# DENOISING DATA WITH MULTI-ECHO EPI

(…Multi-echo EPI, Multi-echo EPI, Multi-echo EPI, Multi-echo EPI, Multi-Echo EPI, Multi-Echo EPI……)

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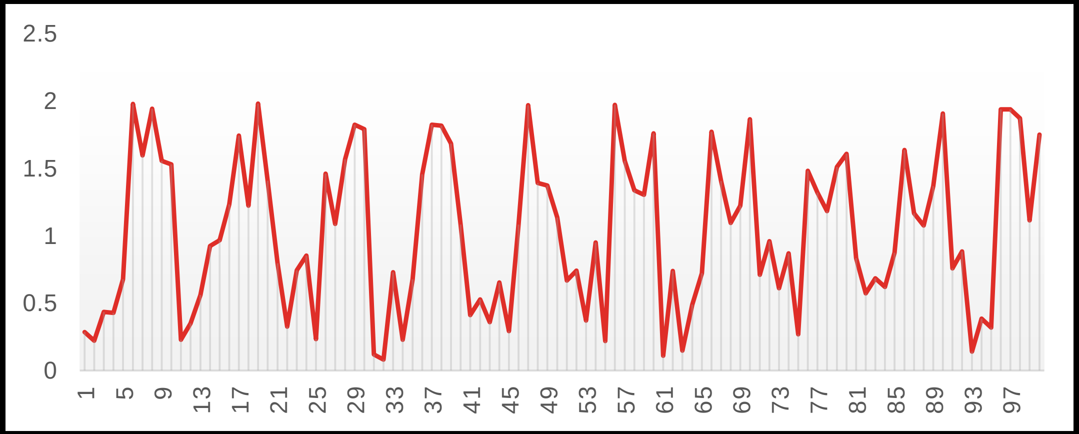
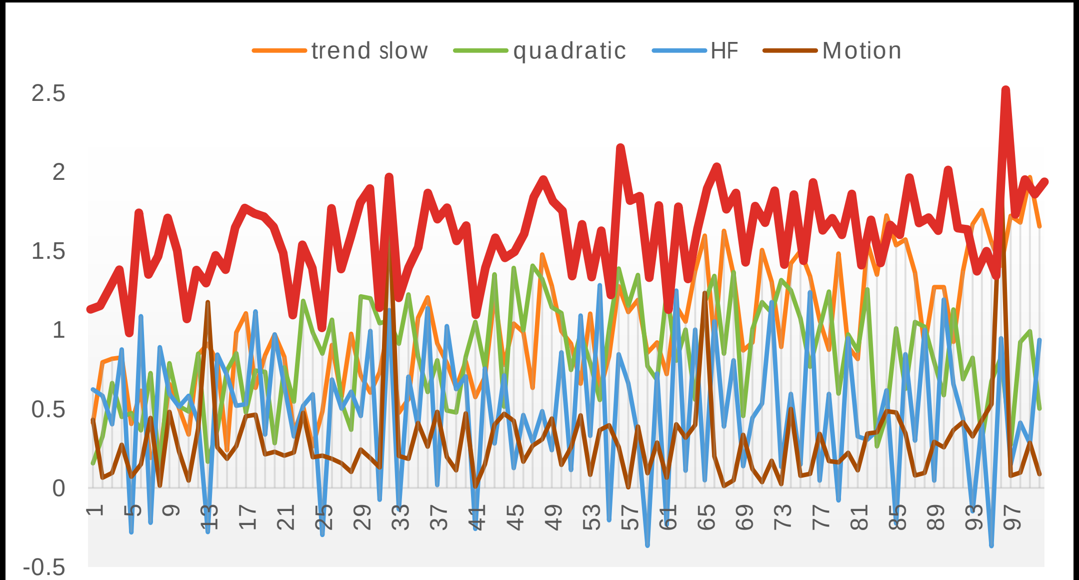
http://montilab.psych.ucla.edu

# THE PROBLEM

"[...] data from standard (i.e. single-echo) fMRI pulse sequences is limited by the fundamental problem that in such experiments, Blood Oxygen Level Dependent (BOLD) signal arising from spontaneous neuronal activity is not differentiable from fluctuations arising from cardiac and respiratory physiology, motion, and many other sources."
Kundu et al., 2012



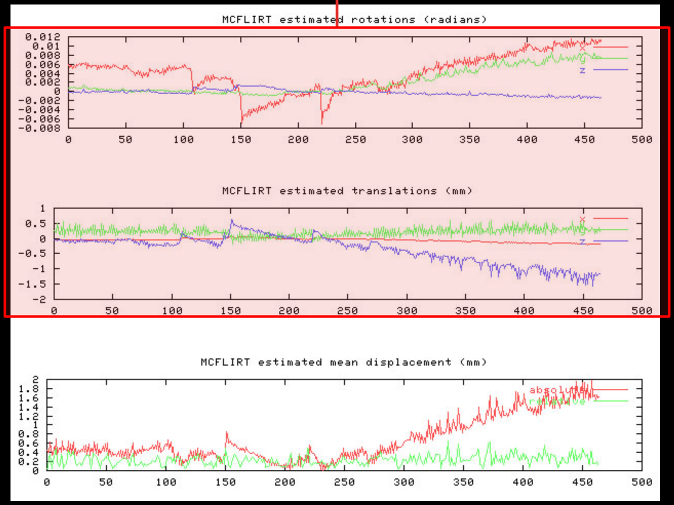
# THE PROBLEM

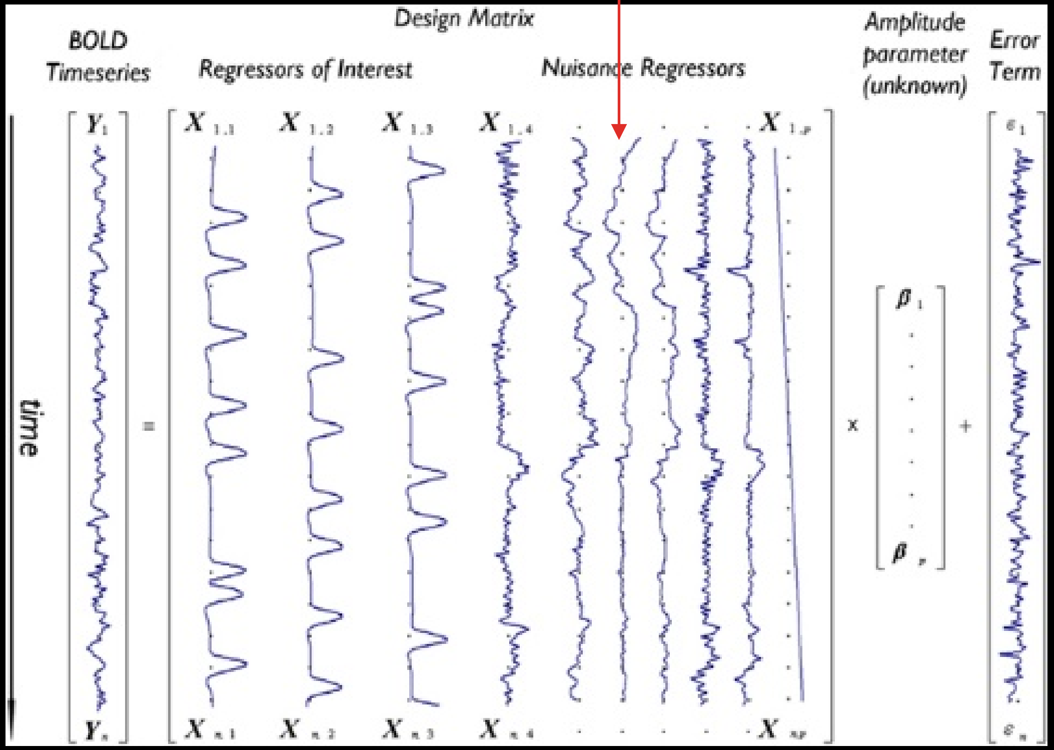
- Task-based fMRI (GLM-based analysis):
  - a-priori hypothesis of the signal of interest. If noise is correlated with the task-related activity it can produce false activations/deactivations/etc.
- Resting state fMRI:
  - NO a-priori hypothesis about the signal of interest: any correlation with noise will produce false positives

Slide from L. Griffanti

# APPROACH #1: THE STANDARD

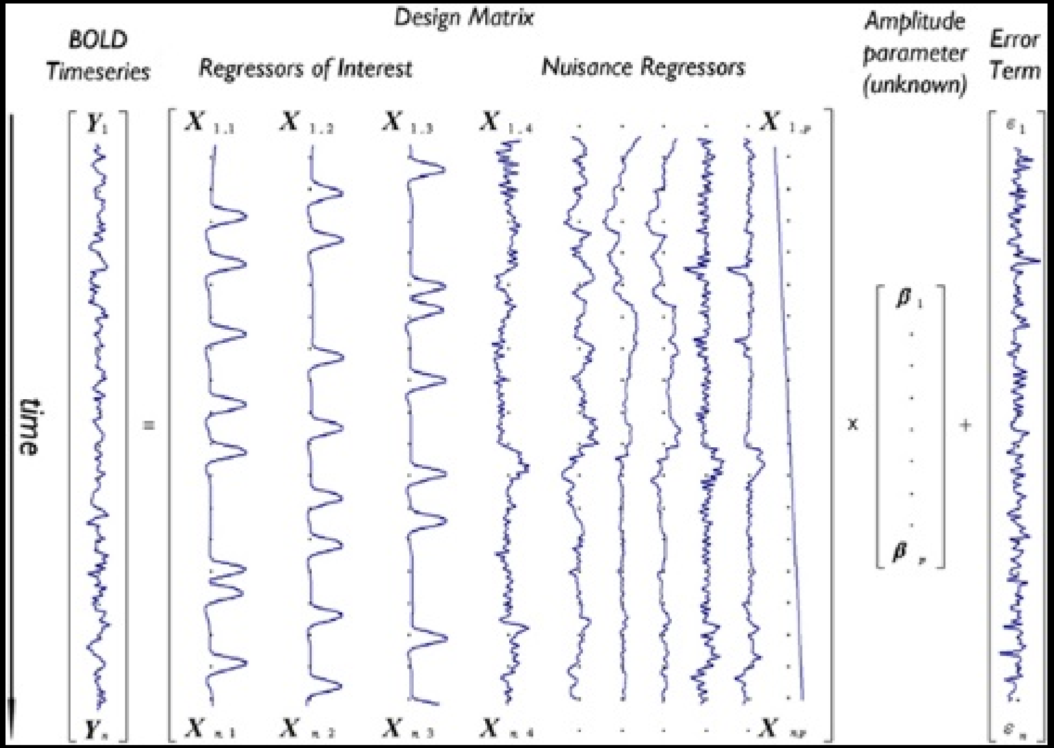
- Motion correction



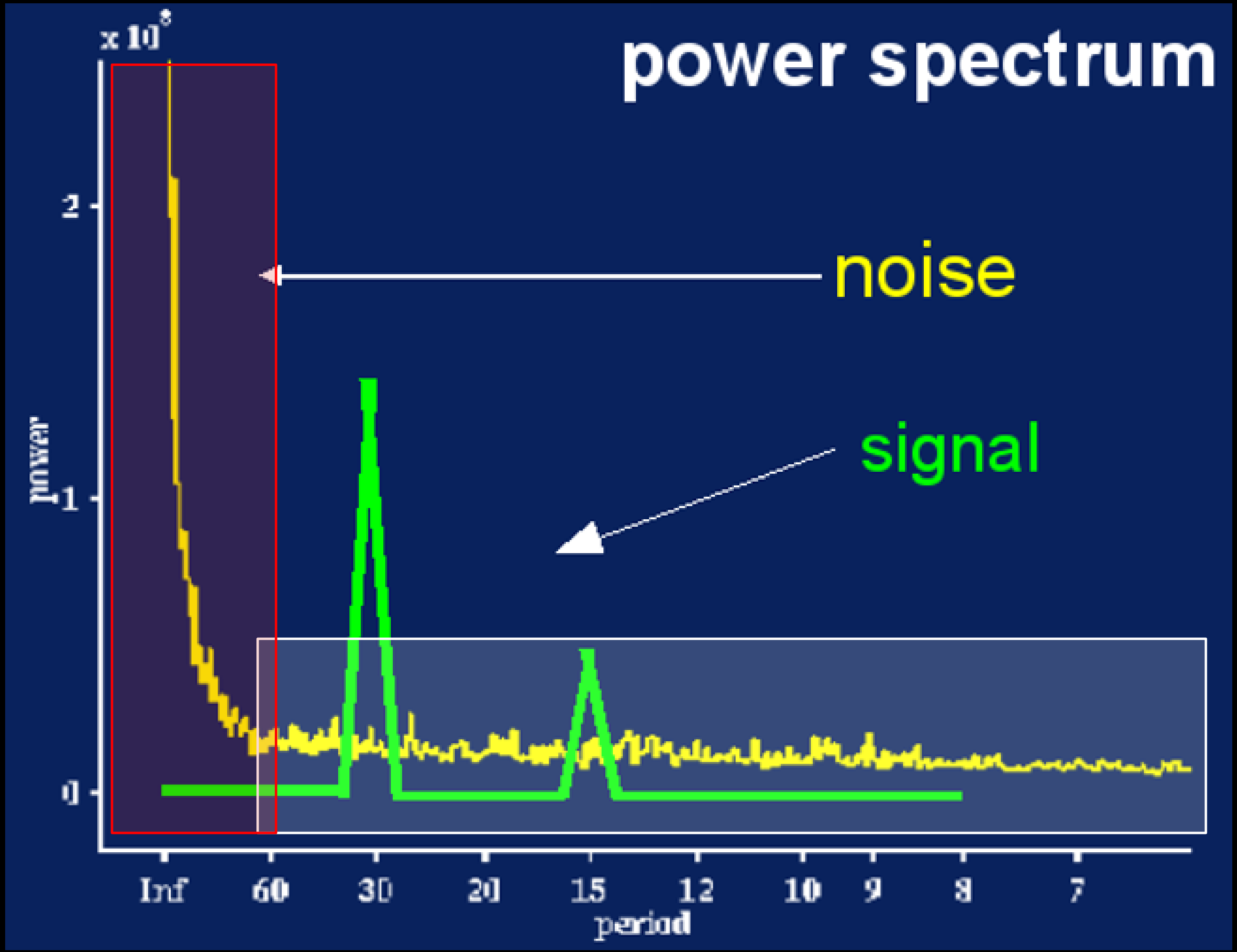
# APPROACH #1: THE STANDARD

- Motion correction
  - But residual motion, intra-TR motion, spin history effects remain
- Outliers/Scrubbing (Power et al., 2012)
  - Might lose a lot of data
- Global Mean Signal regression
  - Anti-correlations issue (Murphy et al., 2009)
- WM/CSF Regression
  - Doesn’t do that much (Power et al., 2012)
- Physiological recording (Glover et al, 2000)



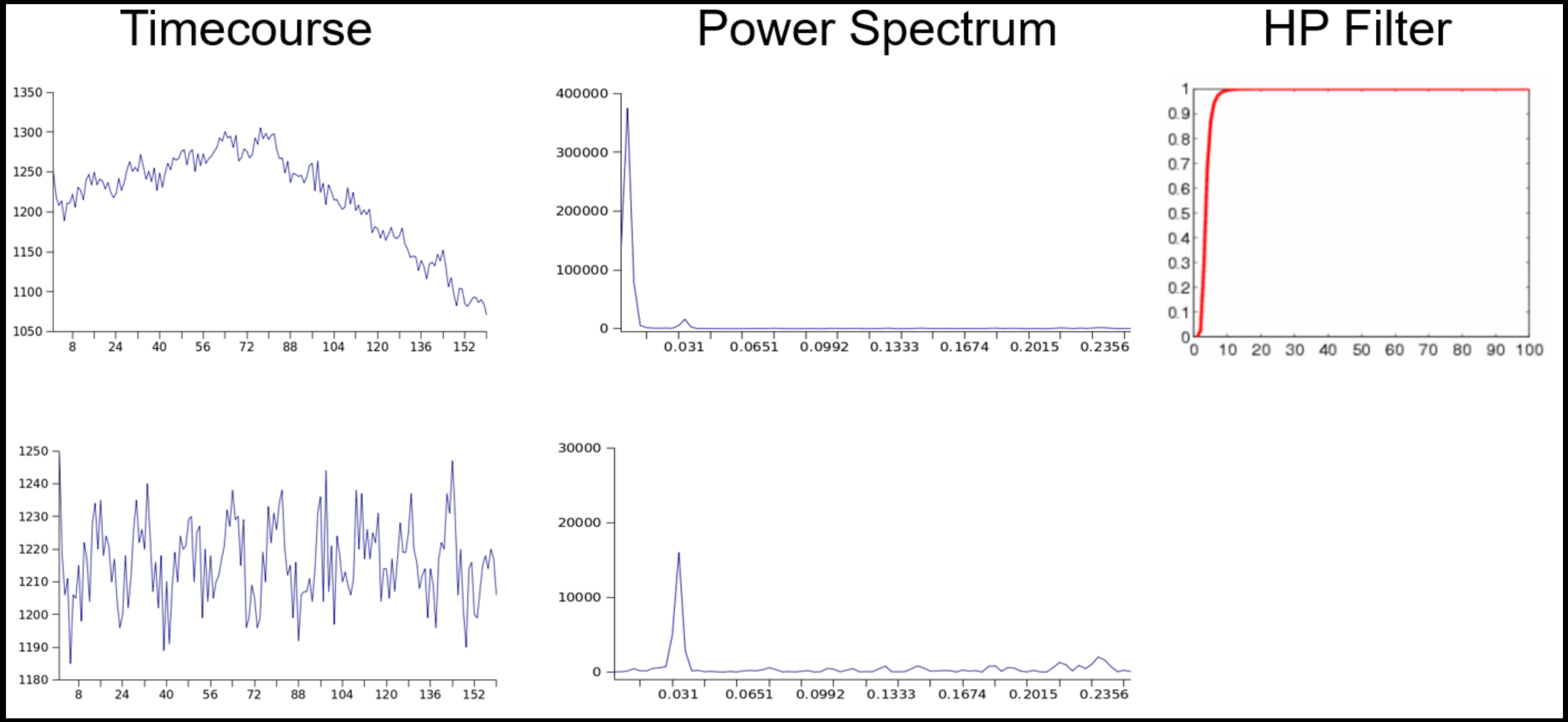
# APPROACH #1: THE STANDARD

- Spatial filtering



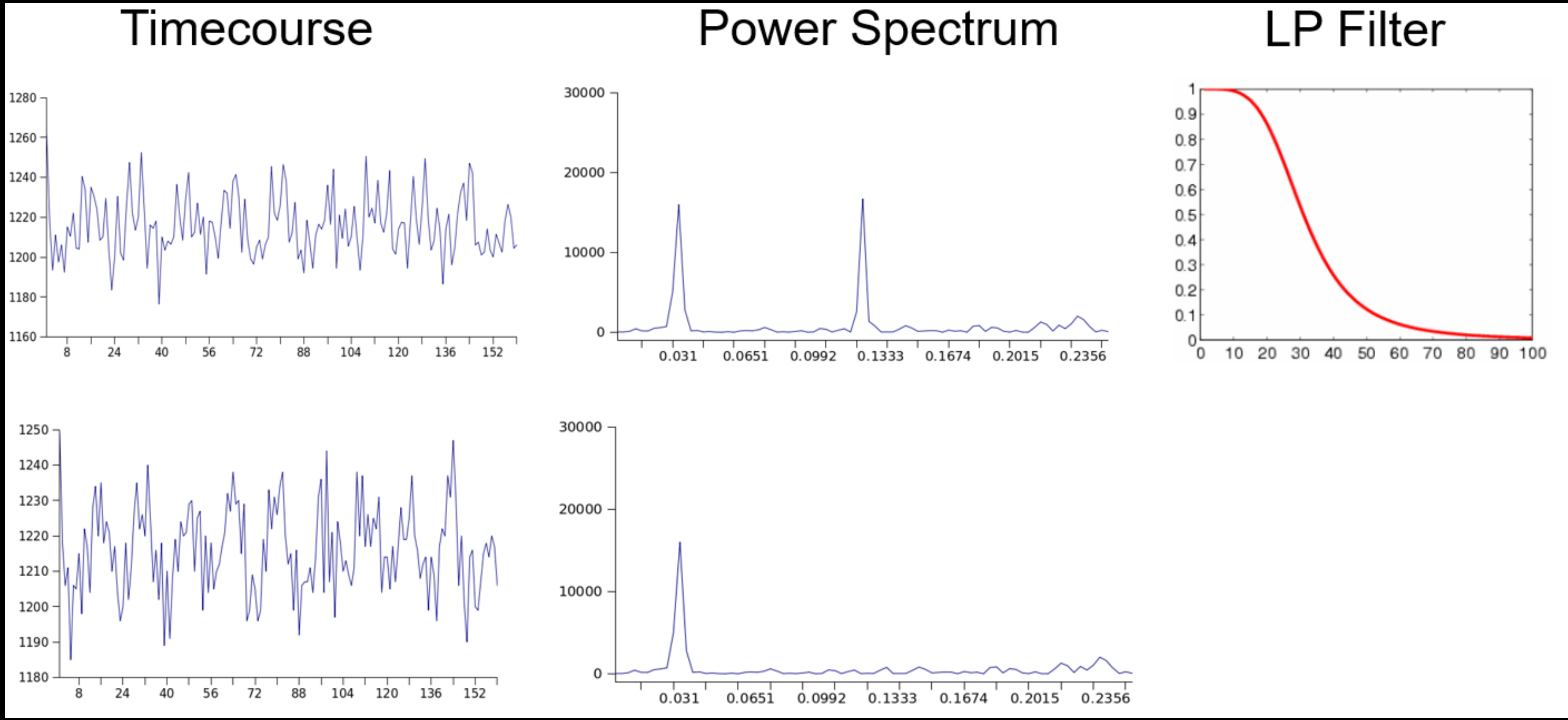
# APPROACH #1: THE STANDARD

- Motion correction
- Spatial filtering
  - Low Freq Noise



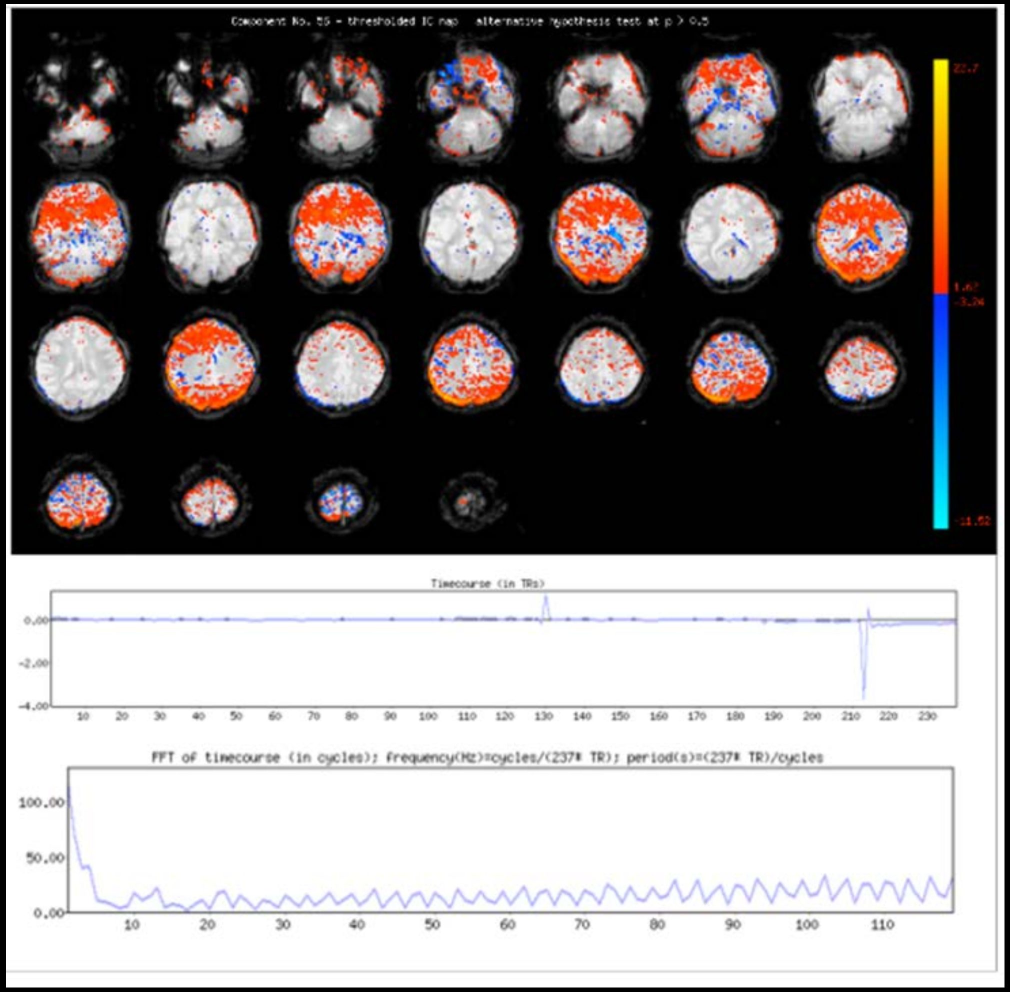
# APPROACH #1: THE STANDARD

- Motion correction
- Spatial filtering
  - Low Freq Noise
  - High Freq Noise



# APPROACH #2: DATA DRIVEN STRUCTURED NOISE REMOVAL

- Use data driven method to find noise and remove it from the data
  - Still have to run standard preprocessing including motion correction, high-pass filtering
- Identify bad components
  - Subjective (if done manually)
- Remove bad components from signal



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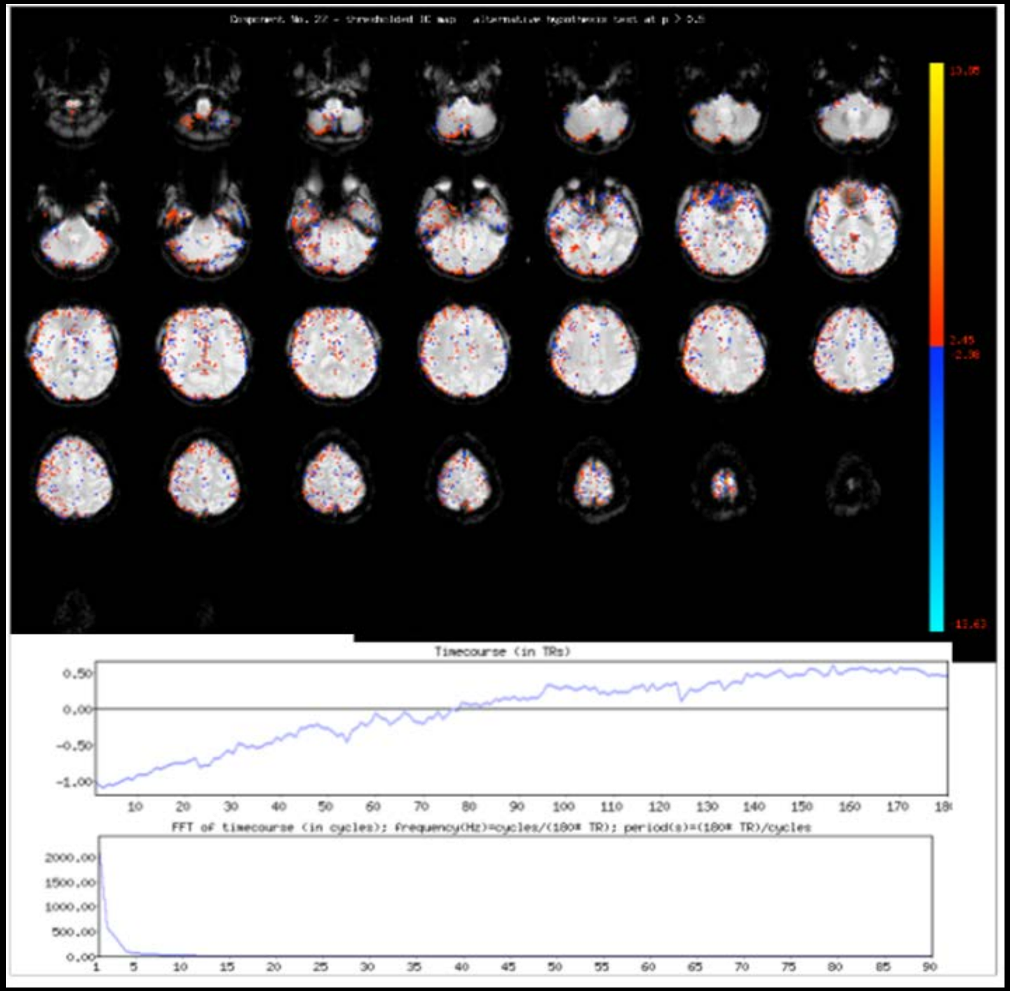

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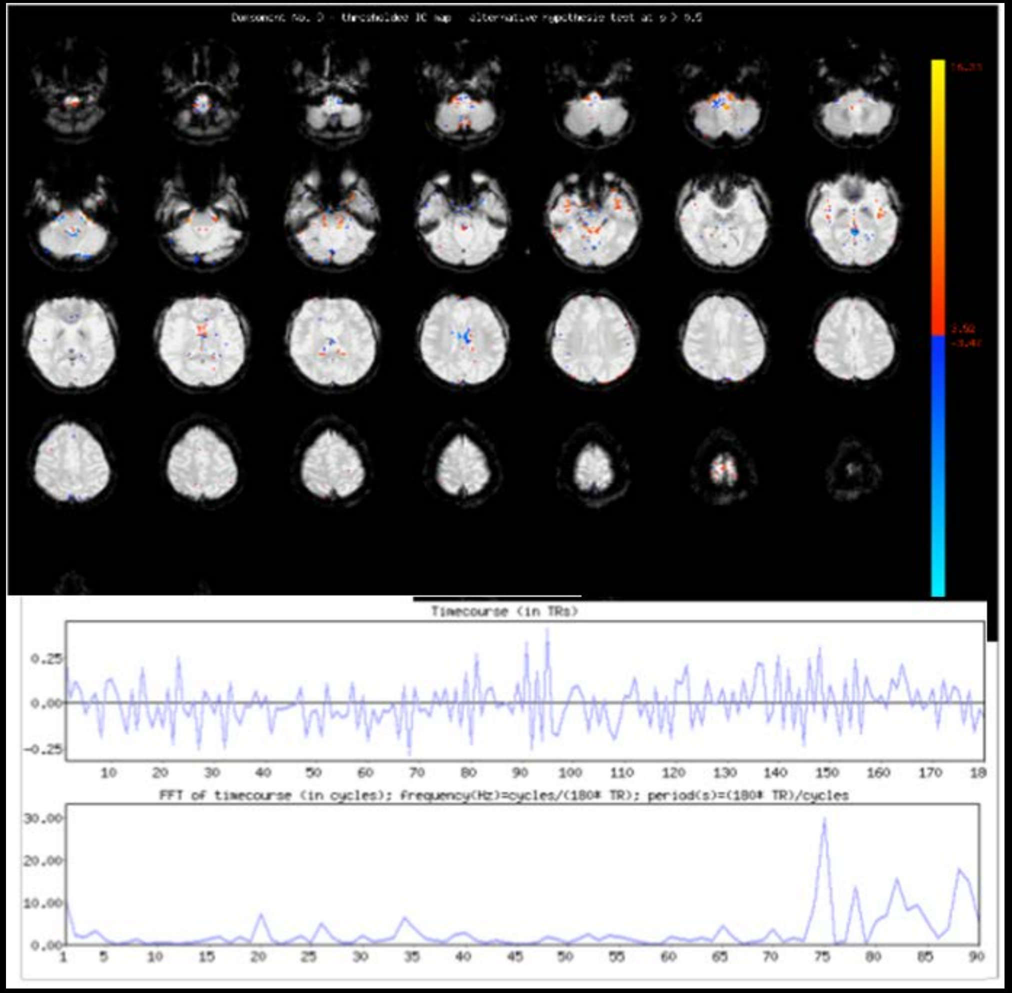

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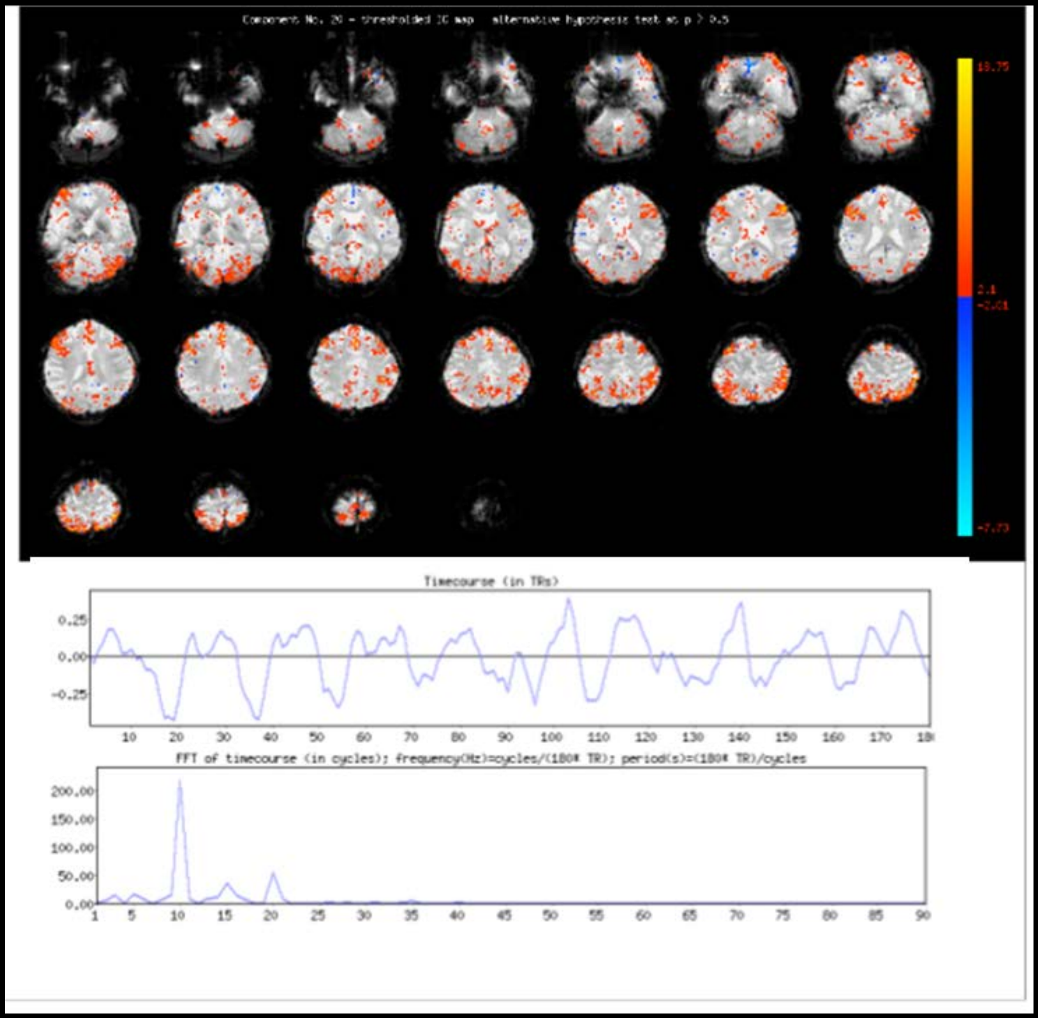
- Today, automated tools exist (FIX)



# APPROACH #3: MULTI-ECHO EPI

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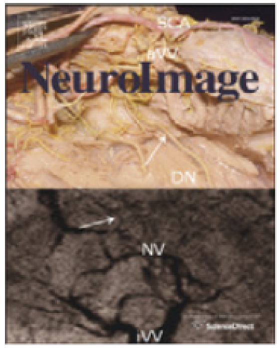


## Differentiating BOLD and non-BOLD signals in fMRI time series using multi-echo EPI

Prantik Kundu [a,c,*], Souheil J. Inati [b], Jennifer W. Evans [a,d], Wen-Ming Luh [b], Peter A. Bandettini [a,b]

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[b] *Functional MRI Facility, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, 20892 USA*
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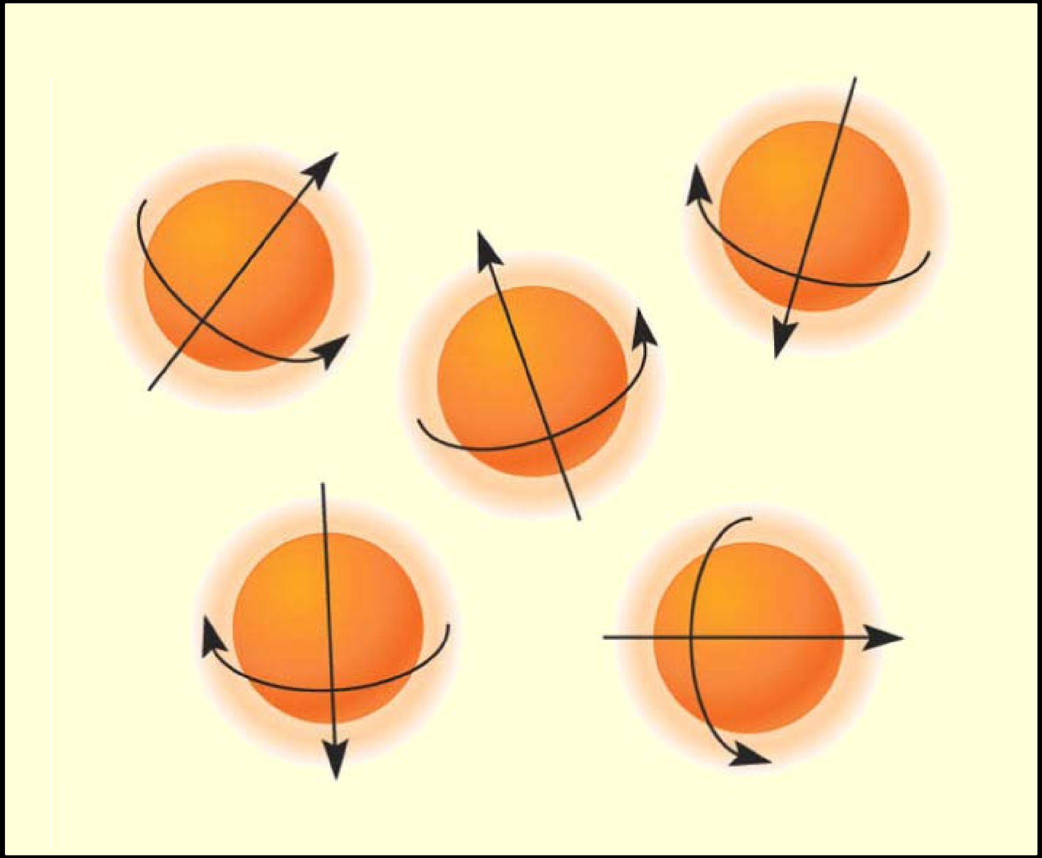
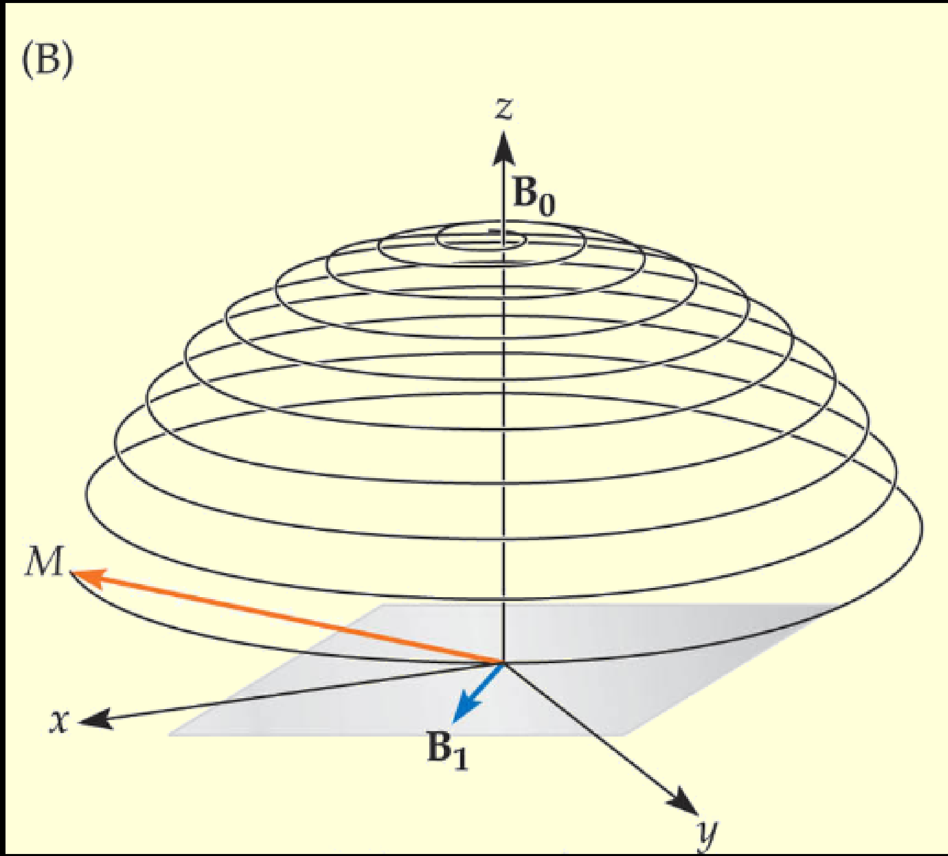
[d] *Center for Neuroscience and Regenerative Medicine, Henry M. Jackson Foundation, Rockville, Maryland, 20852 USA*

# APPROACH #3: MULTI-ECHO EPI

- “We introduce a new method that employs multi-echo acquisition and a TE-dependence test to remove artefactual fluctuations more effectively than these previous approaches by cleanly separating BOLD and non-BOLD signal components of resting state data.” Kundu et al., 2012

# BACK TO BASICS





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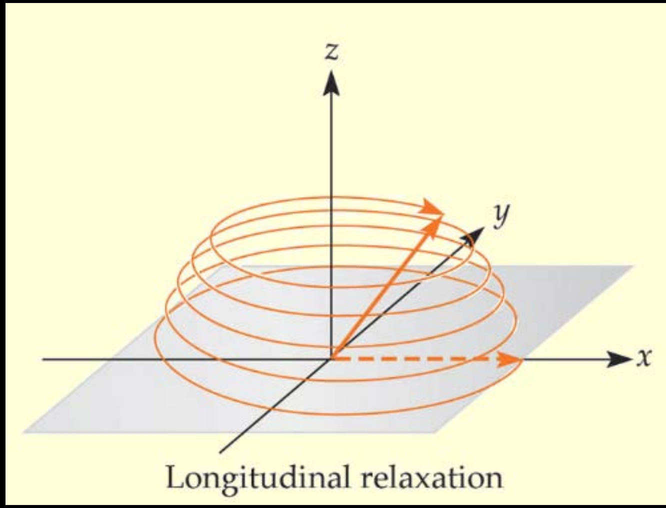


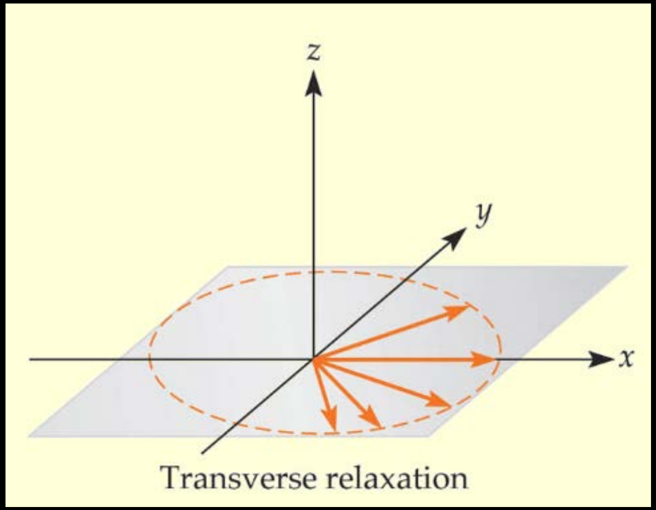


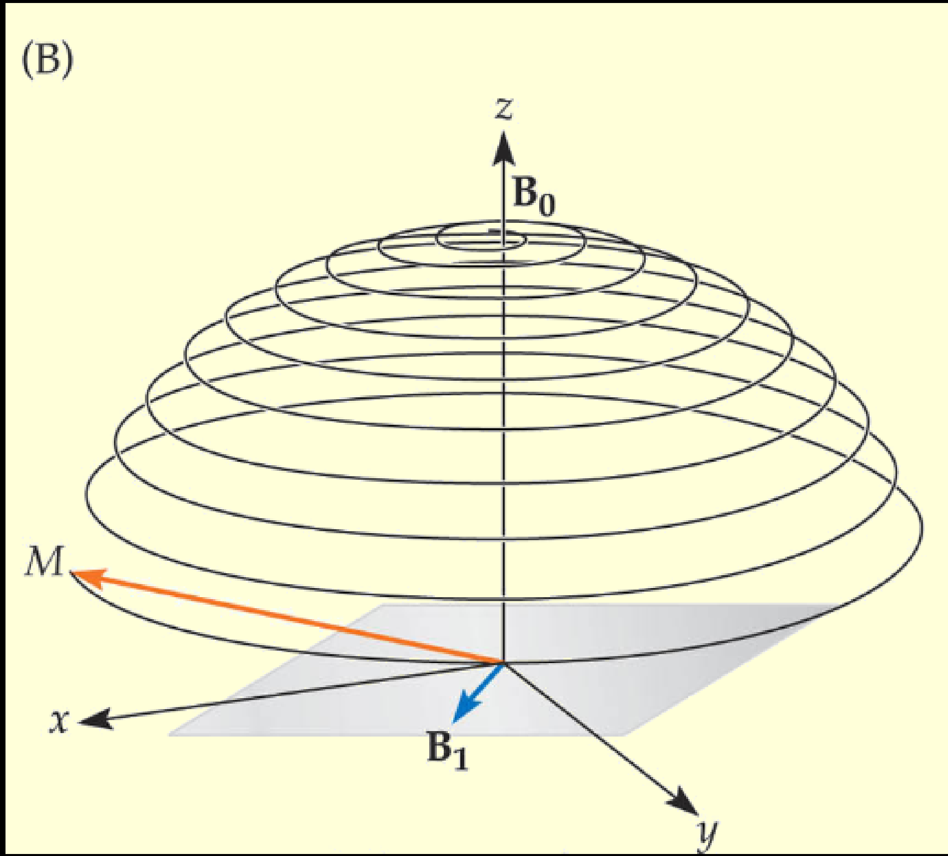


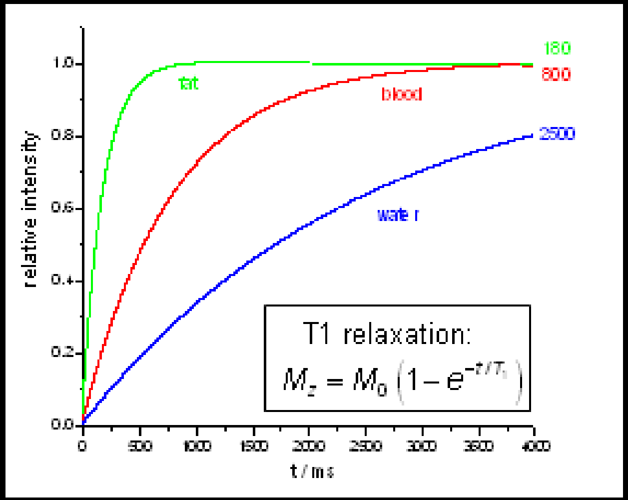


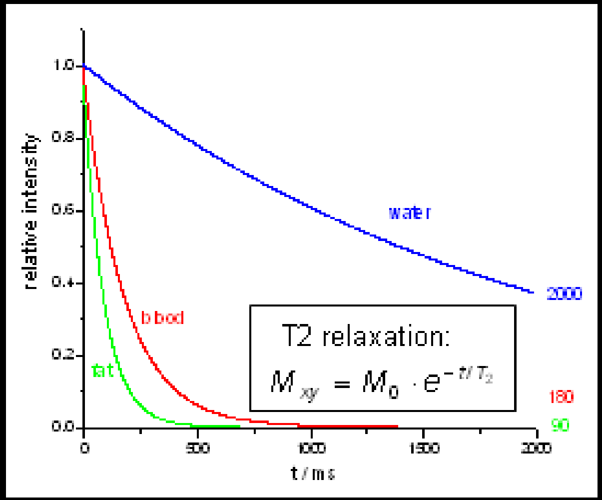

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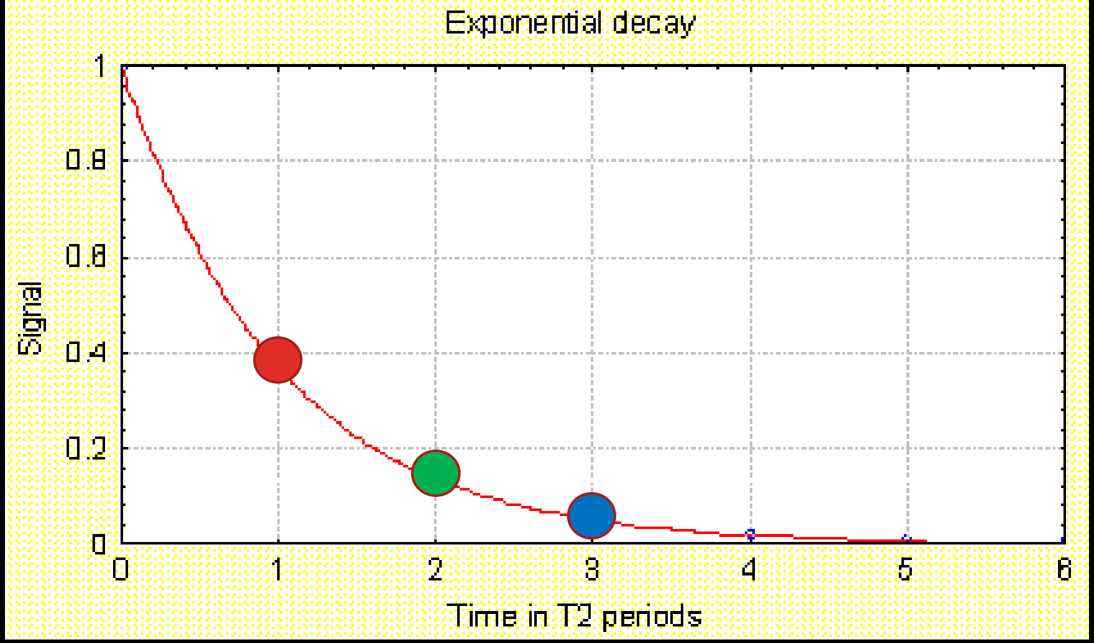


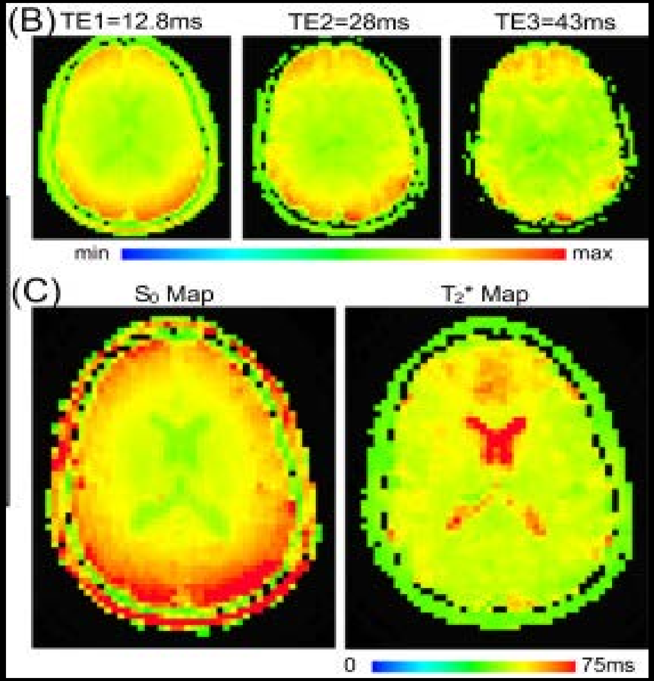

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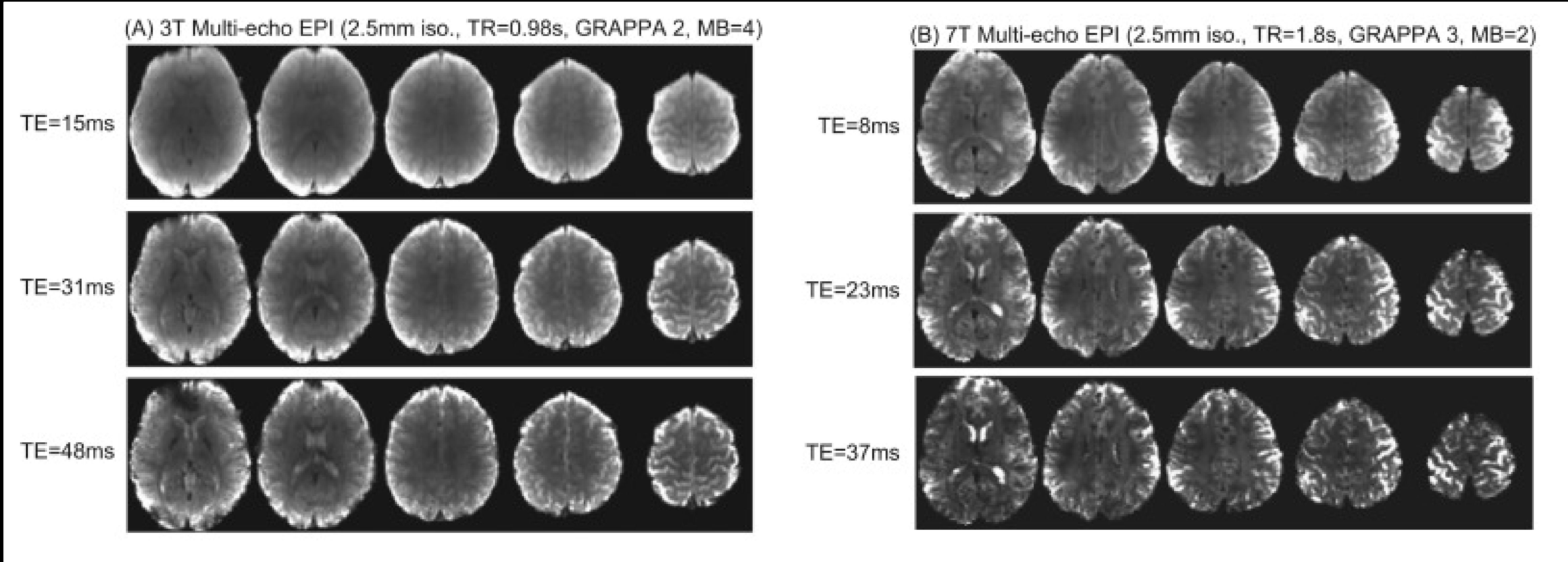

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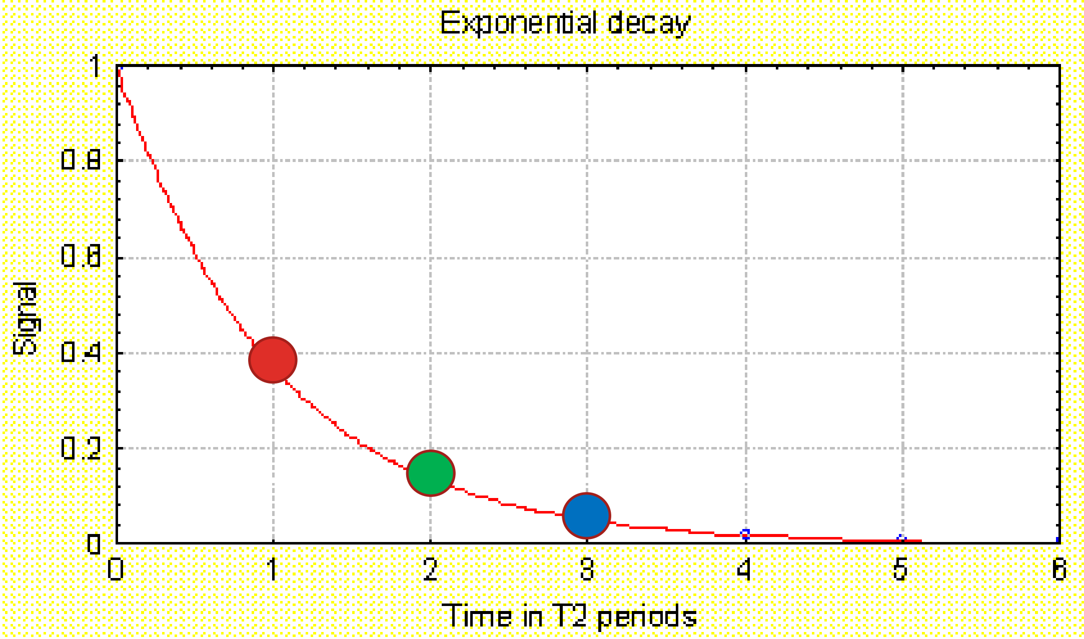
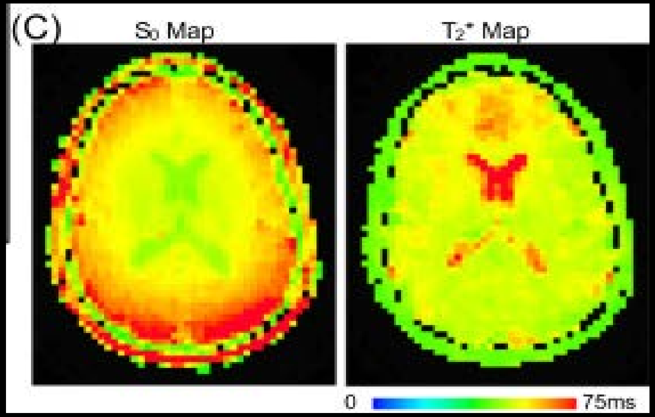



$$S(TE_n) = S_0 \exp(-R_2{}^{*}TE_n)$$



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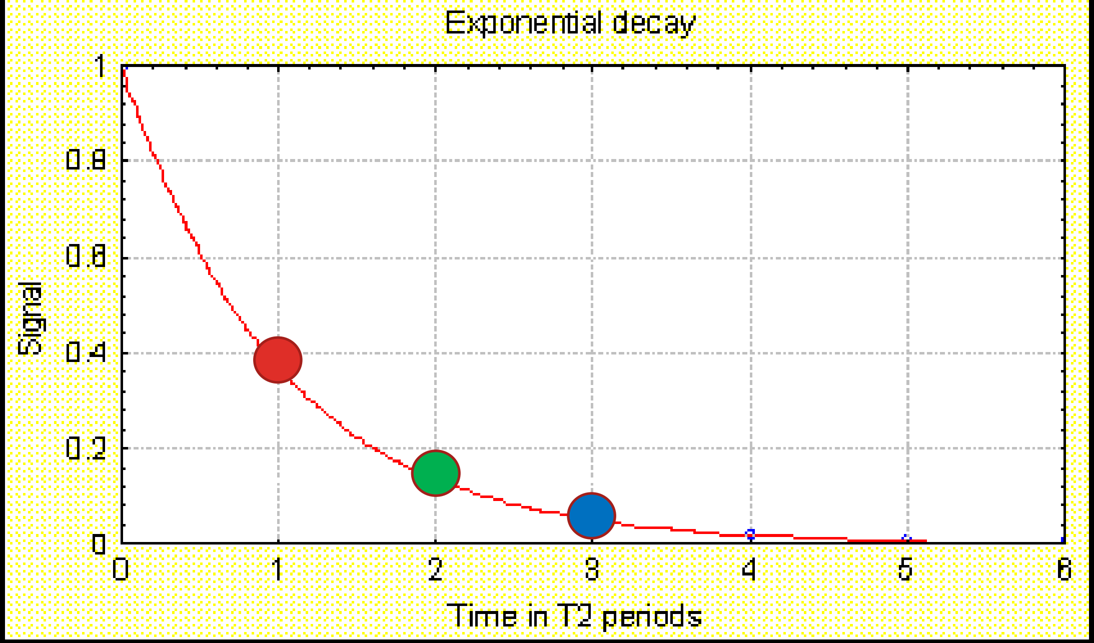



$$S(TE_n) = S_0 \exp(-R_2{}^*TE_n)$$

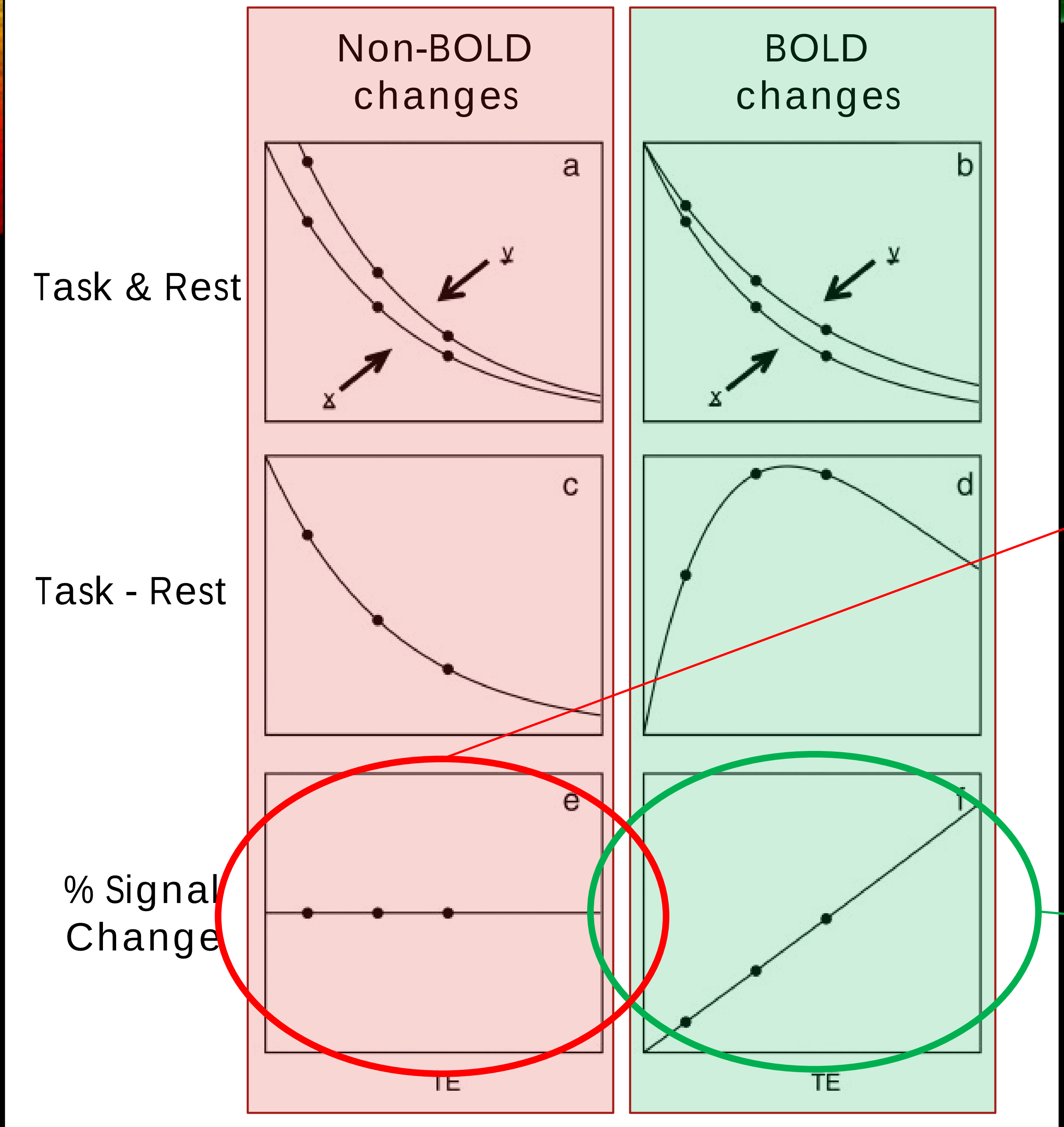
$$\Delta S/S = \Delta S_0/S_0 - \Delta R_2{}^*TE$$

NON-BOLD model

$$\Delta S/S = \Delta S_0/S_0$$

BOLD model

$$\Delta S/S = -\Delta R_2{}^*TE$$



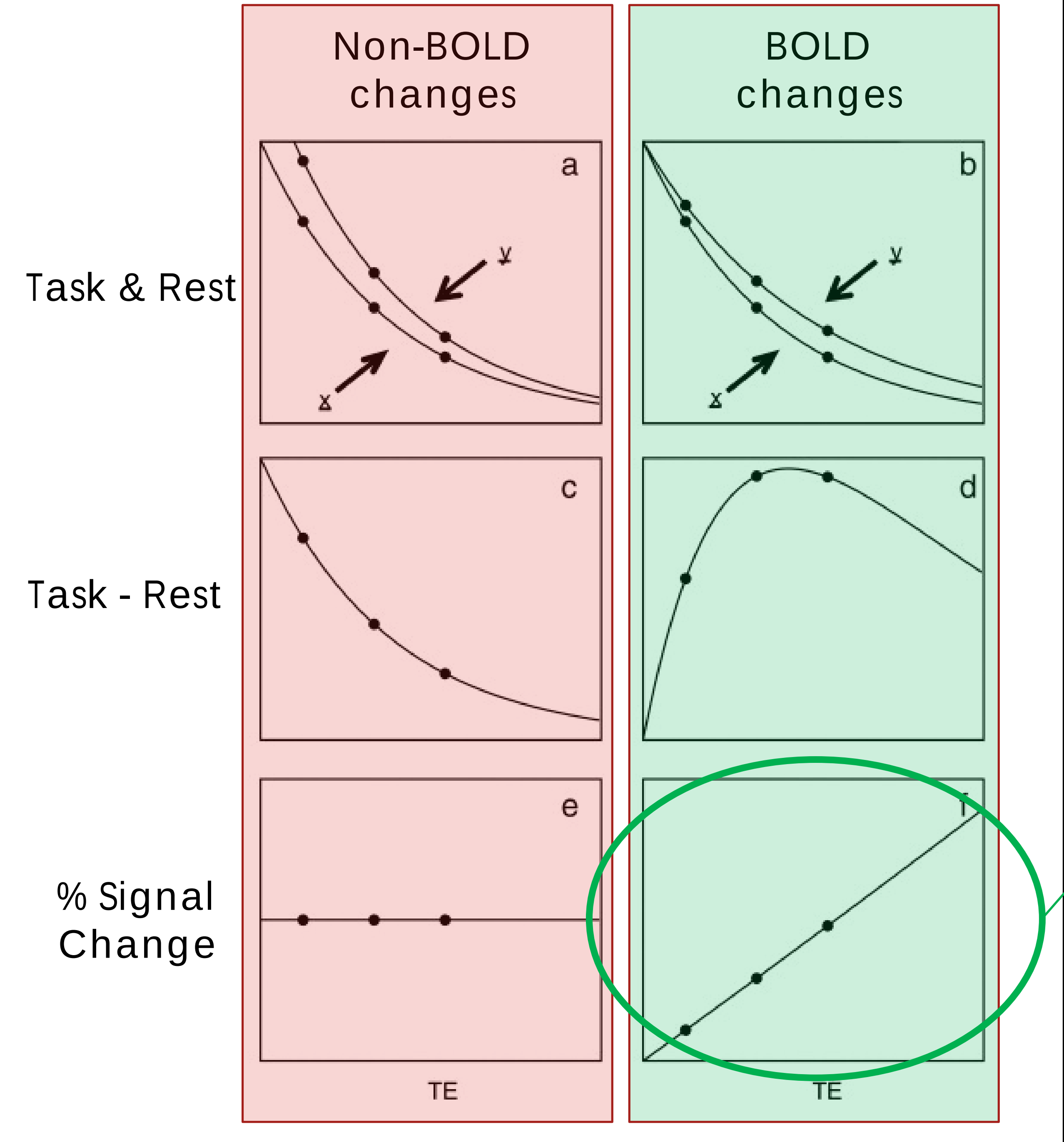

# KUNDU ET AL 2012

IF a signal fits this model (goodness of fit F), then it's not of BOLD origin!

$$\Delta S/S = \Delta S_0/S_0 \quad (\rho)$$

Good signals have to fit this model (goodness of fit F)!

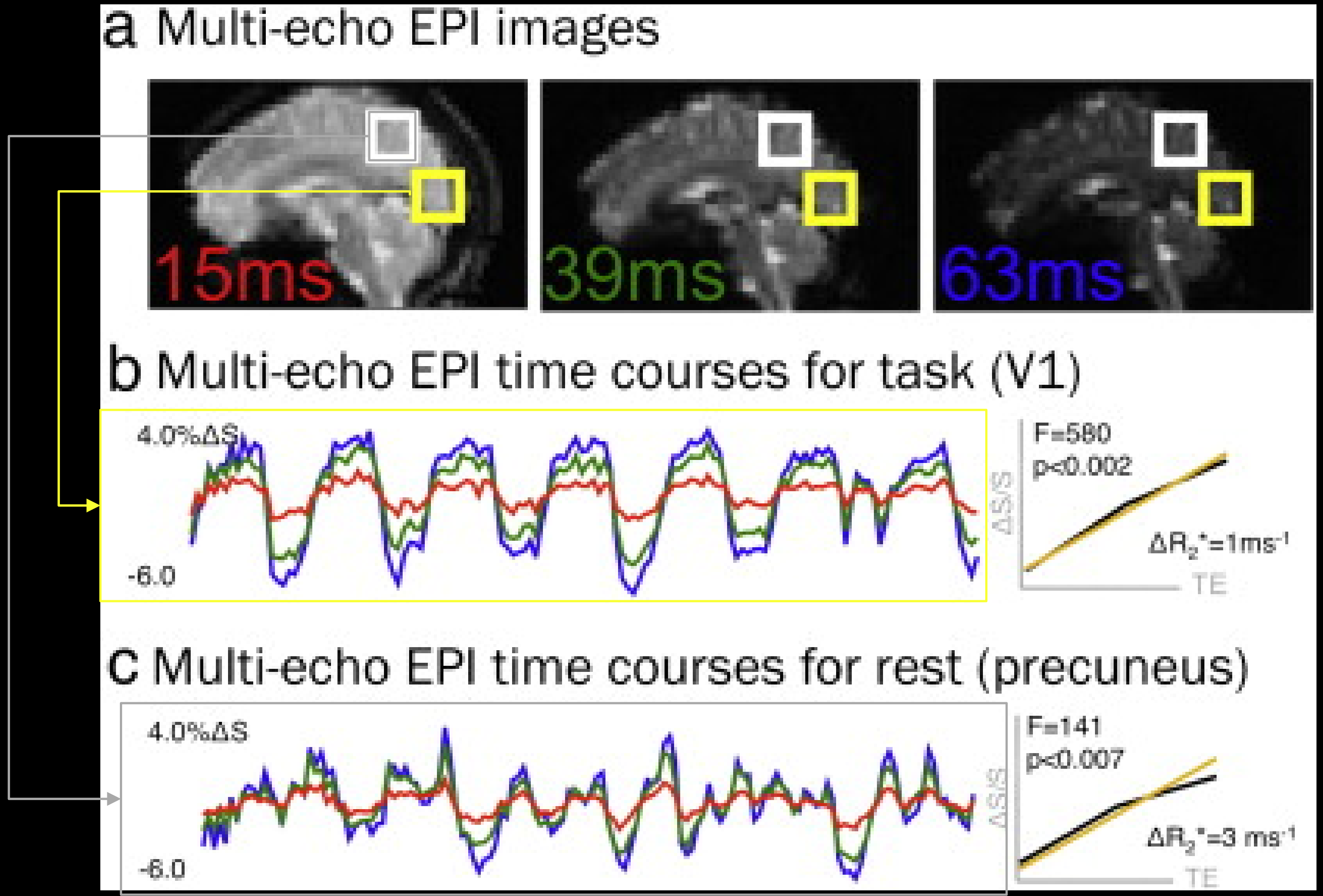
$$\Delta S/S = -\Delta R_2{}^{*}TE \quad (\kappa)$$

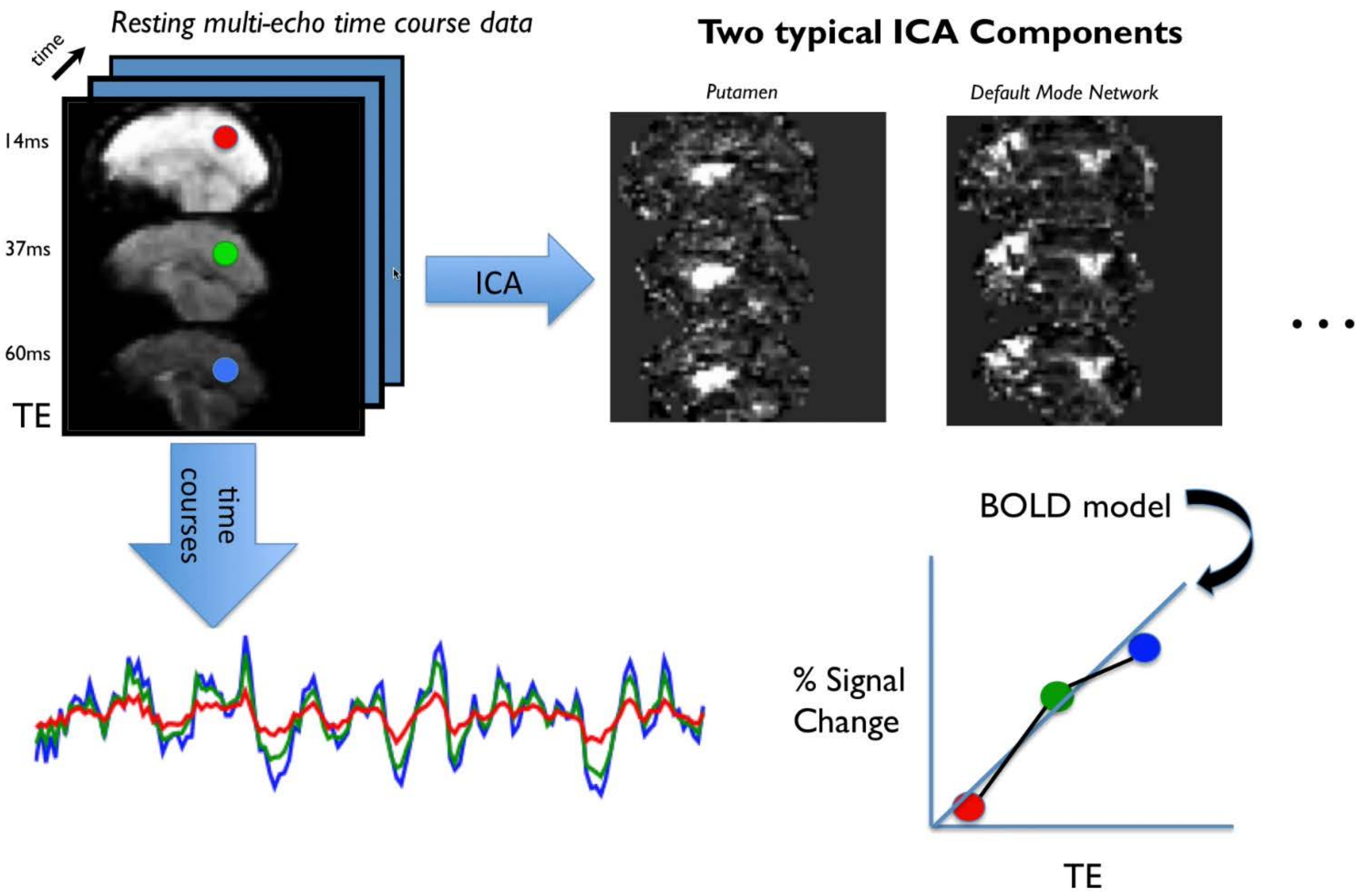



# KUNDU ET AL 2012

The key idea is that, when expressed in terms of ***percent signal change***, we know how the BOLD signal should behave as TE increases.

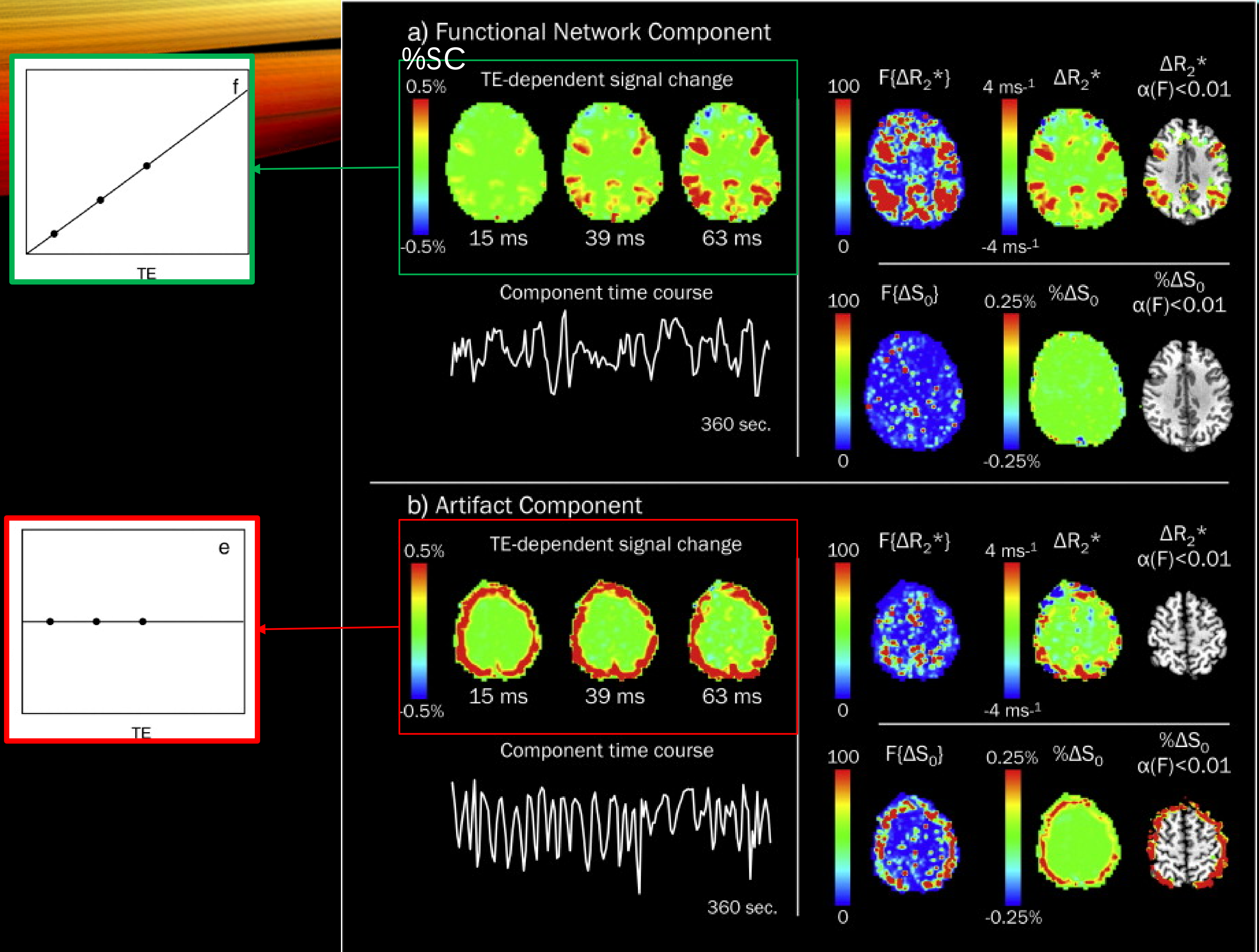
# KUNDU ET AL 2012





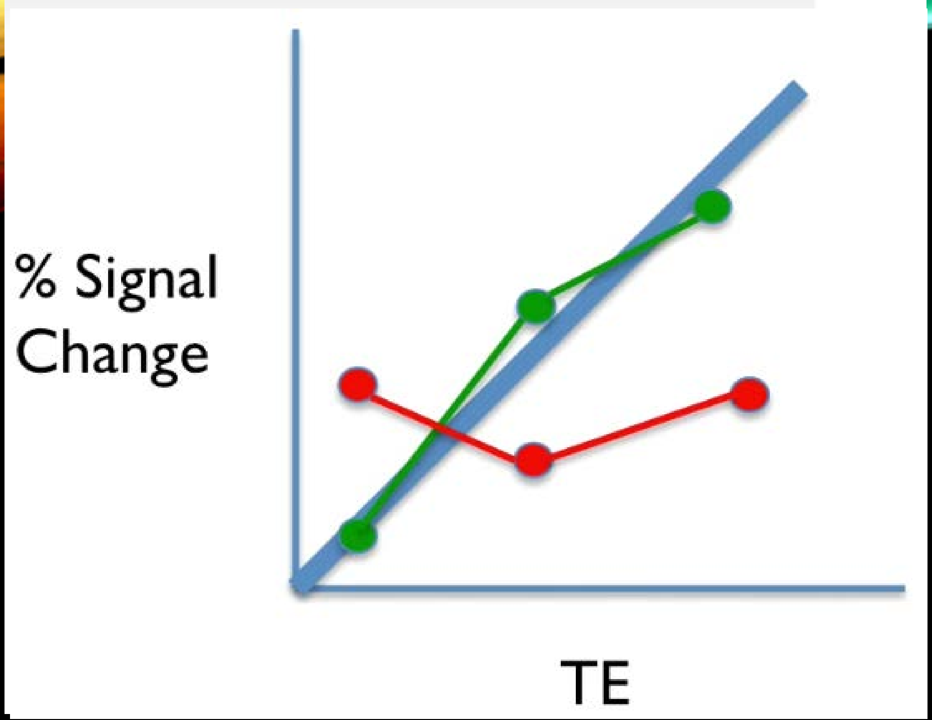
Slide from P. Bandettini

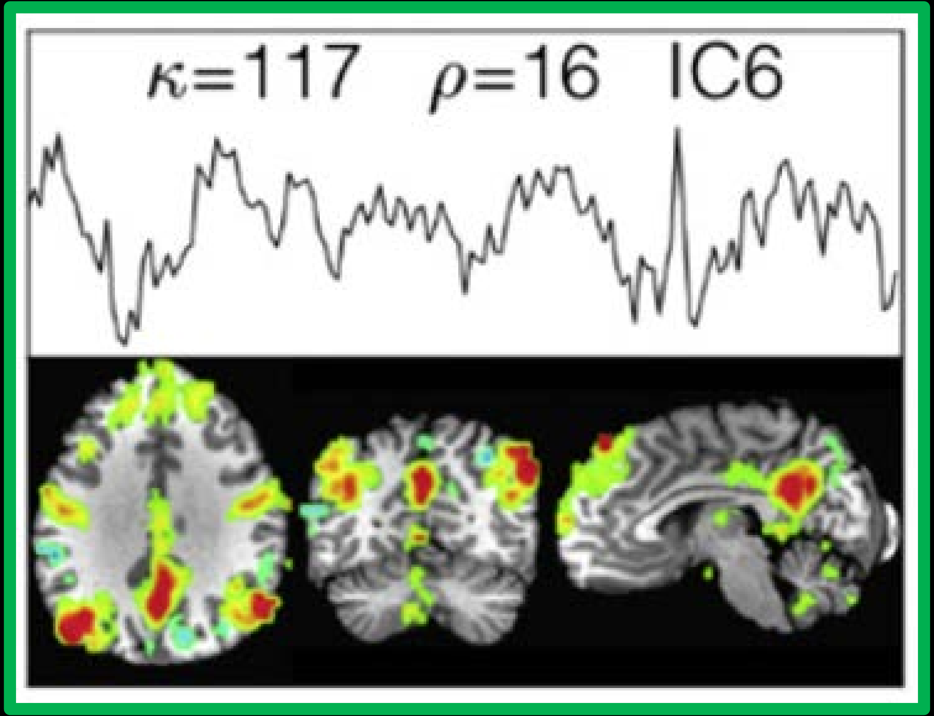
# RESULTS

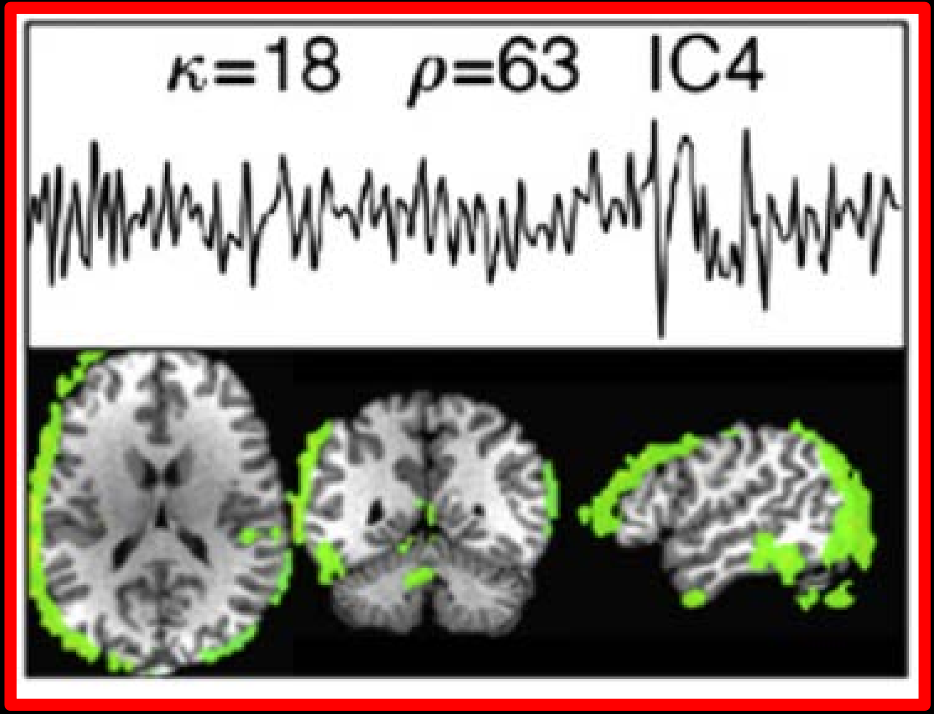


a) Functional Network Component
%SC
TE-dependent signal change
0.5%
-0.5%
15 ms
39 ms
63 ms
f
TE
Component time course
360 sec.
100
0
F{ΔR2*}
4 ms-1
-4 ms-1
ΔR2*
ΔR2* α(F)<0.01
F{ΔS0}
0.25%
-0.25%
%ΔS0
%ΔS0 α(F)<0.01
b) Artifact Component
TE-dependent signal change
0.5%
-0.5%
15 ms
39 ms
63 ms
e
TE
Component time course
360 sec.
100
0
F{ΔR2*}
4 ms-1
-4 ms-1
ΔR2*
ΔR2* α(F)<0.01
F{ΔS0}
0.25%
-0.25%
%ΔS0
%ΔS0 α(F)<0.01

# RESULTS



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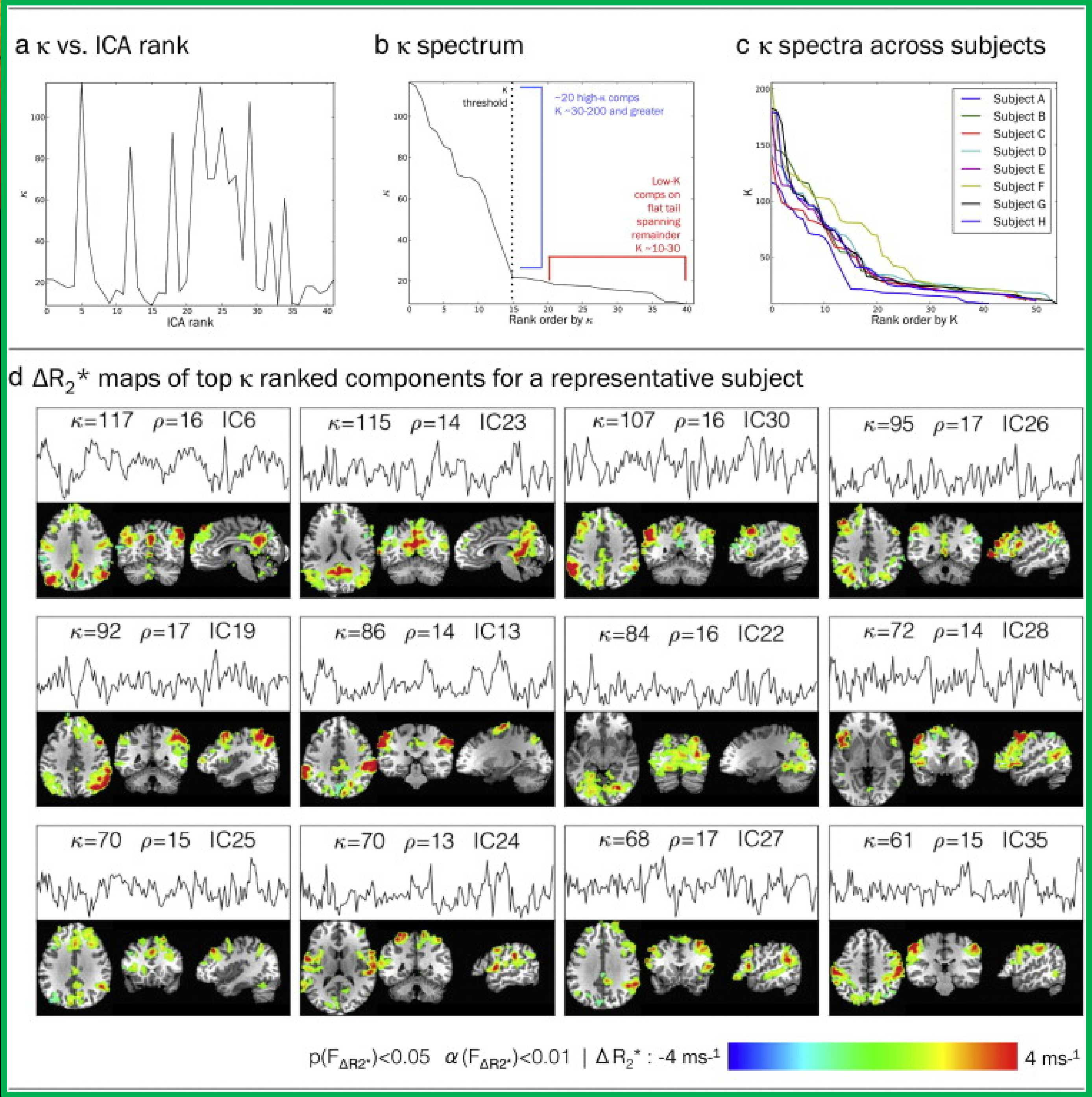
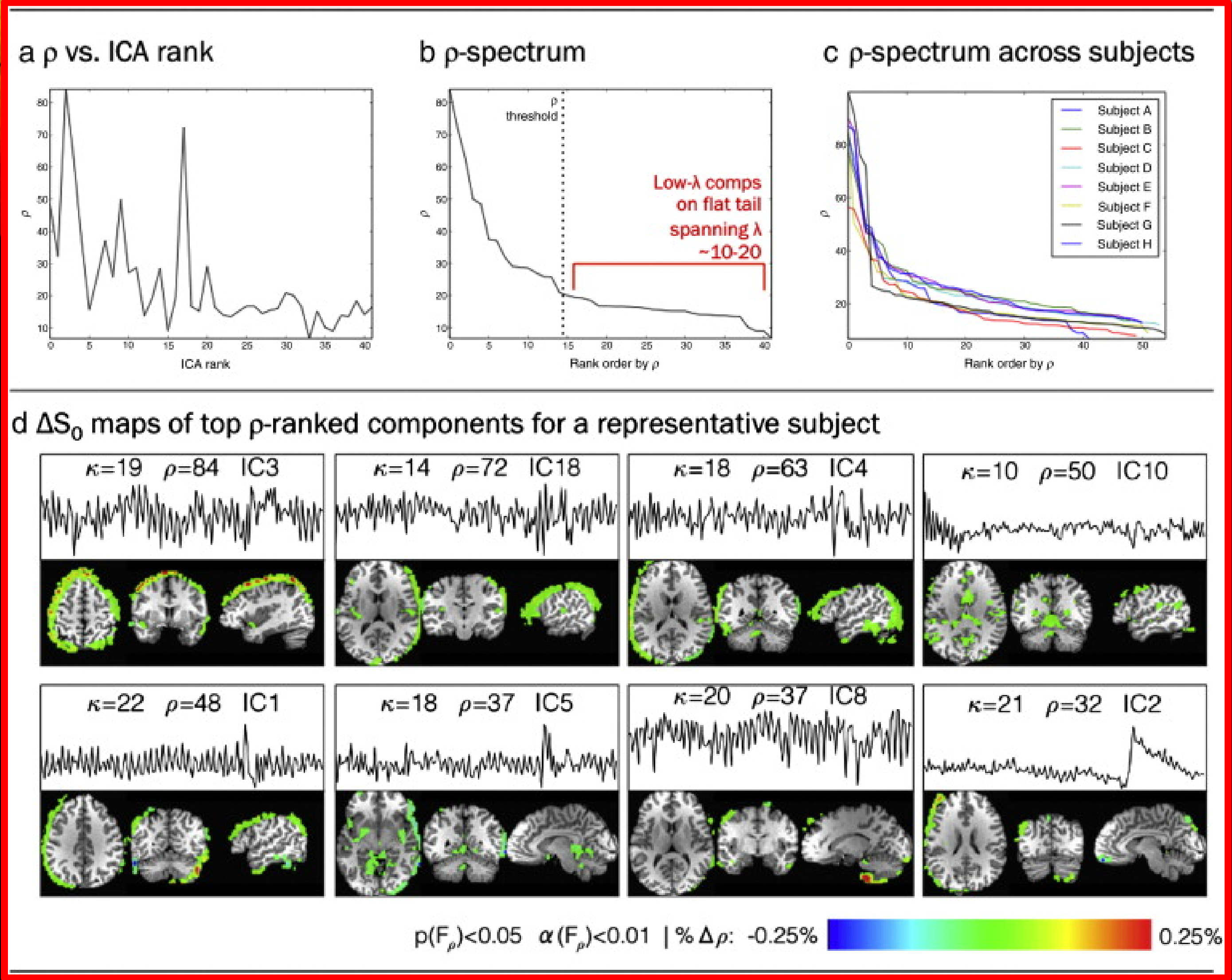
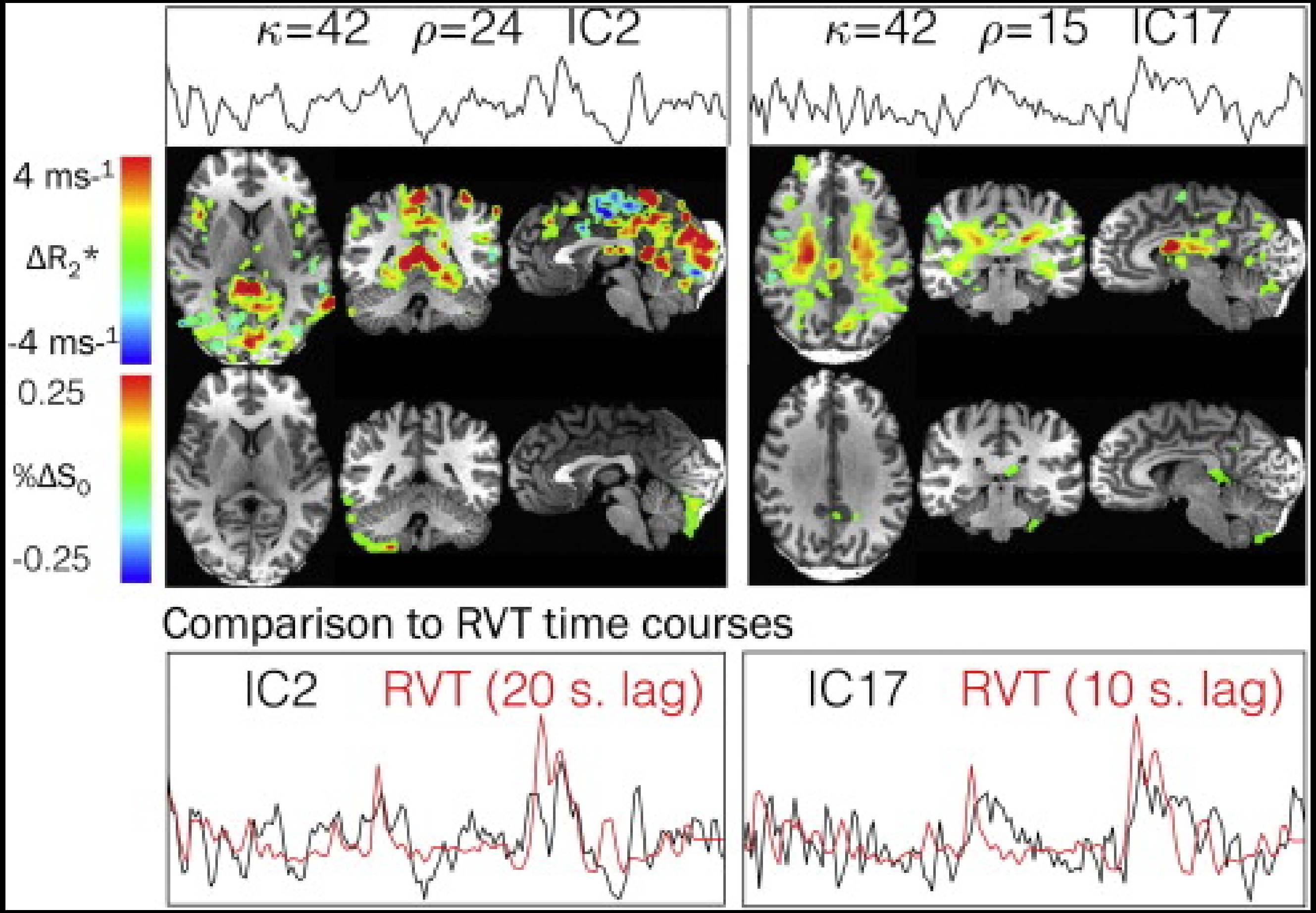

a κ vs. ICA rank
ICA rank
b κ spectrum
κ threshold
~20 high-κ comps
K ~30-200 and greater
Low-K comps on flat tail spanning remainder K ~10-30
Rank order by κ
c κ spectra across subjects
Subject A
Subject B
Subject C
Subject D
Subject E
Subject F
Subject G
Subject H
Rank order by K
d ΔR2* maps of top κ ranked components for a representative subject
κ=117 ρ=16 IC6
κ=115 ρ=14 IC23
κ=107 ρ=16 IC30
κ=95 ρ=17 IC26
κ=92 ρ=17 IC19
κ=86 ρ=14 IC13
κ=84 ρ=16 IC22
κ=72 ρ=14 IC28
κ=70 ρ=15 IC25
κ=70 ρ=13 IC24
κ=68 ρ=17 IC27
κ=61 ρ=15 IC35
p(FΔR2*)<0.05 α(FΔR2*)<0.01 | ΔR2* : -4 ms-1
4 ms-1

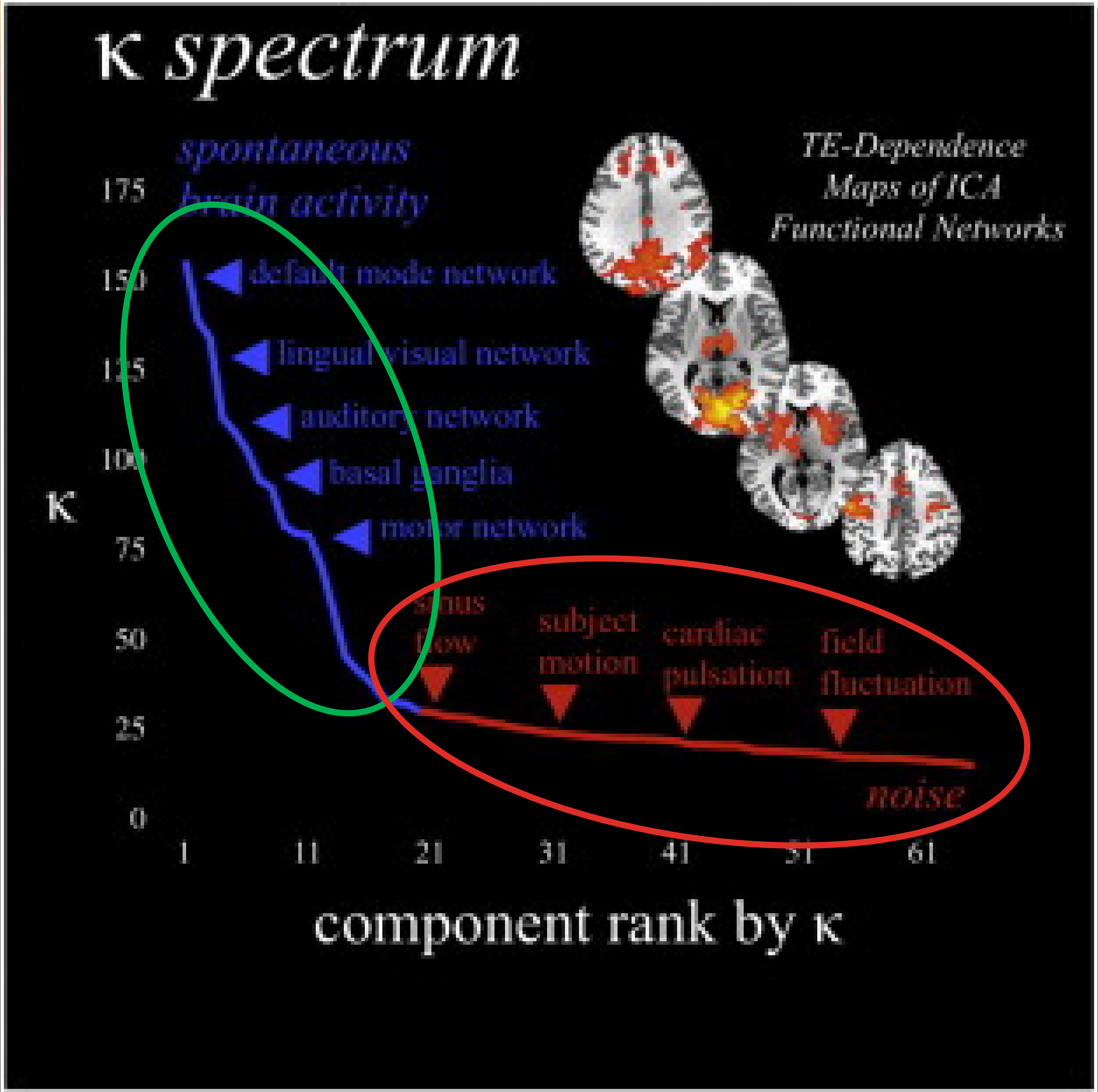
# RESULTS


a ρ vs. ICA rank
ICA rank
b ρ-spectrum
ρ threshold
Low-λ comps on flat tail spanning λ ~10-20
Rank order by ρ
c ρ-spectrum across subjects
Subject A
Subject B
Subject C
Subject D
Subject E
Subject F
Subject G
Subject H
Rank order by ρ
d ΔS0 maps of top ρ-ranked components for a representative subject
κ=19 ρ=84 IC3
κ=14 ρ=72 IC18
κ=18 ρ=63 IC4
κ=10 ρ=50 IC10
κ=22 ρ=48 IC1
κ=18 ρ=37 IC5
κ=20 ρ=37 IC8
κ=21 ρ=32 IC2
p(Fρ)<0.05 α(Fρ)<0.01 | %Δρ: -0.25% 0.25%

# RESULTS



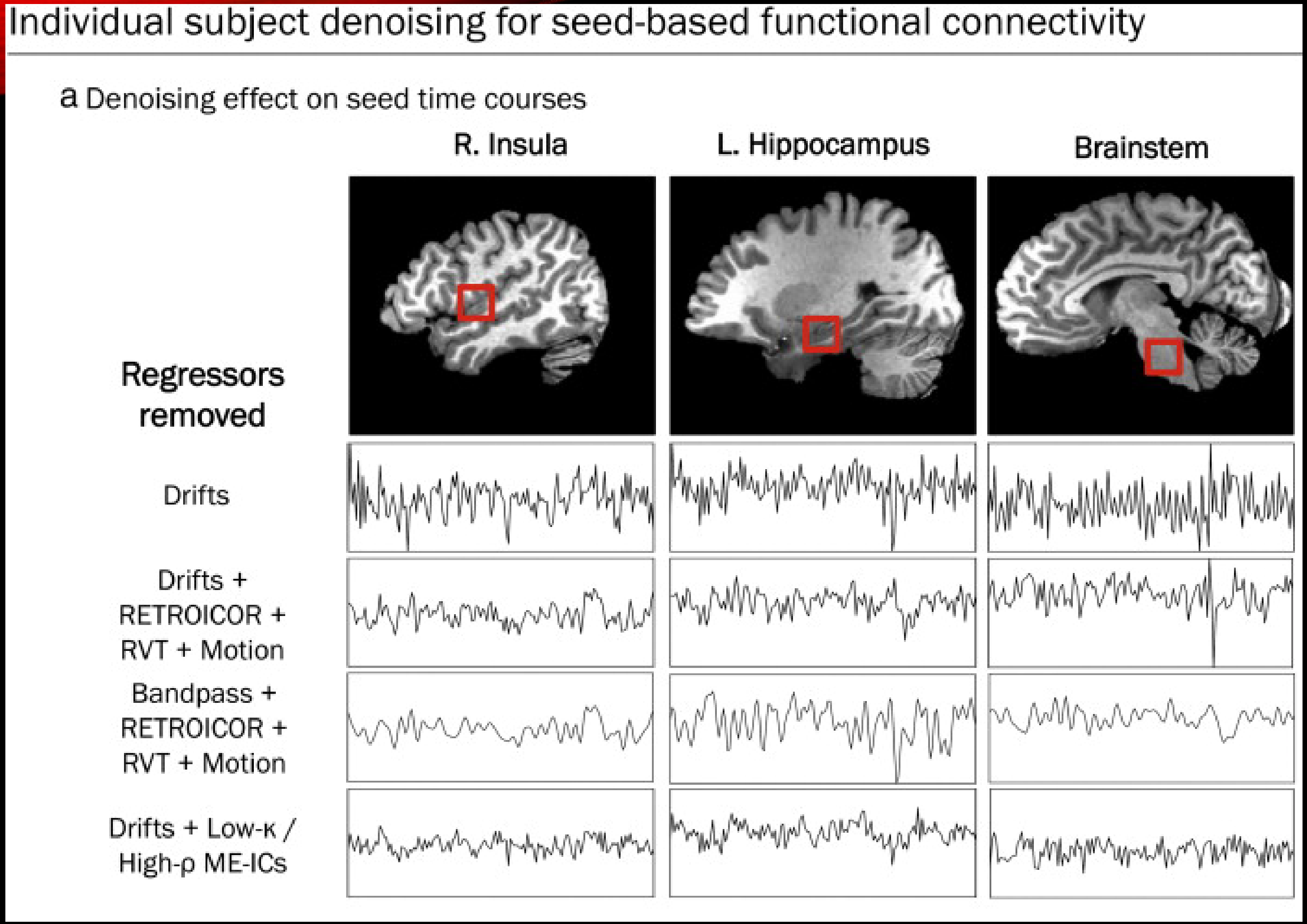

- What happens nearby the κ elbow?
- A component with a near-threshold κ score **could reflect** $\Delta R_2$* modulation from respiratory variation or related BOLD-like effects of no interest.




# DATA DRIVEN ANALYSIS

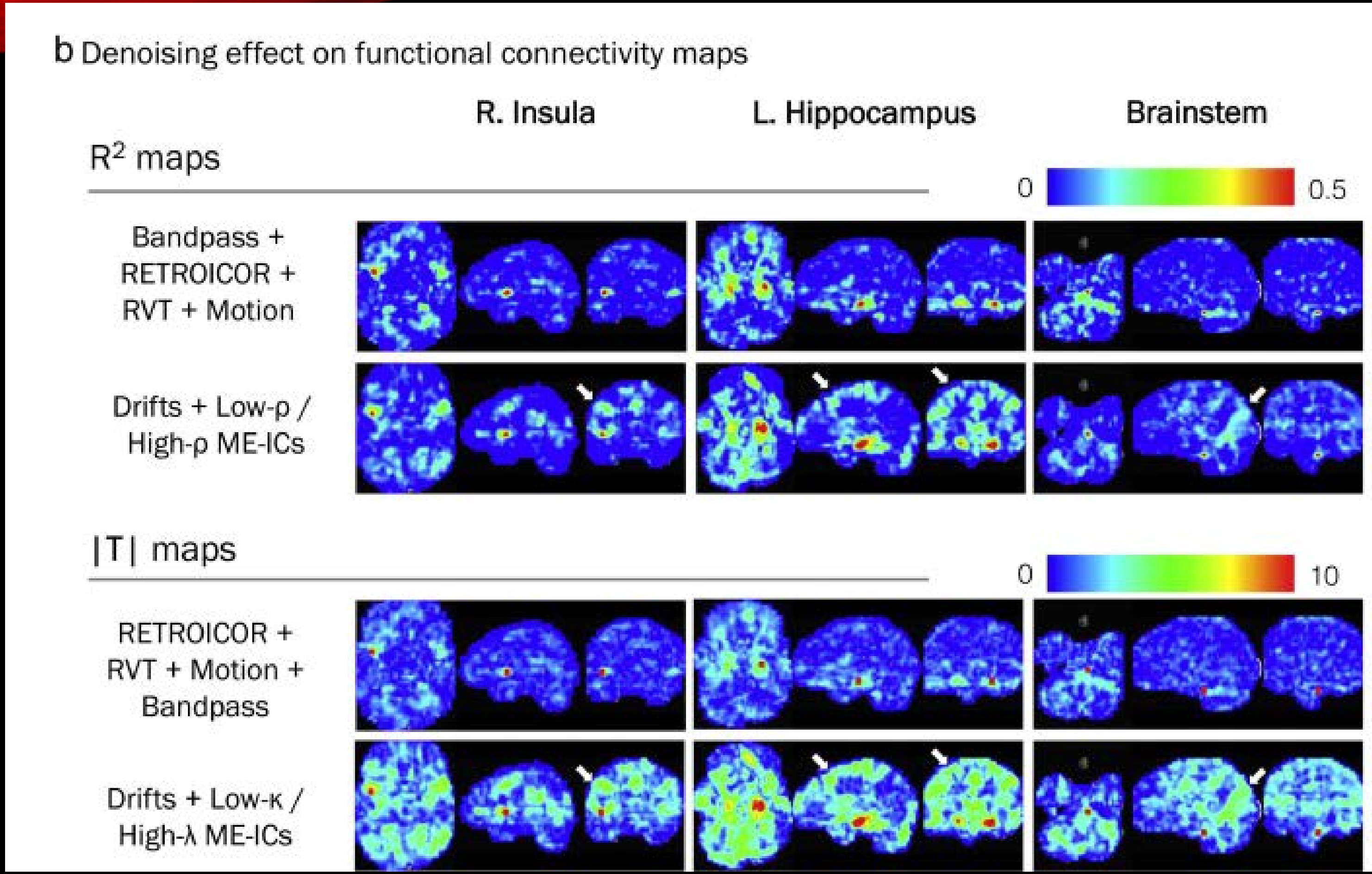
If interested in data **driven analysis**, reject low κ components and keep only high κ components above the elbow.

# SEED-BASED ANALYSIS




If interested in **seed-based connectivity analysis**, then filter out low $\kappa$ and high $\rho$ components from the data (e.g., as in FIX) prior to analysis.

# SEED-BASED ANALYSIS

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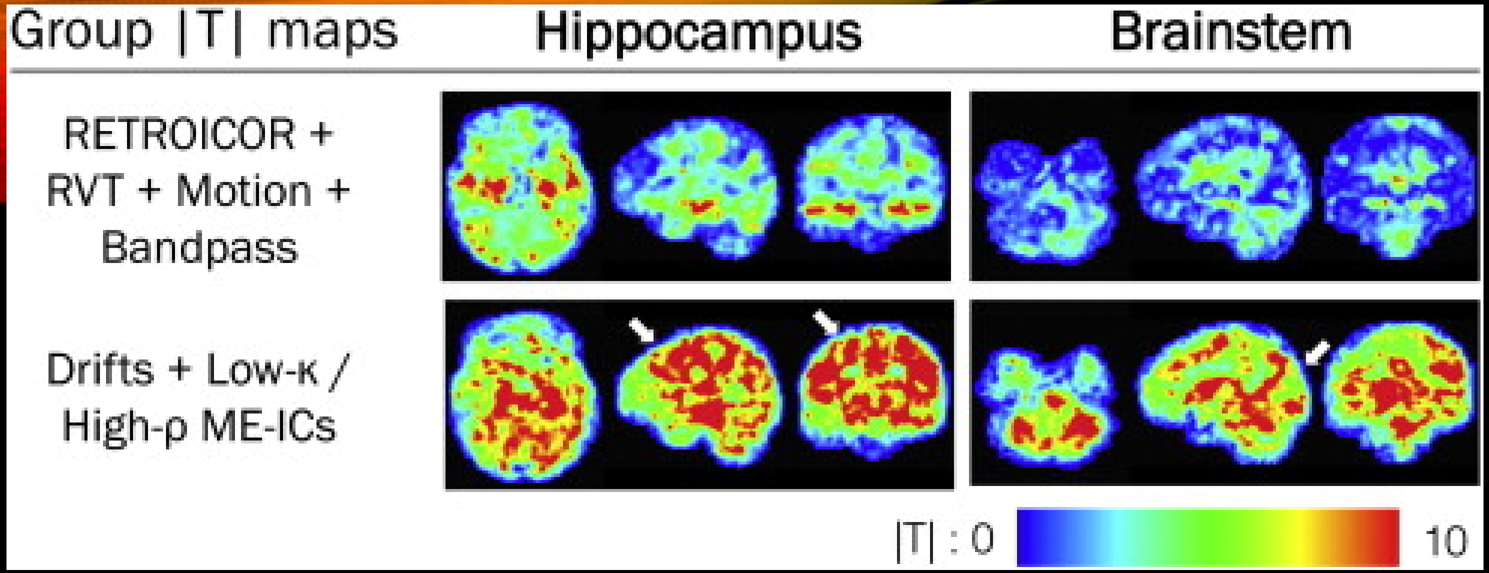
# SEED-BASED ANALYSIS

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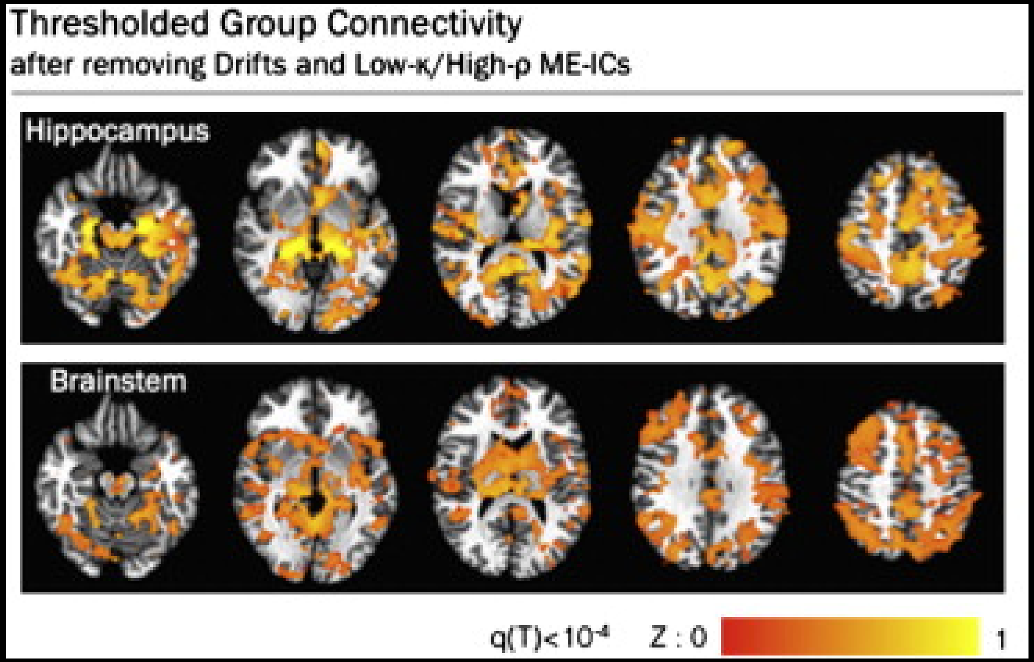


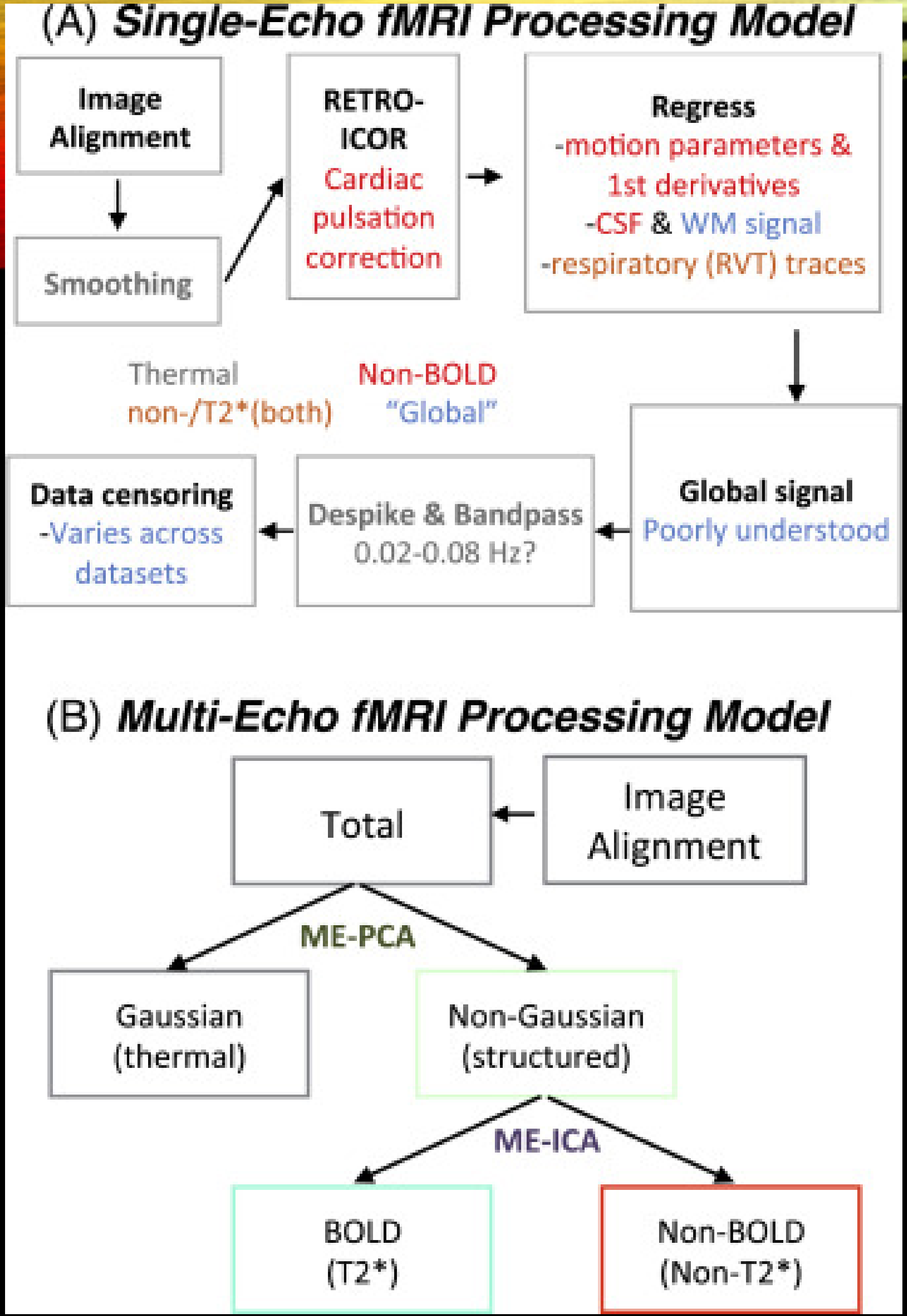

At the same threshold standard approach shows no sig. results

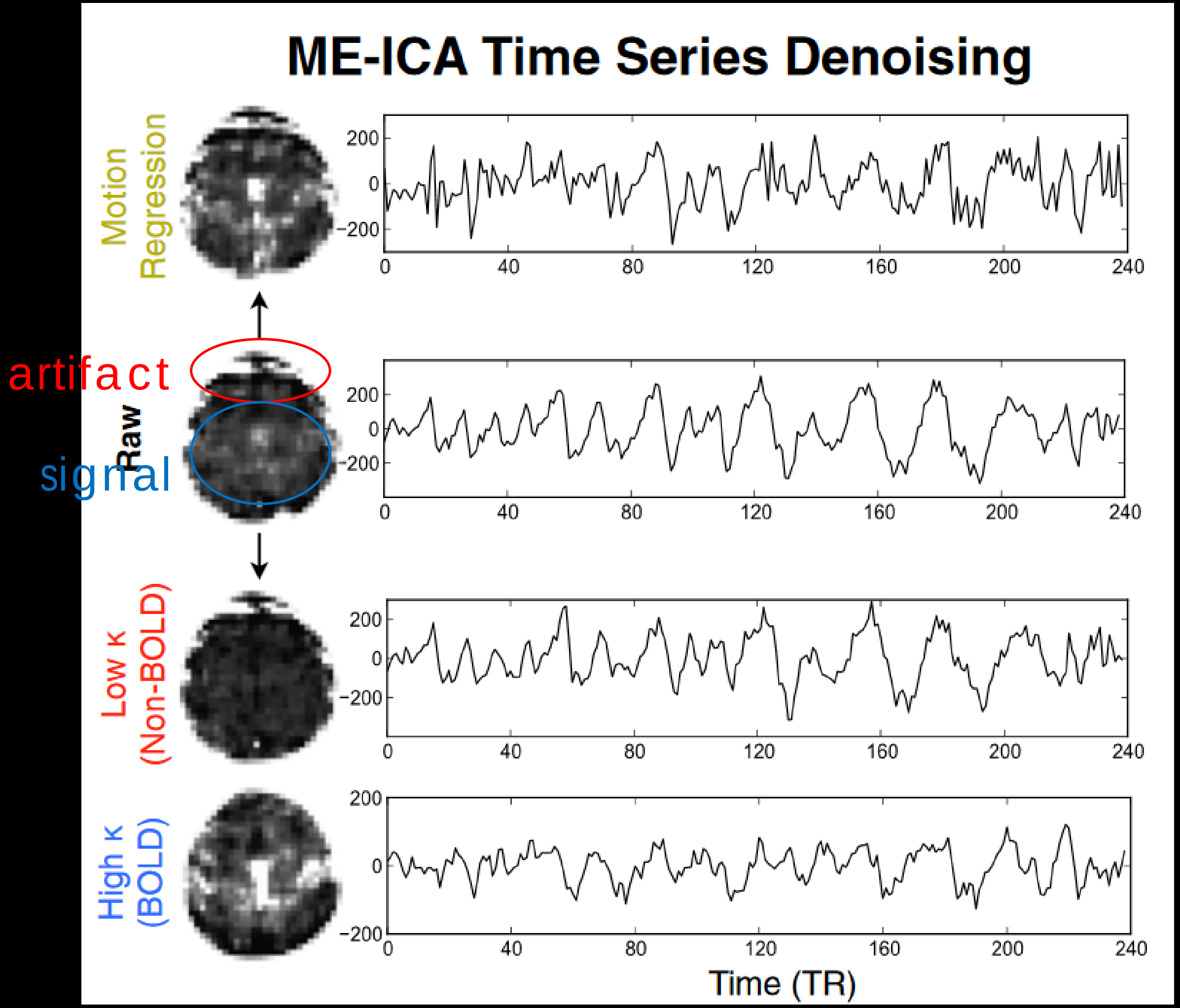
# SUMMARIZING

- This technique allows teasing apart data with multi-echo EPI, identifying **BOLD-like** (high κ, low ρ) **non-BOLD-like** (low κ, high ρ) components directly from the data, and using these non BOLD-like components to obtain nuisance regressors.
- PROs:
  - Based on the characteristic properties of BOLD T2* signal (i.e., transverse susceptibility-weighted relaxation rate).
  - Takes advantage of what ICA does best
  - Does not require external physiologic measures, temporal noise models, or anatomical templates
  - Is fully automated
- CONs:
  - Multi-echo data (multi-echo data, multi-echo data)

Kundu et al., 2012 NI

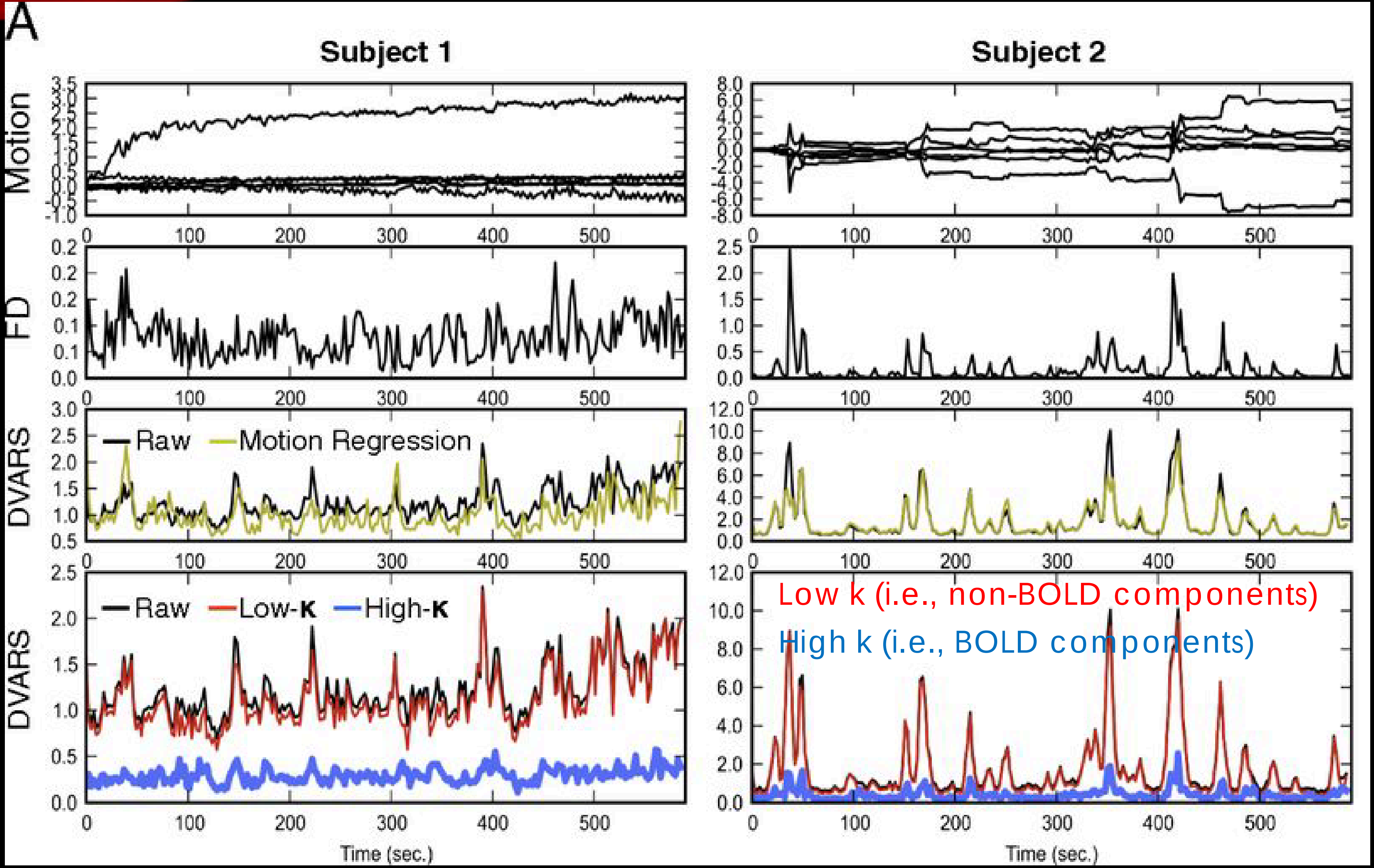
# COMPARING APPROACHES




Kundu et al., 2009, PNAS; 2017 NI

# ME-ICA AND MOTION



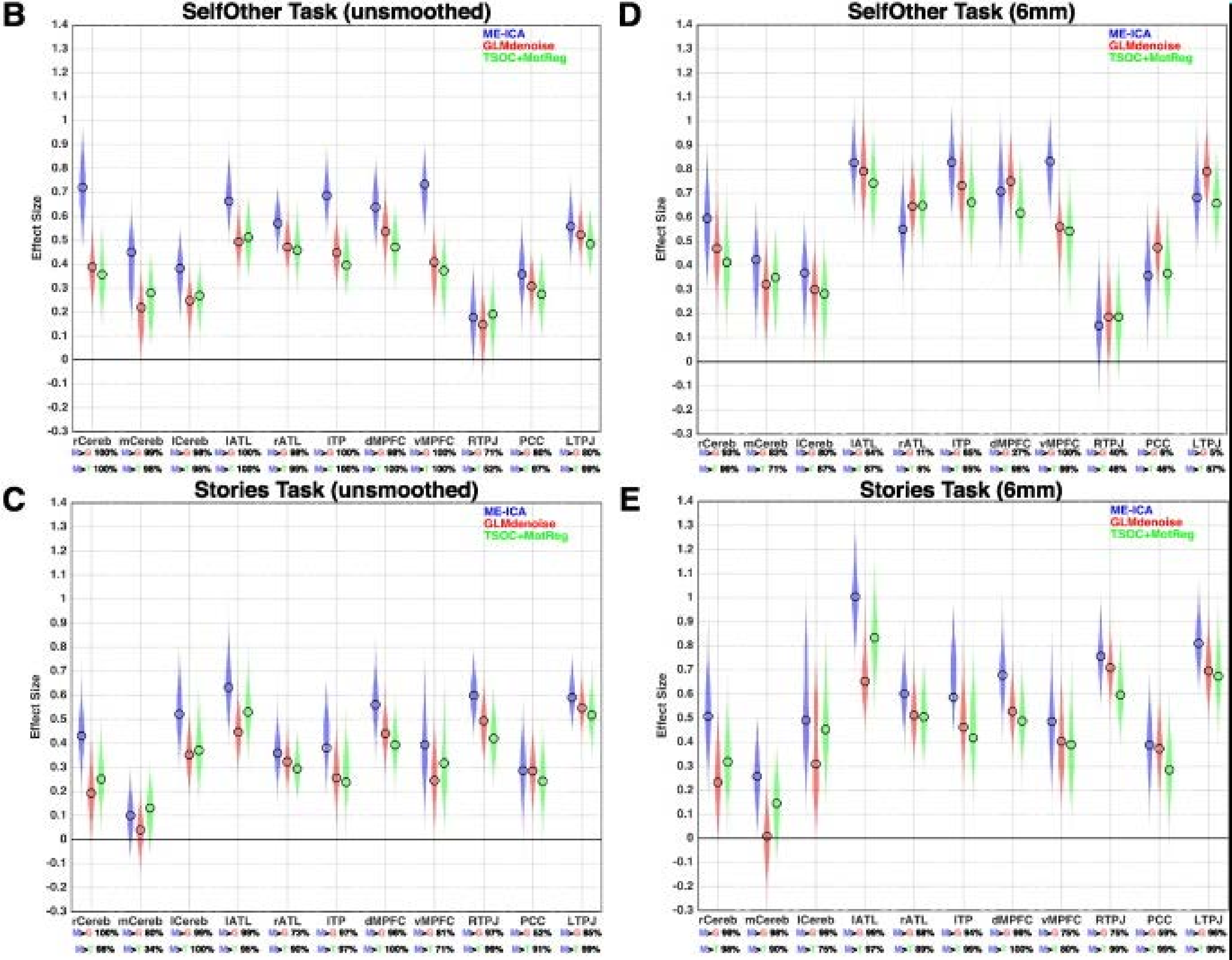

Kundu et al., 2017 NI

# ME-ICA AND TASK-BASED (BLOCK DESIGN) FMRI: MENTALIZING

- Task based approach w/block design
  - Task A: Self/Others (reflective judgments about themselves/HMQ, mentalistic/physical)
  - Task B: Listen to stories (mentalistic/social/physical contents)

- Analyses:
  - ME-ICA denoising
  - Standard approach
  - GLMDenoise (Kay et al 2013)

# ME-ICA AND TASK-BASED (BLOCK DESIGN) FMRI: MENTALIZING



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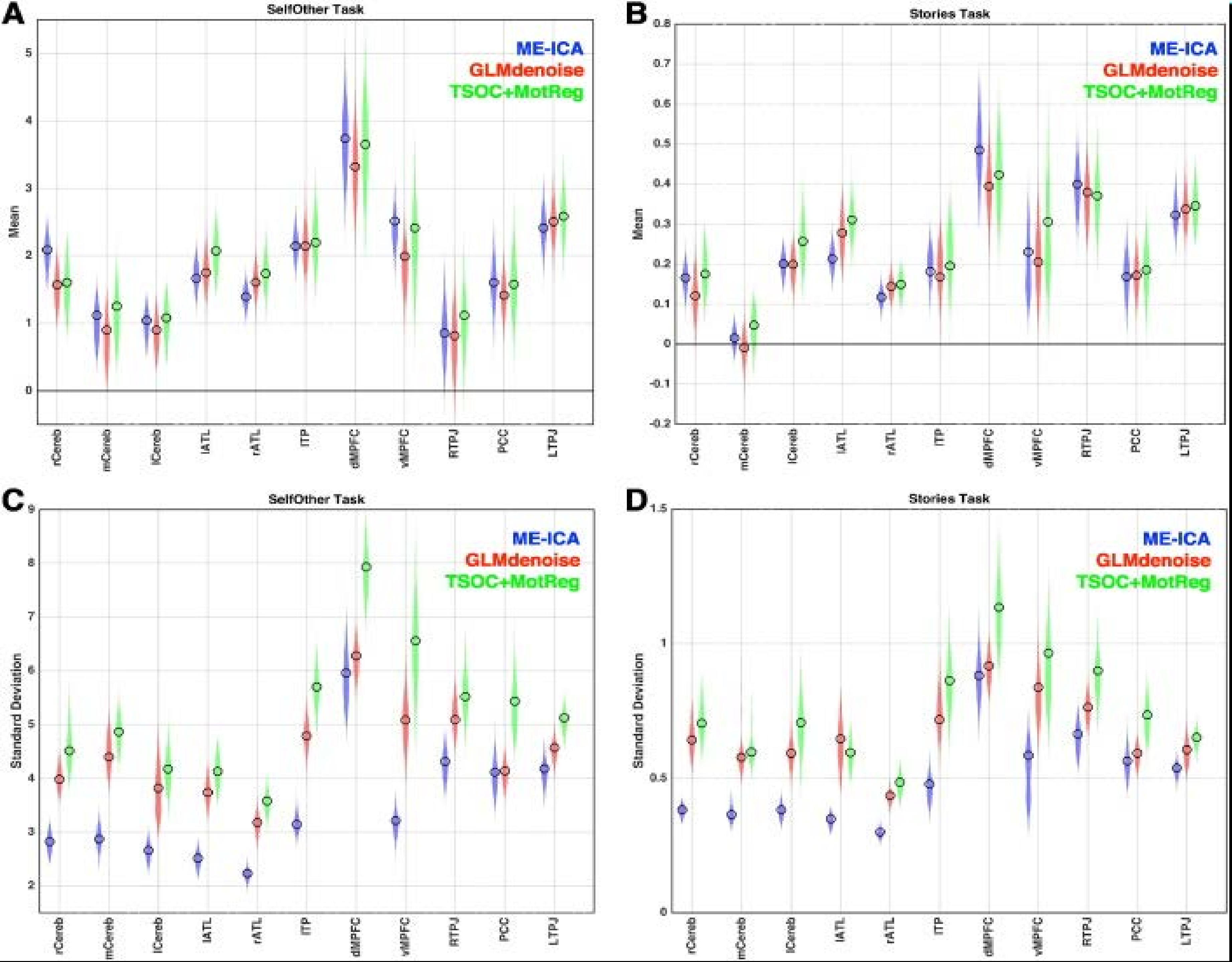

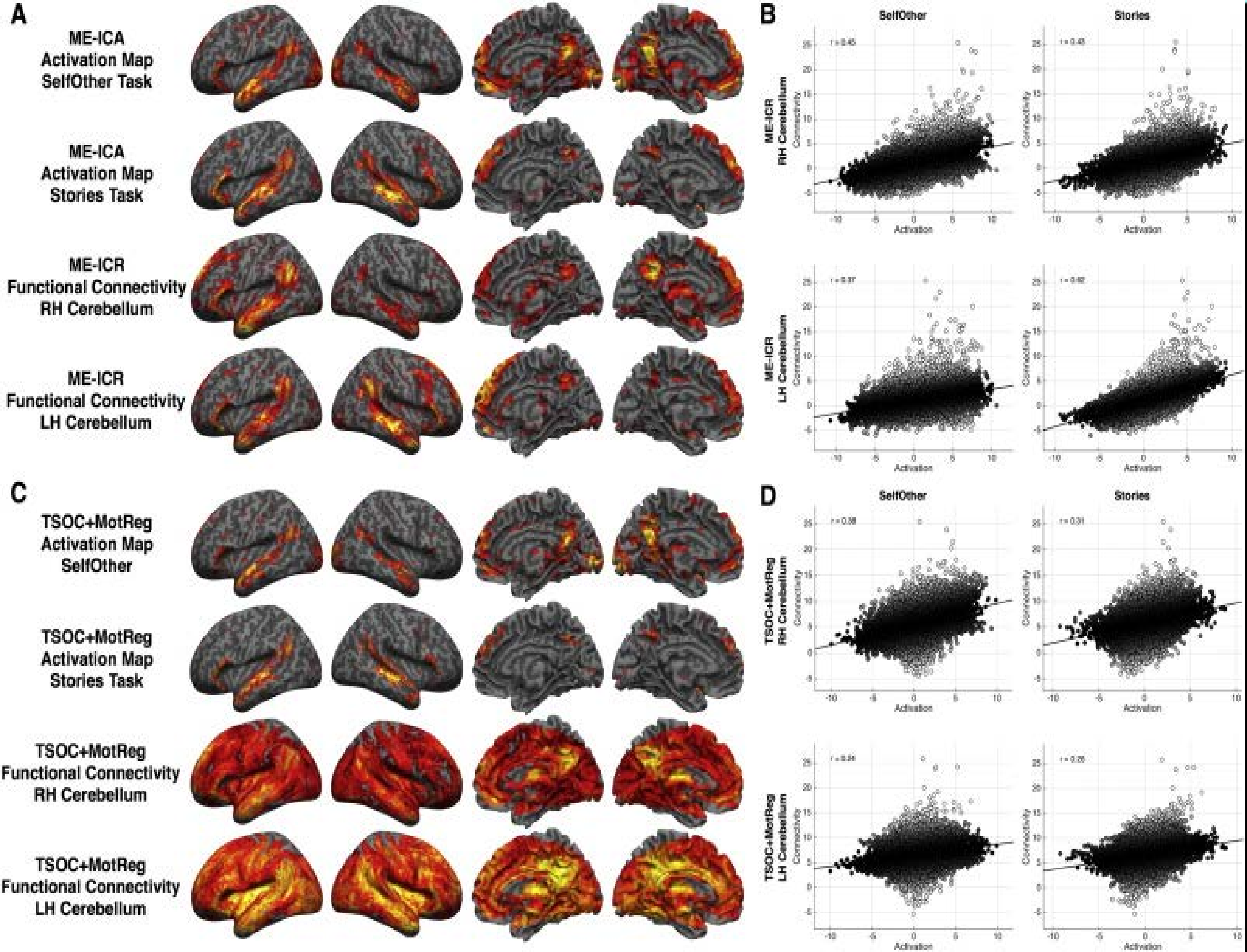


# ME-ICA AND TASK-BASED (BLOCK DESIGN) FMRI: MENTALIZING

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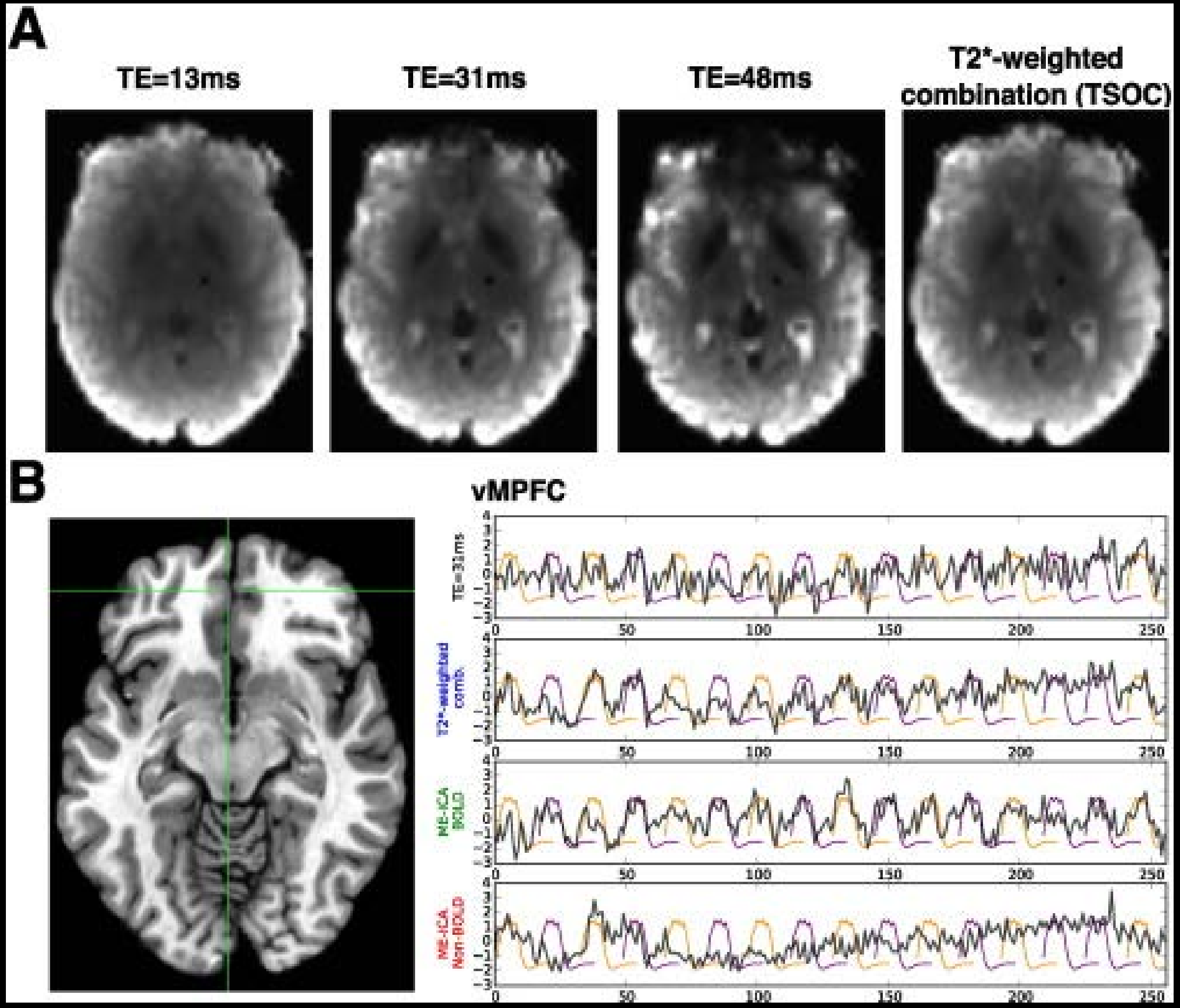
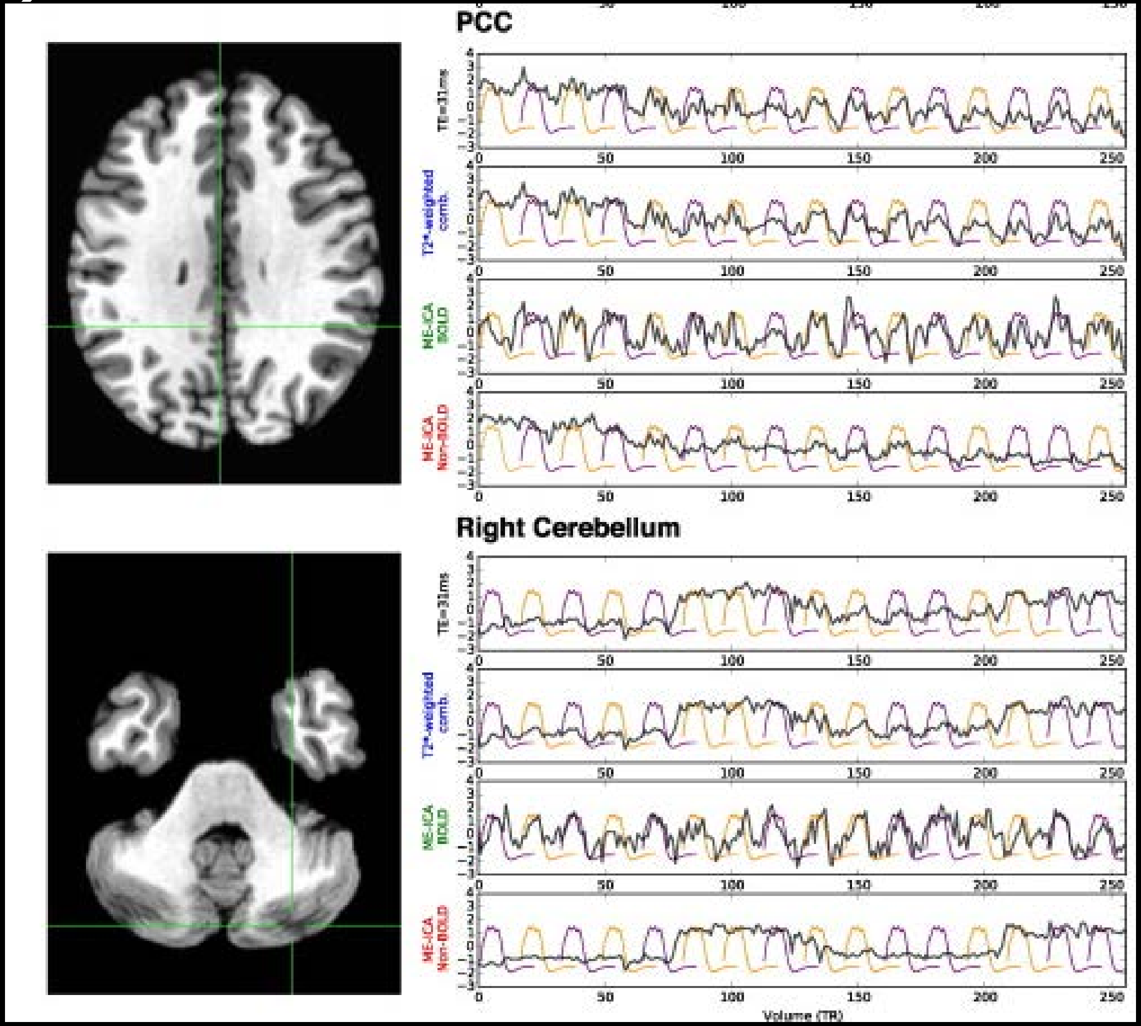
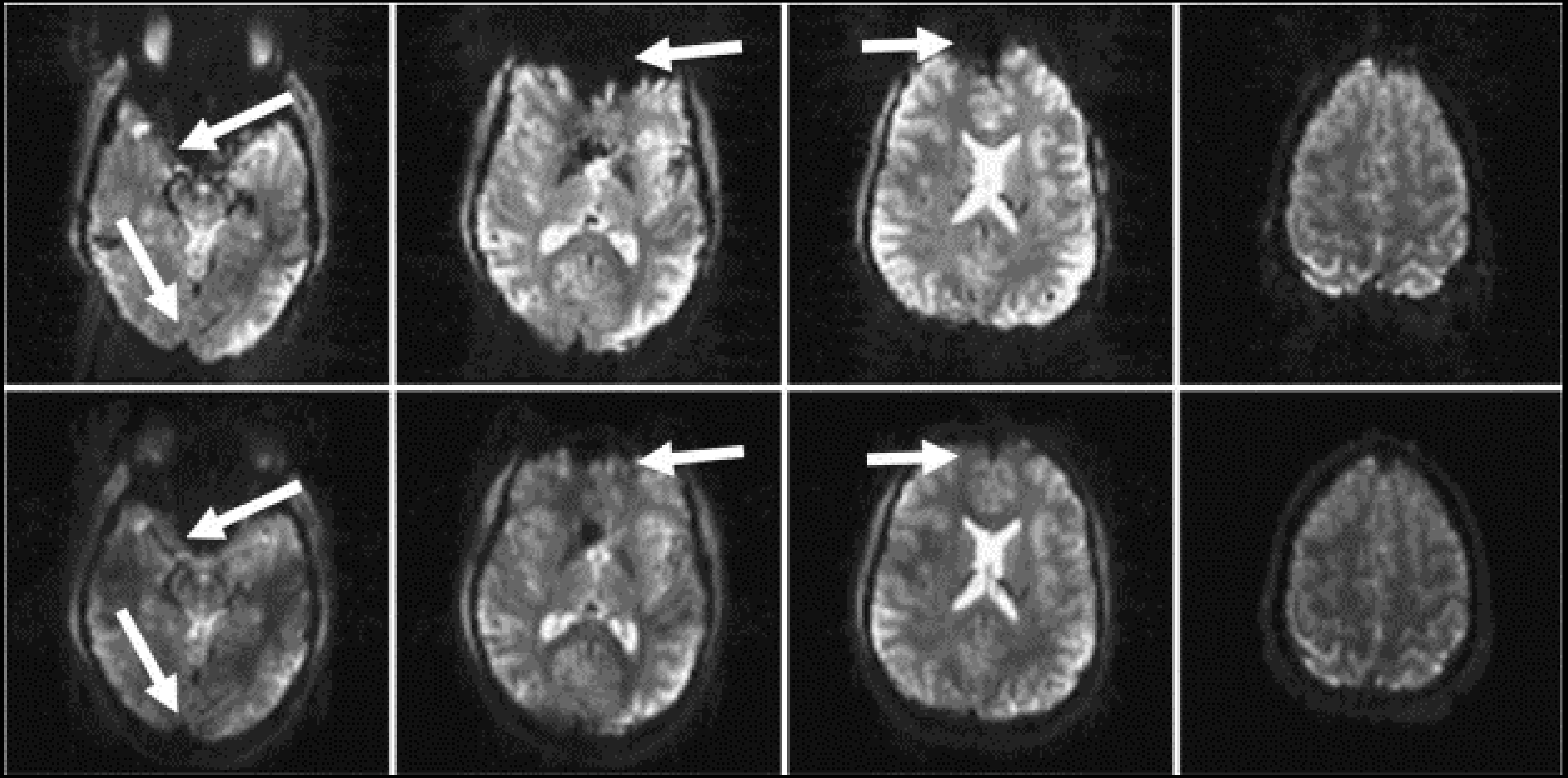


# IMPROVING FMRI AT 7T

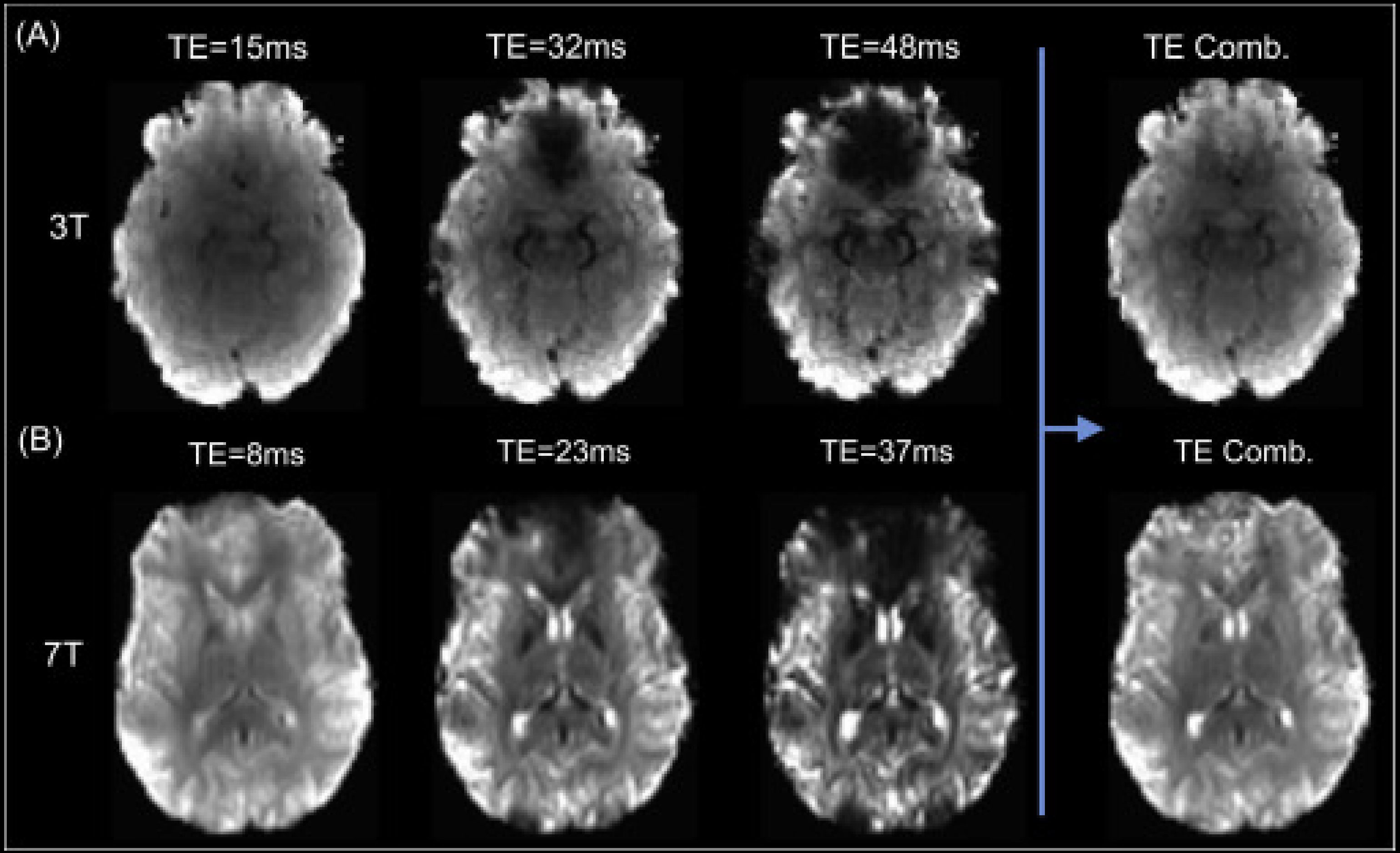
Conventional single EPI



Simple sum of multi-echo EPI

Kundu et al., 2009 NI

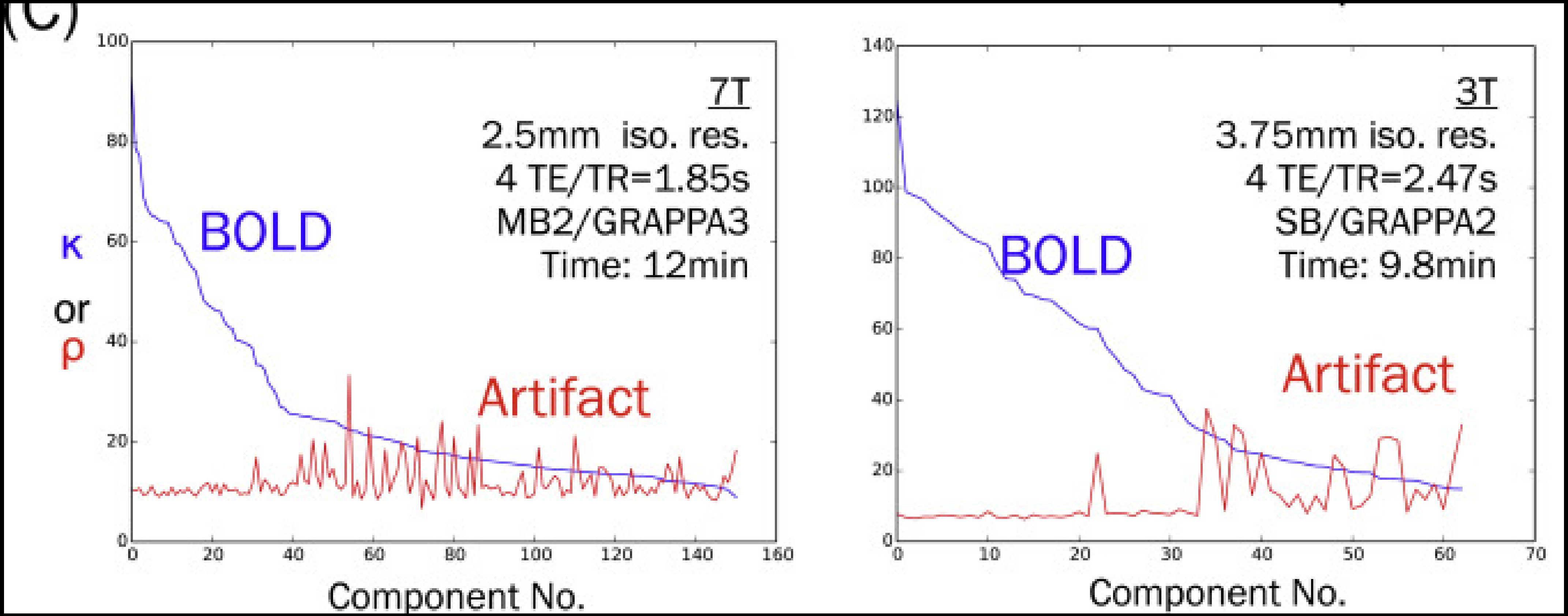
# IMPROVING FMRI AT 7T



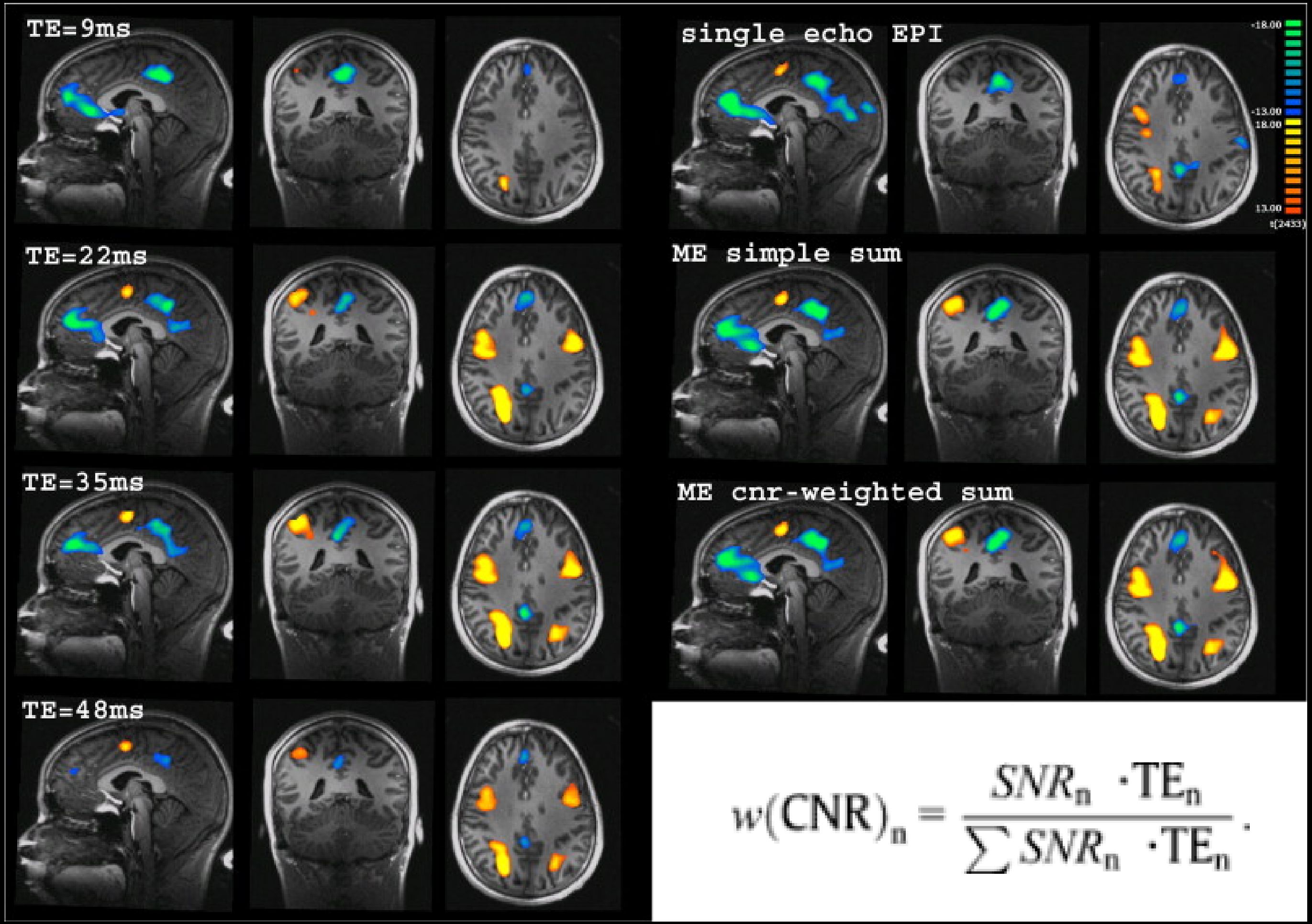

$$w(\mathrm{CNR})_n = \frac{SNR_n \cdot \mathrm{TE}_n}{\sum SNR_n \cdot \mathrm{TE}_n}.$$

Kundu et al., 2017 NI

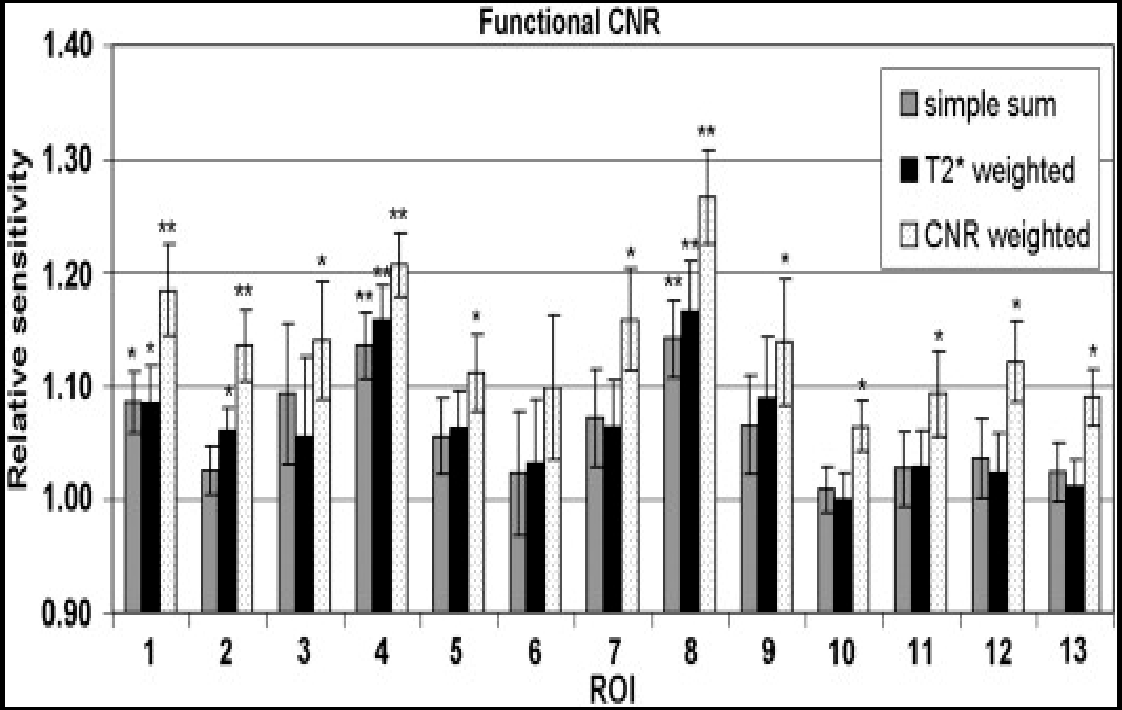
# IMPROVING FMRI AT 7T



# IMPROVING FMRI AT 7T




$$w(\mathrm{CNR})_n = \frac{SNR_n \cdot \mathrm{TE}_n}{\sum SNR_n \cdot \mathrm{TE}_n}.$$




Kundu et al., 2009 NI

# REFERENCES


- Kundu, P., Inati, S. J., Evans, J. W., Luh, W. M., & Bandettini, P. A. (2012). Differentiating BOLD and non-BOLD signals in fMRI time series using multi-echo EPI. *Neuroimage*, *60*(3), 1759-1770.
- Kundu, P., Voon, V., Balchandani, P., Lombardo, M. V., Poser, B. A., & Bandettini, P. (2017). Multi-Echo fMRI: A Review of Applications in fMRI Denoising and Analysis of BOLD Signals. *NeuroImage*.
- Lombardo, M. V., Auyeung, B., Holt, R. J., Waldman, J., Ruigrok, A. N., Mooney, N., ... & Kundu, P. (2016). Improving effect size estimation and statistical power with multi-echo fMRI and its impact on understanding the neural systems supporting mentalizing. *NeuroImage*, *142*, 55-66.
- Kundu, P., Brenowitz, N. D., Voon, V., Worbe, Y., Vértes, P. E., Inati, S. J., ... & Bullmore, E. T. (2013). Integrated strategy for improving functional connectivity mapping using multiecho fMRI. *Proceedings of the National Academy of Sciences*, *110*(40), 16187-16192.