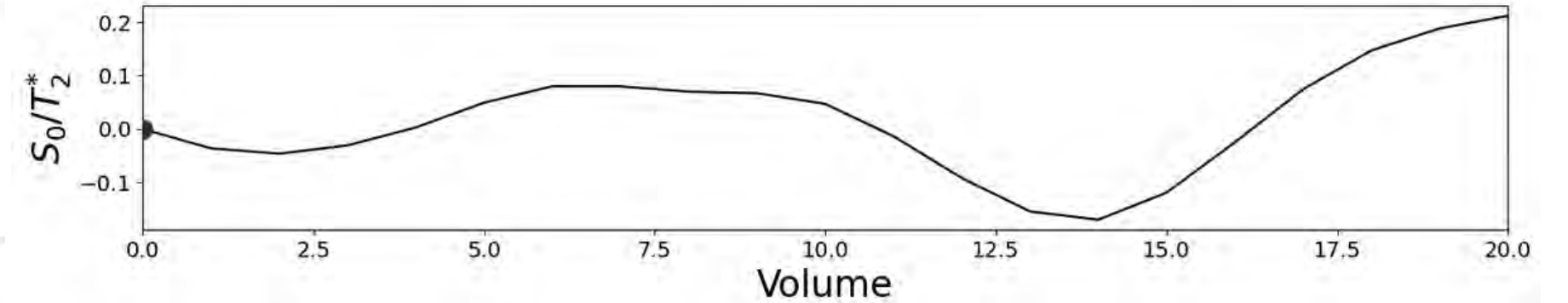
https://me-ica.github.io/multi-echo-data-analysis/content/Signal_Decay.html

DISTINGUISHING T_2^* AND S_0

What we measure with single-echo fMRI



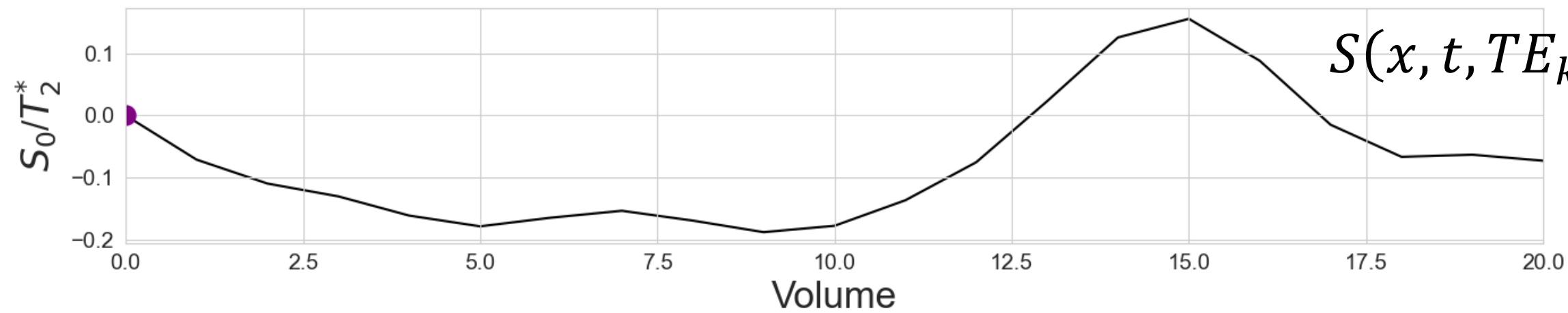
What we measure with multi-echo fMRI



$$S(x, t, TE_k) = S_0(x, t) \cdot e^{-R_2^*(x, t) \cdot TE_k} + n(x, t)$$

https://me-ica.github.io/multi-echo-data-analysis/content/Signal_Decay.html

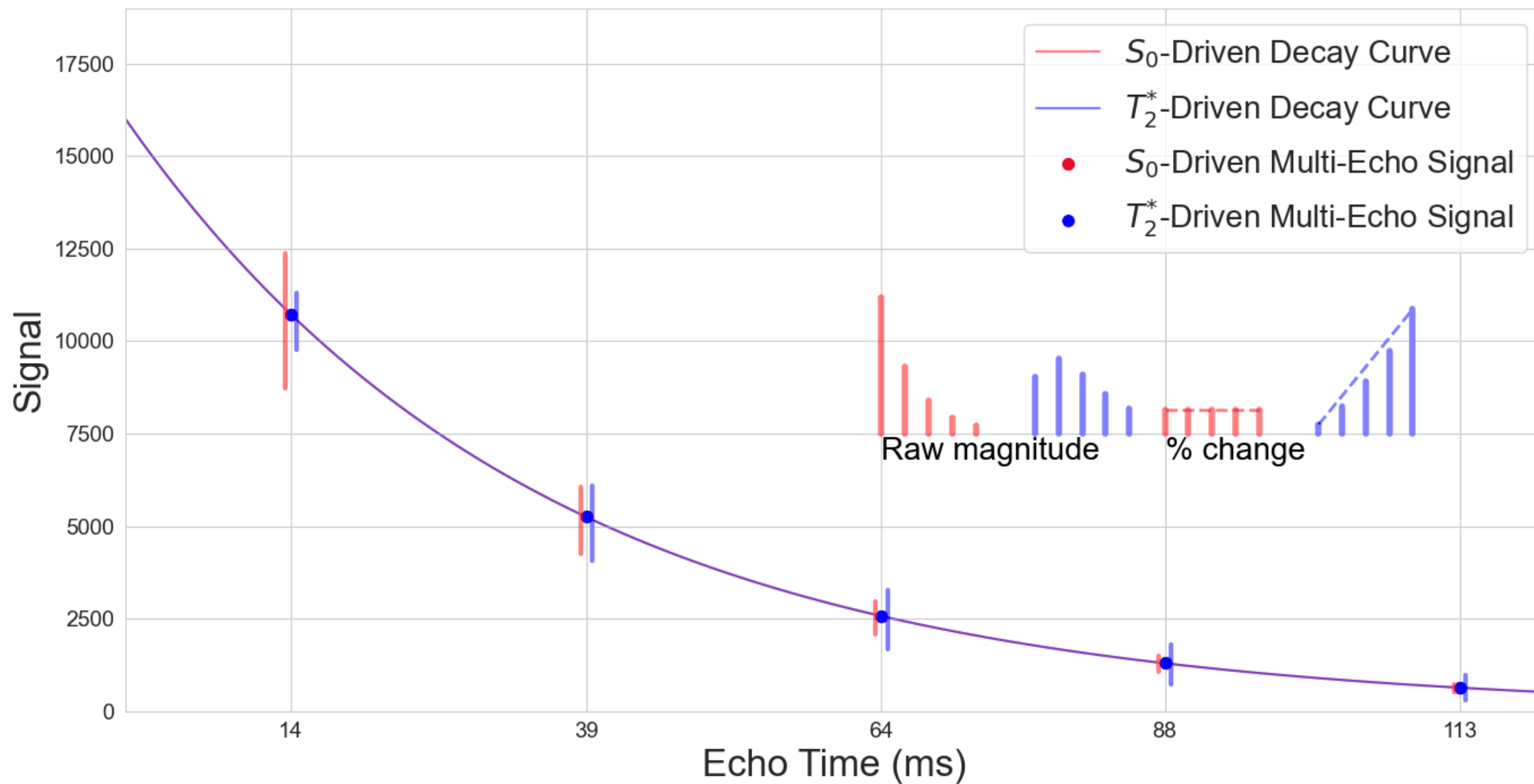
DISTINGUISHING T_2^* AND S_0



$$S(x, t, TE_k) = S_0(x, t) \cdot e^{-R_2^*(x, t) \cdot TE_k} + n(x, t)$$

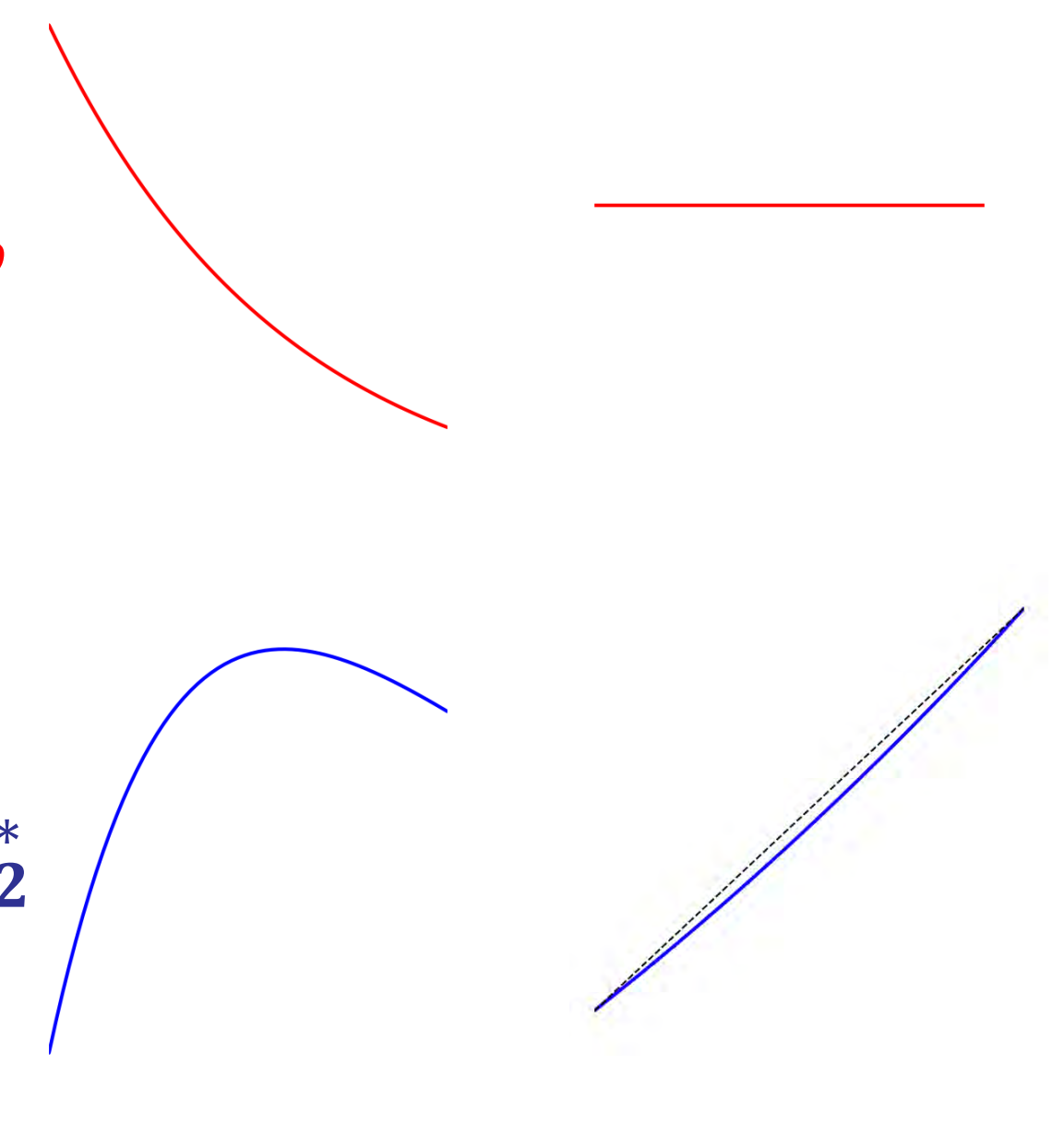
Raw difference

% change difference



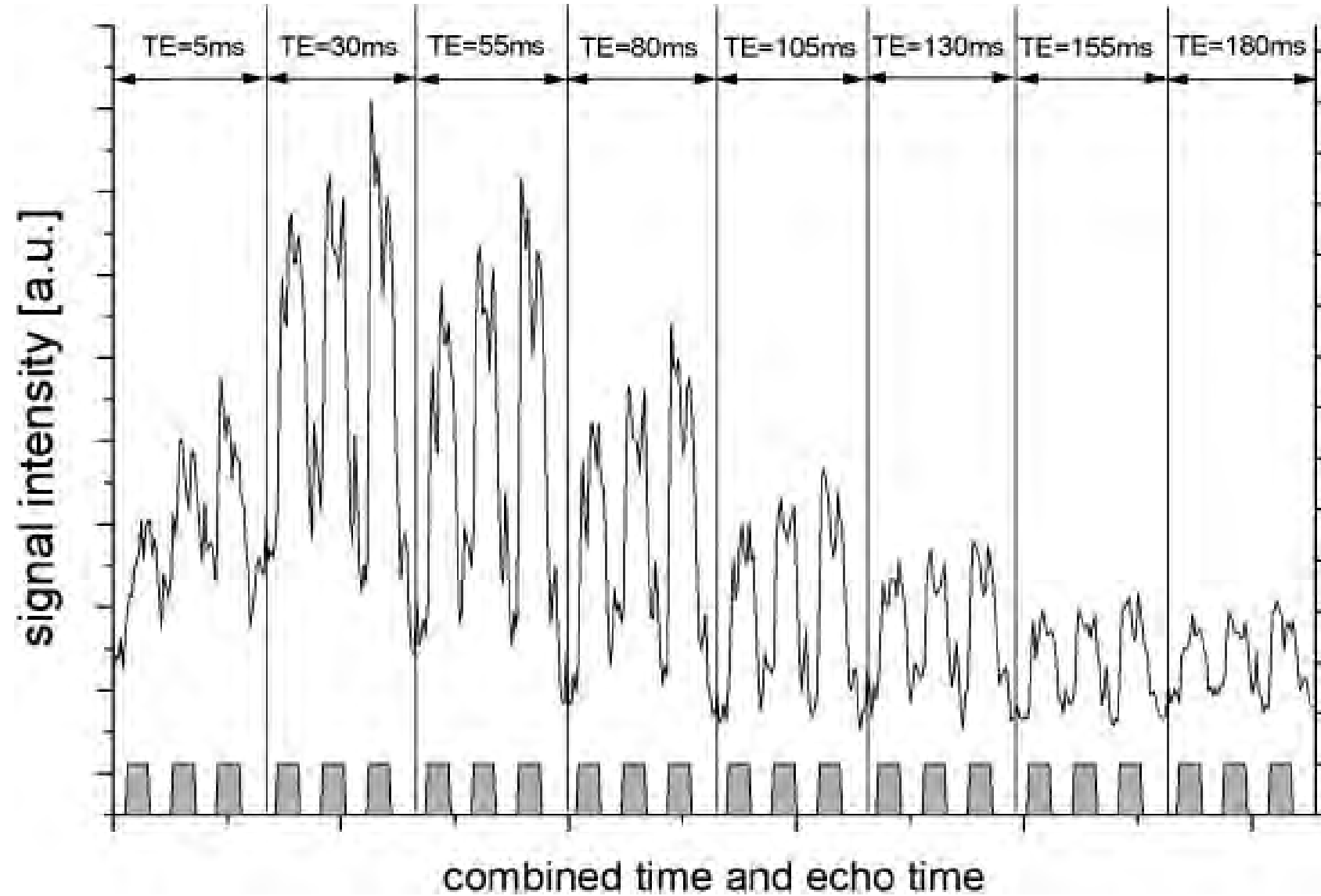
S_0

R_2^*



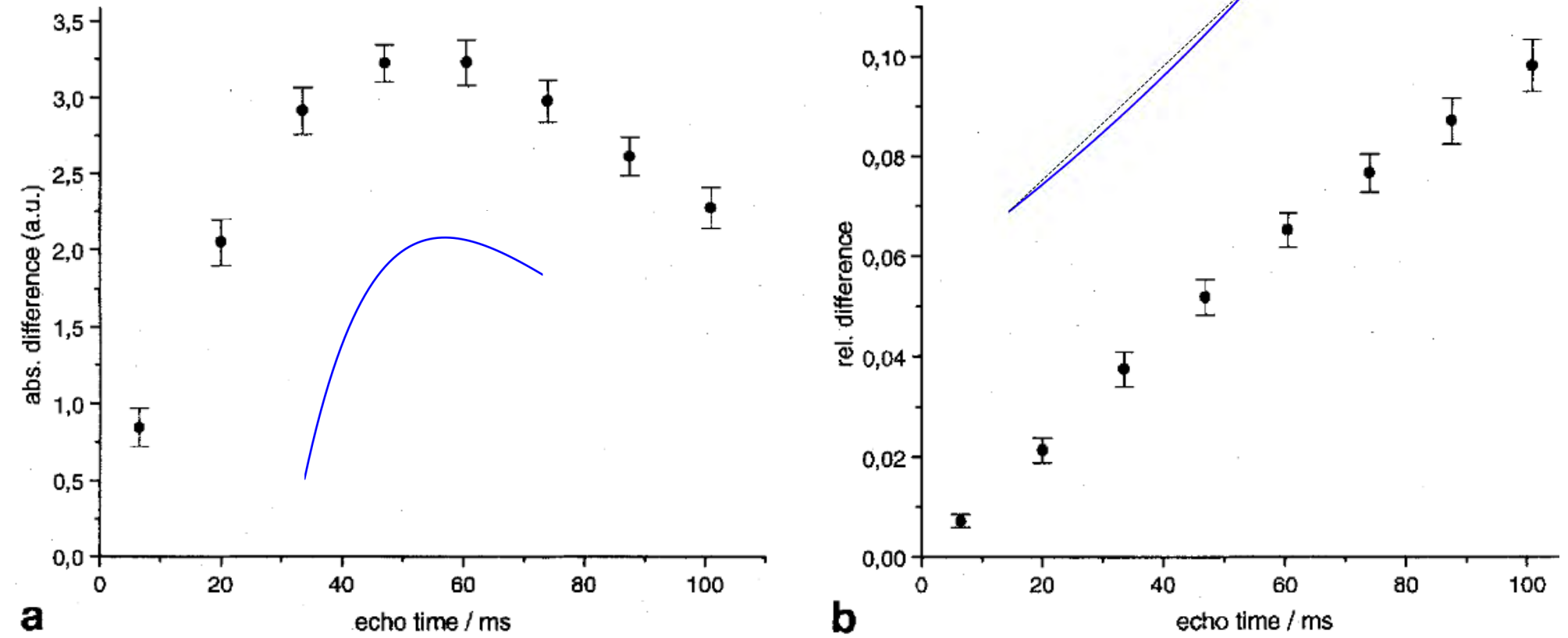
RESPONSE MAGNITUDES BY ECHO TIME

Finger tapping task at 3T



Barth et al NMR Biomed 2001

8Hz flashing checkerboard at 2T



Speck & Hennig 1998

Building off work on functional spectroscopy

Multi-echo Math

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

Assuming $n(x, t)$ is negligible

$$S_o(x, t) = \overline{S_o(x)} + \Delta S_o(x, t) \quad \Delta S_o(x, t) \ll \overline{S_o(x)}$$

$$R_2^*(x, t) = \overline{R_2^*(x)} + \Delta R_2^*(x, t) \quad \Delta R_2^*(x, t) \ll \overline{R_2^*(x)}$$

$$S_{\%change} = \frac{S(x, t, TE_k) - \overline{S(x, TE_k)}}{\overline{S(x, TE_k)}} = \left(1 + \frac{\Delta S_o(x, t)}{\overline{S_o(x)}} \right) \cdot e^{-TE_k \cdot \Delta R_2^*(x, t)} - 1$$

First order Taylor Expansion of: $e^{-TE_k \cdot \Delta R_2^*(x, t)}$

$$S_{\%change} = \frac{\Delta S_o(x, t)}{\overline{S_o(x)}} - TE_k \cdot \Delta R_2^*(x, t)$$

$$\frac{TE_k \cdot \Delta R_2^*(x, t) \cdot \Delta S_o(x, t)}{\overline{S_o(x)}}$$

Assuming this is negligible

Multi-echo Math

$$S_{\%change} \approx \frac{\Delta S_o(x, t)}{S_o(x)} - TE_k \cdot \Delta R_2^*(x, t)$$

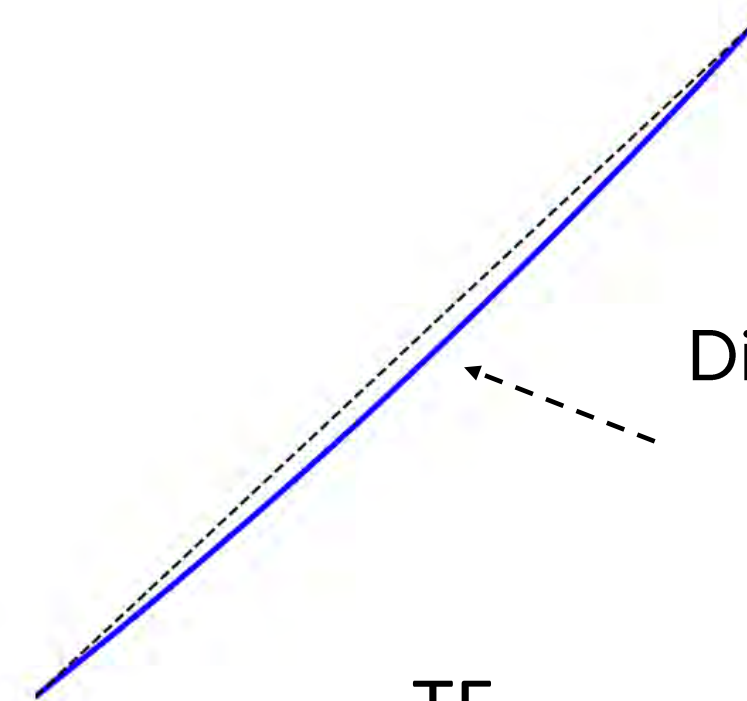
$$\frac{\Delta S_o(x, t)}{S_o(x)} = \Delta \rho(x, t)$$



TE

Net Magnet. Fluctuations
in at location 'x', time 't'

$$\Delta R_2^*(x, t)$$



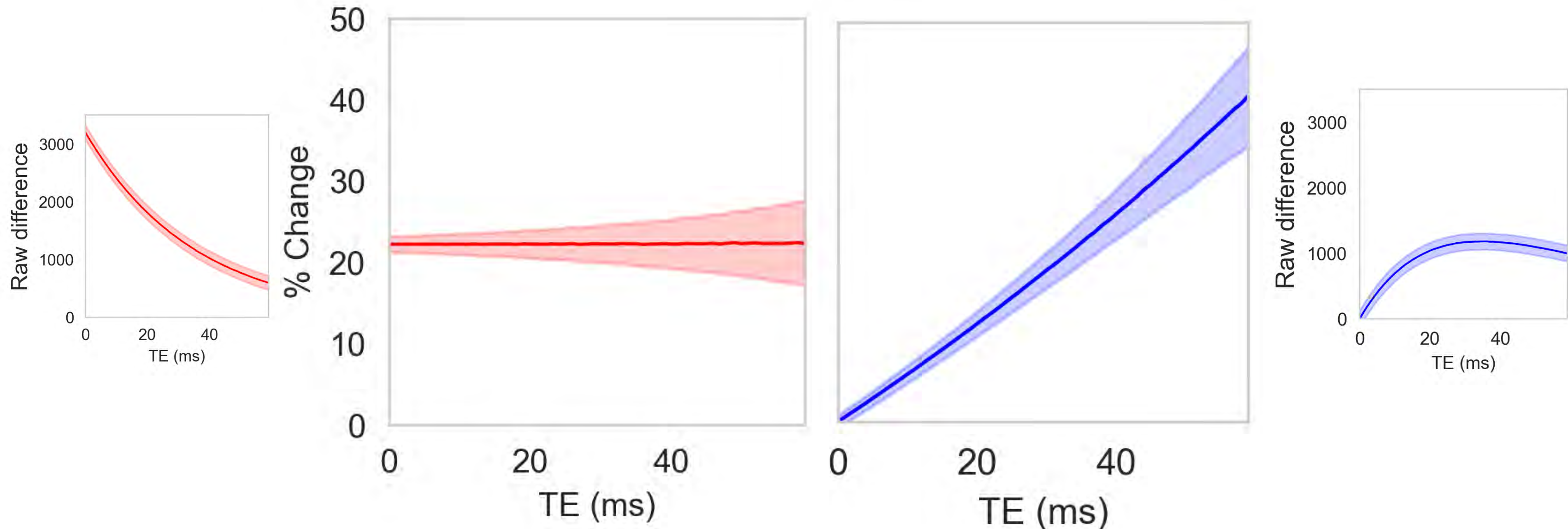
Diff between approx.
on Taylor Approx
& linear

TE

BOLD Fluctuations at
location 'x', time 't'

WITHOUT IGNORING THERMAL NOISE

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



$n(x, t)$ is not TE dependent, so later echoes have relatively more noise

A linear fit across 3-5 noisy data points is... challenging

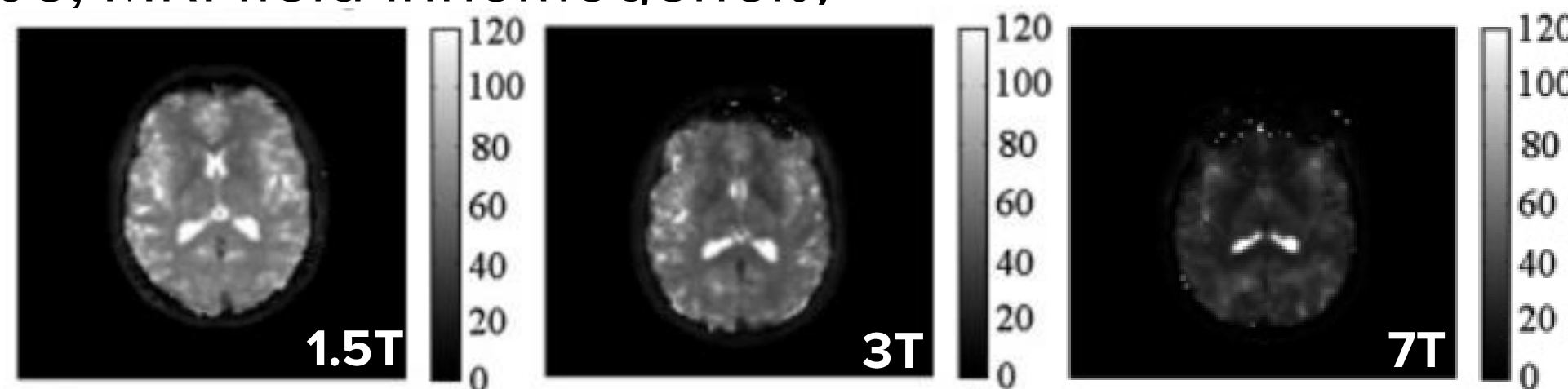
OPTIMAL ECHO TIME

The optimal echo time (TE) = T_2^* of tissue

- T_2^* varies by MRI field strength, tissue type, MRI field inhomogeneity

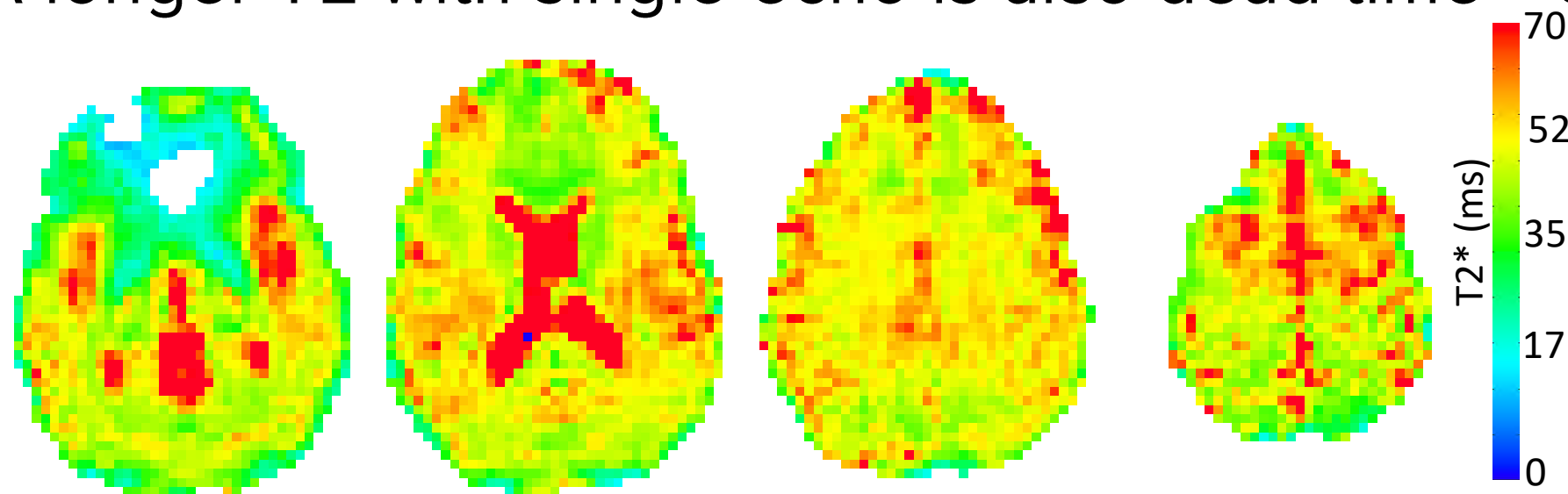
Table 1. Mean corrected T_2^* values for all regions and field strengths

Field strength (T)	Grey matter (ms)	White matter (ms)	Caudate (ms)	Putamen (ms)
1.5	84.0±0.8	66.2±1.9	58.8±2.4	55.5±2.3
3	66.0±1.4	53.2±1.2	41.3±2.3	31.5±2.5
7	33.2±1.3	26.8±1.2	19.9±2.0	16.1±1.6



Peters, Brooks et al. MRM (2007)

- Since T_2^* varies, the optimal TE varies. We pick a TE with “good enough” contrast in most of the brain without losing signal in areas of interest
- A longer TE with single echo is also dead time + slower acquisition



T_2^* also varies by age.
(See Julia Moser’s talk on developmental neuroimaging)

Multi-echo acquisition means we collect data that covers a range of optimal TEs

USING MULTI-ECHO TO REDUCE NOISE

Weighted average of echoes

Method	Weights	Requires T2* estimates	Weights vary by voxel	Weights vary with time
Simple Summation (Posse 1999)	$w_n = 1/N$	No	No	No
TE-Combined	$w_n = \frac{TE_n}{\sum_{i=1}^N TE_i}$	No	No	No
T ₂ *-Combined (OC ⁺ /BOLD ⁺⁺) (Posse 1999)	$w_n = \frac{TE_n \cdot e^{-TE_n/T_2^*}}{\sum_{i=1}^N TE_i \cdot e^{-TE_i/T_2^*}}$	Yes	Yes	No
tSNR-Combined (Poser 2006)	$w_n = \frac{tSNR_n \cdot TE_n}{\sum_{i=1}^N tSNR_i \cdot TE_i}$	No	Yes	No
T ₂ *-FIT Combined (Heunis 2021)	$w_n(t) = \frac{TE_n \cdot e^{-TE_n/T_2^*-FIT(t)}}{\sum_{i=1}^N TE_i \cdot e^{-TE_i/T_2^*-FIT(t)}}$	Yes	Yes	Yes

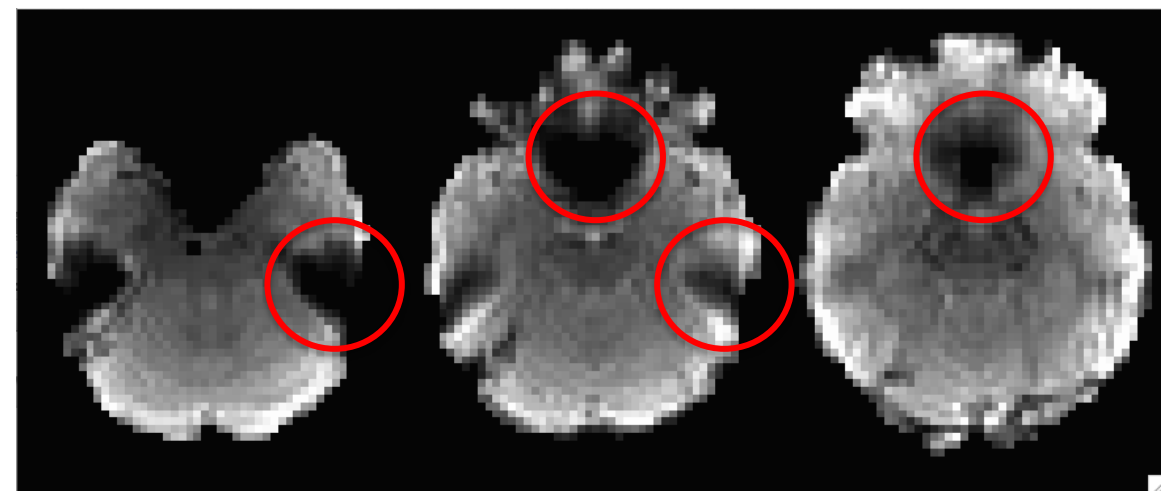
Adding thermal noise across X independent measurements is $\approx \sqrt{X}$ reduction in thermal noise

† a.k.a. Optimally Combined (OC) in Kundu et al. 2012
 †† a.k.a. BOLD weighting in Poser et al. 2006

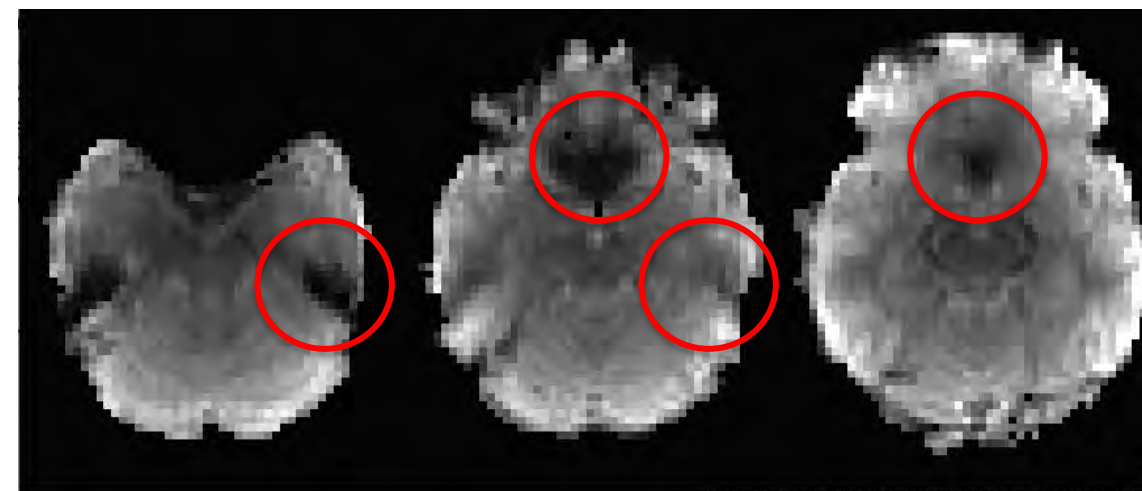
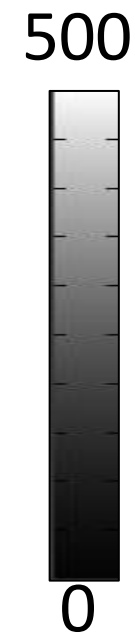


WEIGHTED AVERAGE OF ECHOS

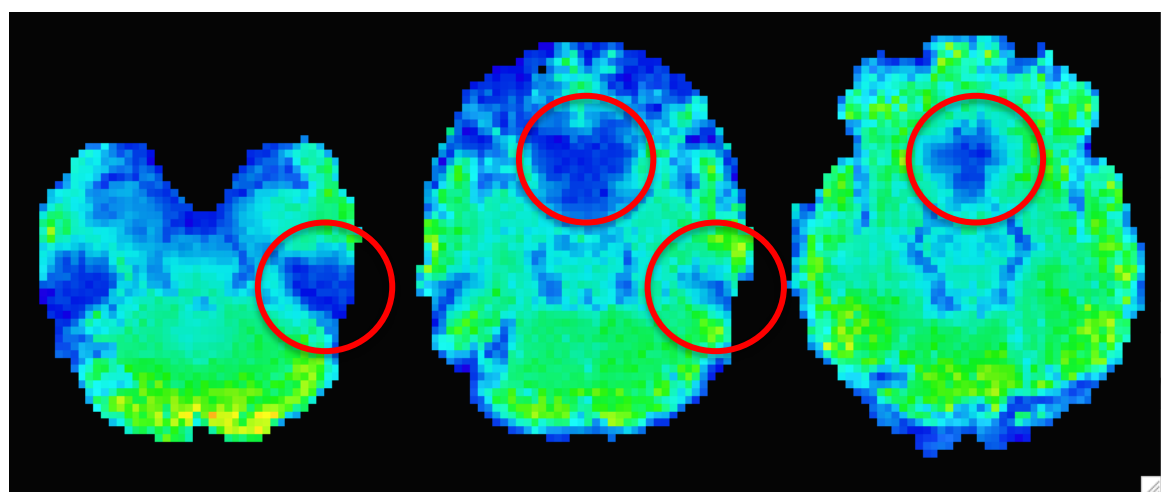
T₂*-Combined Method



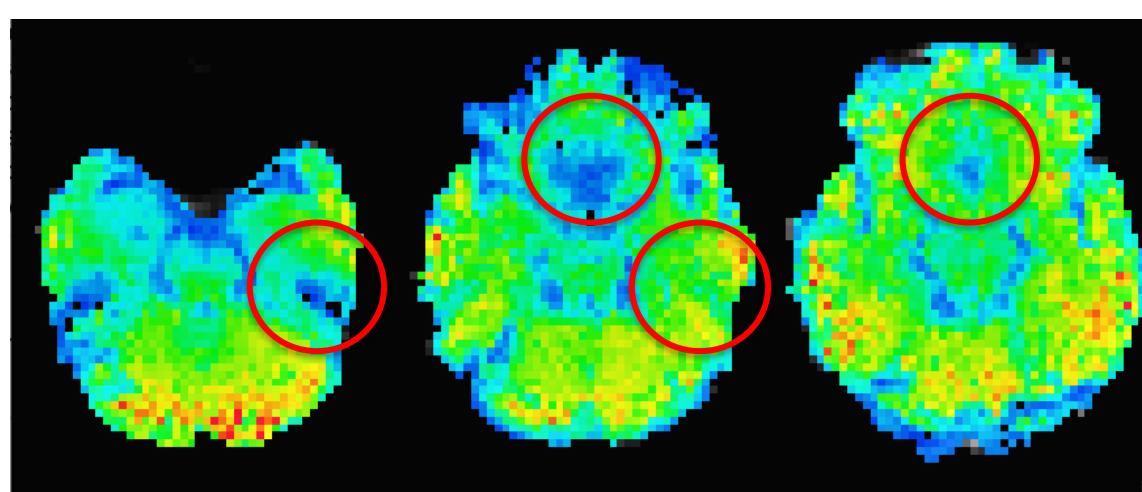
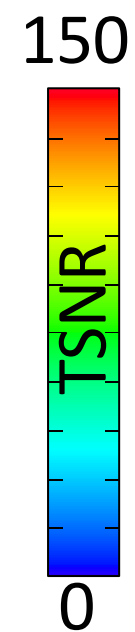
SINGLE ECHO



"OPTIMALLY" COMBINED



SINGLE ECHO



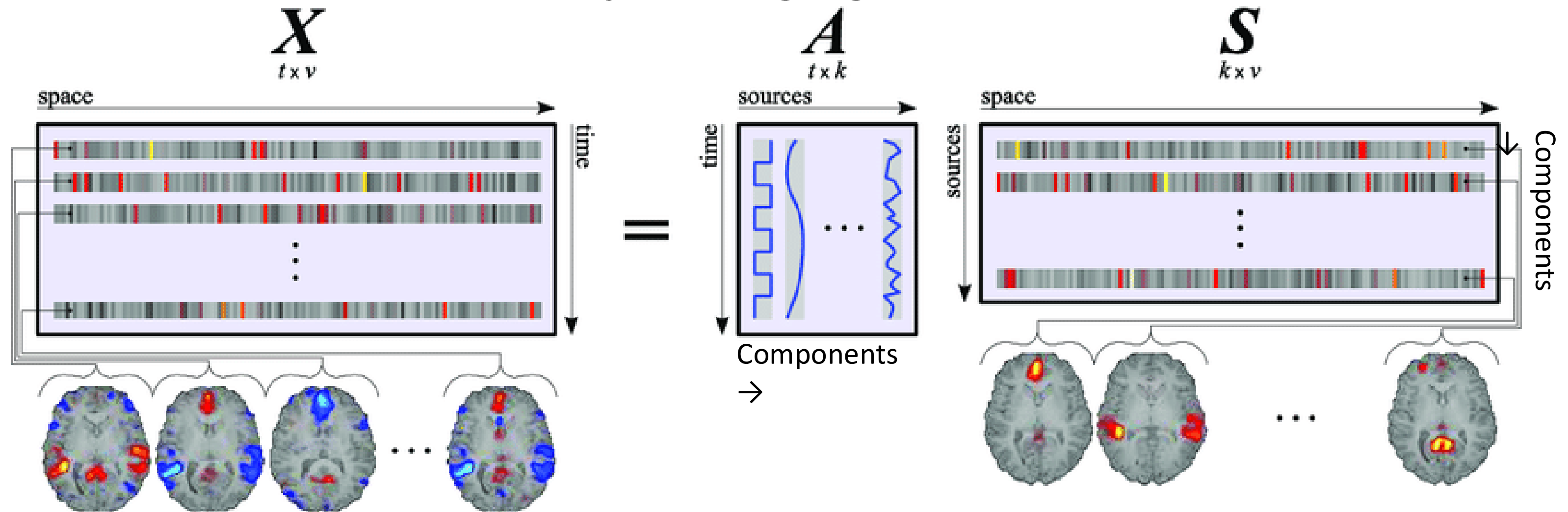
"OPTIMALLY" COMBINED

- Average of echoes weights towards voxelwise mean T_2^*
- Recovers signal in some dropout regions
- Straightforward math
- Only fit is on a lower-noise average across time
- Automatically calculated in AFNI, fMRIPrep, tedana, +
- Reliable improvements
 - Improvement should be equal or better than SNR loss from a small increase in acquisition acceleration to acquire multi-echo

USING ICA FOR DENOISING

Weighted average reduces noise in model fit by averaging across time

ICA reduces noise in model fit by averaging across spatio-temporal components

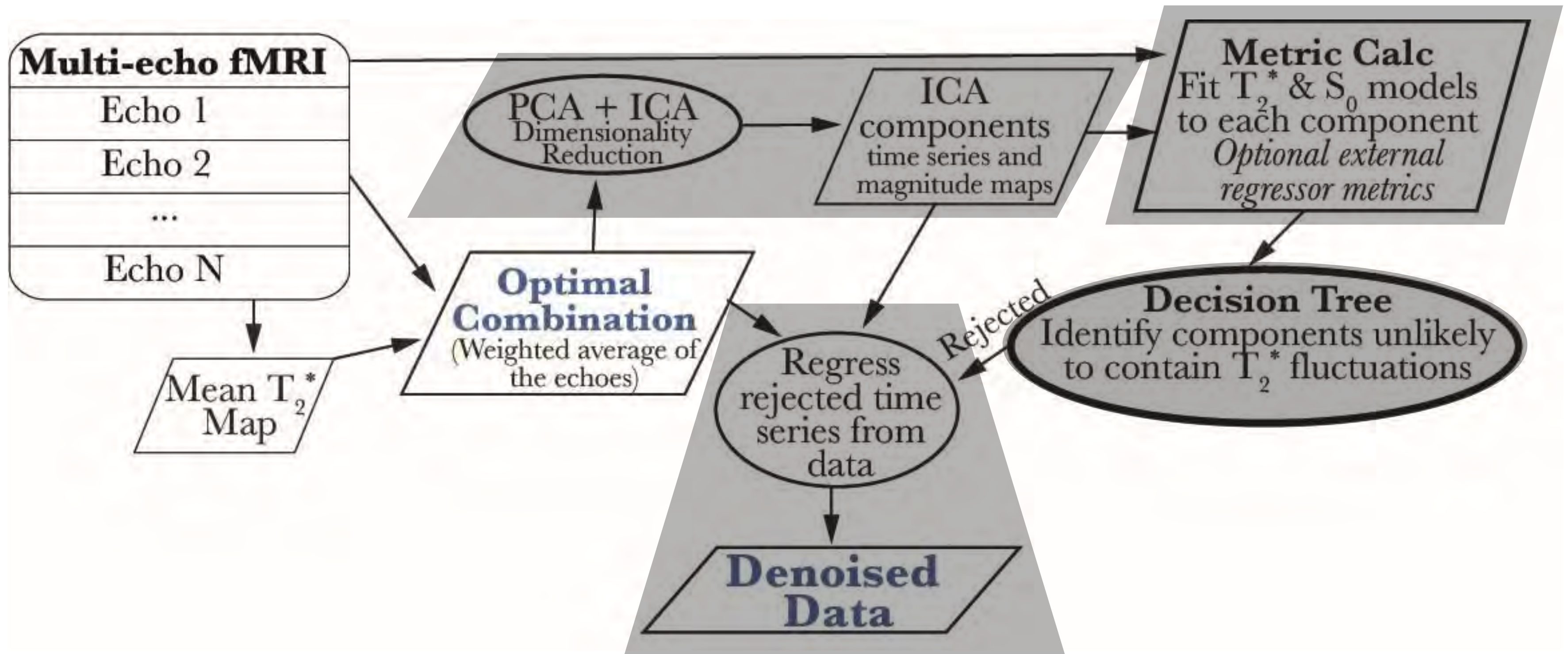


Ylipaavalniemi, *Variability of Independent Components in functional Magnetic Resonance Imaging*

Originally applied to multi-echo denoising by Buur, *IEEE J. Sel. Top. Signal Process* (2008)

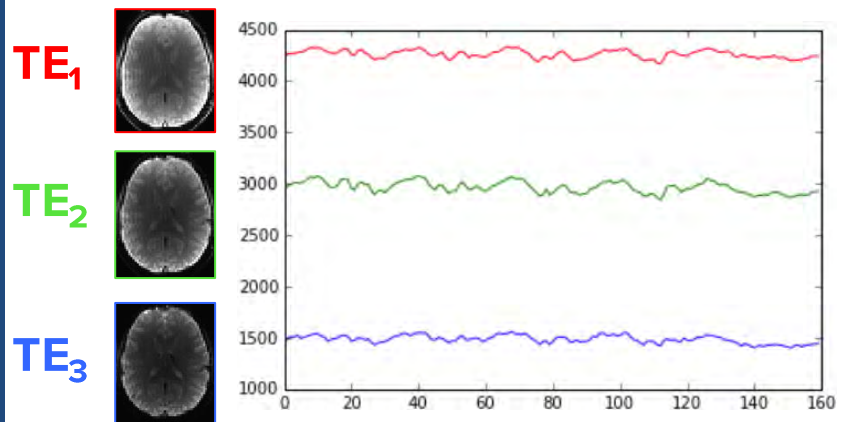
Method in ME-ICA and tedana software initially developed in Kundu, *NeuroImage* (2012)

MEICA/TEDANA PIPELINE



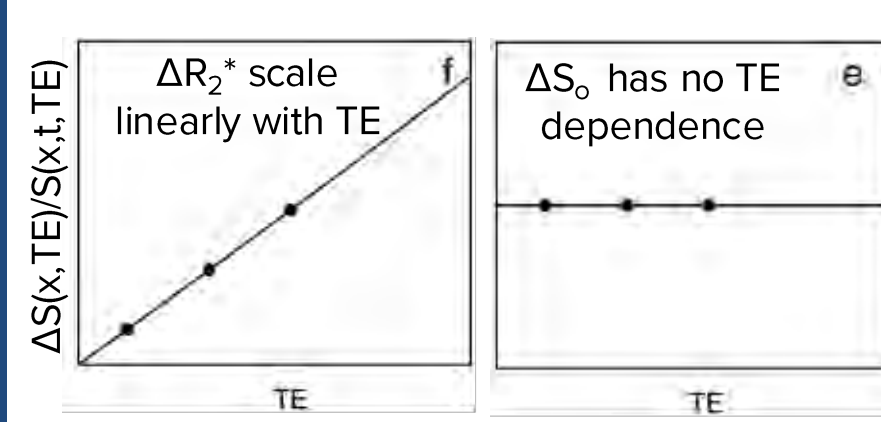
CLASSIFYING ICA COMPONENTS

MULTI-ECHO
DATASET



Linear fit of ICA component time series to each voxel and echo

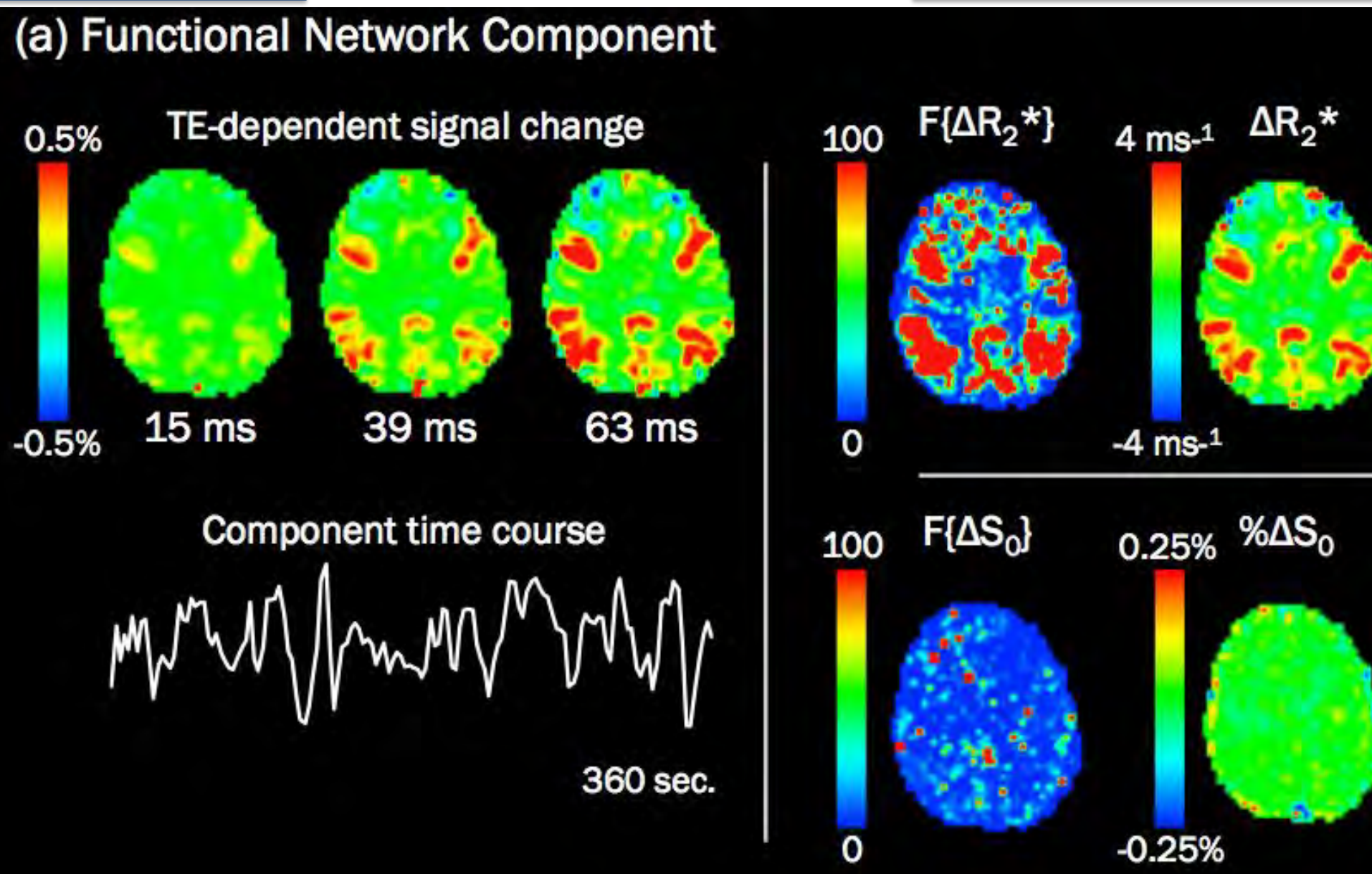
TE-DEPENDENCE
MODEL



Fit across echoes to

$$R_2^* \left(\frac{1}{T_2^*} \right)$$

or S_0 models



Calculate the weighted sum of the ICA component weight map and the model fit to T2* (Kappa) and S0 (Rho)

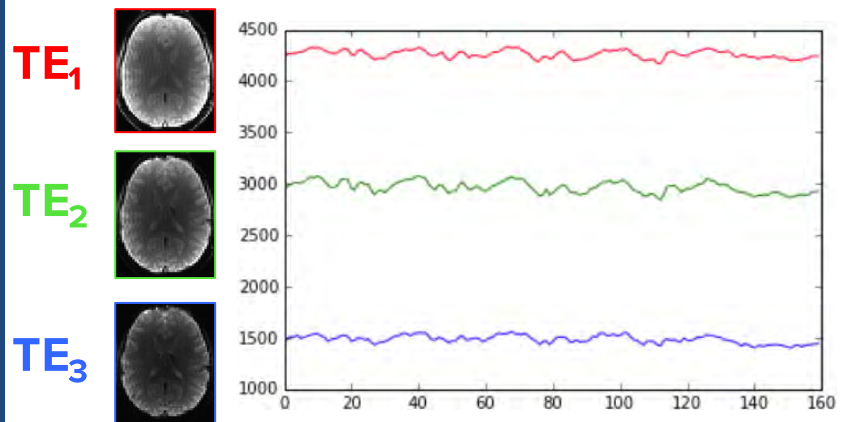
$$\text{Kappa } (\kappa) = 210$$

$$\text{Rho } (\rho) = 10$$

Kundu et al., NeuroImage 2012

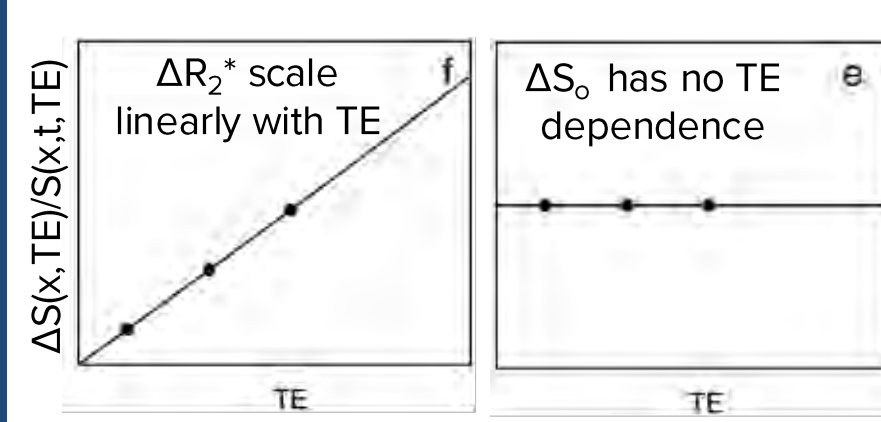
CLASSIFYING ICA COMPONENTS

MULTI-ECHO
DATASET



Linear fit of ICA component time series to each voxel and echo

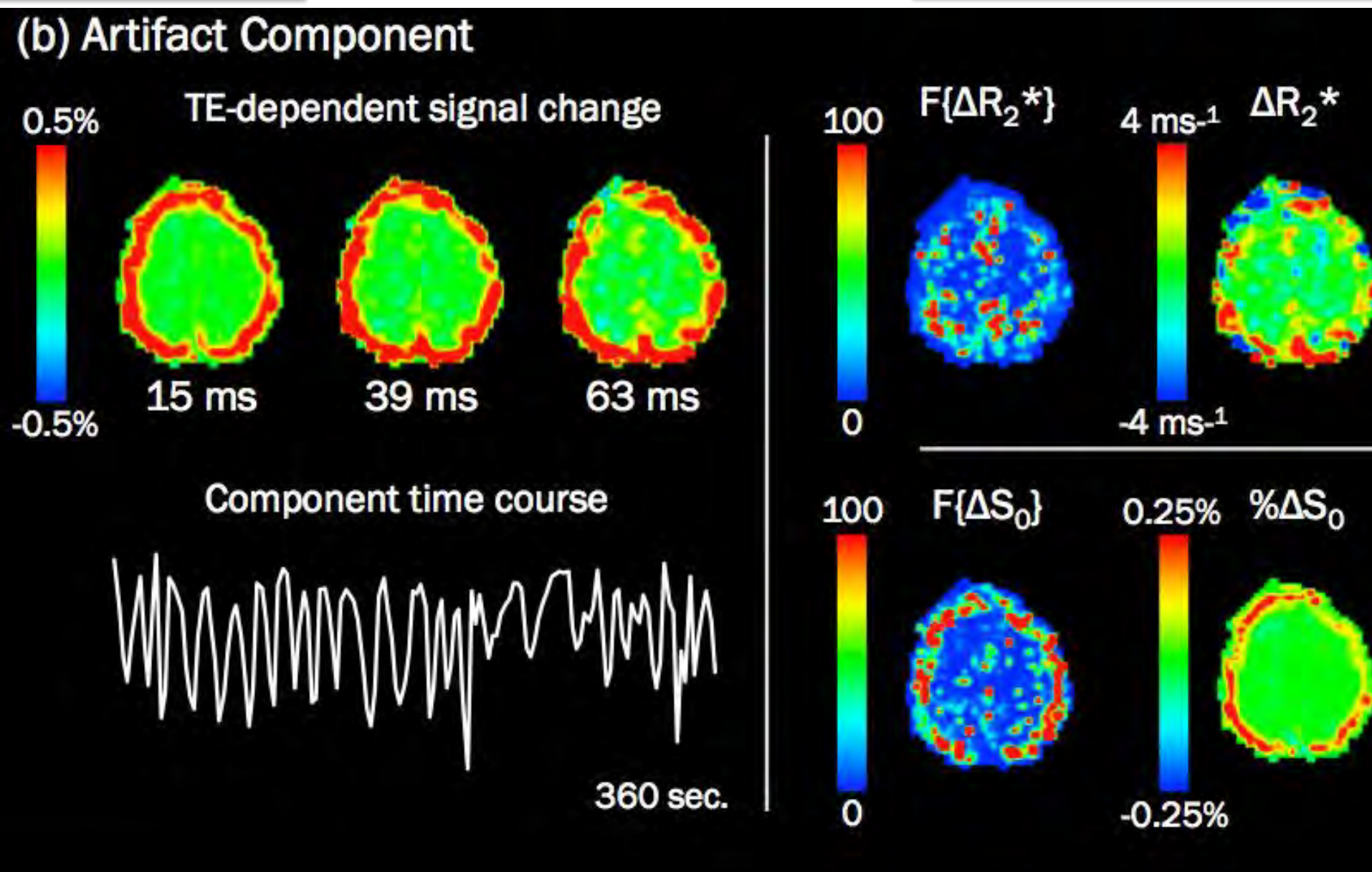
TE-DEPENDENCE
MODEL



Fit across echoes to

$$R_2^* \left(\frac{1}{T_2^*} \right)$$

or S_0 models



Calculate the weighted sum of the ICA component weight map and the model fit to T_2^* (Kappa) and S_0 (Rho)

Kappa (κ) = 32

Rho (ρ) = 81

Kundu et al., NeuroImage 2012

ACCEPTED AND REJECTED COMPONENTS



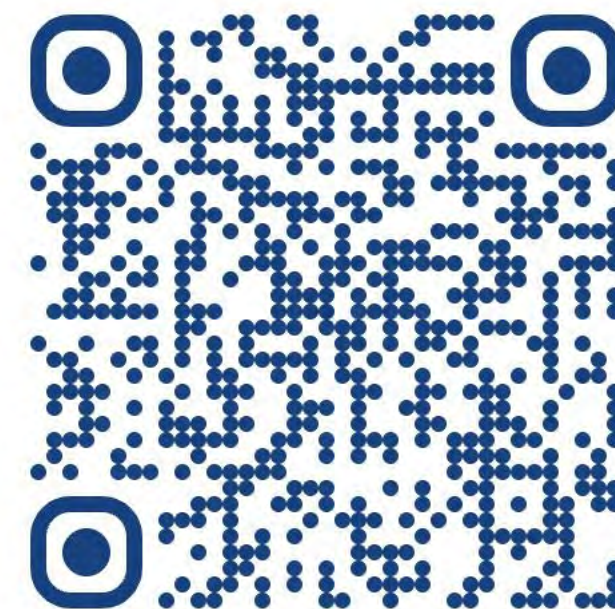
Interactive component browser in RICA
rica-fmri.netlify.app

Component	Kappa	Rho	Variance %	κ Rank	ρ Rank	Dice FT2	Dice FS0	S/N t	Classification	Tags
ICA 29	105.57	18.36	0.54	7.00	16.00	0.79	0.67	13.35	accepted	Likely BOLD
ICA 30	68.46	17.99	0.37	14.00	18.00	0.75	0.64	17.81	accepted	Likely BOLD
ICA 31	136.49	28.57	9.08	1.00	2.00	0.72	0.63	5.96	accepted	Likely BOLD

RUNNING TEDANA

```
pip install tedana
tedana -d data_e1.nii data_e2.nii data_e3.nii \
  -e 15 30 45 \
  -tree minimal \
  --mask mask_file.nii \
  --convention bids
```

Code & Interactive Reports



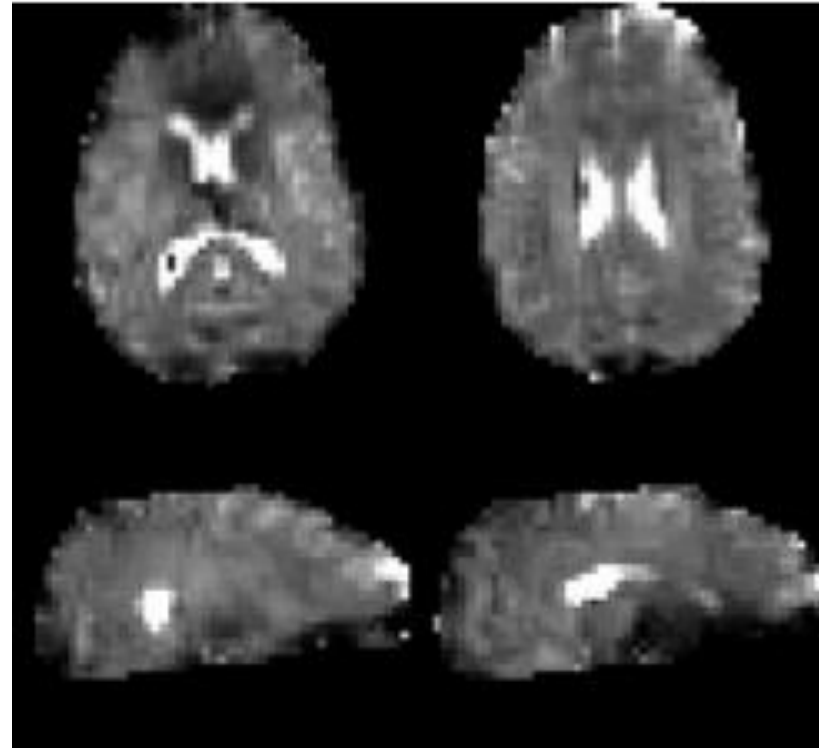
Built into AFNI & fMRIPrep pipelines

tedana.readthedocs.io includes:

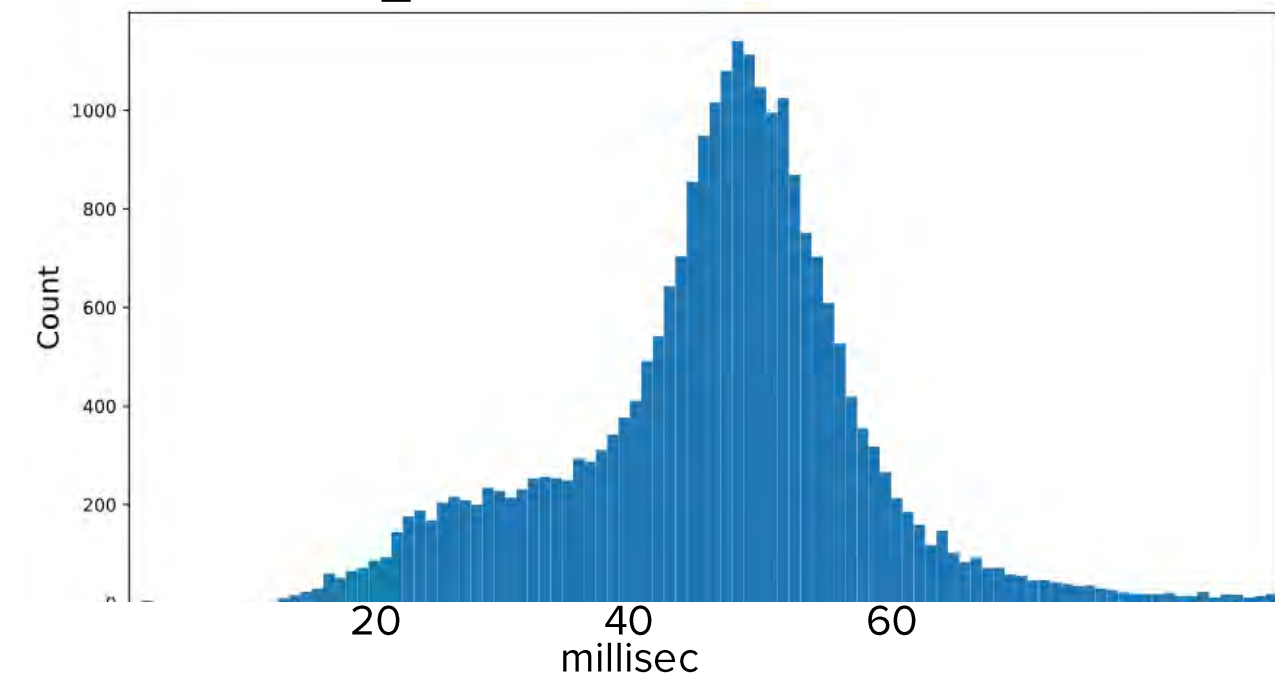
- Instructions on expected preprocessing steps
- Descriptions of options, output files, and visualizations
- Can also run from within python

TEDANA QUALITY CHECK REPORT

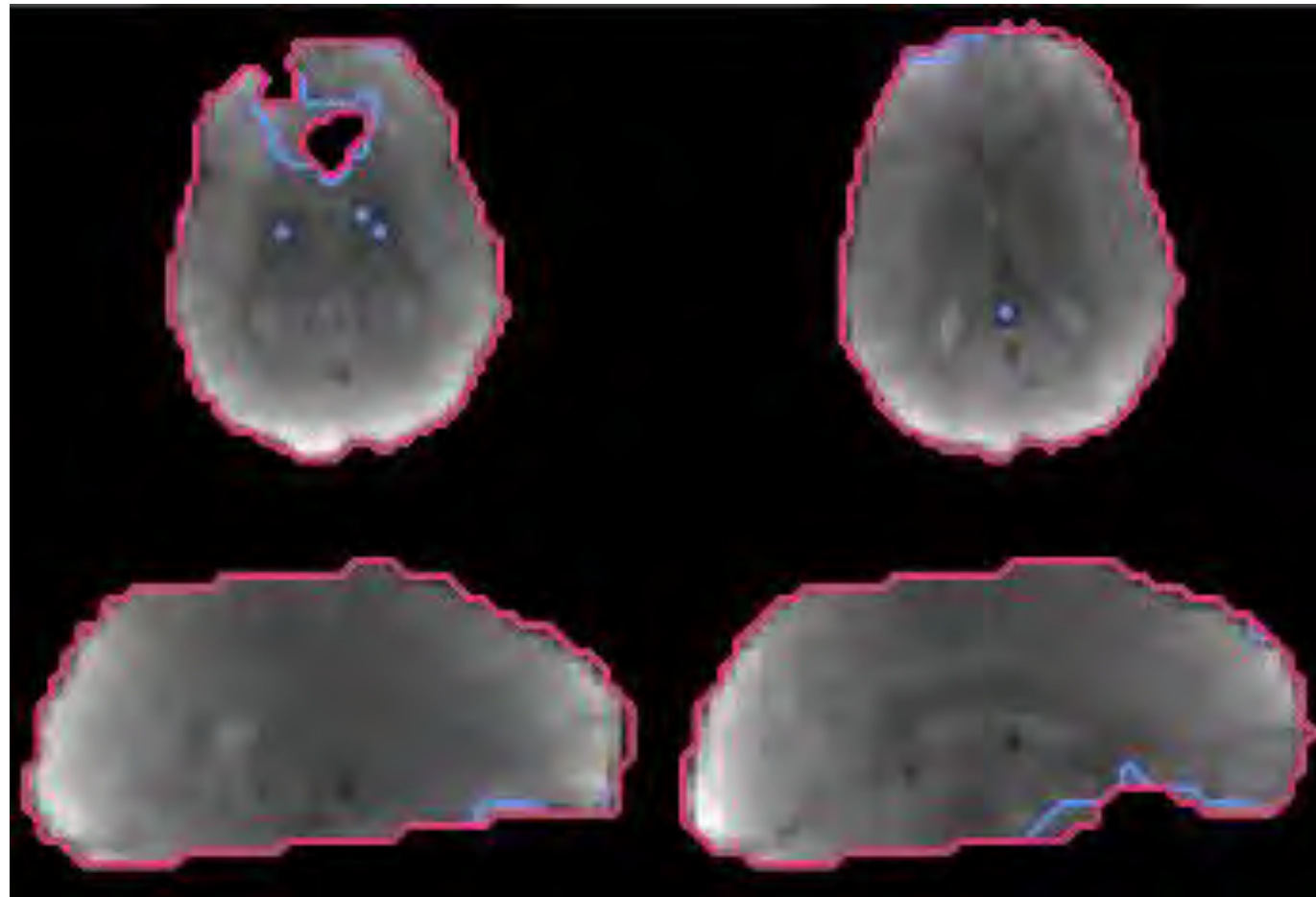
Mean T_2^*



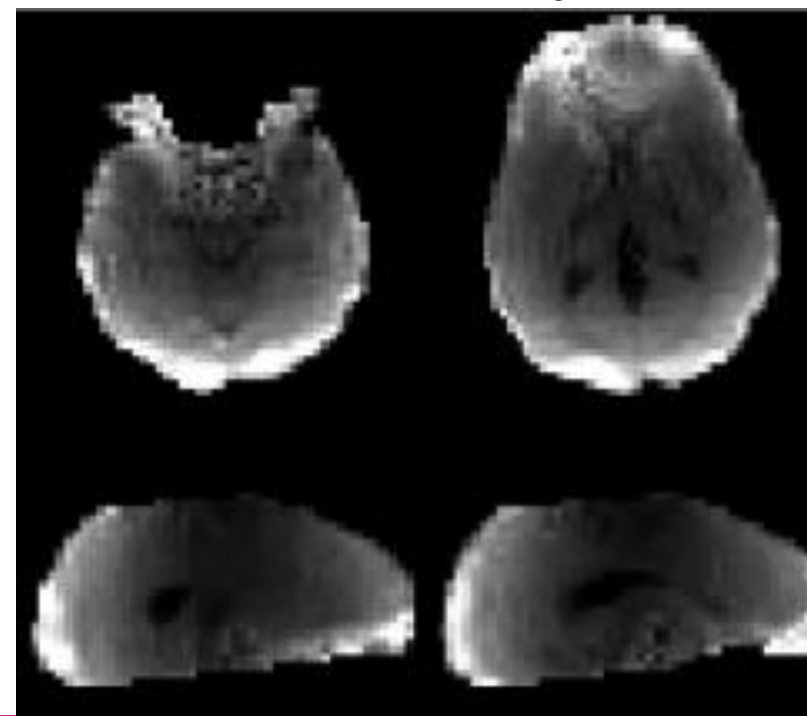
T_2^* Distribution



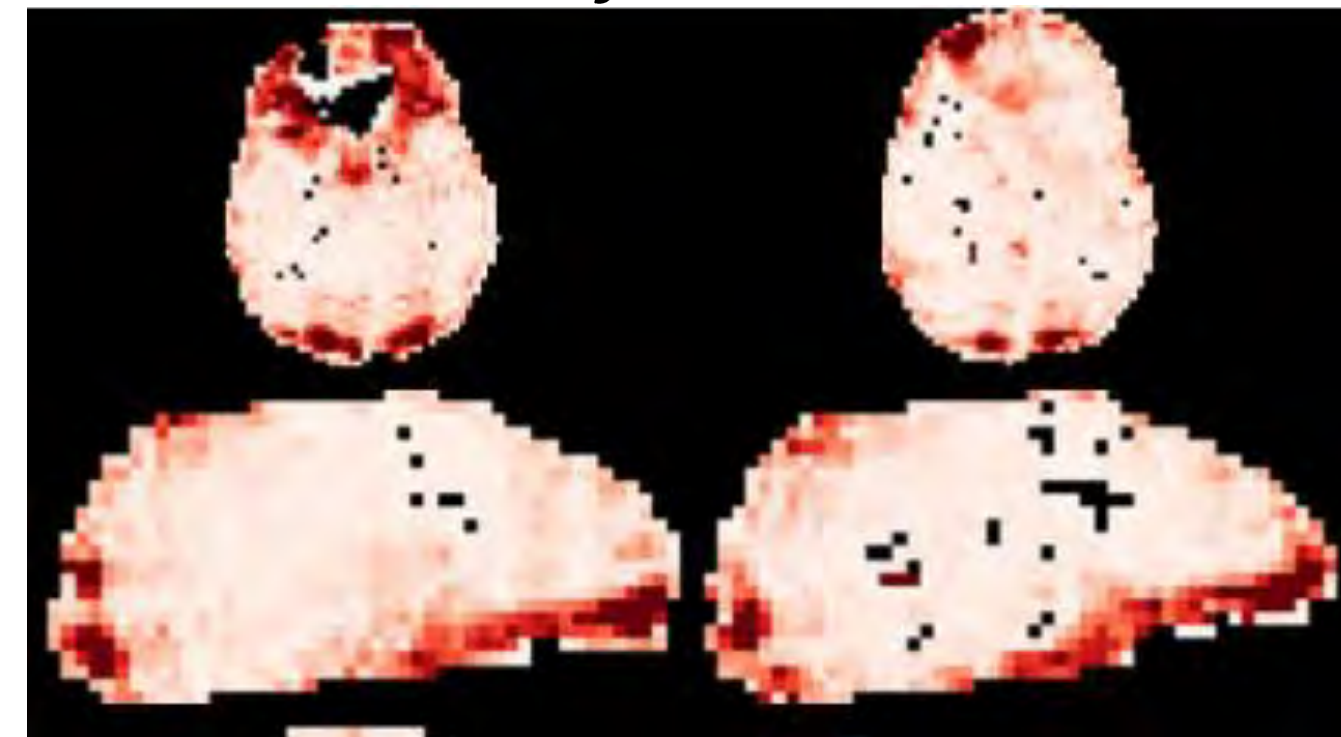
Initial & mask with 3 good echoes



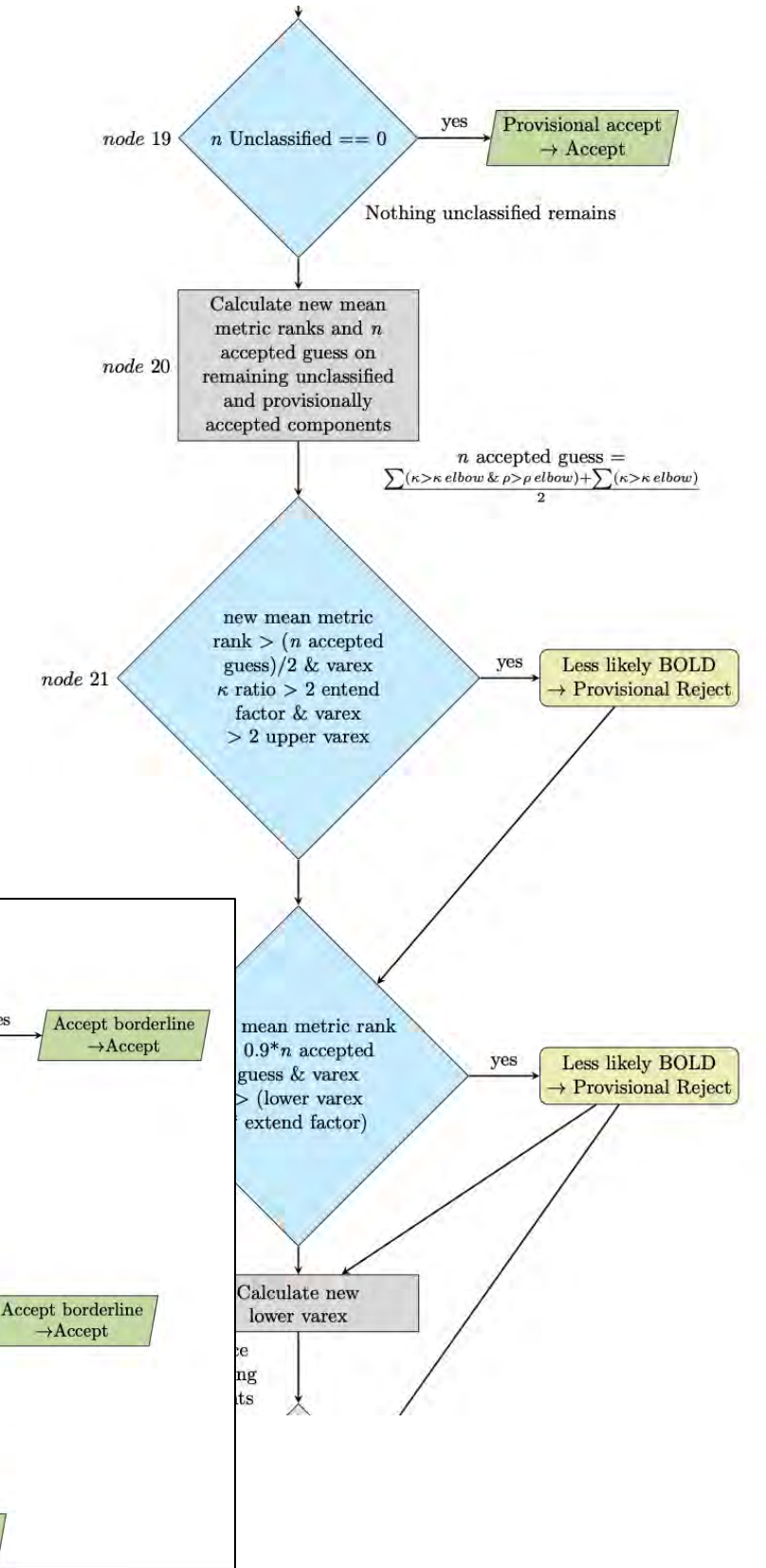
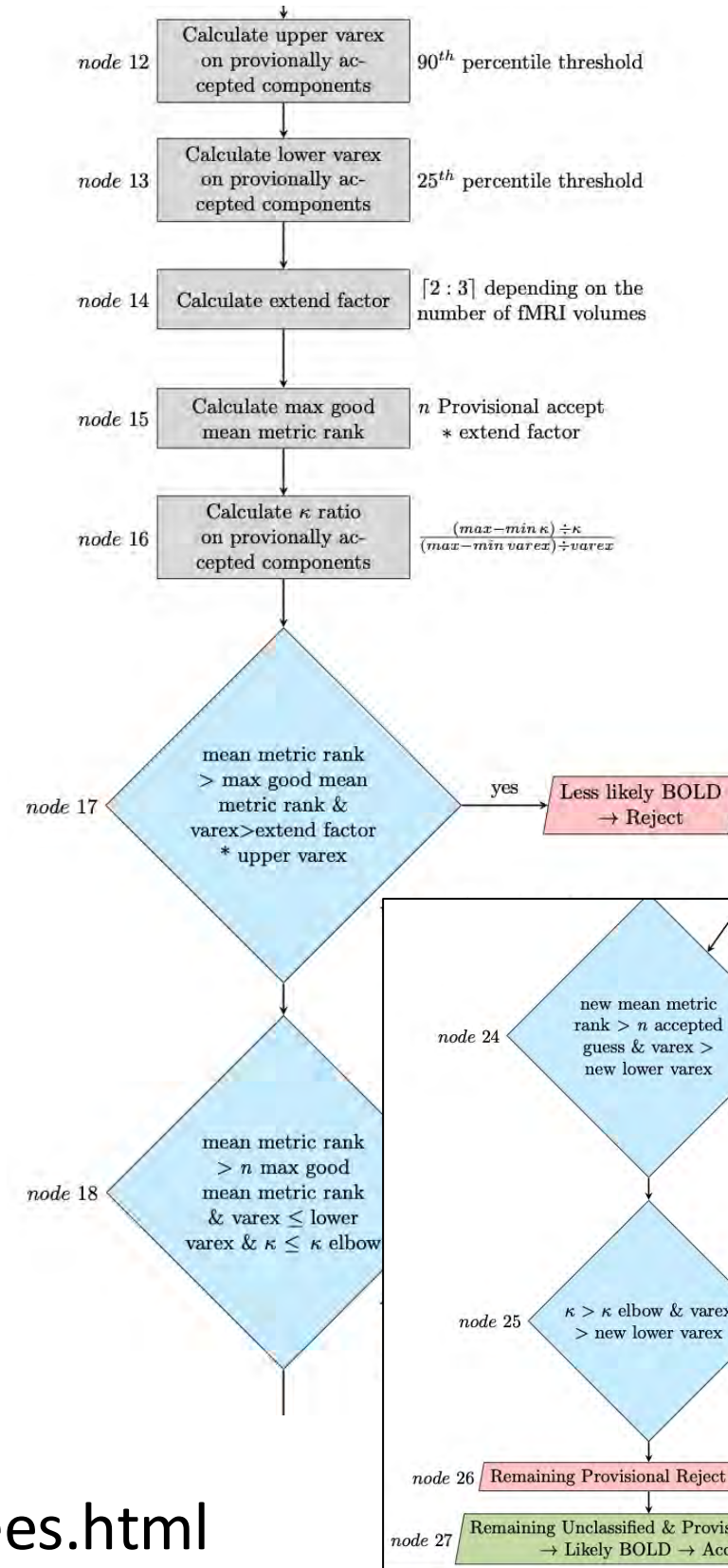
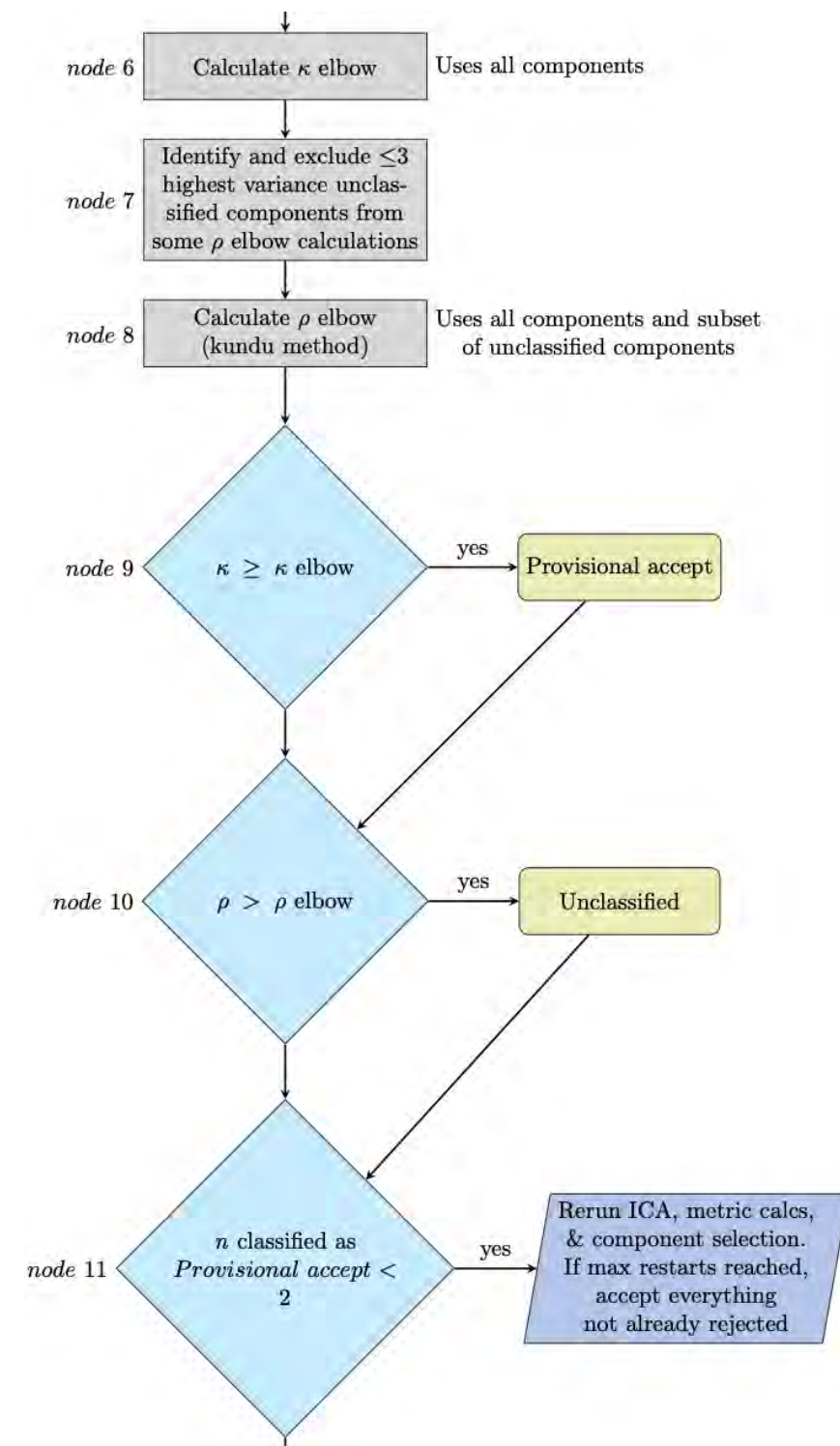
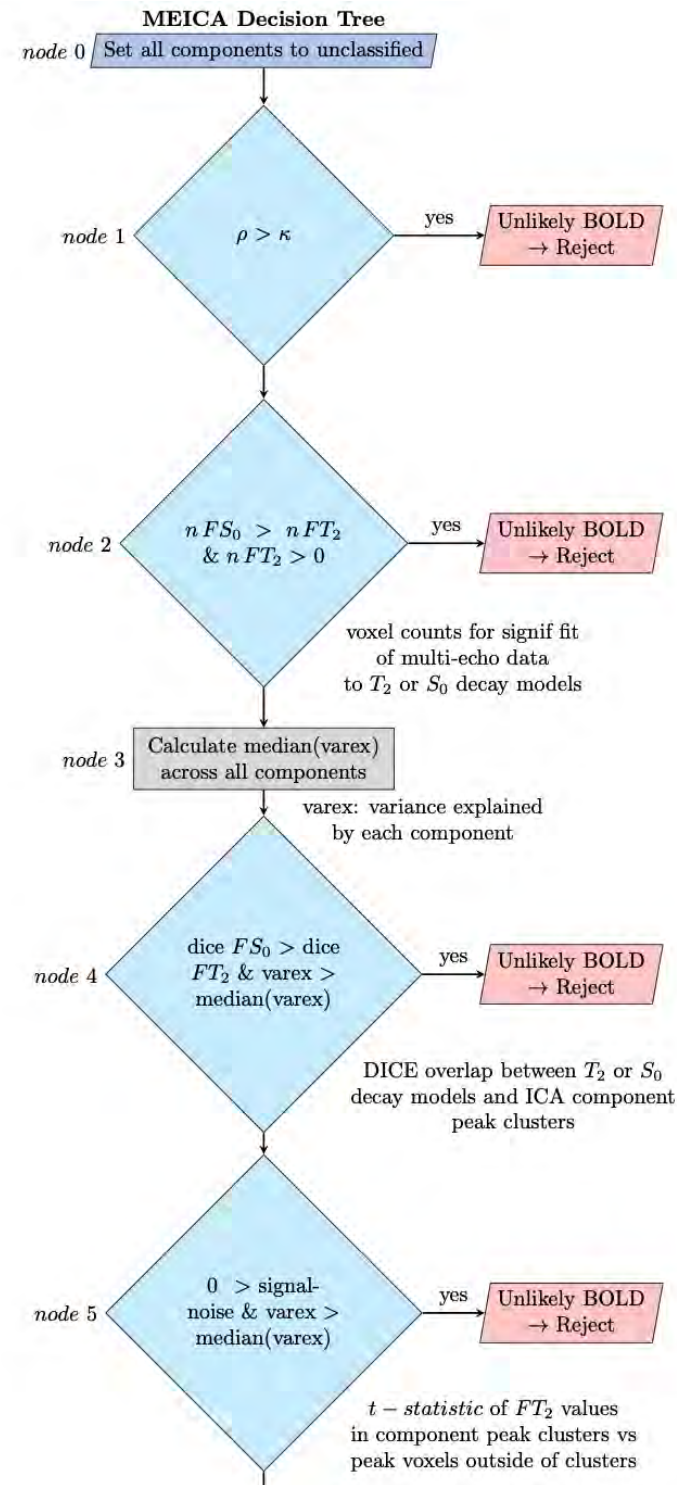
Mean S_0



Mean decay model fit error



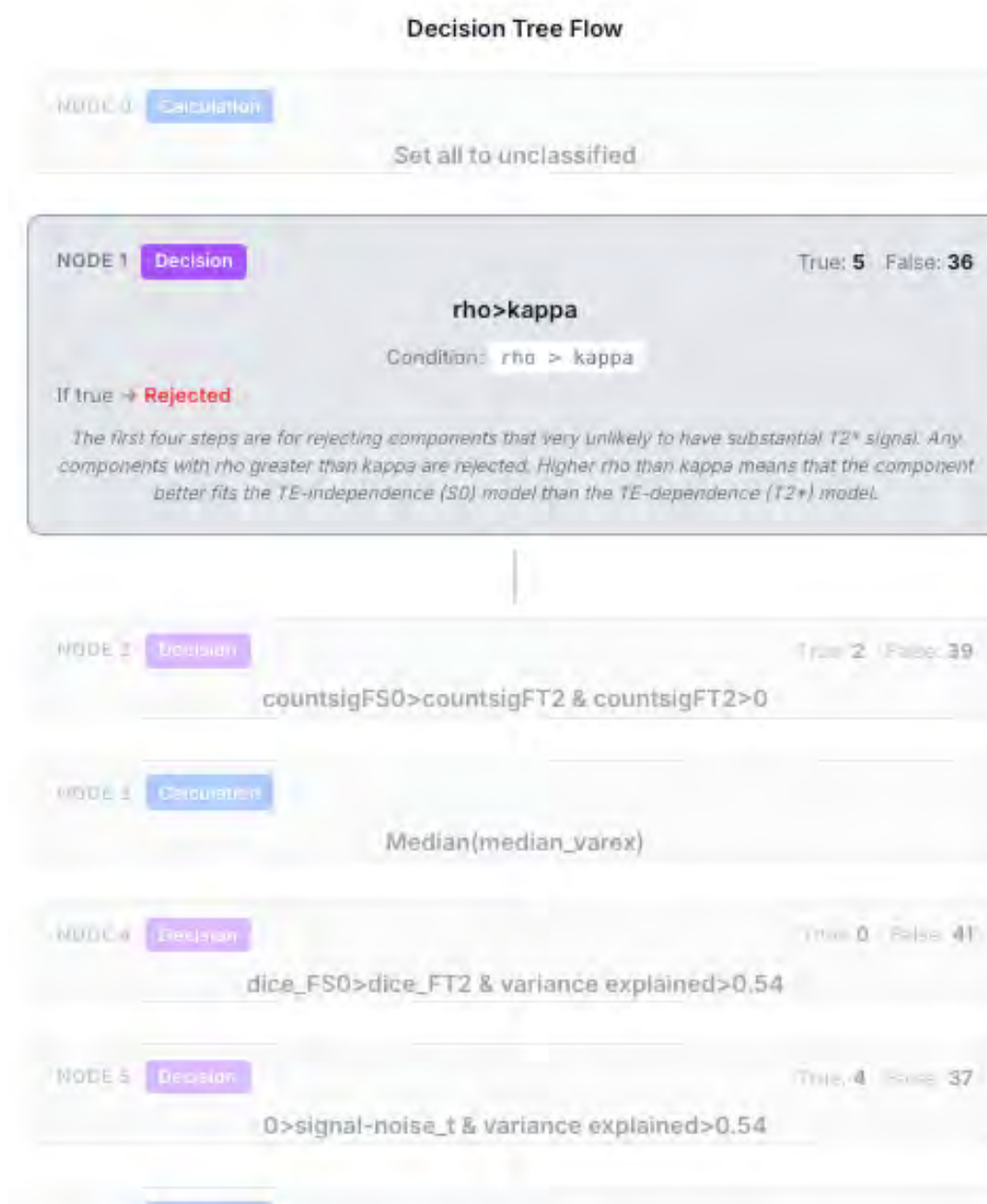
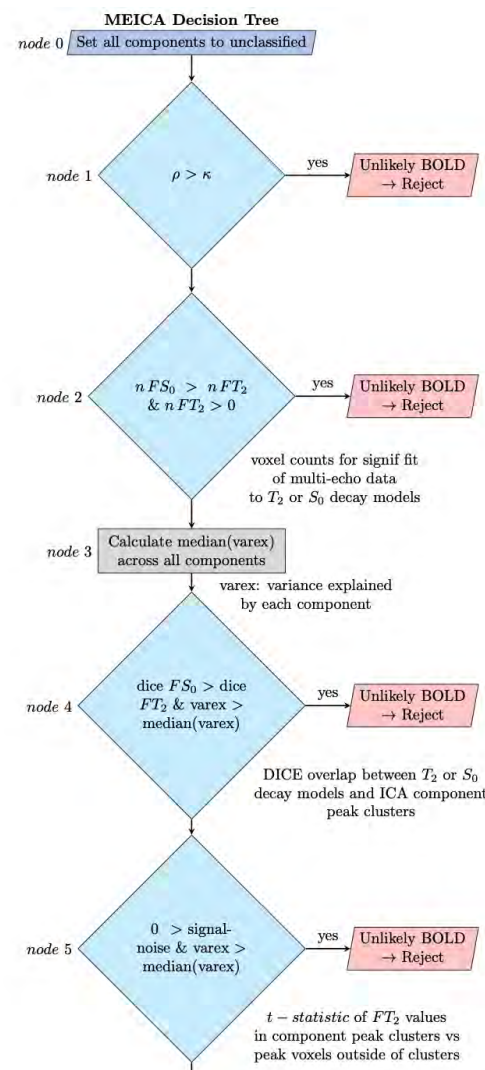
DECIDING WHAT TO REJECT IS NOT SOLVED



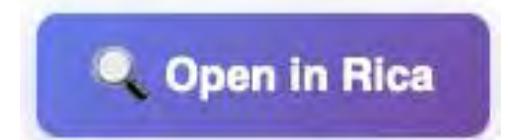
https://tedana.readthedocs.io/en/stable/included_decision_trees.html

DECIDING WHAT TO REJECT IS NOT SOLVED

- Tedana is designed to allow for multiple decision tree options
 - Supports continued innovation
 - Supports dataset-specific changes (more/less aggressive, infants, patients)



Interactive view of the accept vs reject decision tree process using



COULD EXTERNAL REGRESSORS HELP?



“Standard” tedana evaluates:

- Kappa (BOLD-like signal)
- Rho (non-BOLD signal)
- Variance explained
- Spatial features



External Regressor Decision Tree:

- Head motion
- Respiration
- Heart rate
- CSF signal
- Task regressor

Classifies ICA component as
“Accept” or Reject”

Does this ICA component look like
something I already know about?



COULD EXTERNAL REGRESSORS HELP?

“Standard” tedana evaluates:

- Kappa (BOLD-like signal)
- Rho (non-BOLD signal)
- Variance explained
- Spatial features



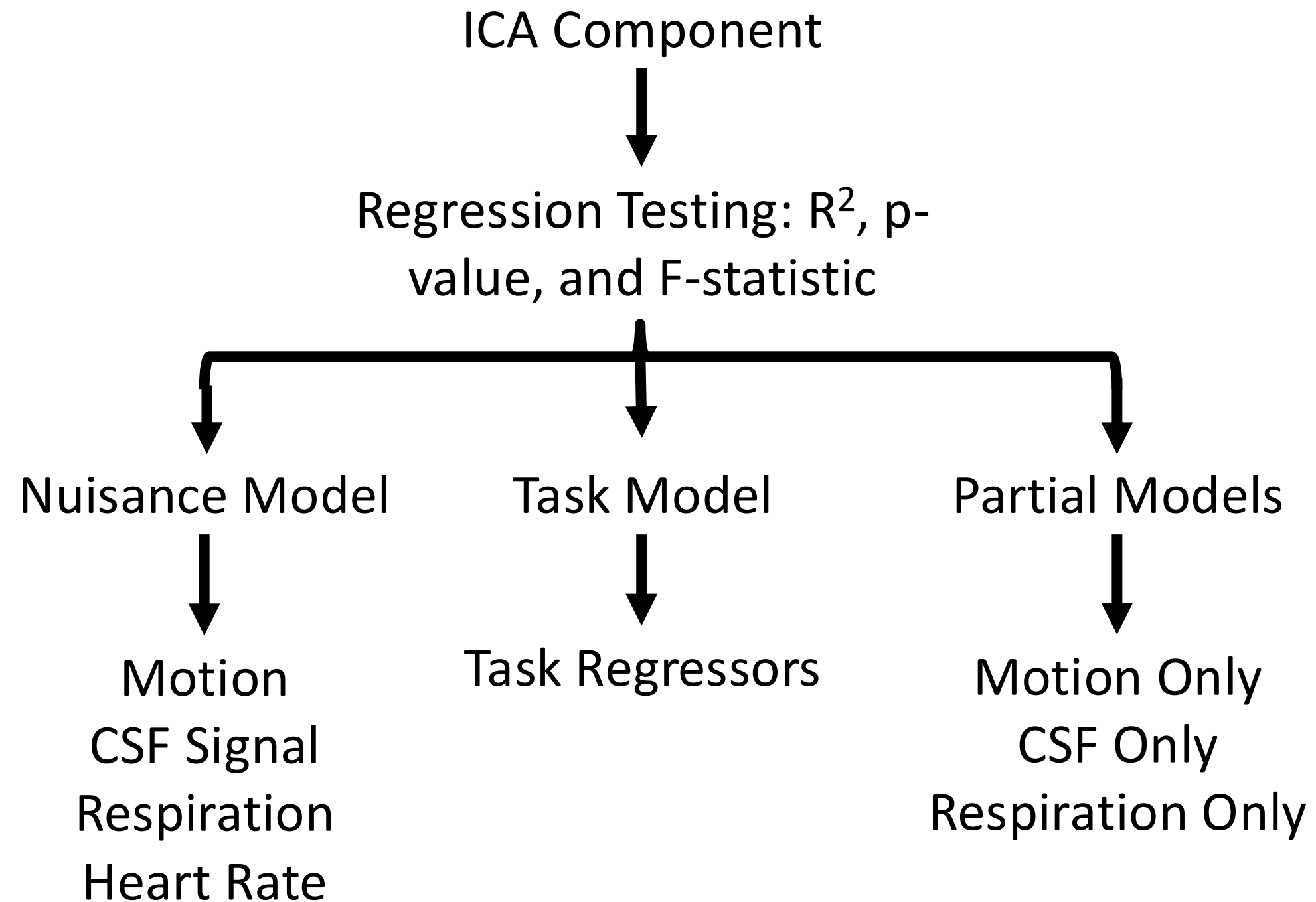
External Regressor Decision Tree:

- Head motion
- Respiration
- Heart rate
- CSF signal
- Task regressor

Classifies ICA component as
“Accept” or Reject”

Does this ICA component look like
something I already know about?

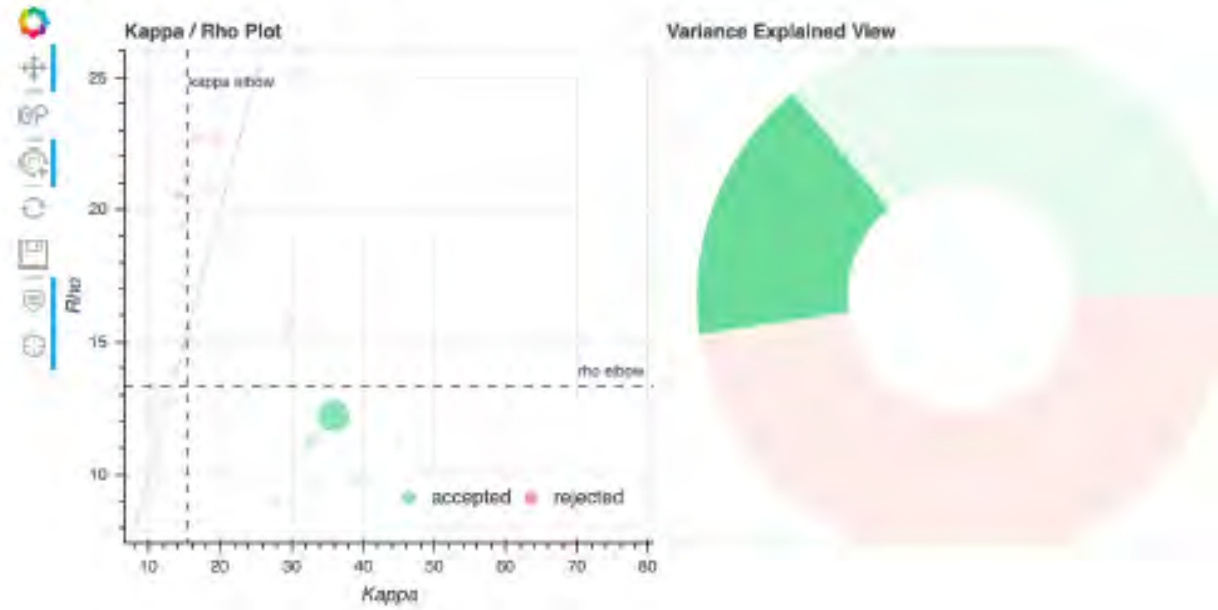
COULD EXTERNAL REGRESSORS HELP?



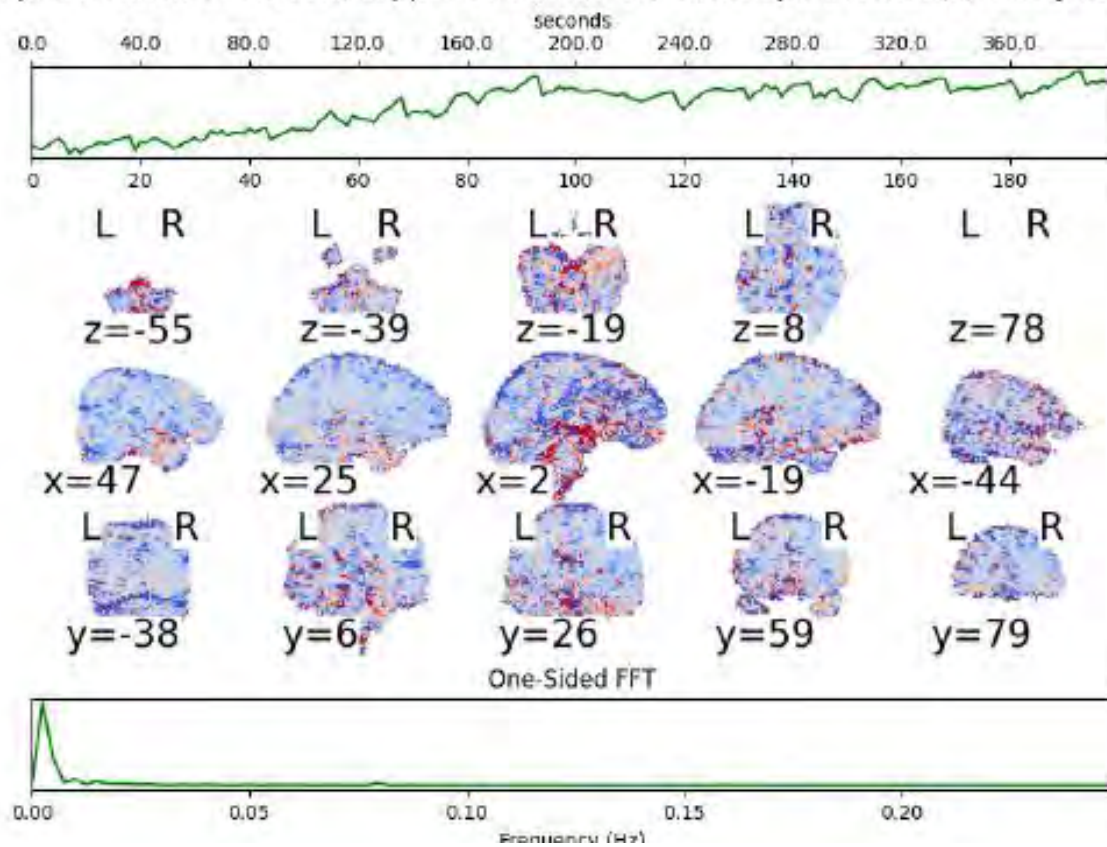
** important note: tedana is doing component classification, not voxel wise inference

NUISANCE MODEL

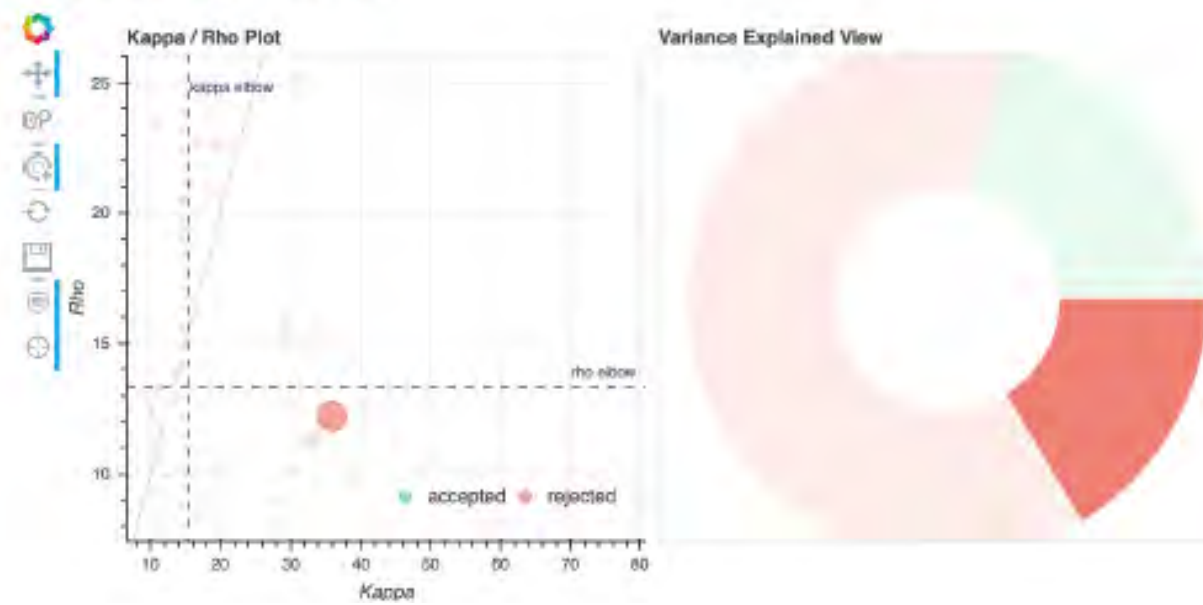
ICA components



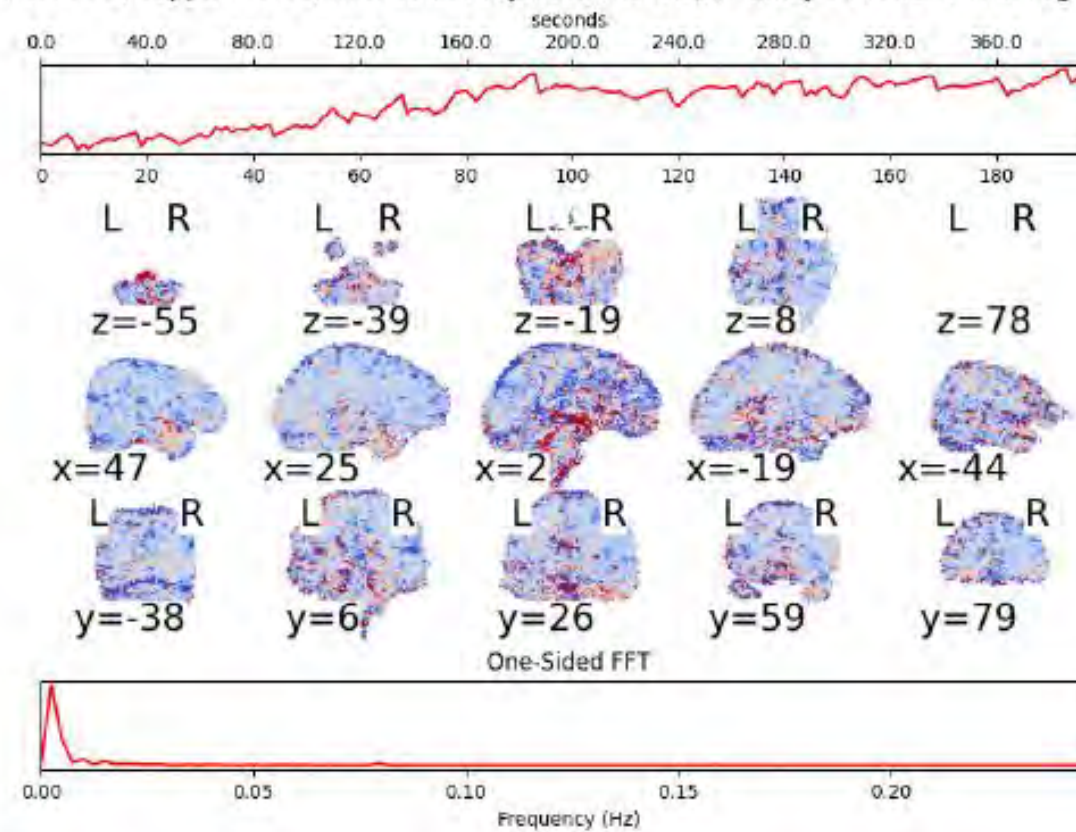
Comp. 13: variance: 16.39%, kappa: 35.90, rho: 12.20, accepted reason(s): Likely BOLD



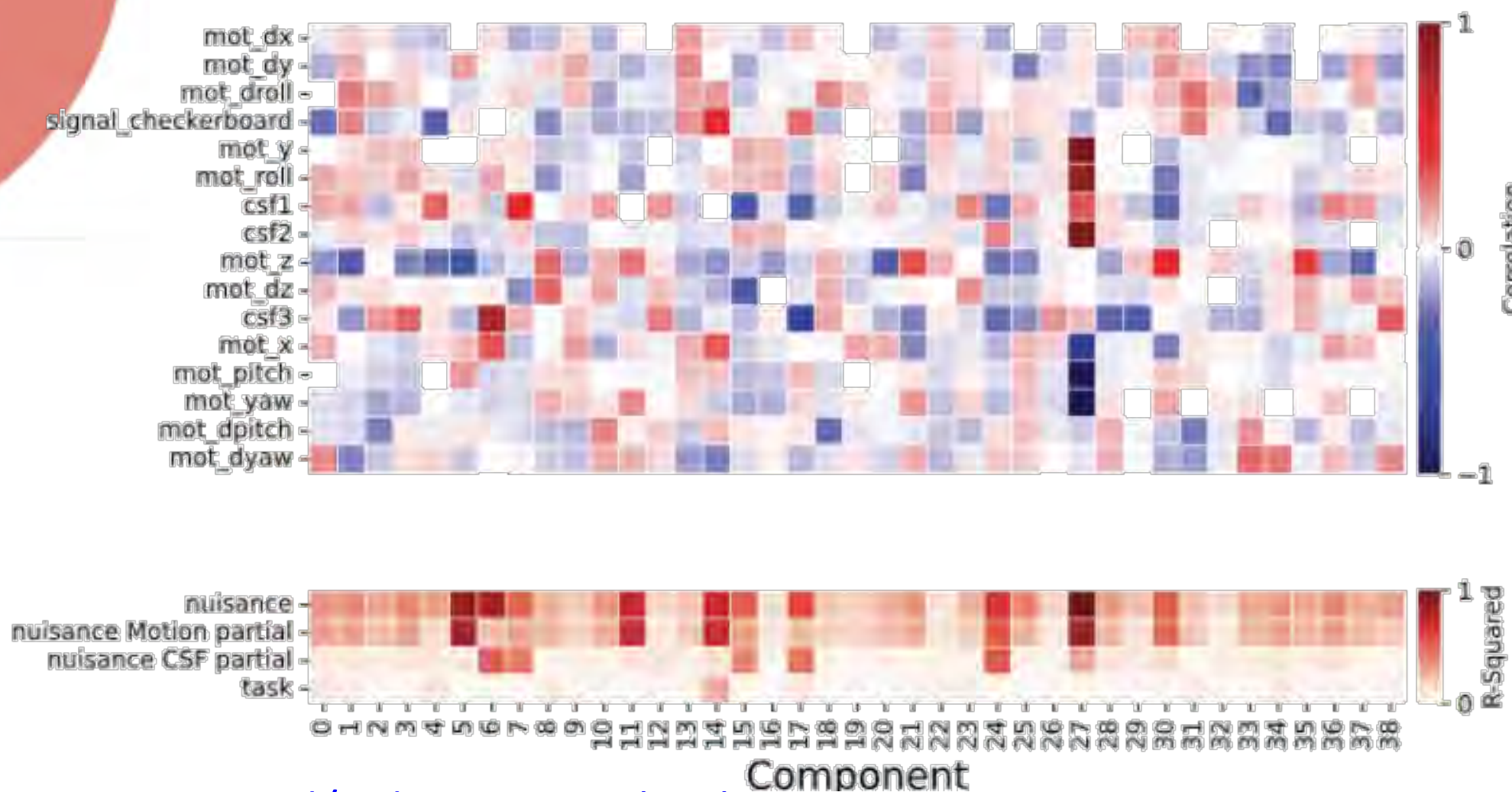
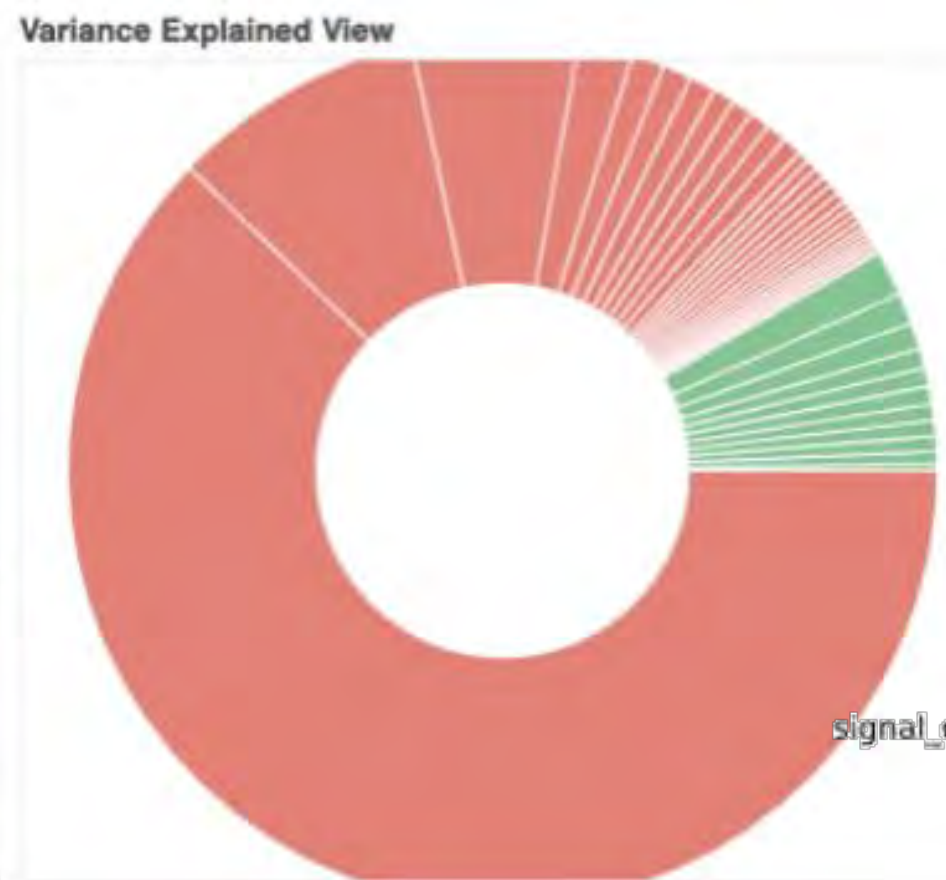
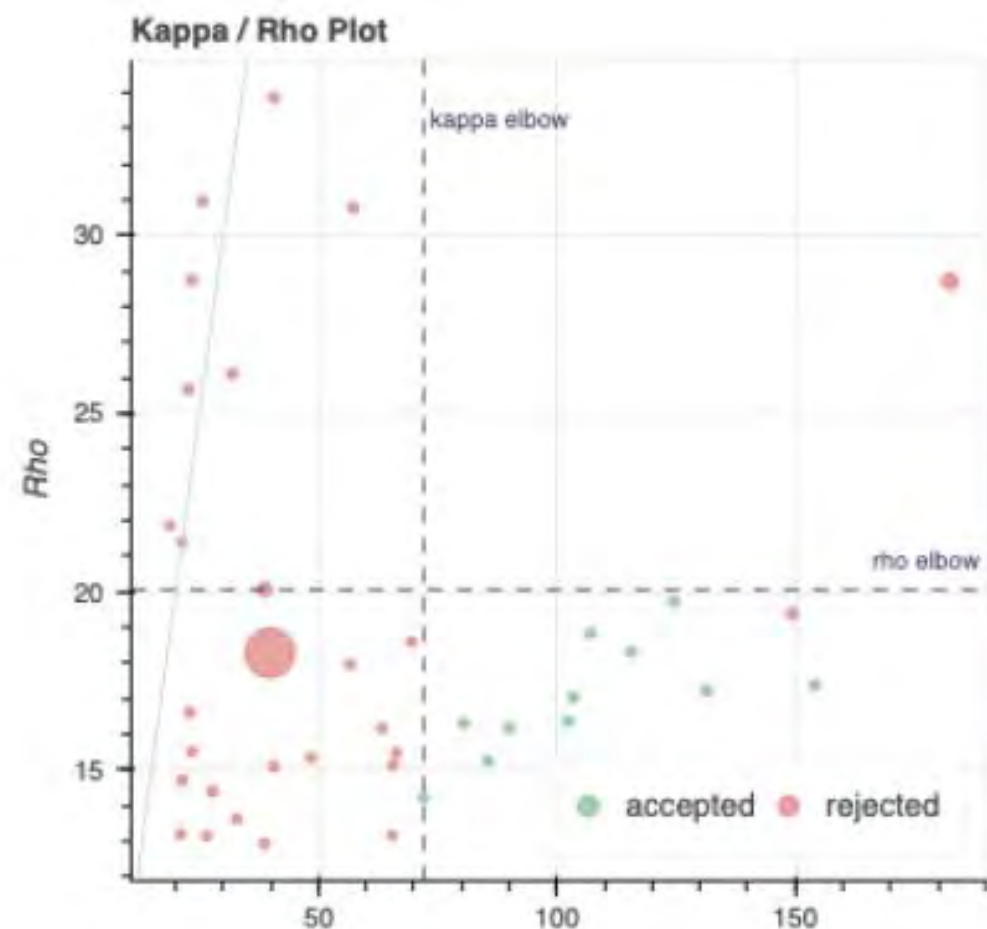
ICA components



variance: 16.39%, kappa: 35.90, rho: 12.20, rejected reason(s): Likely BOLD, External regressors, Unlit



TASK/PARTIAL MODELS



https://me-ica.github.io/ohbm-2026-multiecho/tedana_external_regress_processed/tedana_report.html

TAKE HOME MESSAGES

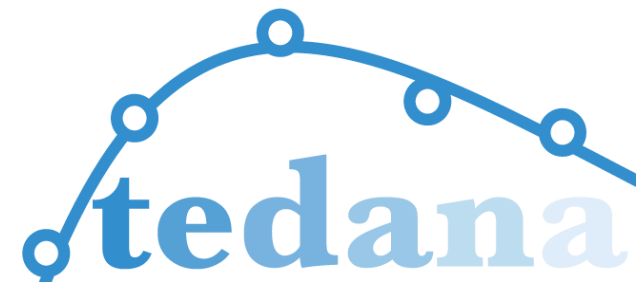
Multi-echo fMRI

- Improves data quality now
- Keeps improving with advances in MRI acquisition and processing
- Is an active area for research & innovation

Things to notice across this course

- Speakers will highlight different methods
- Differences *may* be due to different applications & scientific priorities
- Anyone working in this space see benefits from using multi-echo fMRI

ACKNOWLEDGEMENTS



Many, including:

- **Taylor Salo**
- Eneko Uruñuela
- Sarah Goodale
- Katie Lamar Bruno
- Brandon Forys
- Stefano Moia
- Elizabeth DuPre
- **Peter Bandettini**
- Javier Gonzalez-Castillo
- Vinai Roopchansingh
- Tyler Morgan
- Catherine Walsh
- Marlene Smith
- Ka Chun Lam
- NIH Grant ZIAMH002783

COURSE OVERVIEW

INTRODUCTION & CONCEPTS

9:00	Dan Handwerker (+ Sarah Goodale): Introduction to multi-echo fMRI and tedana
9:50	Mélanie Garcia: Multi-echo fMRI data quality control
10:25	Javier Gonzalez-Castillo: Now that I have multi-echo data, what else can I do with it?
11:00	Discussion and Q&A: Best practices for collecting and validating multi-echo fMRI data
11:20	Break

RESEARCH & CLINICAL APPLICATIONS

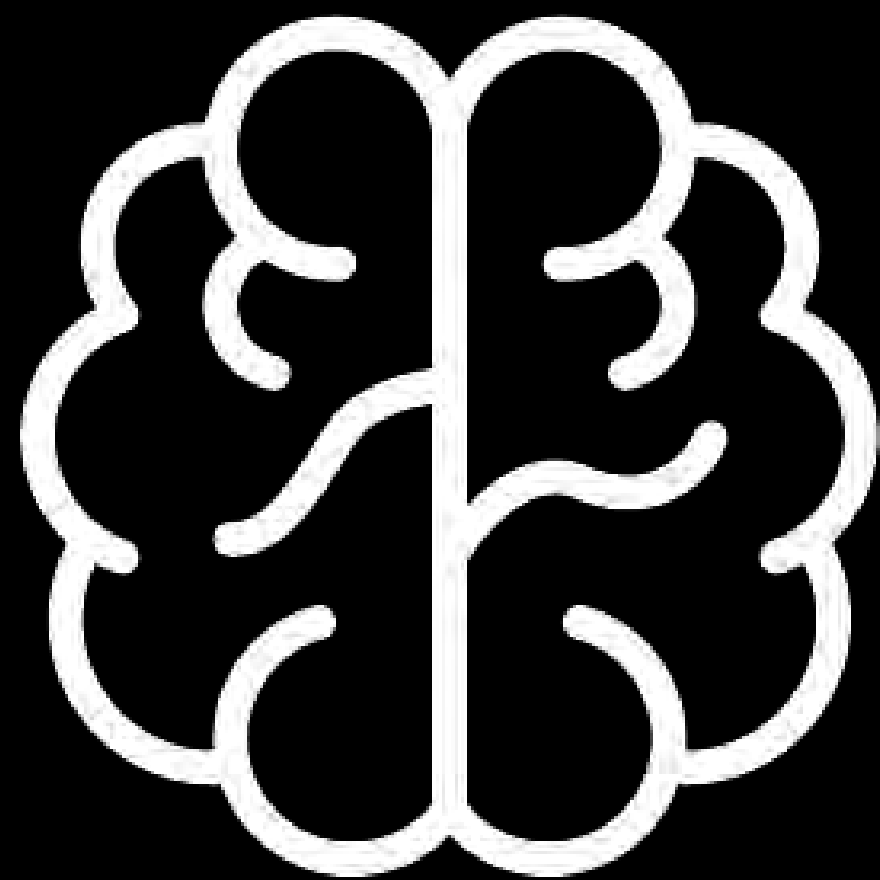
11:30	Eric Pierre: Multi-echo fMRI in a large clinical study — insights from the Australian Epilepsy Project
12:05	Eui-Jin Jung: Enhancing predictive modeling using multi-echo fMRI in pain
12:40	Lunch break 🥪🧀🍇 with informal Q&A for the final 20 minutes of the break
13:40	Julia Moser: Multi-echo fMRI in developmental neuroimaging
14:15	Discussion and Q&A: Advice & challenges for using multi-echo fMRI in clinical studies

PUSHING METHODS

14:35	Kathryn Lamar-Bruno: Benefits and challenges of Echo Planar Time-Resolved Imaging (EPTI) for multi-echo fMRI
15:10	Nathan Spreng + Prantik Kundu: Subcortical connectivity at 3T & 7T with ME fMRI
15:45	Break
15:55	Logan Dowdle: The higher the field, the faster it falls — challenges and opportunities of multi-echo fMRI at 7T
16:40	Eneko Uruñuela: Is generative AI the next step in multi-echo fMRI denoising?
17:05	Panel Discussion and Q&A: Unmet needs, future goals and challenges

This schedule & other resources including a fast OHBM abstract browser





OHBM 2026