The strategies and challenges of noise reduction or removal

Why is noise removal so hard to solve?
Noise during acquisition

Daniel Handwerker

NOISE !?

- "Impacting the effect of fMRI **noise** through hardware and acquisition choices – Implications for controlling false positive rates"
Wald & Polimeni, *NeuroImage* (2017)

- First sentence of their introduction
  - Applied to the intensity fluctuations of a pixel in an fMRI time- series, the term "noise" is so non-specific and carries such negative connotations that it should probably be eliminated from the fMRI vocabulary.

What is noise?

Noise

- Merriam Webster: "Irrelevant or meaningless data or output occurring along with desired information"

- Stuff that gets in the way of of measuring what we want to measure
  - Noise is defined by each study's goals
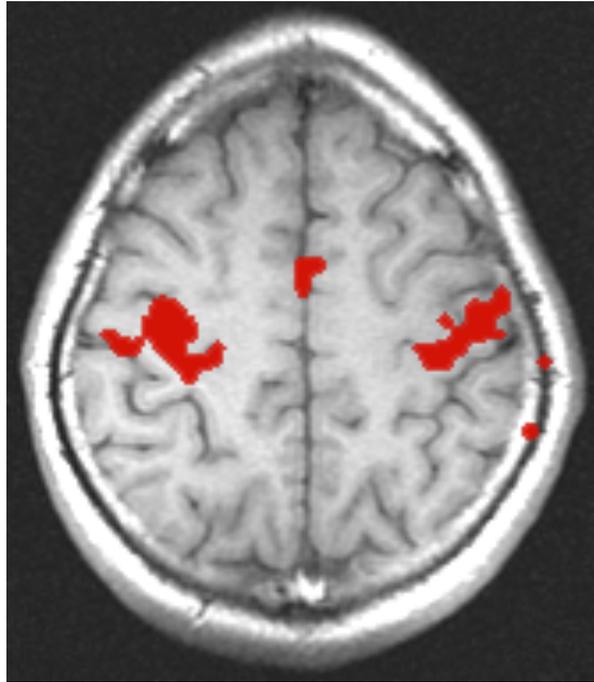 - One study's noise can be another study's signal

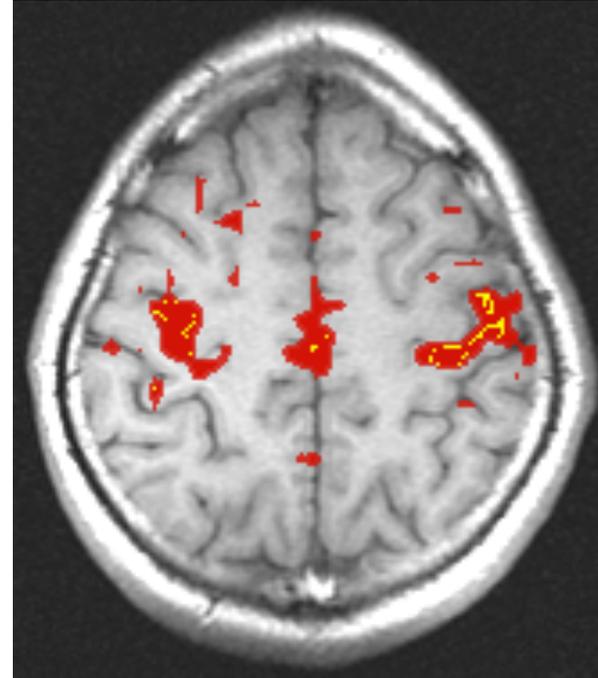# One study's noise can be another study's signal
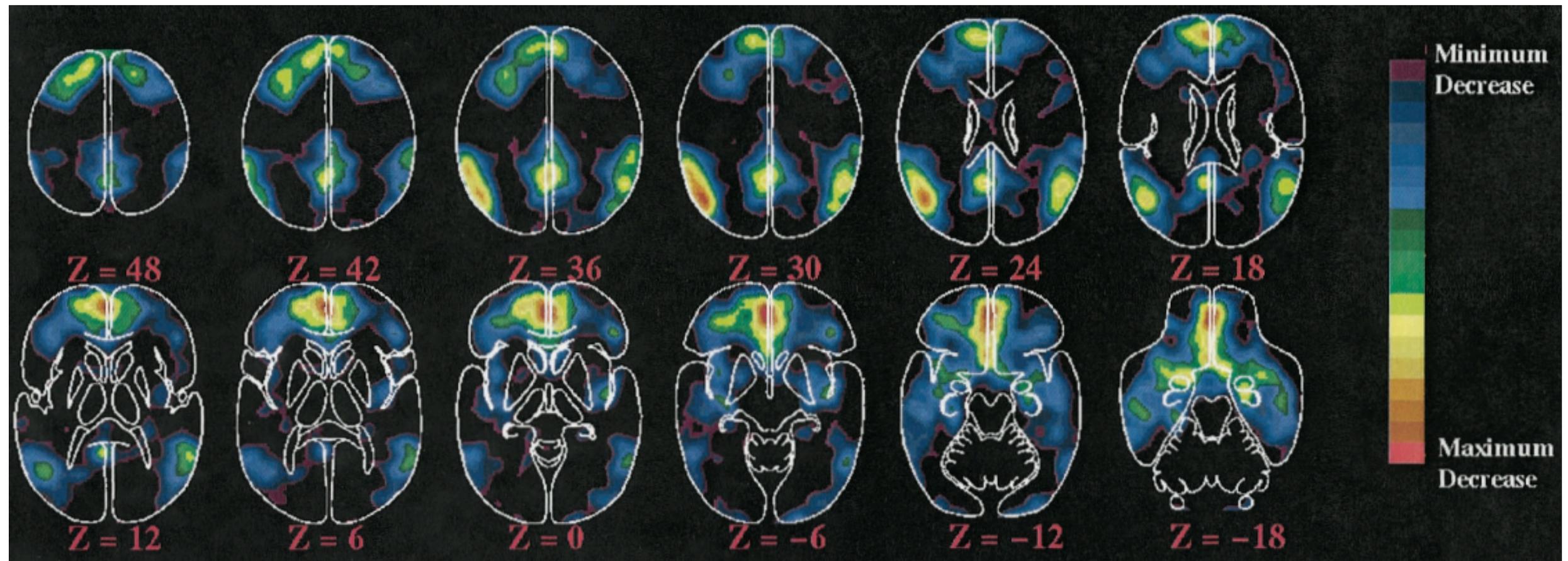
Areas of the brain that decrease activity across a wide range of cognitive tasks

Raichle, MacLeod et al, PNAS 2001 "A default mode of brain function"
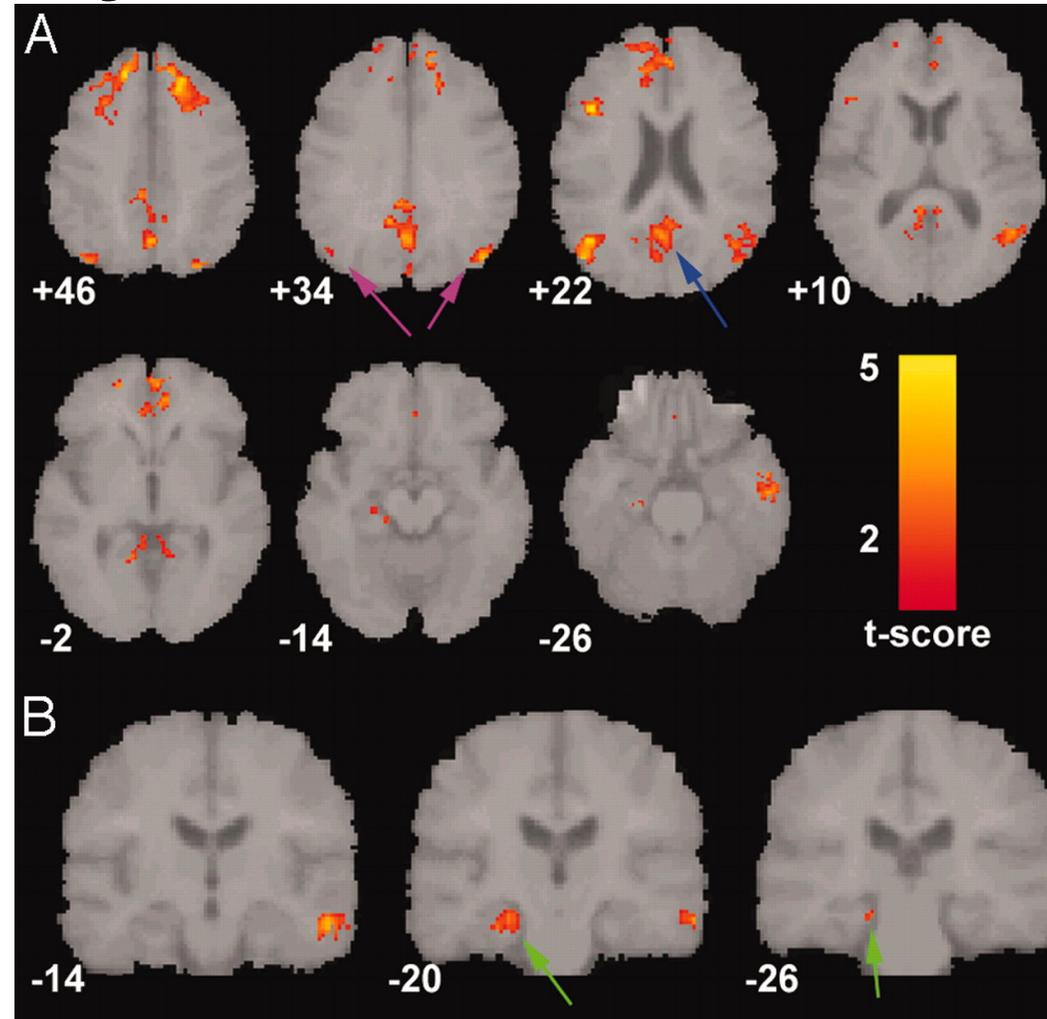
"Random" fluctuations become signal

Activation during finger-tapping

Correlations with "seed voxel" in motor cortex **during rest**
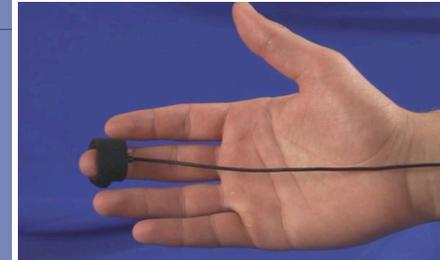
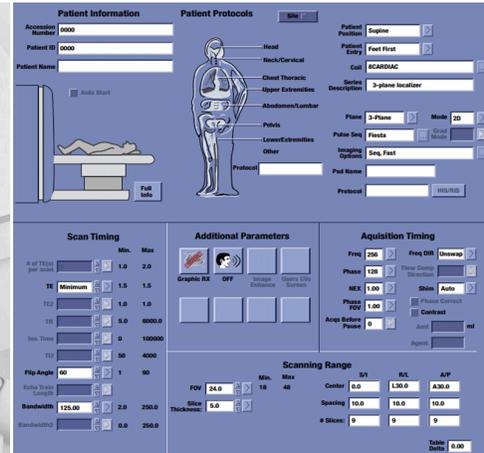*B. Biswal* et al., *MRM, 34:537 (1995)*

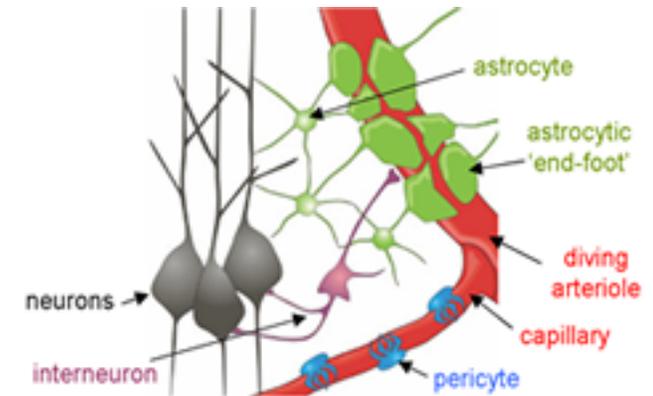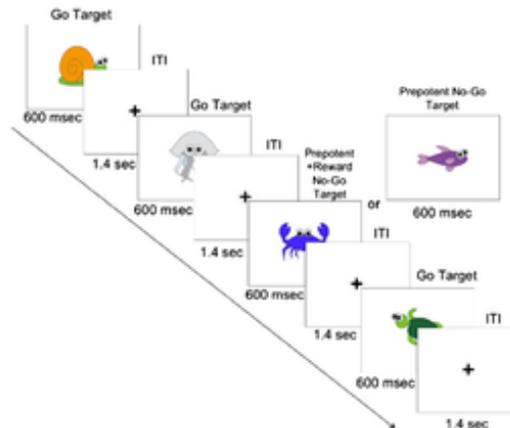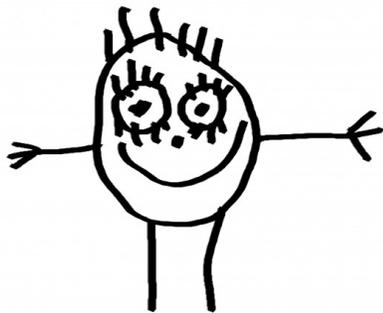# Noise in one study can be a clinical biomarker in another

Default mode brain regions distinguish
Alzheimer's Disease patients from healthy elderly

Ways to categorize noise
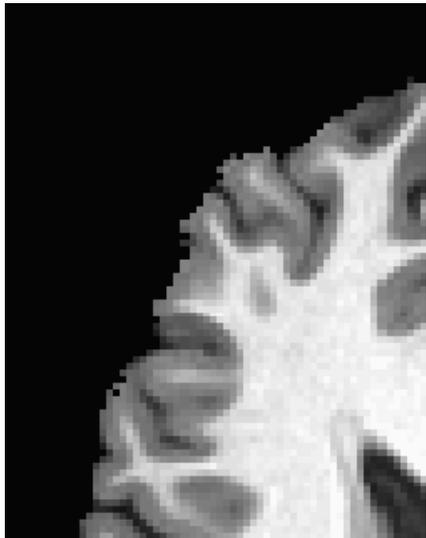
From the measurement tools

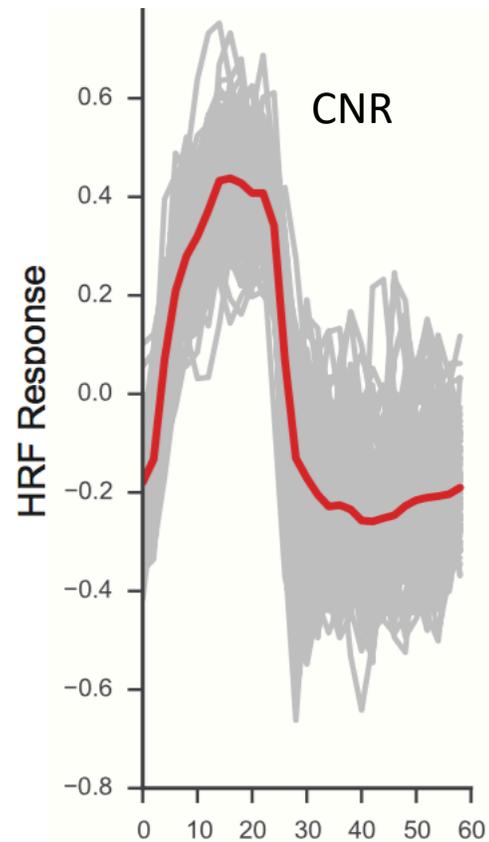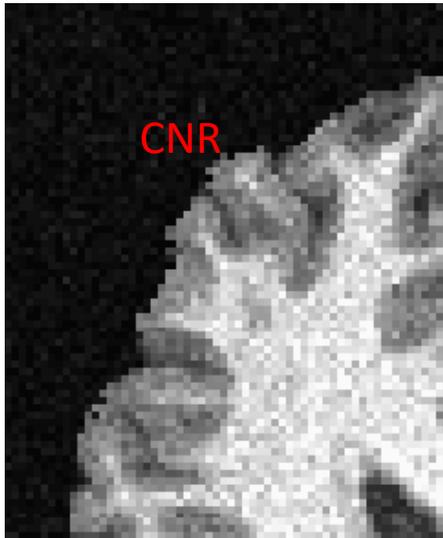
From the system being measured

Measures of noise

- Signal-To-Noise Ratio (SNR)

- Temporal Signal-To-Noise Ratio (TSNR)

- Contrast-To-Noise Ratio (CNR)

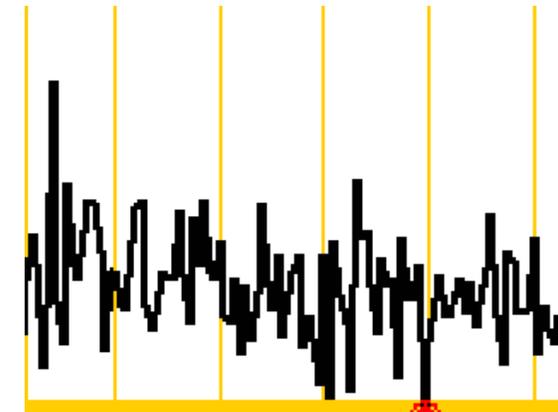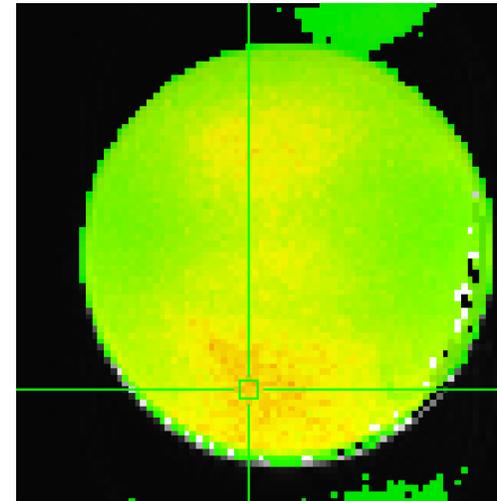# How to think about noise reduction or removal
Unstructured random noise
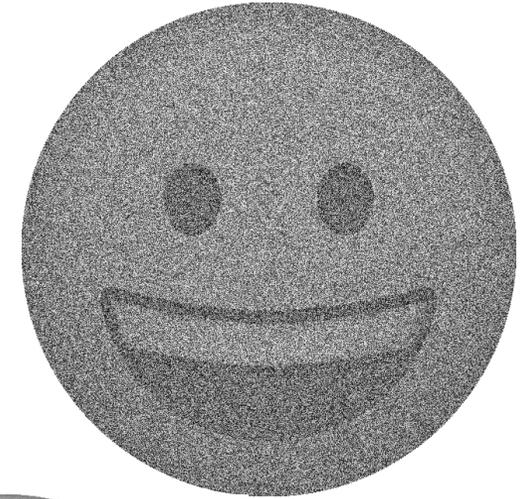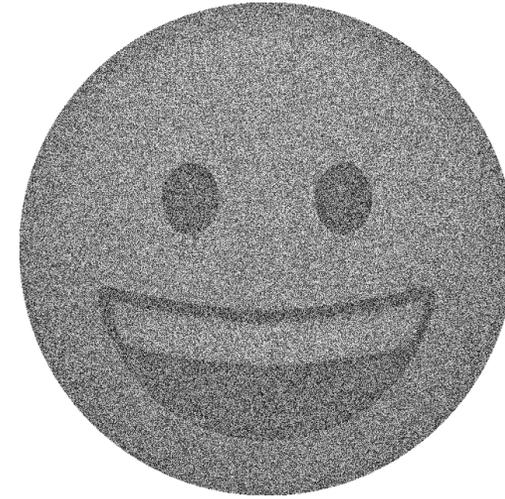
No noise

"White" noise

100 averages

1000 averages

- Less noise in original data is better
- **IF** all data are similarly noisy, unlikely to bias results
- More repetitions reduces noise
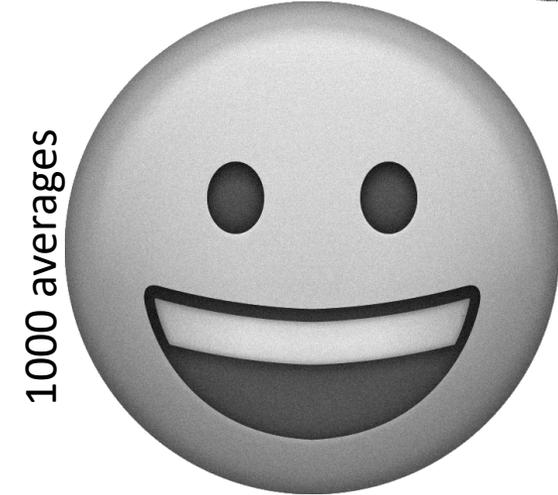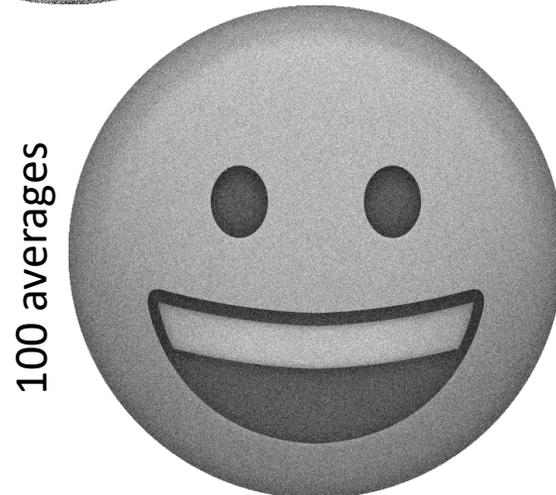
Unstructured random noise
More repetitions reduces noise

3 volunteers
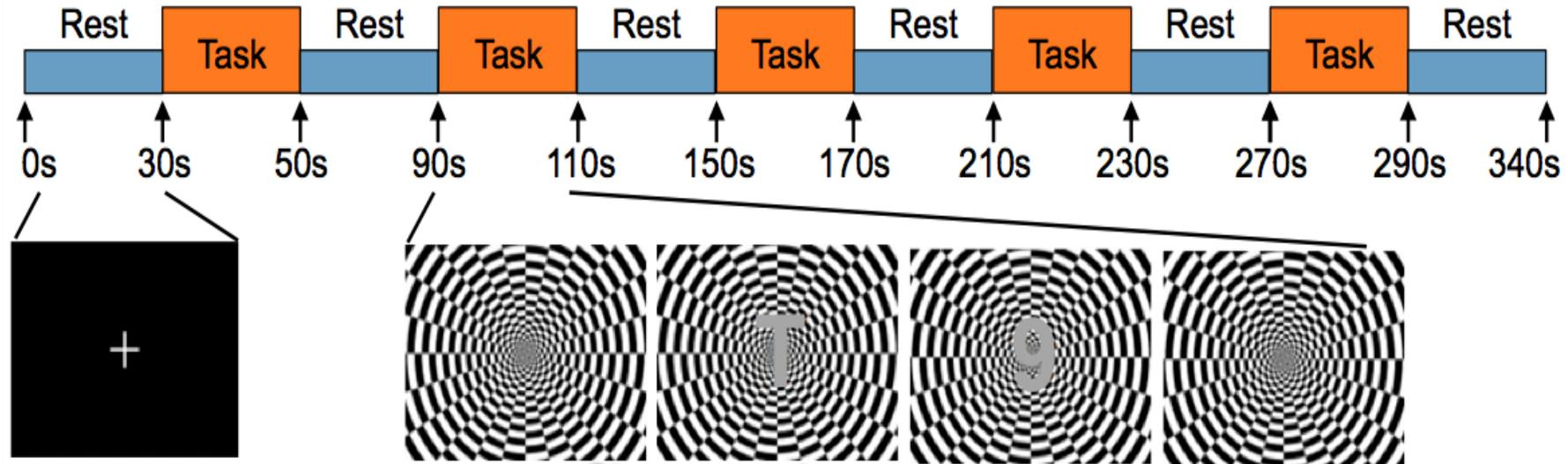
100 five minute runs
9 hours of functional data per volunteer

100 runs of responses in primary visual cortex

LEFT   RIGHT   RIGHT   LEFT

Rest **TASK** Rest **TASK** Rest **TASK** Rest **TASK** Rest **TASK** Rest

0s   30s 50s   90s 110s   150s 170s   210s 230s   270s 290s   340s

INDIVIDUAL RUNS   **AVERAGING**

RUN=001 N_{avg}=001

30 50   90 110   150 170   210 230   270 290

Time (s)
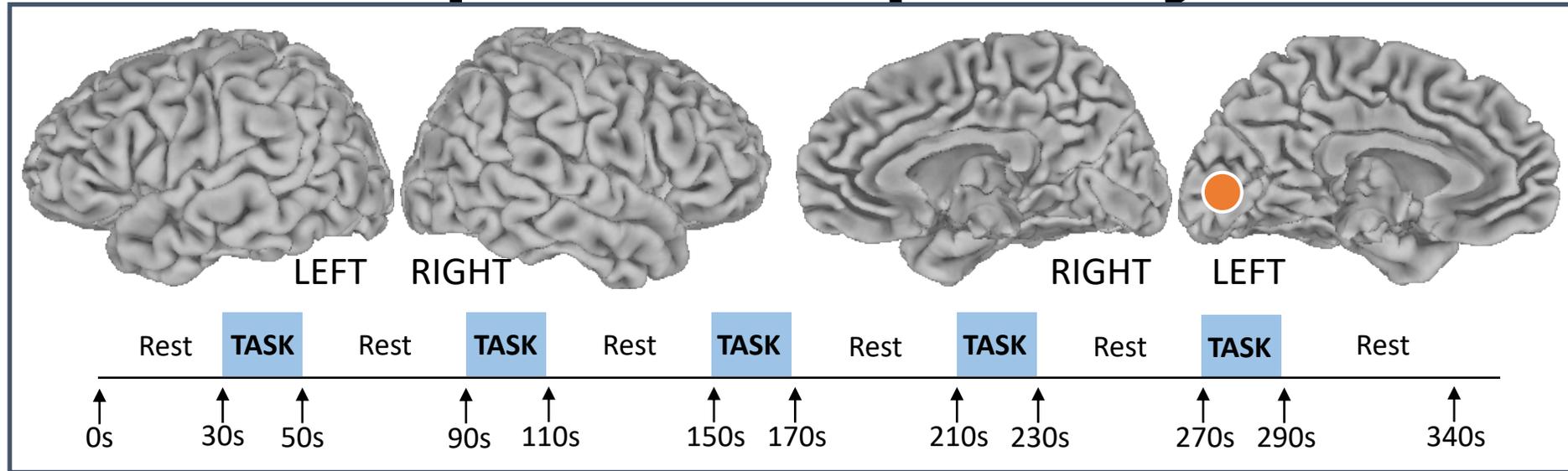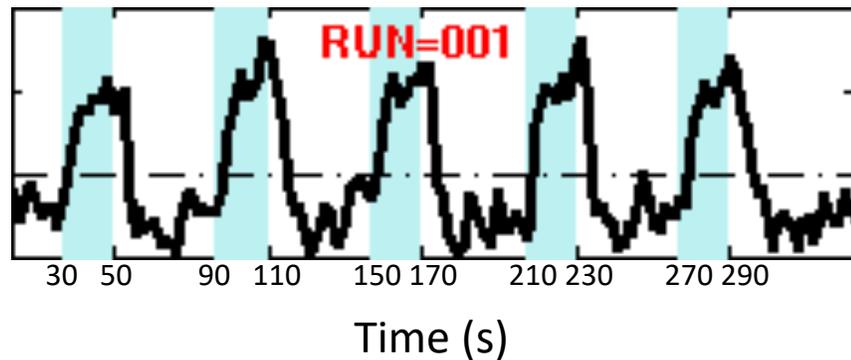
100 runs of responses in primary auditory cortex
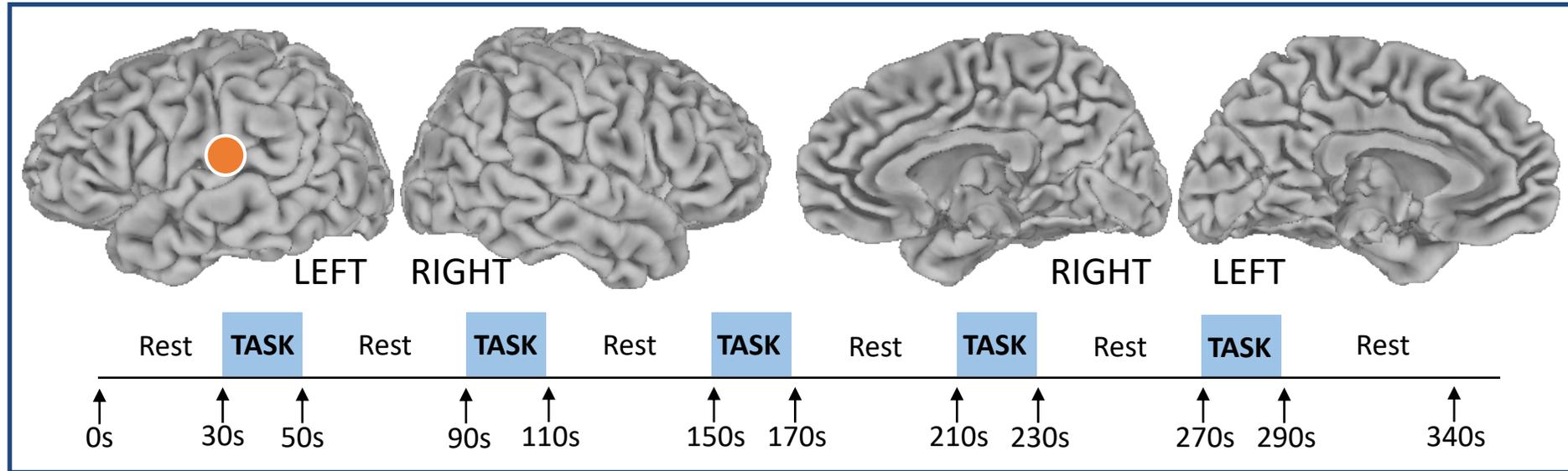
INDIVIDUAL RUNS
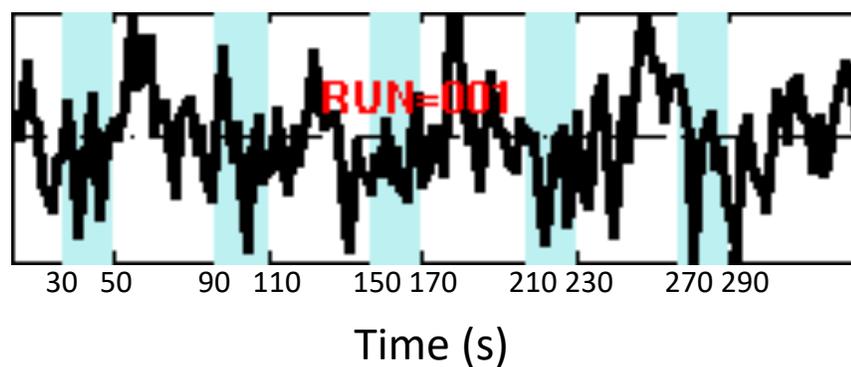
AVERAGING
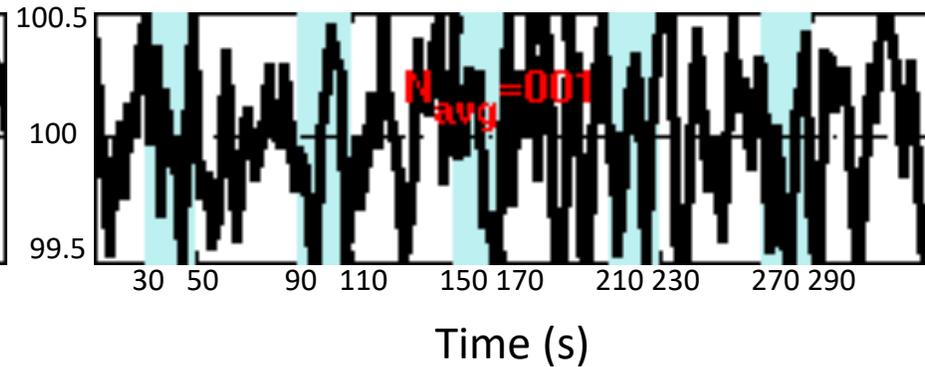
More data means more of the brain is significantly modeled by the task
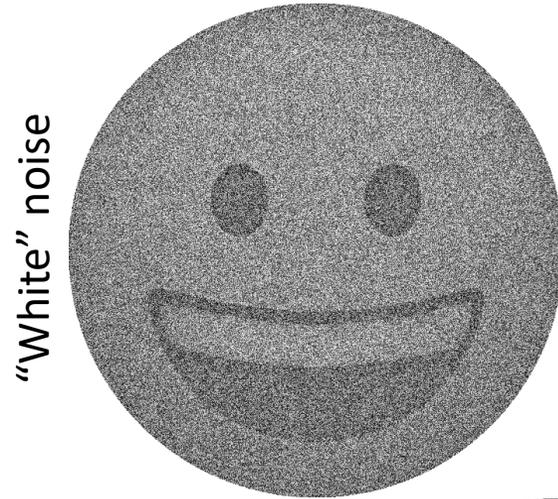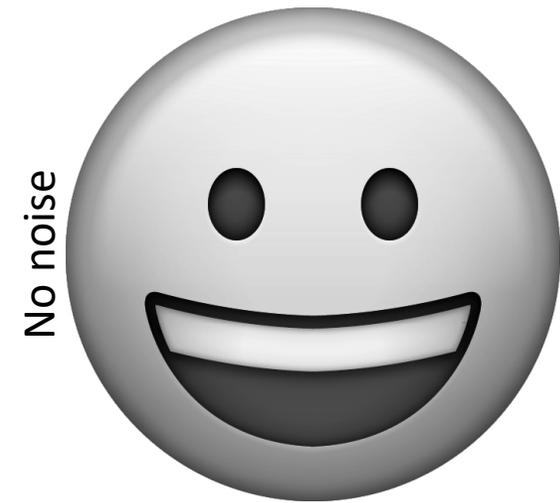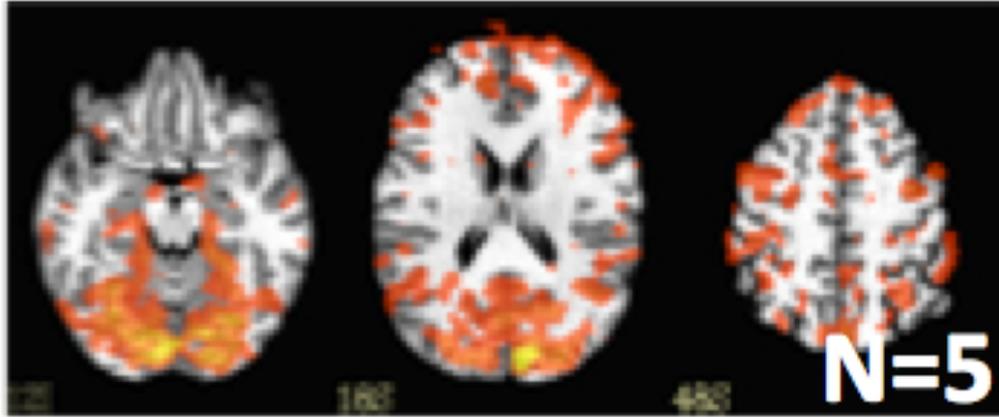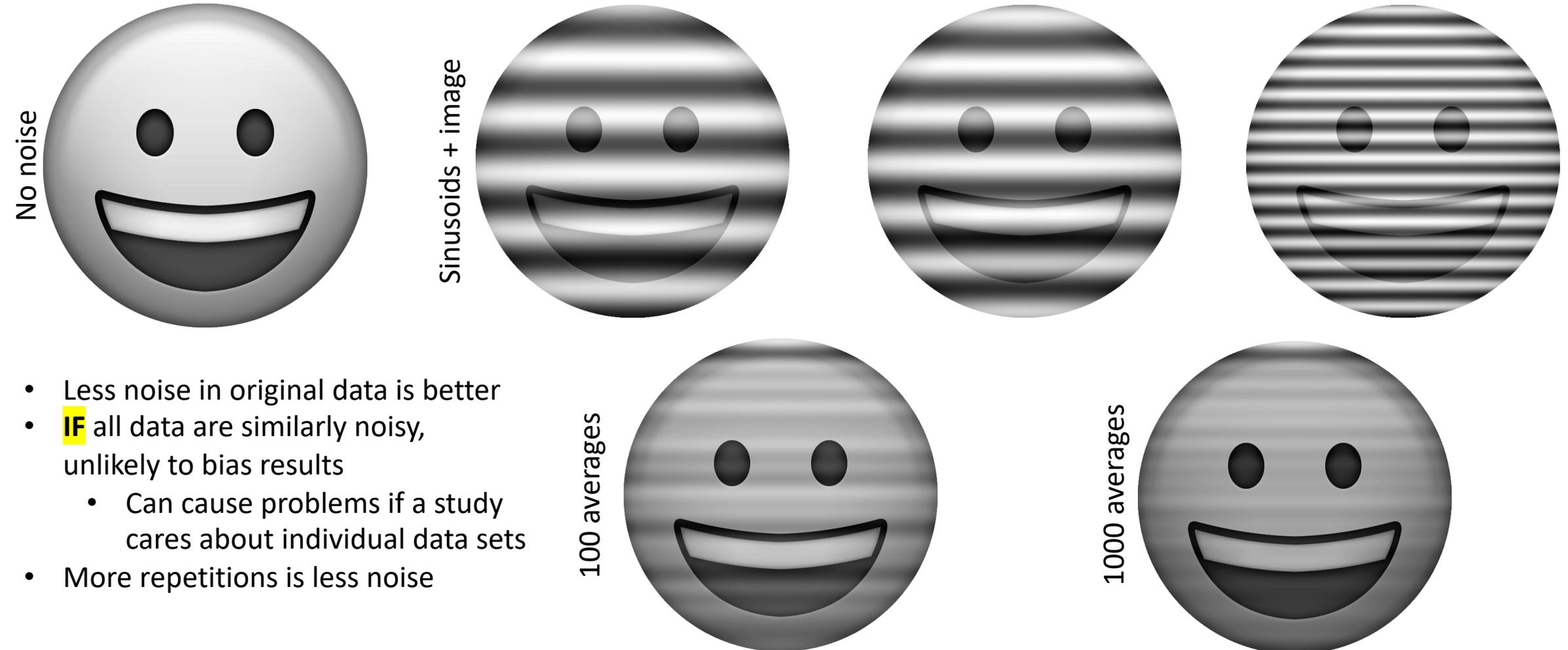

F = 0 [color bar] F = 20

How to think about noise reduction or removal
Structured random noise

No noise

Sinusoids + image

100 averages

1000 averages

- Less noise in original data is better
- **IF** all data are similarly noisy, unlikely to bias results
  - Can cause problems if a study cares about individual data sets
- More repetitions is less noise

# How to think about noise reduction or removal
Structured random noise

- Task-based fMRI
  - Head motion
  - Respiration and heart rate
  - Neurovascular coupling variation
  - Trial-to-trial behavioral variation

- These variations *ideally* cancel each other out over time
- Worrying about these from a noise perspective was a peripheral concern for the first decade+ of fMRI

How to think about noise reduction or removal
Structured non-random noise

No noise

Drop out

100 averages
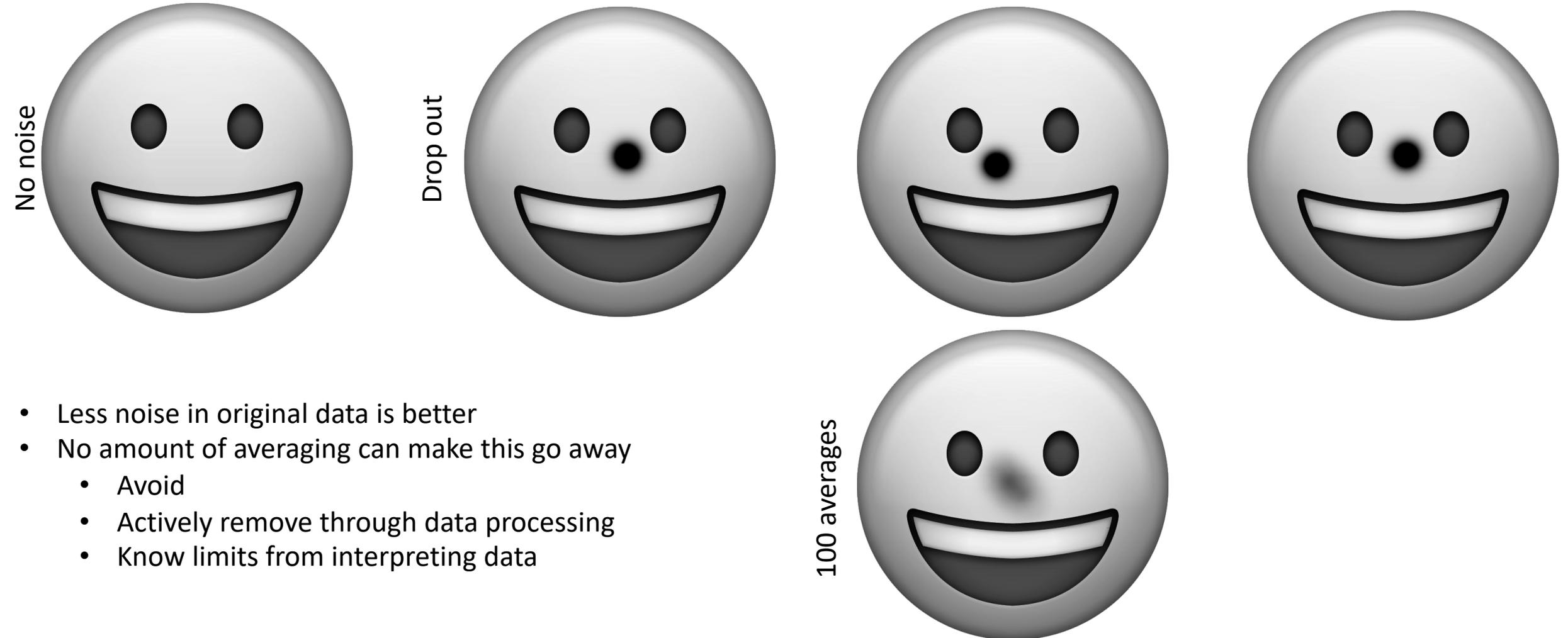
- Less noise in original data is better
- No amount of averaging can make this go away
  - Avoid
  - Actively remove through data processing
  - Know limits from interpreting data

Structured non-random noise
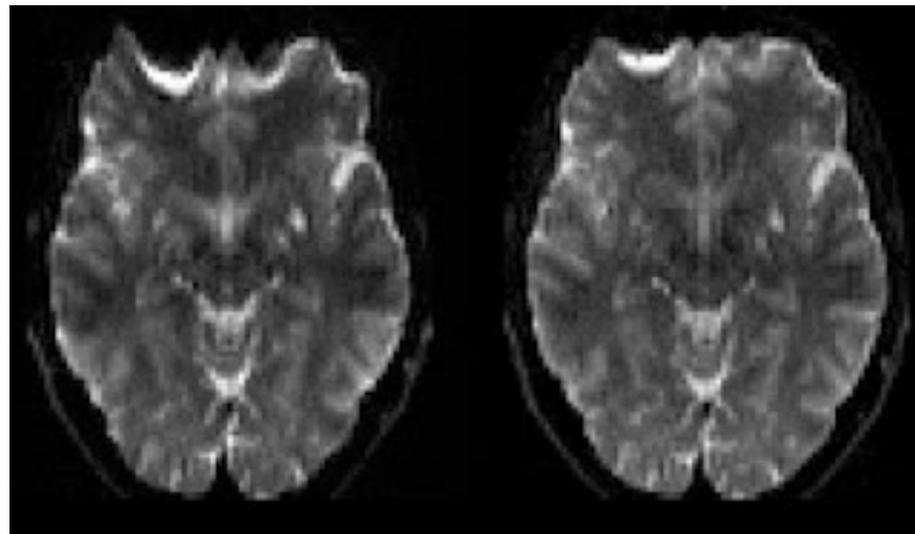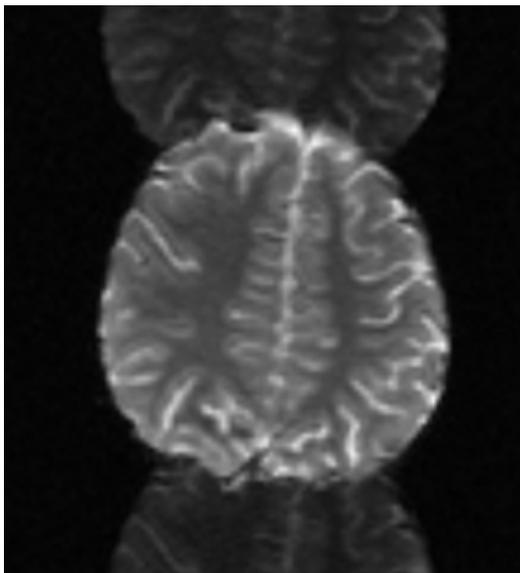
Structured non-random noise

- Task-based fMRI
  - **Task correlated** Head motion
  - **Task correlated** Respiration and heart rate
  - Unmodeled systemic behavioral variation
- Connectivity based fMRI analyses
  - All head motion
  - All respiration & heart rate fluctuations
  - Unmodeled structured behaviors

- Image drop-out, mis-alignment, and distortions
- Unmodeled Hemodynamic Responses / Neurovascular Coupling

Signal & noise are correlated for functional connectivity

Original "neuronal" time series

r=1.0
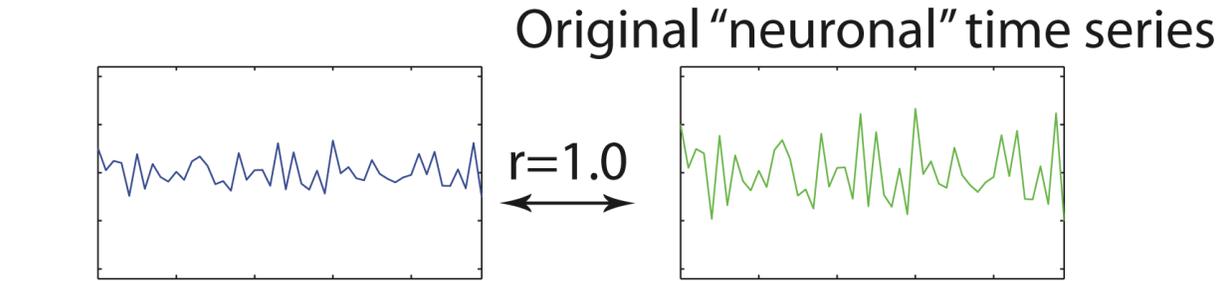
fMRI Signal Change

Seconds

Model-based fMRI
Noise that isn't time-locked to a task is annoying.

Connectivity-based fMRI
Common noise across regions can contaminate results

Functional Brain Networks Develop from a "Local to Distributed" Organization

Fair... Petersen, PLoS Comp Bio 2009
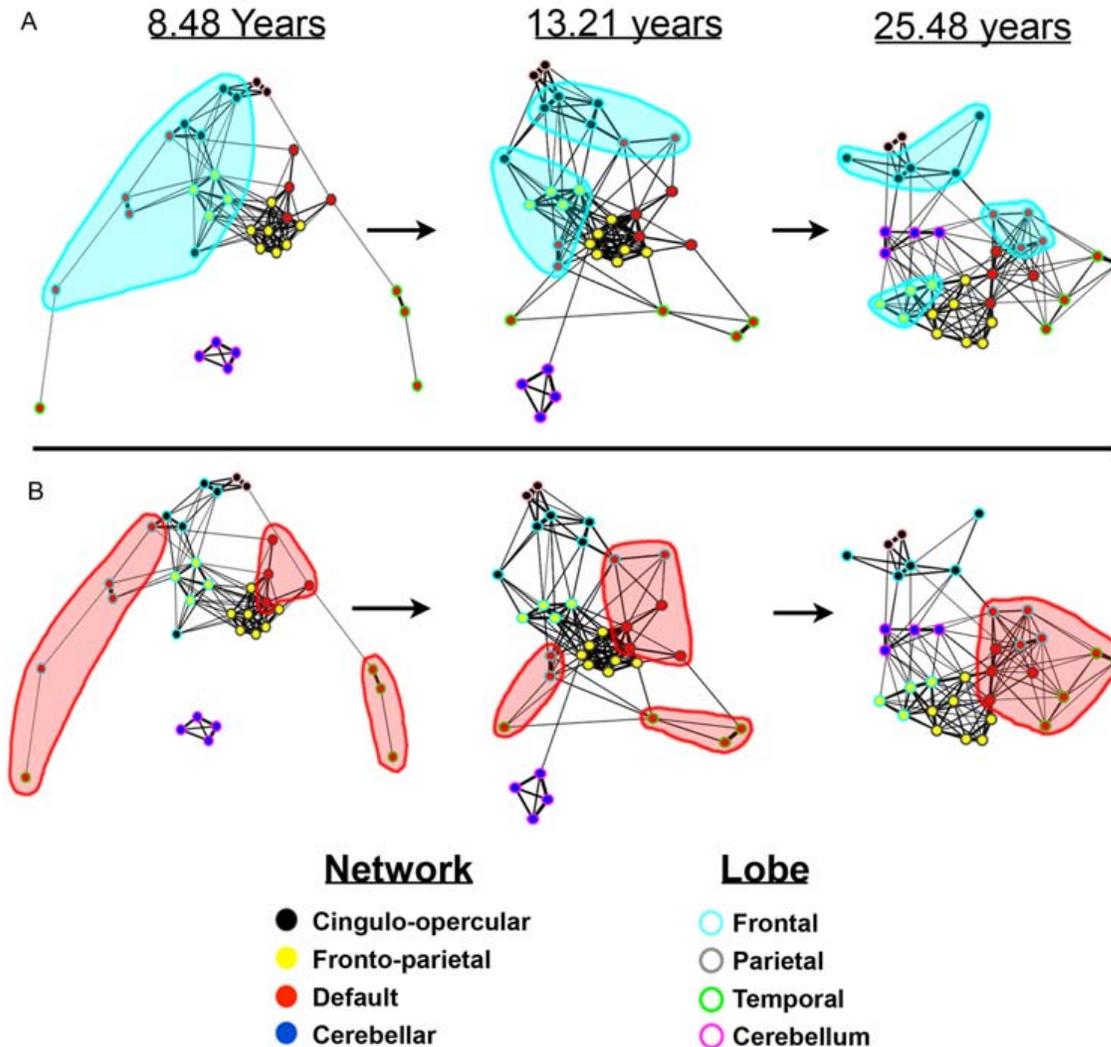
Noise from head motion drove the network result

unscrubbed | scrubbed

Cohort 1: 3T children

0.69

0.56 prior to scrubbing

0.70 after motion scrubbing
0.58 ± 0.01 after random scrubbing

Cohort 3: 3T adults

0.94
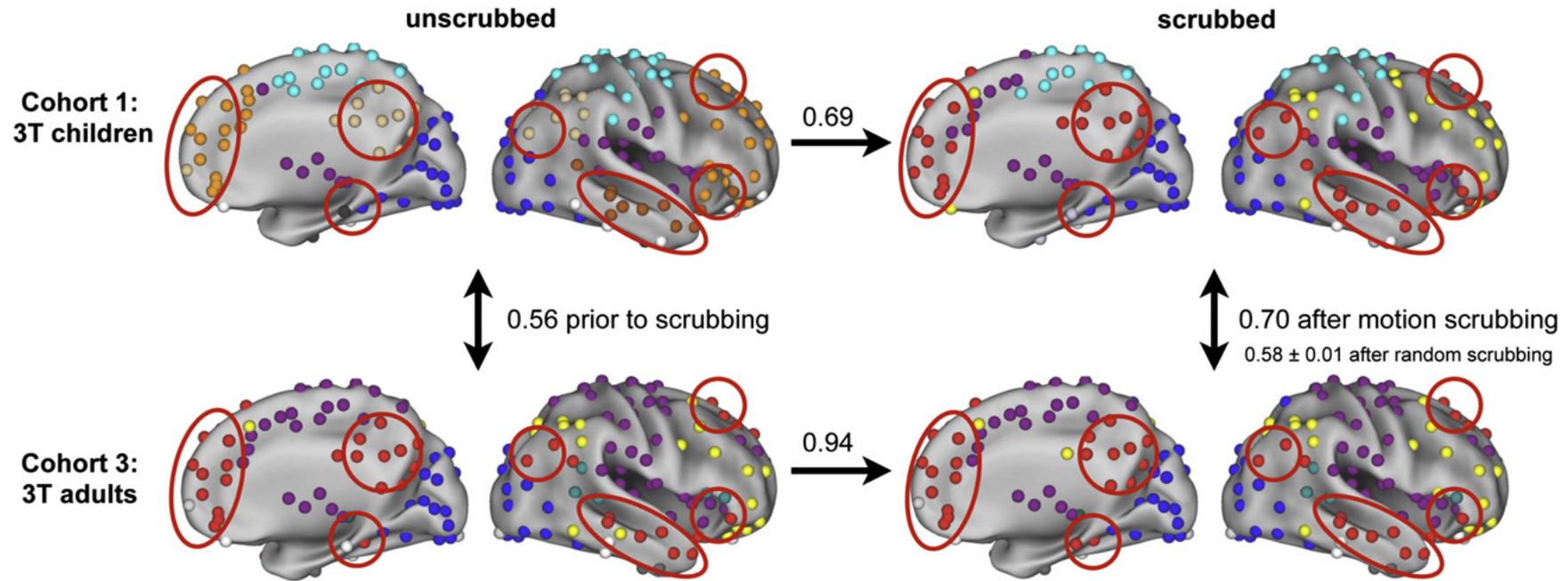
When they scrubbed data for areas of higher head motion (more common in children), the main network differences disappeared

Power, … Petersen, Neuroimage 2012

"It really, really, really sucks. My favorite result of the last five years is an artifact," Steve Petersen

http://sfari.org/news-and-opinion/news/2012/movement-during-brain-scans-may-lead-to-spurious-patterns

Noise can be task correlated

Respiration depth over time (RVT) during a letter/number discrimination task

Neurovascular coupling noise

| | + | - | ? |

Neural Activity

Cerebral Oxygen Metabolism

Cerebral Blood Flow

Cerebral Blood Volume

DeoxyHb Concentration

BOLD

0　　~2　　　　　~4　　　~7　　　　~20-40

Seconds
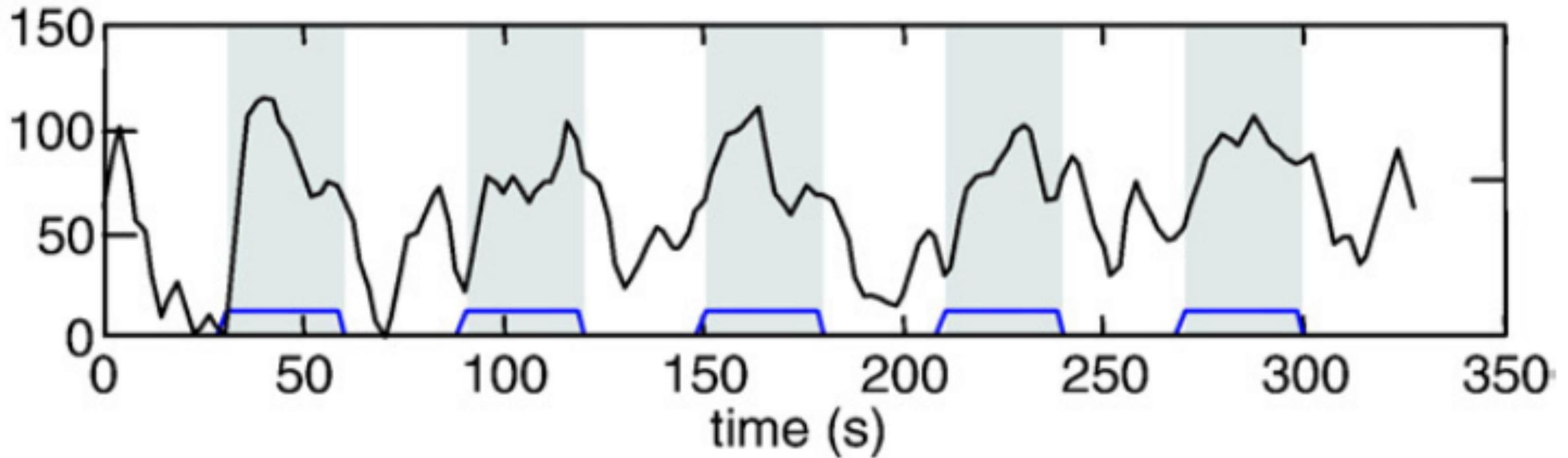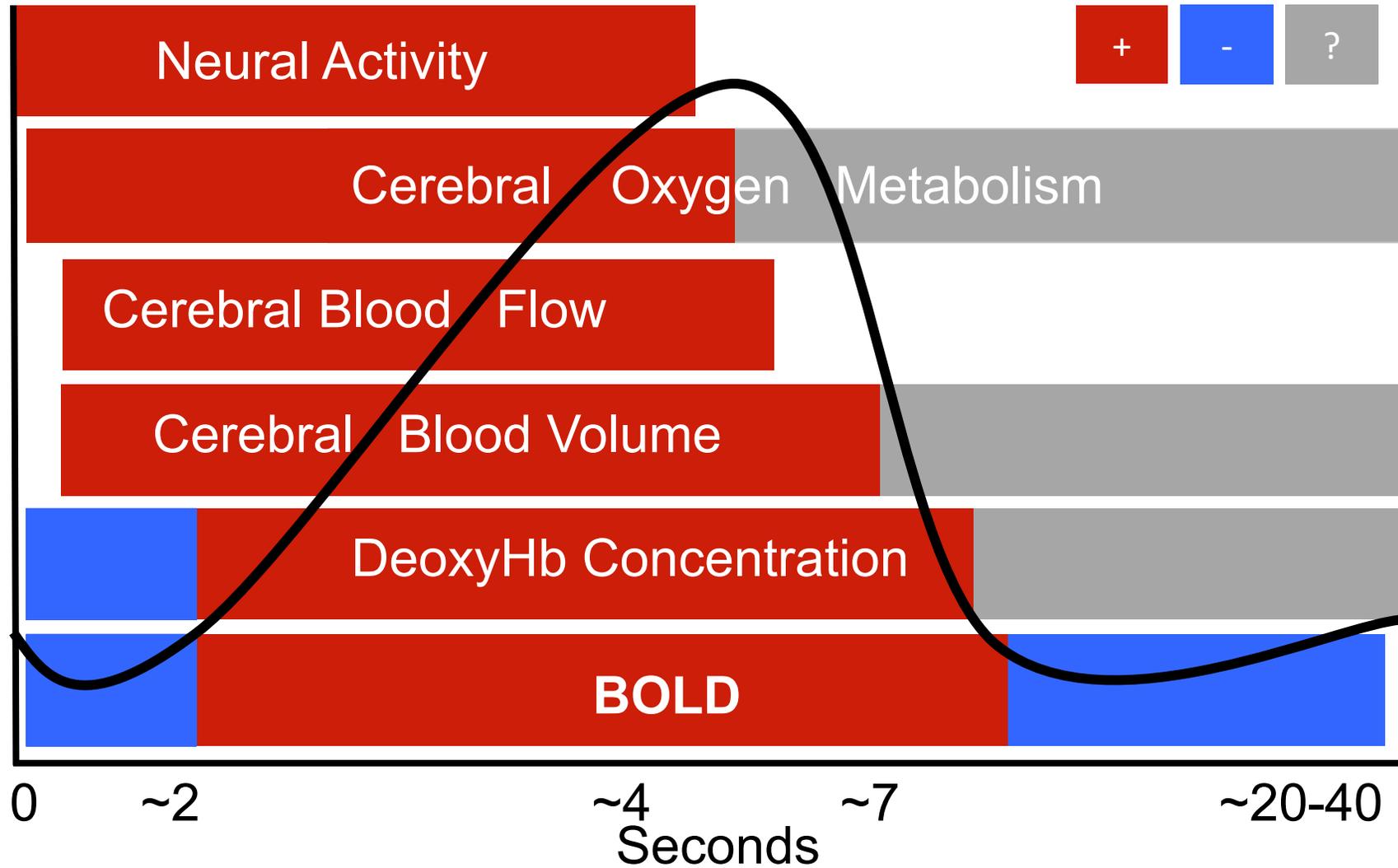
This shows what happens, not why it happens

We know a lot about neurovascular coupling
It's not directly driven by oxygen or energy needs

Elizabeth Hillman, Annual Review of Neuroscience 2014. 37:161–81

There's still a lot we don't know about neurovascular coupling

Population differences can occur from non-neural variation
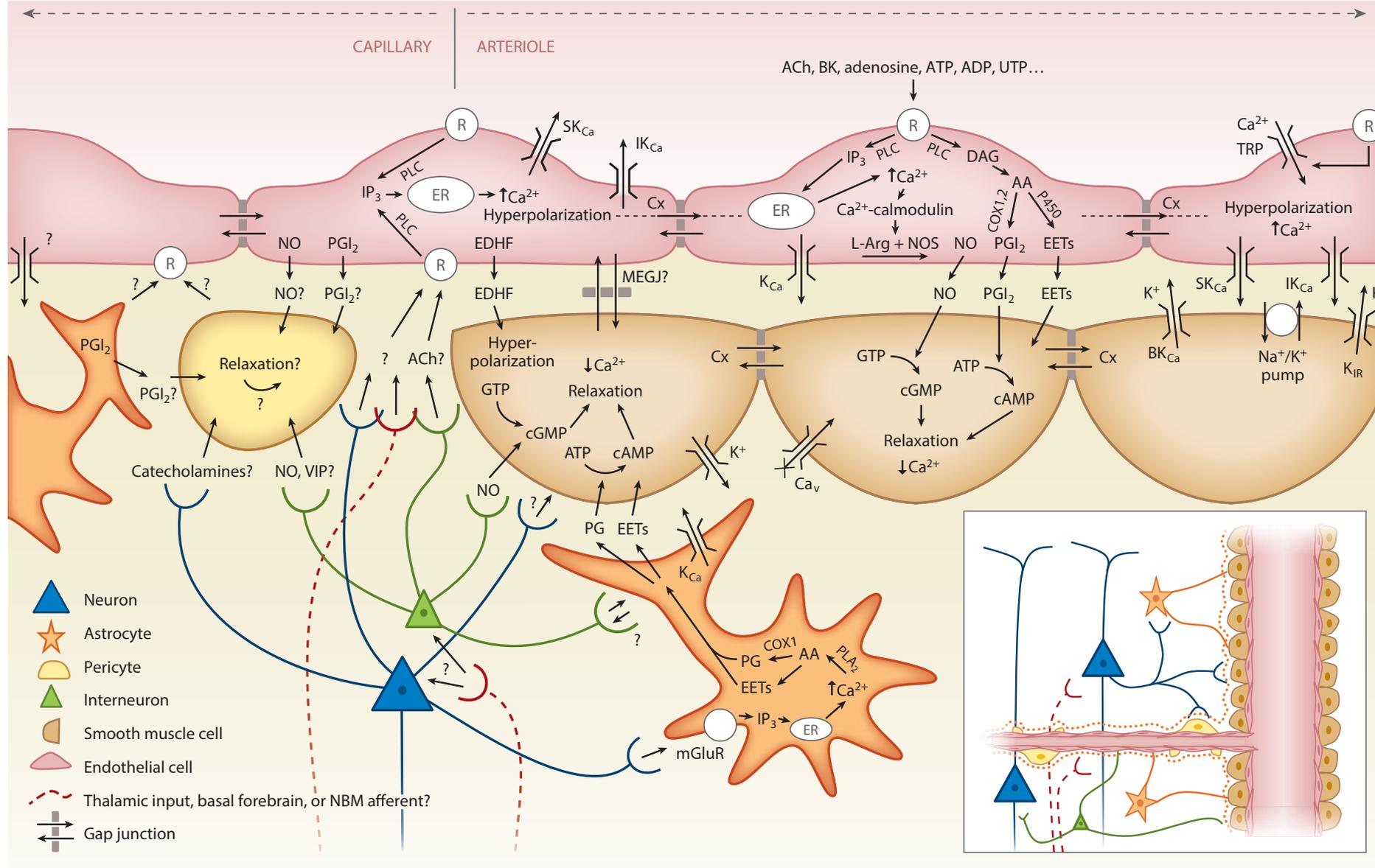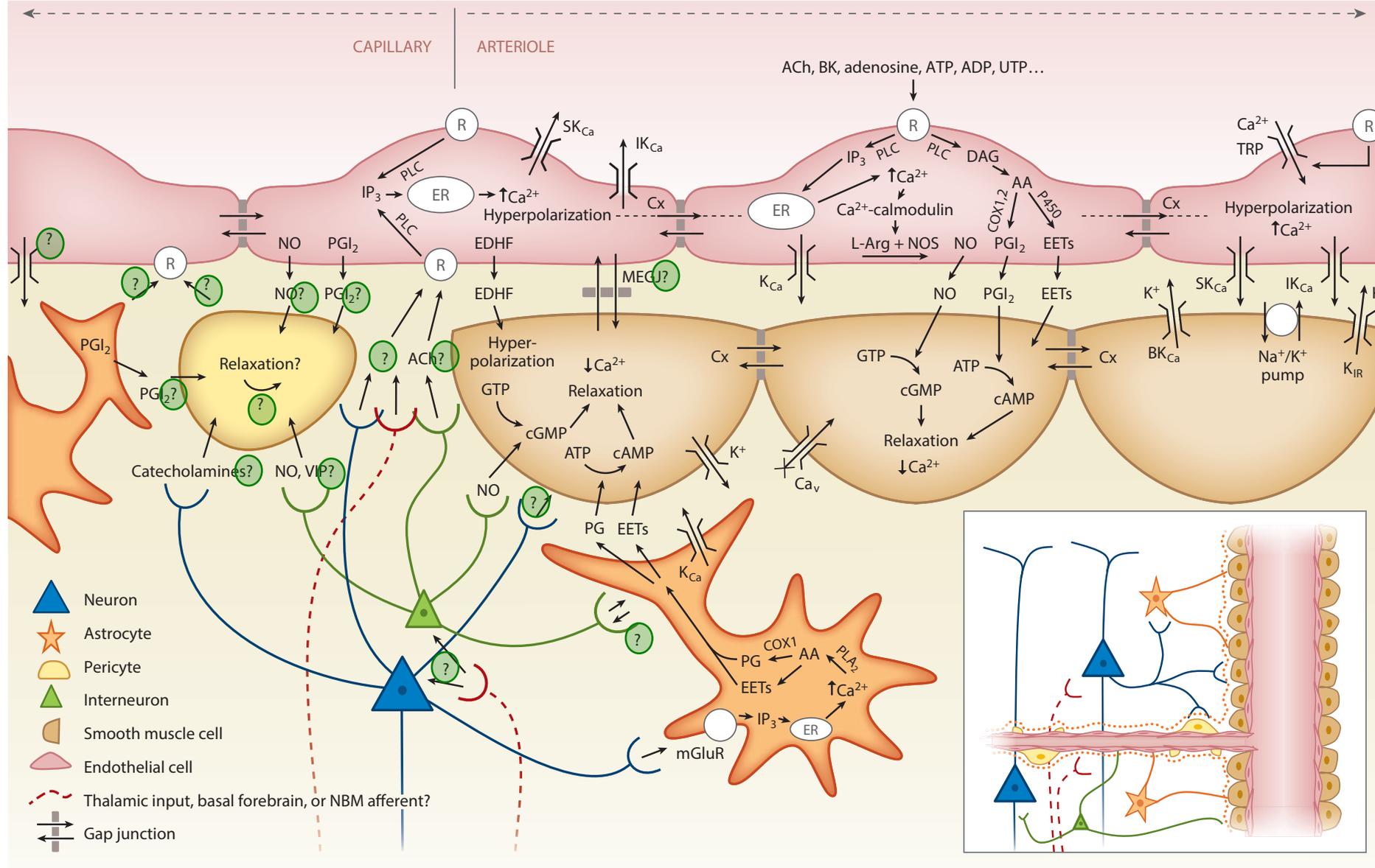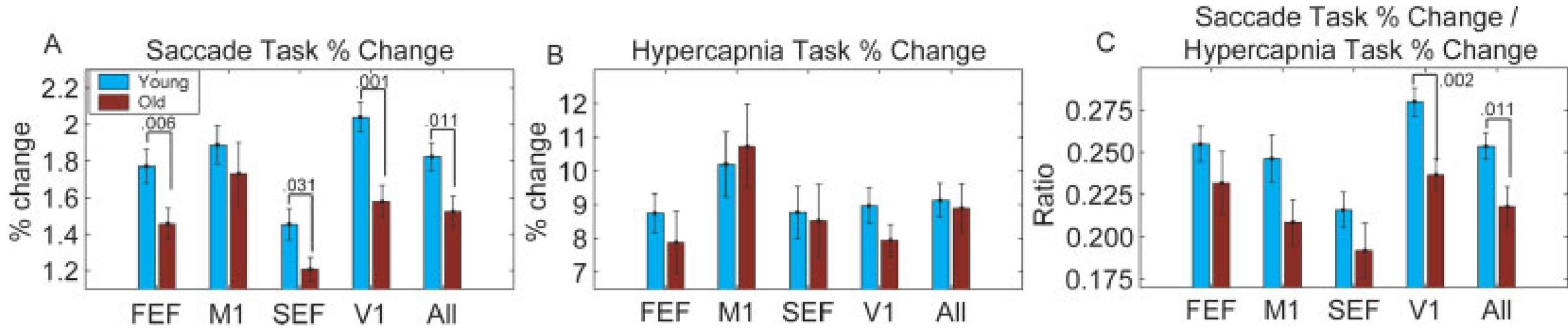

Response magnitudes in several brain regions vary during a cognitive task and a primarily vascular breath holding task.

Separate measures of simple tasks, enriched gas breathing, baseline CBF, standard deviation of resting scans can provide calibration or simply sanity checks

These can take scanner time away from studying the effects of interest, which has limited their popularity

Handwerker et al, Human Brain Mapping 2007

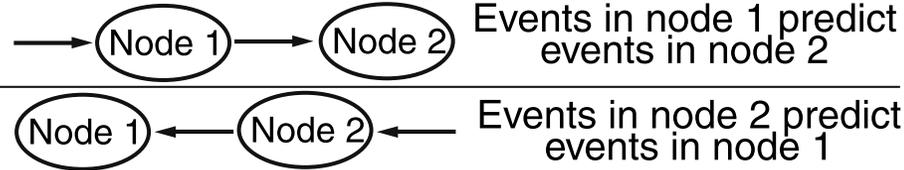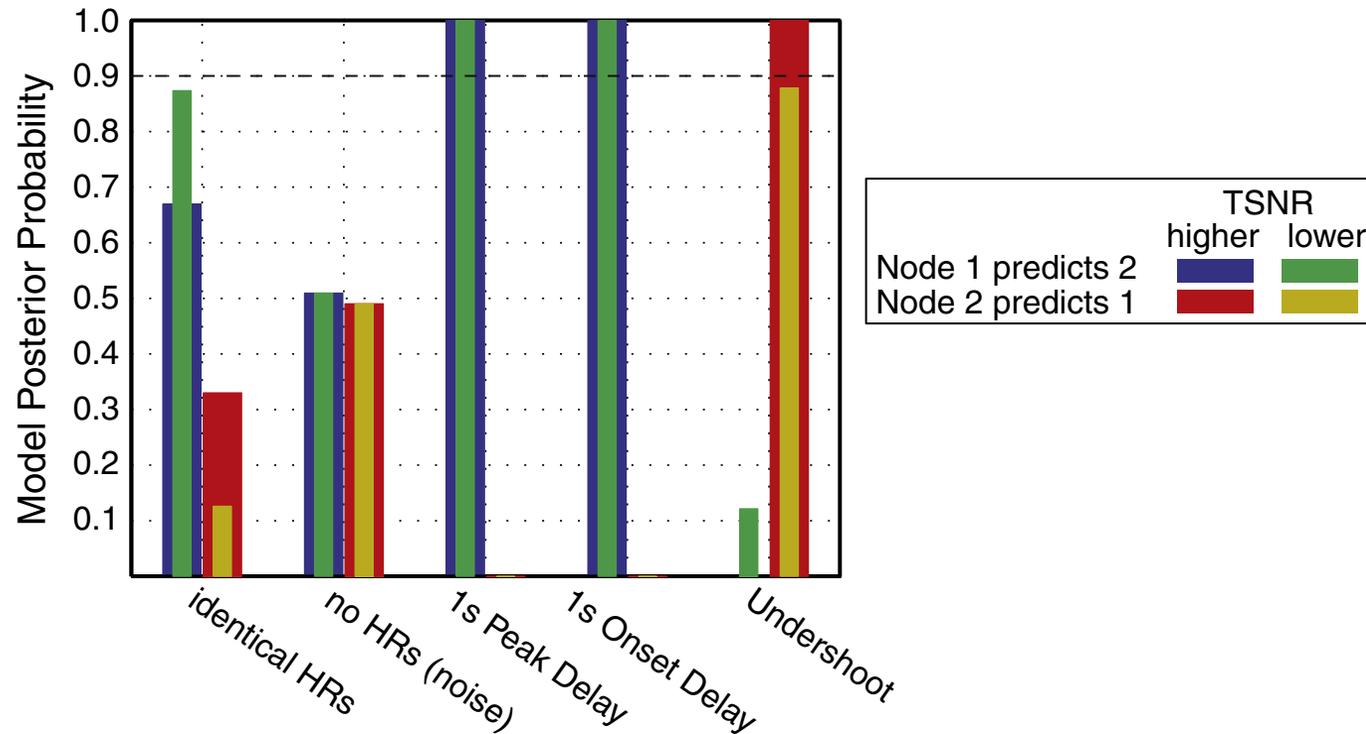# Modeling the order of neural events with fMRI is fundamentally problematic

Which Model is more likely to accurately represent the data?
Actual stimulus timing is identical in both nodes

Node 1 → Node 2   Events in node 1 predict events in node 2

Node 1 ← Node 2   Events in node 2 predict events in node 1

An example using Dynamic Causal Modeling

Summary: Why is noise removal so hard to solve?

- Signal vs Noise is defined by a study's goals
- Annoying noise vs result-biasing noise also depends on a study's goals
- Some factors are easily measurable:
  Motion, breathing, pulse
  - But they aren't always measured or examined closely
  - Measuring can identify problems, but not necessary solutions
- Some factors aren't easily measurable:
  Neurovascular coupling, non-task-specific behavior

Minimizing noise during data acquisition

- Maximize Signal-To-Noise Ratio (SNR)
- Maximize Contrast-To-Noise Ratio (CNR)
- Maximize Temporal Signal-To-Noise Ratio (TSNR)
- Minimize specific artifacts
- Minimize distortions & signal dropout
- Minimize subject-induced or unmodeled variation
- Improve temporal resolution
- Improve spatial specificity

We want fast data at super high resolution where responses can be resolved in just a few trials with no distortion, dropout, or artifacts

Everything is a balance of priorities with no definitive right answer, but many wrong ones

General acquisition goals

- Give thought to the specific priorities of a study
  - Response shape sensitivity vs specificity
  - Anatomical accuracy
  - Robustness against general artifacts
  - Robustness against artifacts that can bias a study

- The optimal acquisition options aren't always obvious.

  - What is the best flip angle for an fMRI study?

Optimal flip angle?

Grey Matter
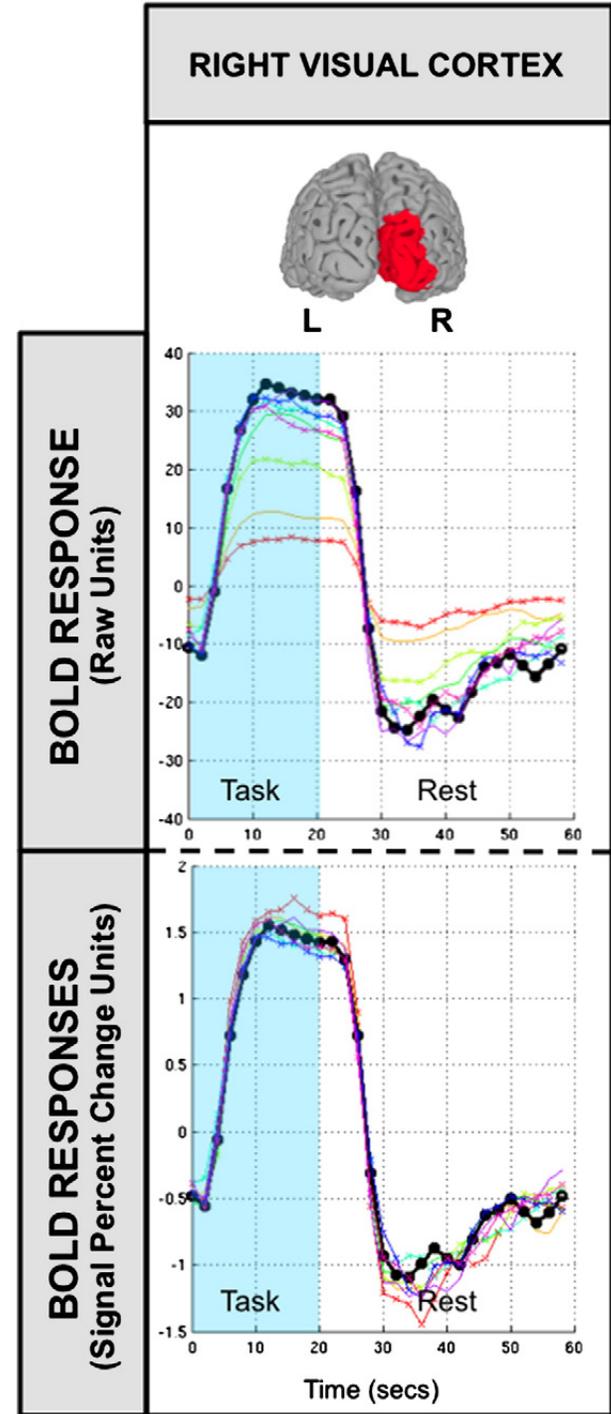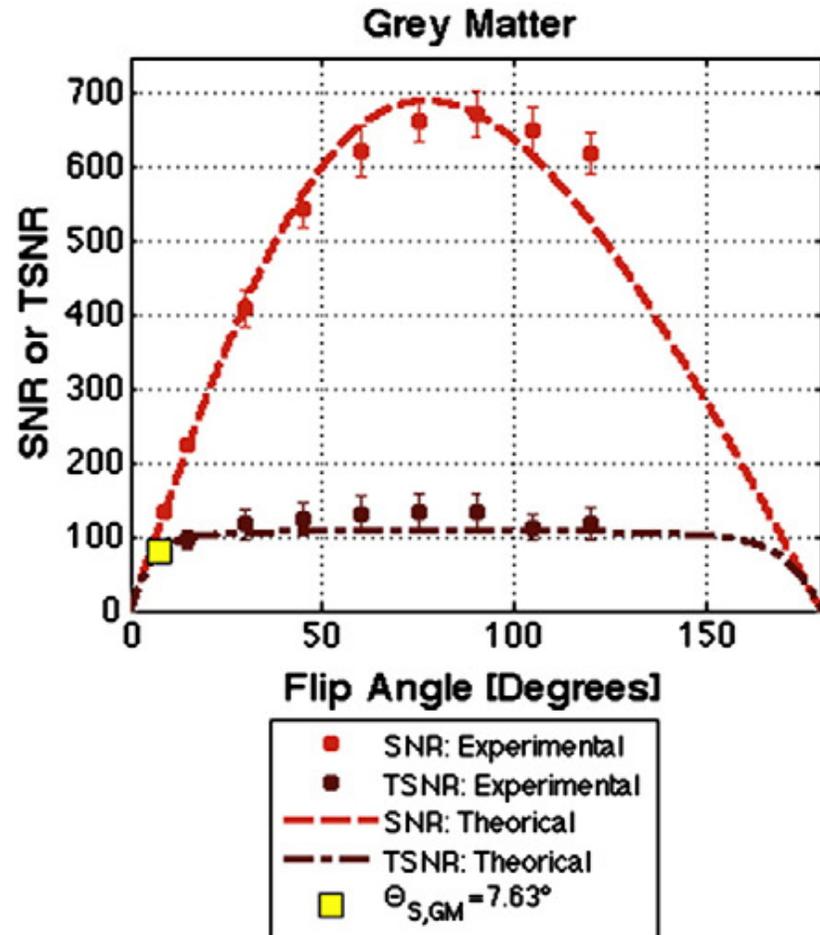
$$TSNR = \frac{SNR}{\sqrt{1 + \lambda^2 \cdot SNR^2}}$$

λ is amount of physiological noise

Increases in SNR also increase the physiological noise signal and dampen the temporal SNR benefits from a signal increase

Gonzalez-Castillo, Roopchansingh, et al 2011

Selecting the right voxel size

- Smaller -> Lower SNR

- Smaller -> More anatomical specificity -> Higher TSNR of interest

$3x3x3mm^3$ voxels = 27 mm^3
$1x1x1mm^3$ voxels = 1 mm^3
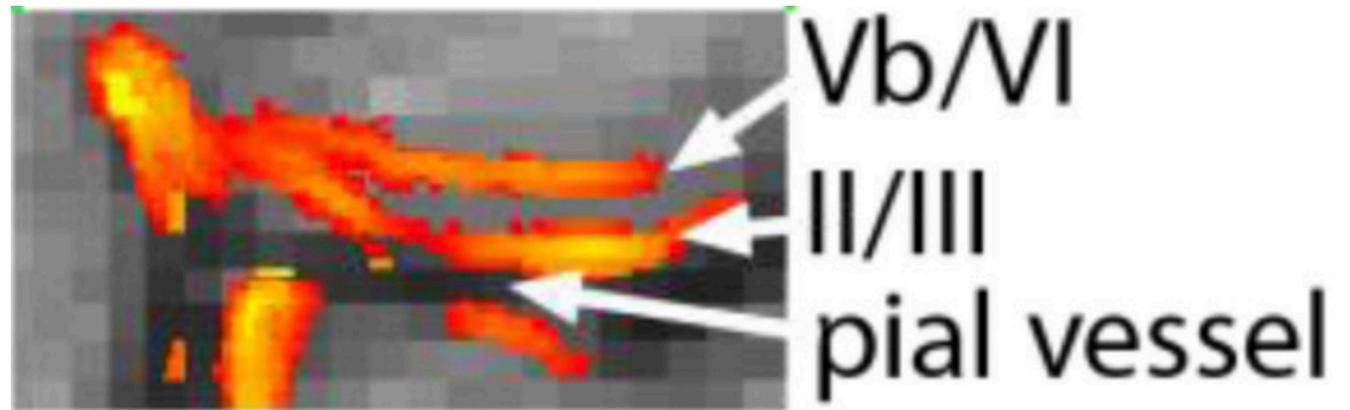
Huber, Tse et al NeuroImage (2018)
VASO imaging with spatial smoothing

Temporal Sampling Rate (TR)

- Shorter -> lower SNR, but better temporal resolution and possibly higher TSNR

- Shorter -> Better filtering of high frequency artifacts (if not removed using other methods)

- Still limited by the speed of the hemodynamic response

Griffanti et al NeuroImage 2014
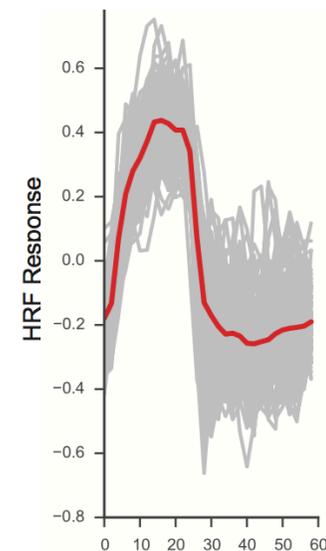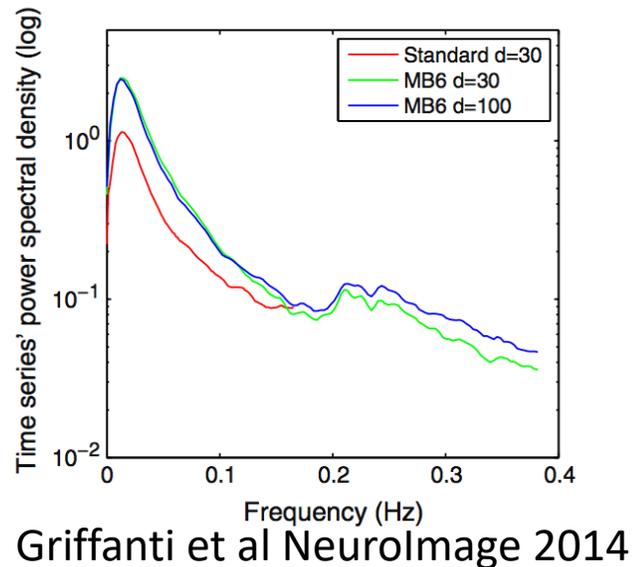
Pay attention to artifacts:
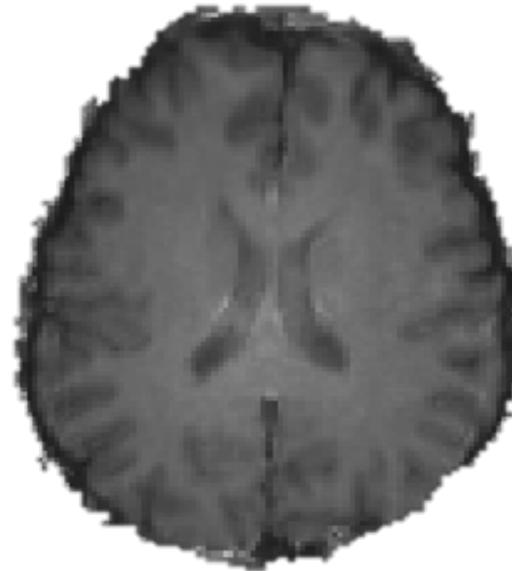# Fat ghosts can have small signal but large instability
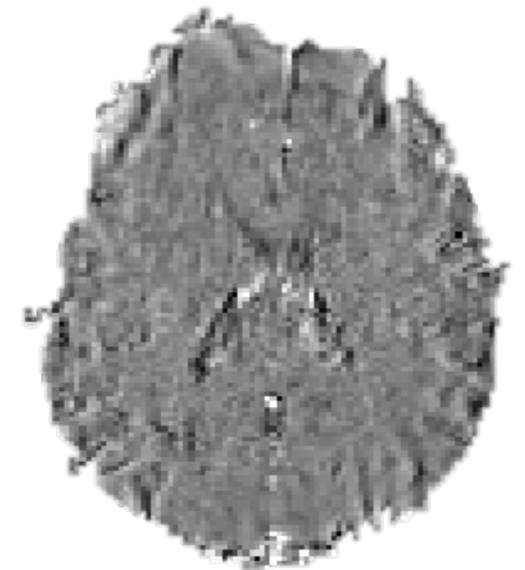

Mean signal with normal fat saturation
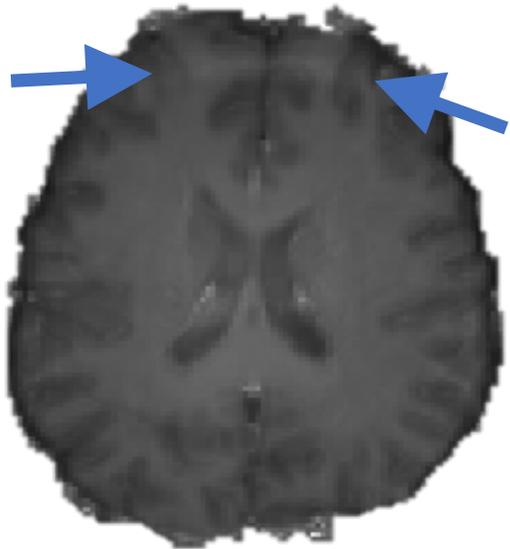
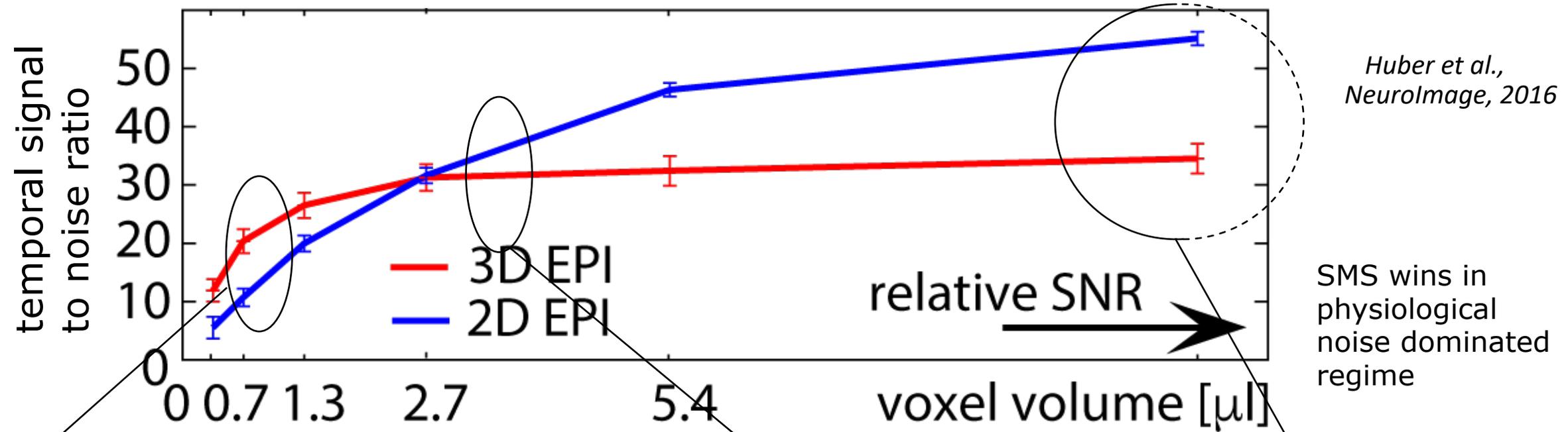Standard devision with normal fat saturation

Mean signal with ultra strong fat saturation

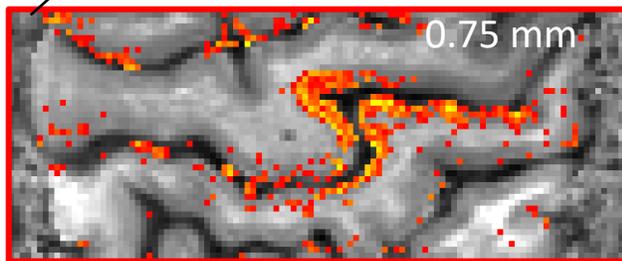Standard deviation with ultra strong fat saturation

VASO data presented at OHBM 2016. Handwerker, Huber et al

The "best" pulse sequence interacts with voxel size & SNR

Huber et al., NeuroImage, 2016

SMS wins in physiological noise dominated regime

SMS is challenged in thermal noise dominated regime]

Pulse sequence sensitivies

large veins

small vessels

large arteries

GE-BOLD

VASO

SE-EPI BOLD

diff-weighted
T2-prep

T1ρ–prep

T2-prep
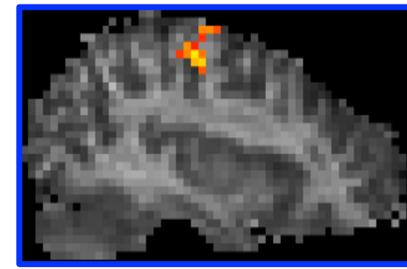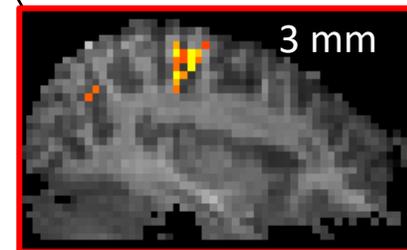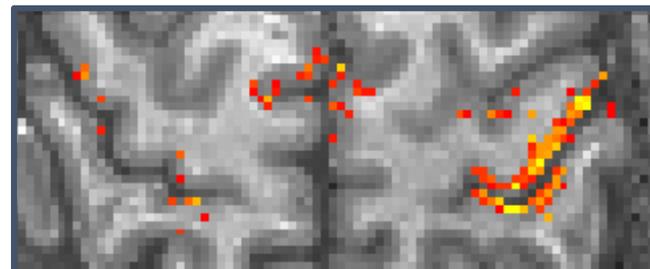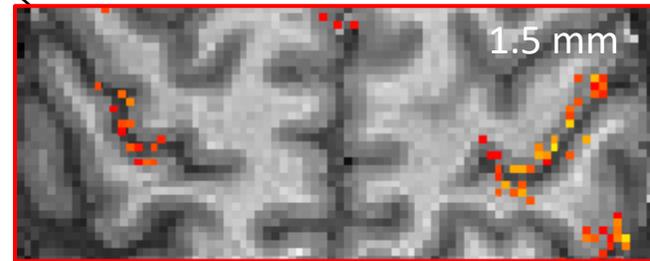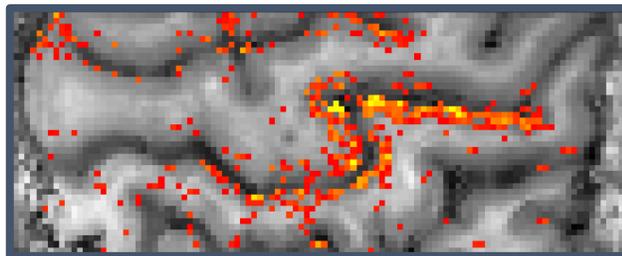
Images from Laurentius Huber
graphical depiction of review articles [Uludaĝ and Blinder 2017] and [Huber et al., 2017]
drawn based on Duvernoy, 1981 Brain Res

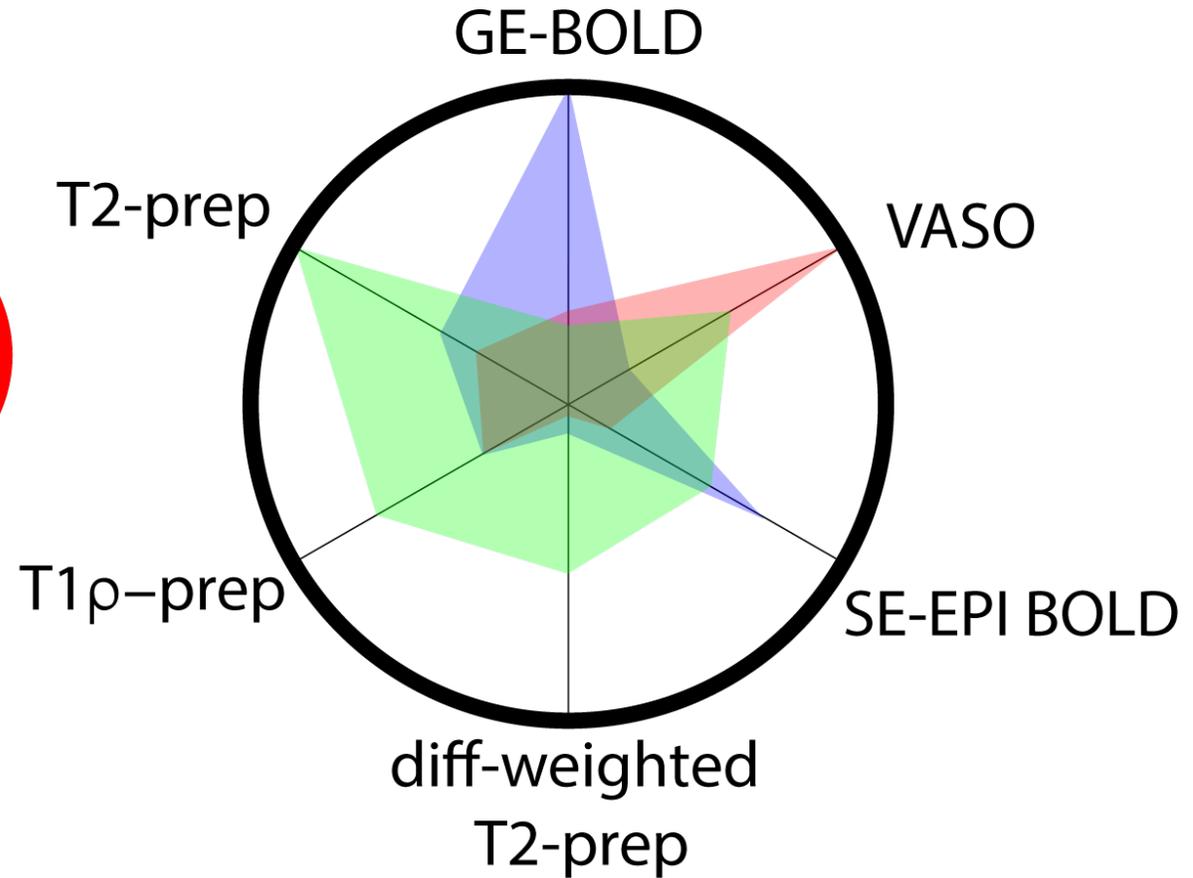# Pulse sequence sensitivies

Functional Response

Images from Laurientius Huber
[Huber et al., ISMRM, 2017]
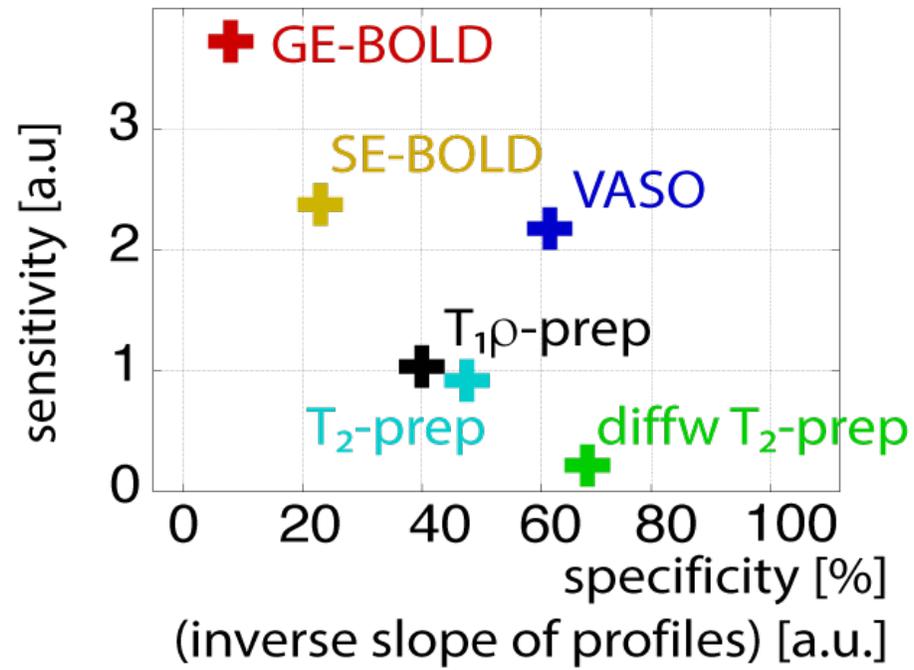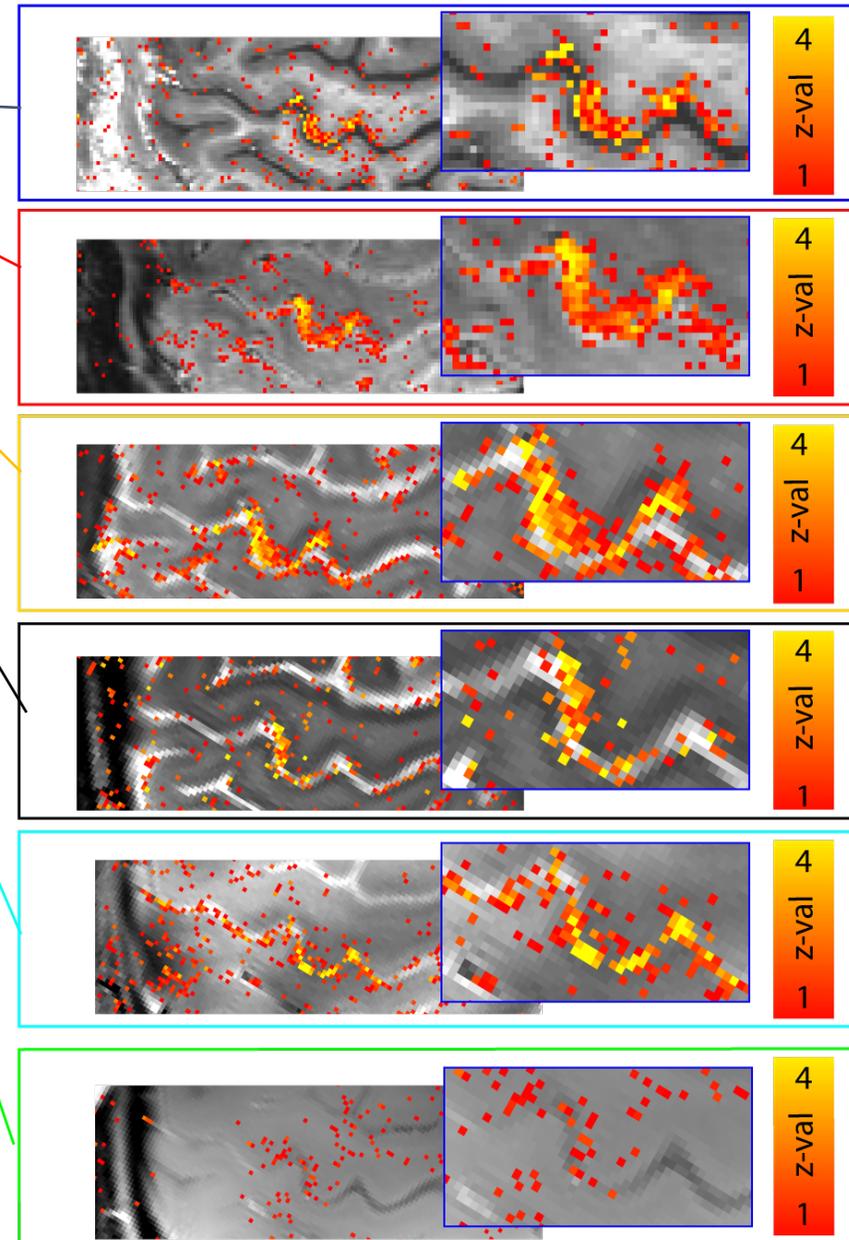
Using peripheral measures: Eye tracking

Correlation between behavioral arousal (eye) index and fMRI
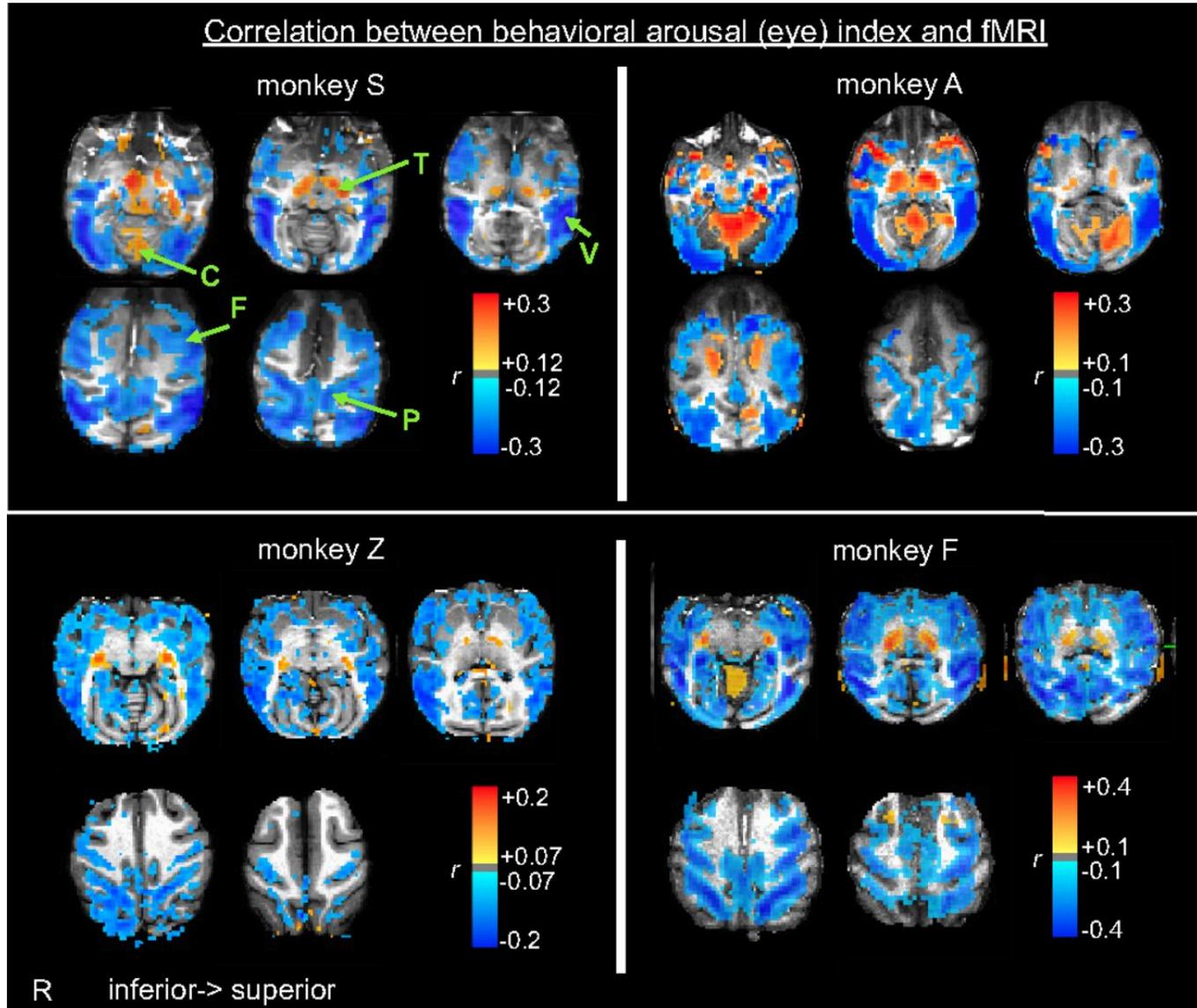
- Correlations to eyelids open vs closed
- Other studies have shown gaze to also be an arousal/attention measure
- This variation my have a neural origin, but it can still be noise when unmodeled

Chang, Leopold, et at 2016

Head movement can be reduced

- Less head motion -> Less need to remove motion in data processing

- Head movement may systematically vary across populations

- Don't assume the way you saw someone else restrict head movement is the best way
  - "The best" varies by head coil, head size, & population
  - There are more and more options

http://www.magmedix.com/pearltec-multipad-slim.html

caseforge.co

Prepare participants

- Take the time to make sure a participant knows what to do in the MRI and is comfortable
- The more feedback you get in a task, the better you know what a participant is doing
  - For classic "resting state" scans, peripheral measurements are particularly useful
- Noise IS NOT independent from task design

Task design & head movement
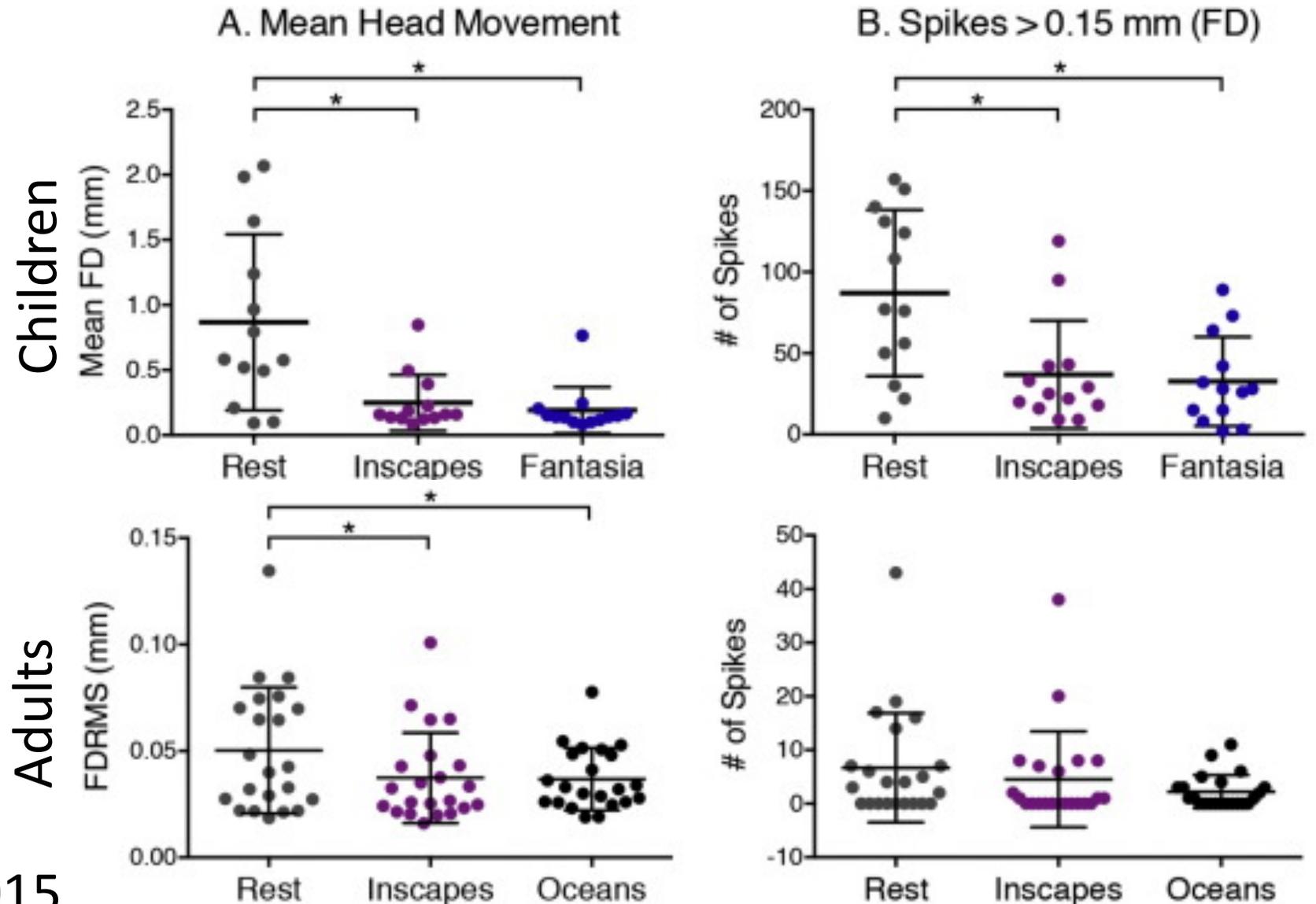
Experimental design affects head motion

Huijbers, Van Dijk, et al 2017

Task design & head movement

Experimental design affects head motion

A. Mean Head Movement

B. Spikes > 0.15 mm (FD)

Children

Adults

Vanderwal, Kelly, et al 2015
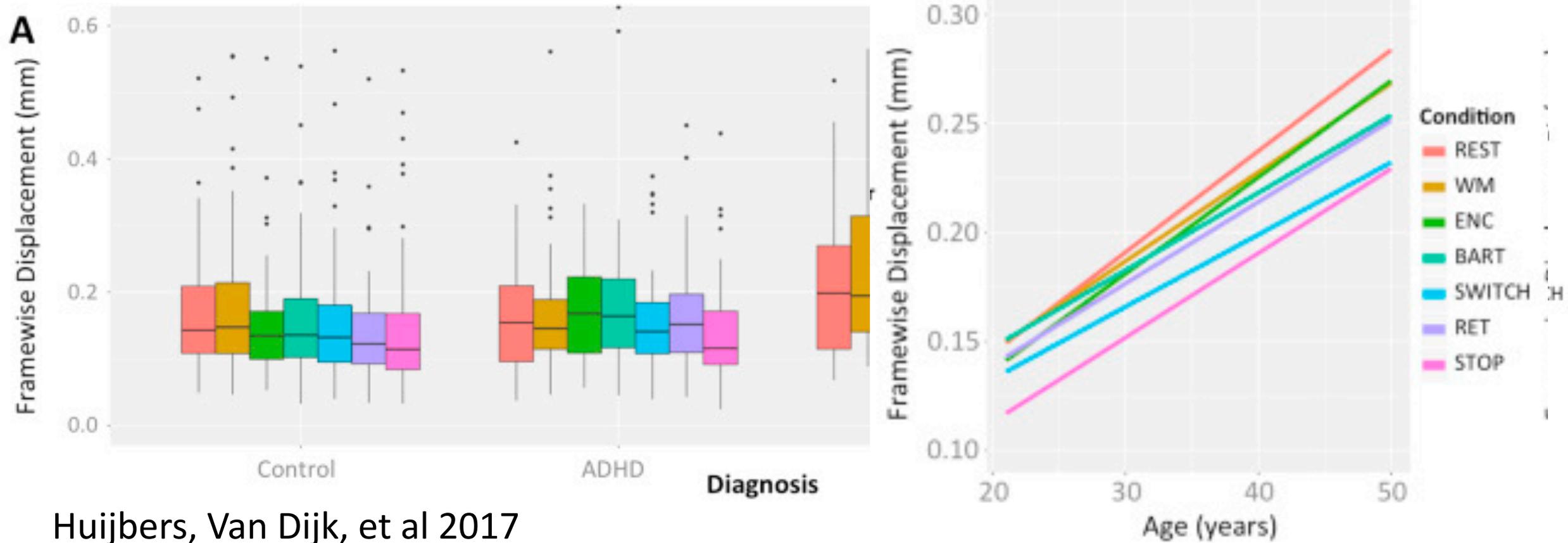
MRI Quality Assessment Scans
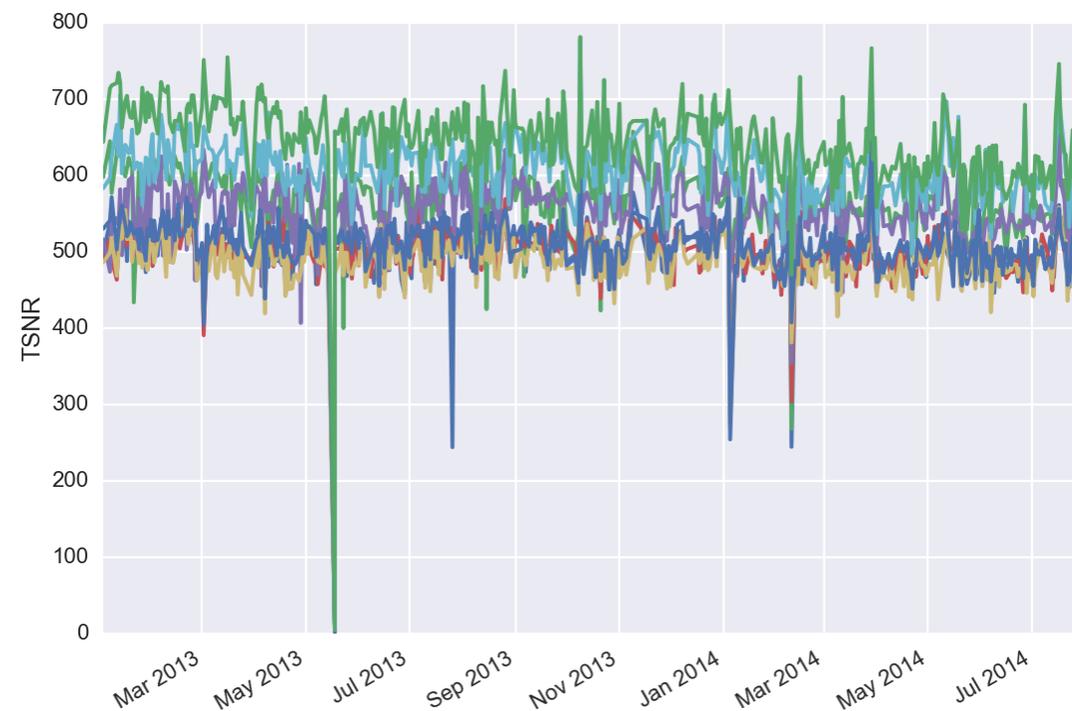## NIH Intramural example

- Approximately daily scans of an oil phantom for every commonly used head coil on every scanner

- Parameters that can provide long-term consistency
  - Single Echo EPI, no acceleration; 72x72 grid; 37 slices; 3mm^3 voxels; 5-10 min of data per receiver coil

- Save reconstructed & (sometimes) raw data

- Try to automate processing & recording pipeline

Sample QA Plots of Temporal Signal To Noise Ratio

From different scanners
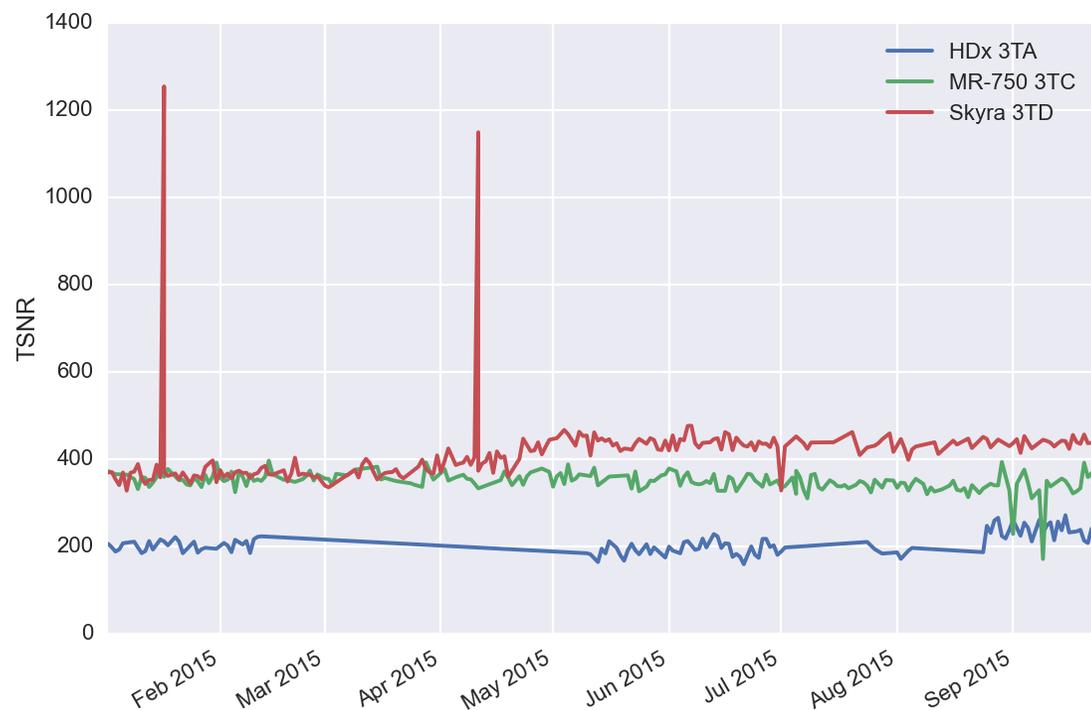
From each receiver coil on one scanner

Images from Vinai Roopchansingh

Regular Results Evaluations

MRIQC: group anatomical report

Summary

Image from: http://mriqc.readthedocs.io/en/stable/reports/group.html

MRIQC code: https://github.com/poldracklab/mriqc
MRIQC new web API: https://mriqc.nimh.nih.gov/
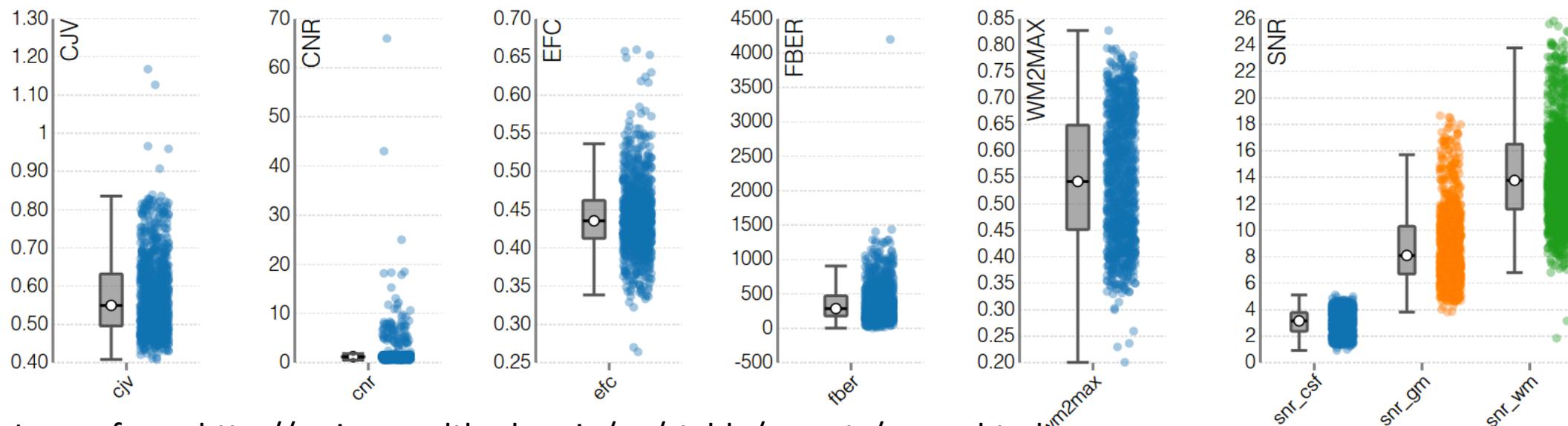
Summary: Removing Noise during acquisition

- Every MRI pulse sequence parameter choice is a compromise
  - Need to know what the priorities of a study are
- Noise at acquisition is about more than pulse sequences and MRI hardware
  - Undesired Head motion and behavioral changes can be reduced through study design and working proactively with volunteers
  - Peripheral measures like respiration, pulse, and eye movement can model some noise sources
- Scanner quality can vary with time. Regular quality assurance scans can prevent undesired surprises

Next time

The least bad ways to remove noise