Noise and Artifacts in MRI and fMRI

Daniel Handwerker

Section on Functional Imaging Methods
National Institute of Mental Health

June 18, 2024

Other noise removal talks in this series

- Preprocessing Pipelines & QC: Paul Taylor
  - Particularly the section on quality control near end
- High resolution MRI & fMRI: Renzo Huber & Tyler Morgan
  - Covers multiple types of imaging artifacts
- Physiologic Confounds in fMRI: Burak Akin
  - Covers a range of respiratory and cardiac signals and potential ways to reduce noise
- Multi-echo fMRI: Me
- Probably most talks in this series

https://www.youtube.com/@nimhcmn

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.

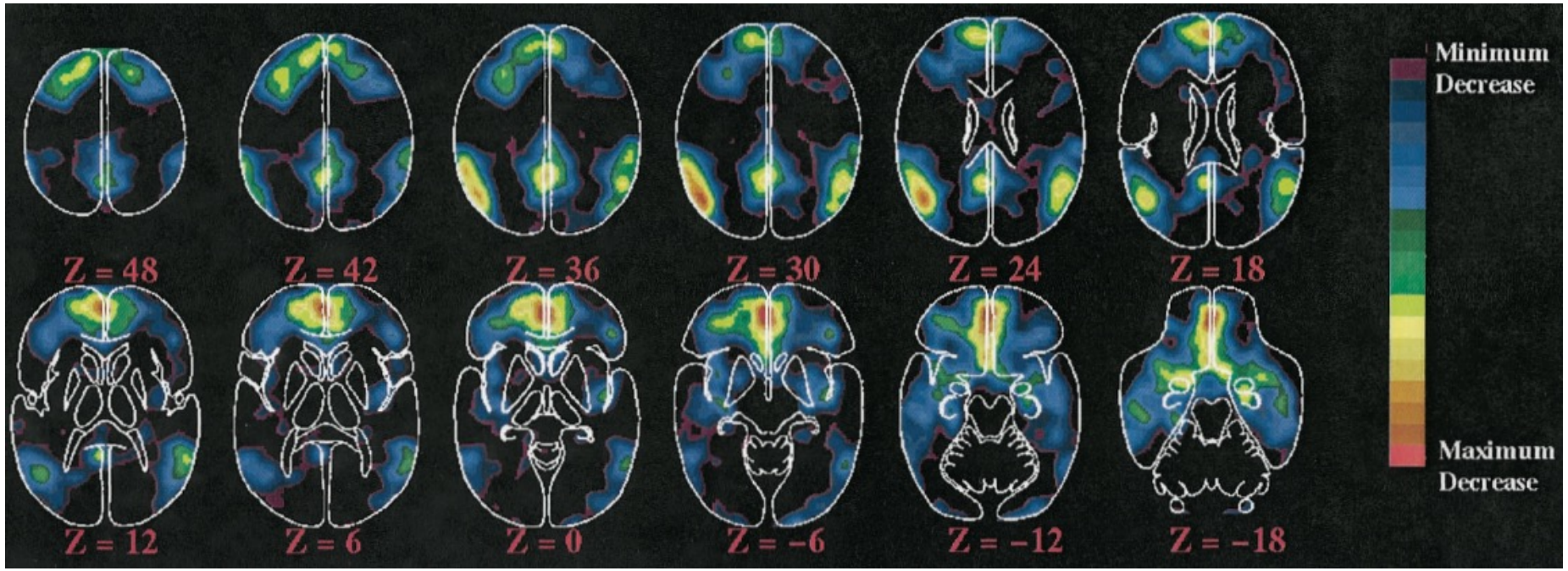
What is noise?

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

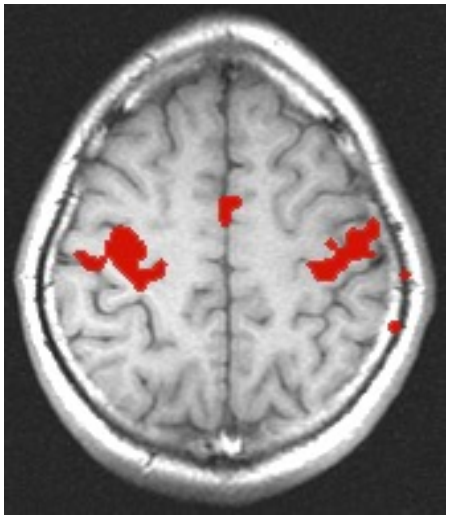
One study's noise can be another study's signal



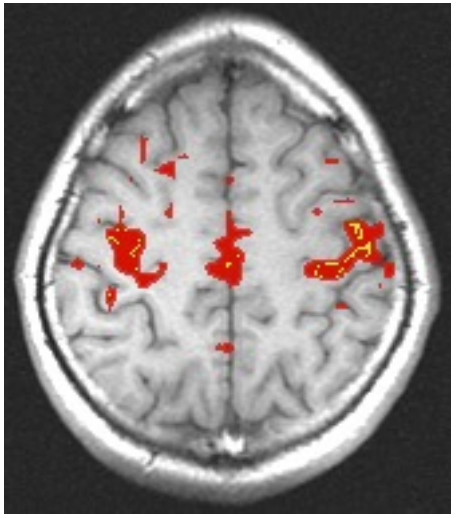
Areas of the brain that decrease activity across a wide range of cognitive tasks

Raichle, MacLeod et al, PNAS 2001 "A default mode of brain function"

“Random” fluctuations become signal



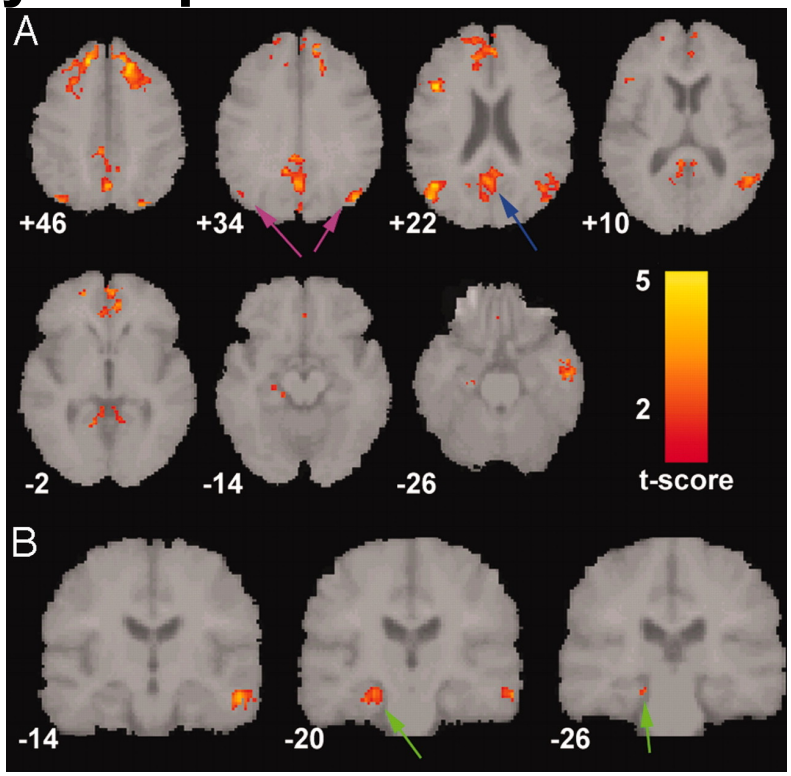
Activation during finger-tapping



Correlations with “seed voxel” in motor cortex **during rest**

B. Biswal *et al., MRM, 34:537 (1995)*

Noise in one study is a potential clinical biomarker in another

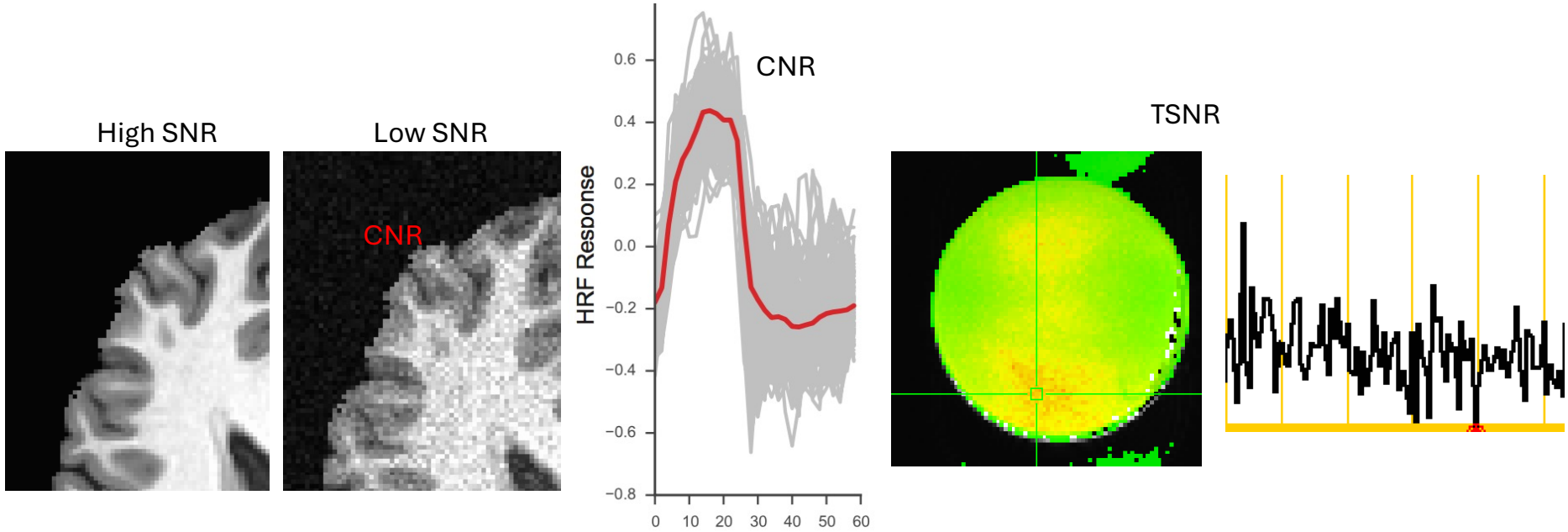


Default mode brain regions distinguish
Alzheimer's Disease patients from healthy elderly

Greicius M D et al. PNAS 2004;101:4637-4642

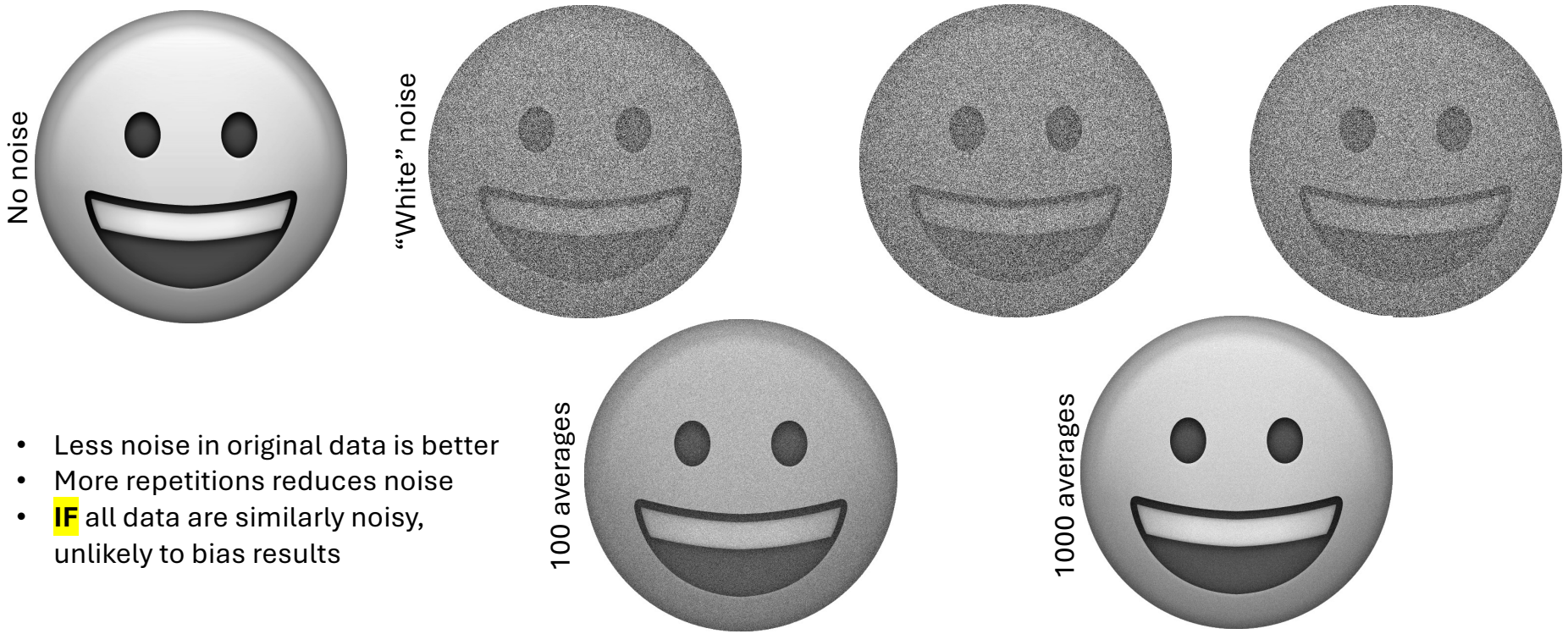
Measures of noise

- 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

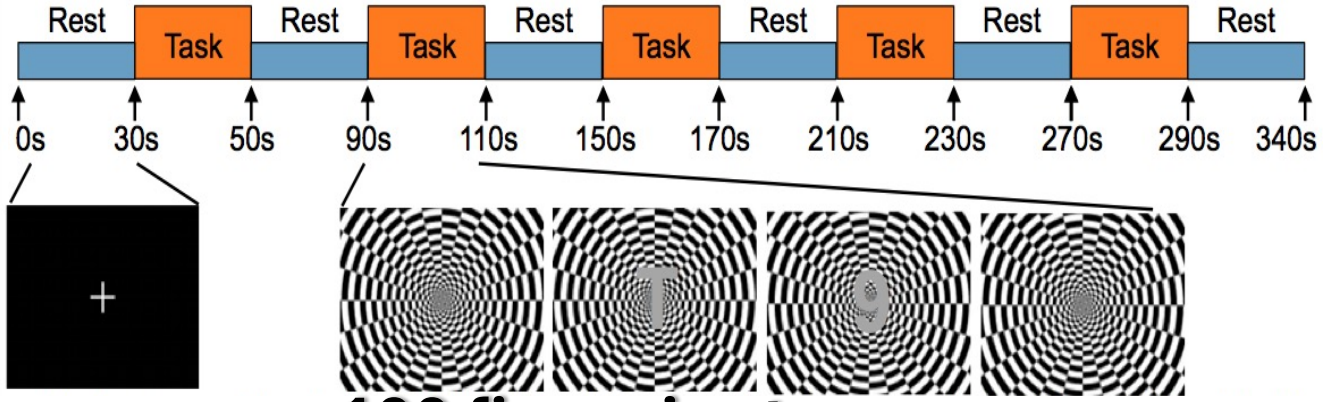


- Less noise in original data is better
- More repetitions reduces noise
- **IF** all data are similarly noisy, unlikely to bias results

Unstructured random noise

More repetitions reduces noise

3 volunteers

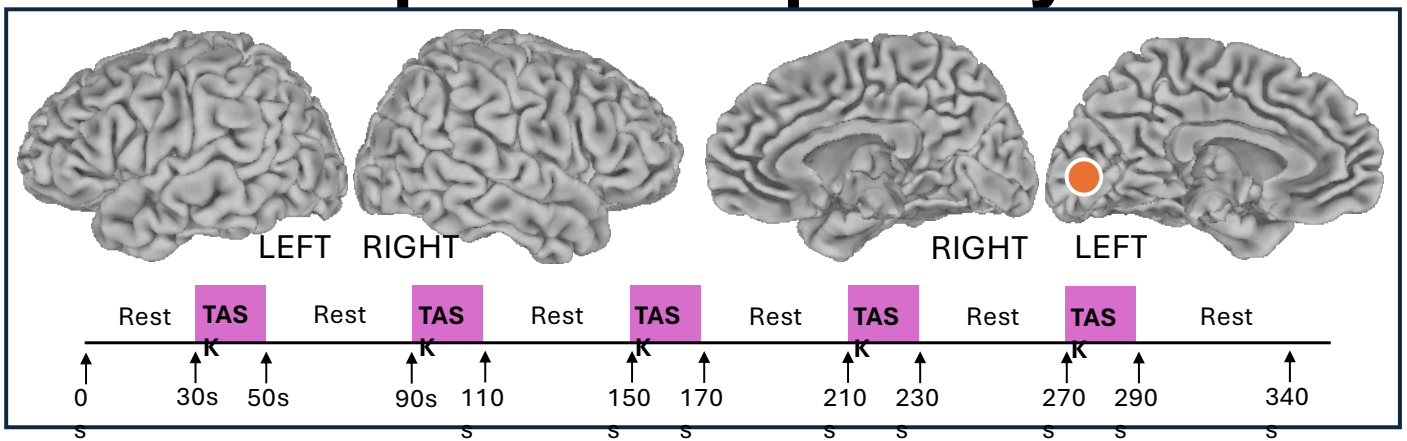


100 five minute runs

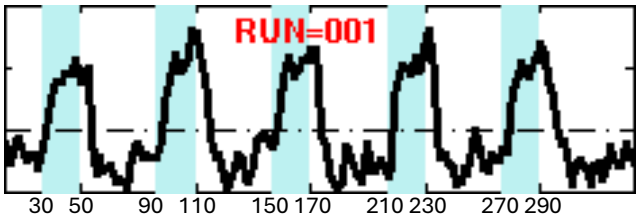
9 hours of functional data per volunteer

Gonzalez-Castillo PNAS 2012

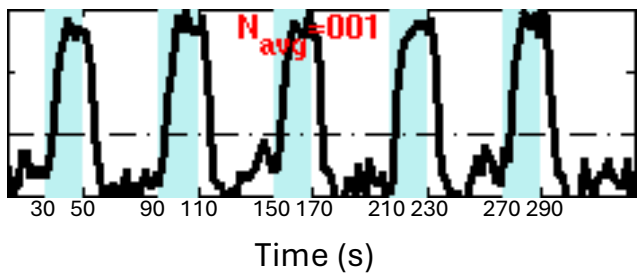
100 runs of responses in primary visual cortex



INDIVIDUAL RUNS

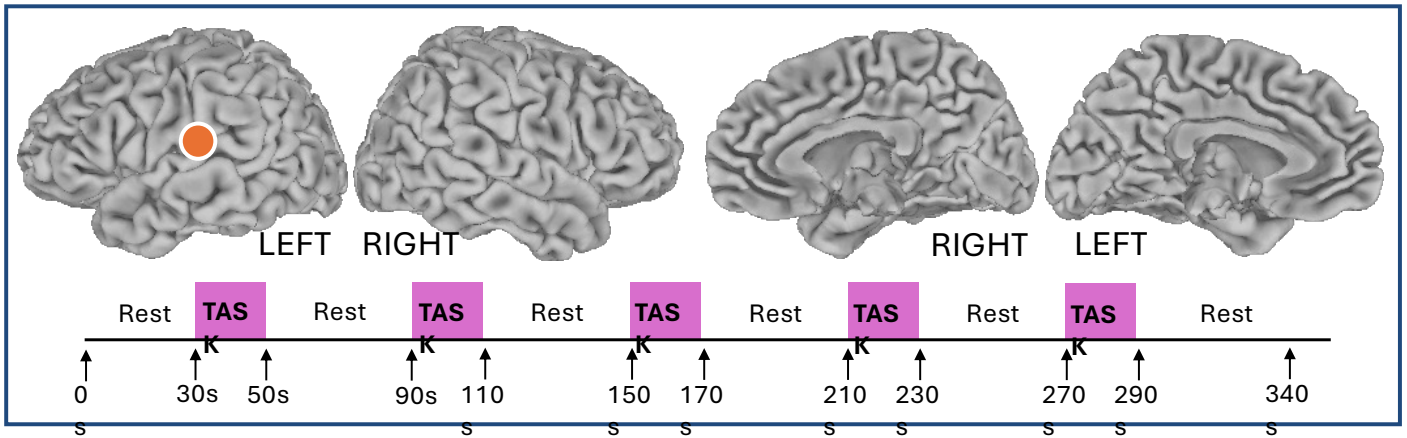


AVERAGING

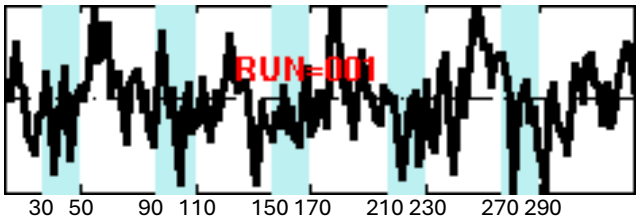


Gonzalez-Castillo PNAS 2012

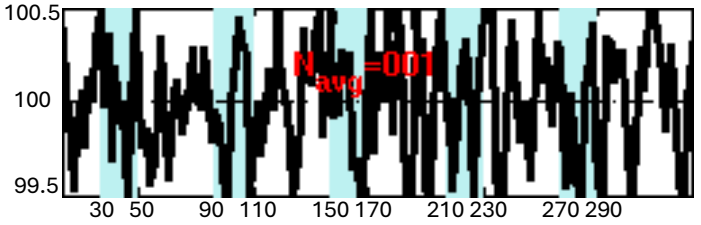
100 runs of responses in primary auditory cortex



INDIVIDUAL RUNS

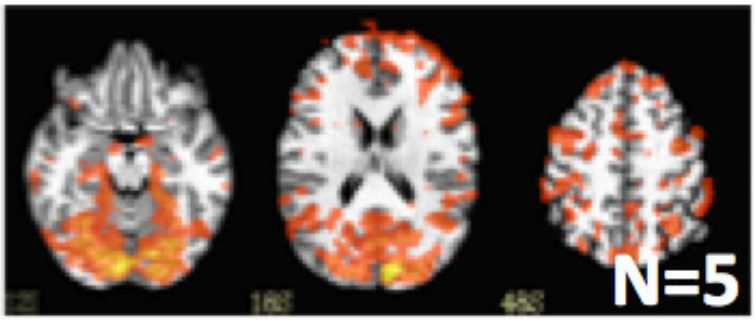


AVERAGING



Gonzalez-Castillo PNAS 2012

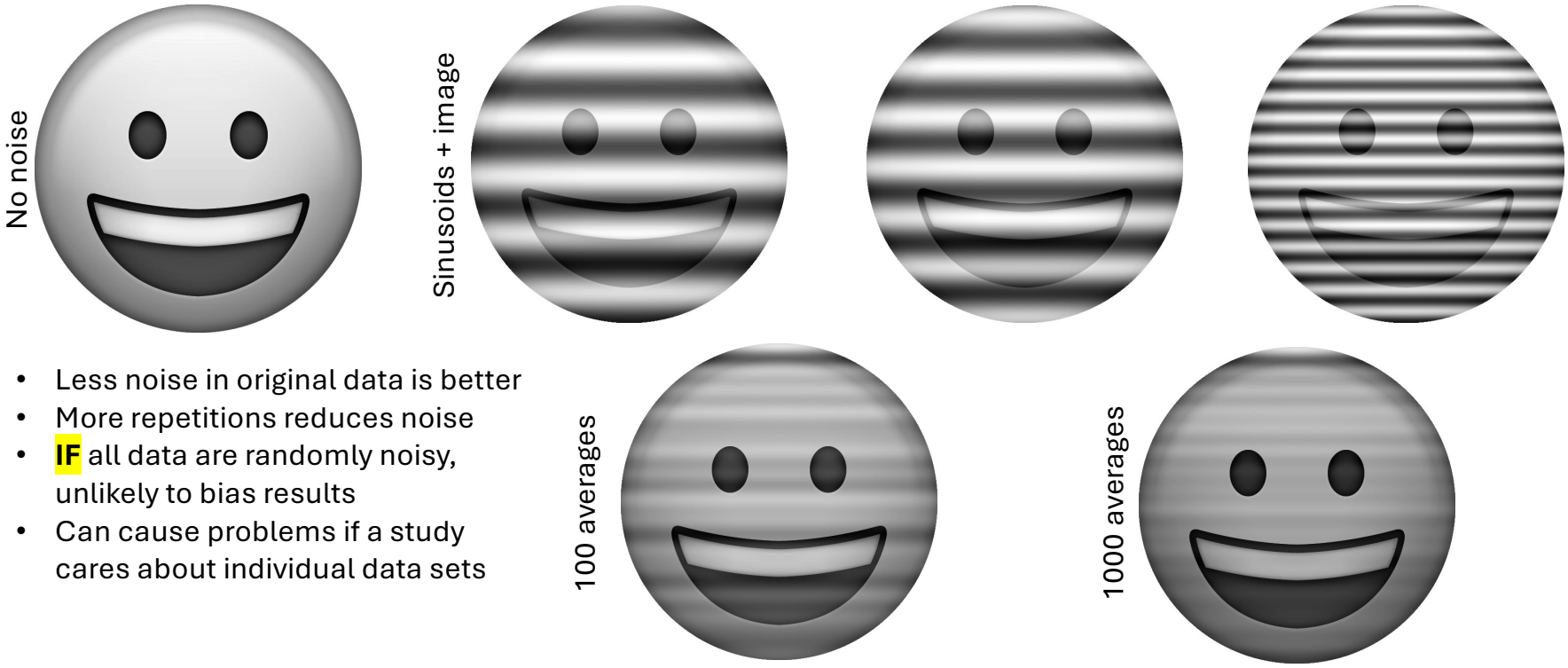
More data means more of the brain is significantly modeled by the task



Gonzalez-Castillo PNAS 2012

How to think about noise reduction or removal

Structured random noise



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

How to think about noise reduction or removal

Structured random noise

- If NOT correlated to task or behavior conditions
  - 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

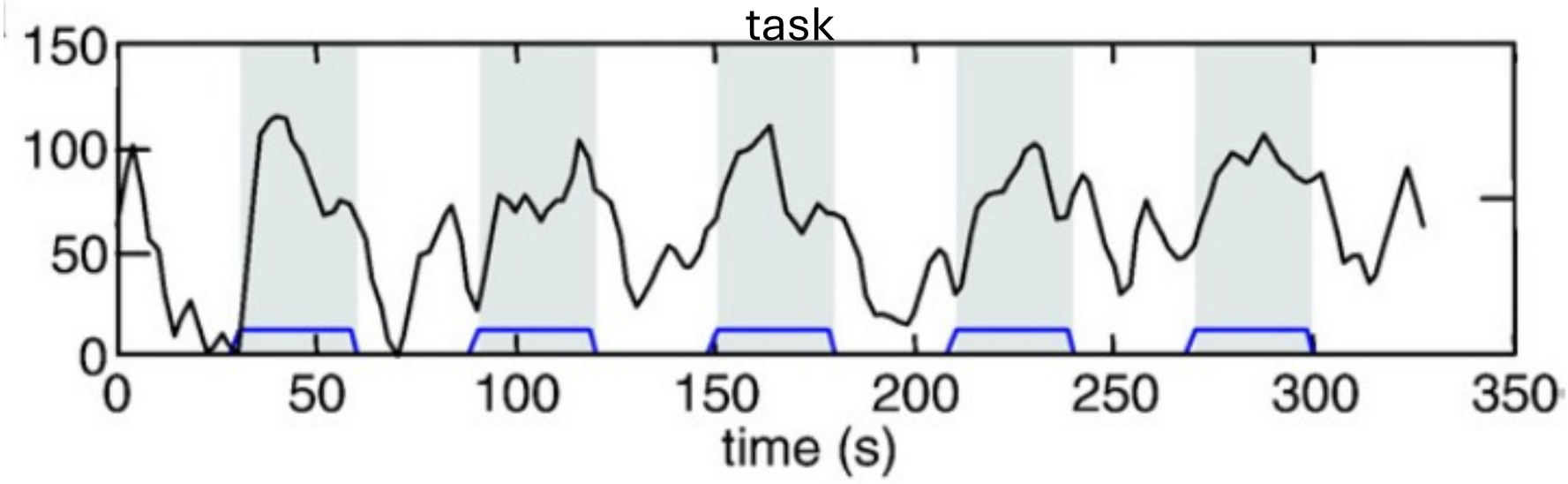
Structured non-random noise

- 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

Noise can be task correlated

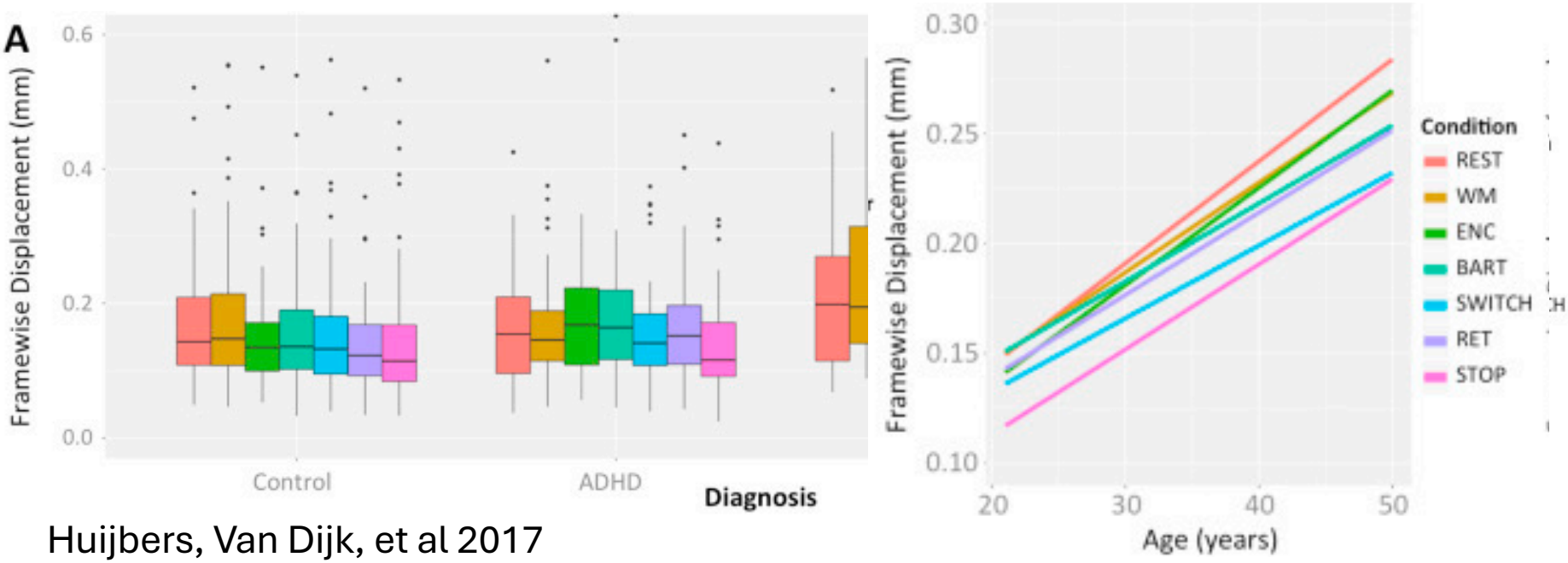
Respiration depth over time (RVT) during a letter/number discrimination task



Birn, Murphy et al NeuroImage 2009 “fMRI in the presence of task-correlated breathing variations”

Task design & head movement

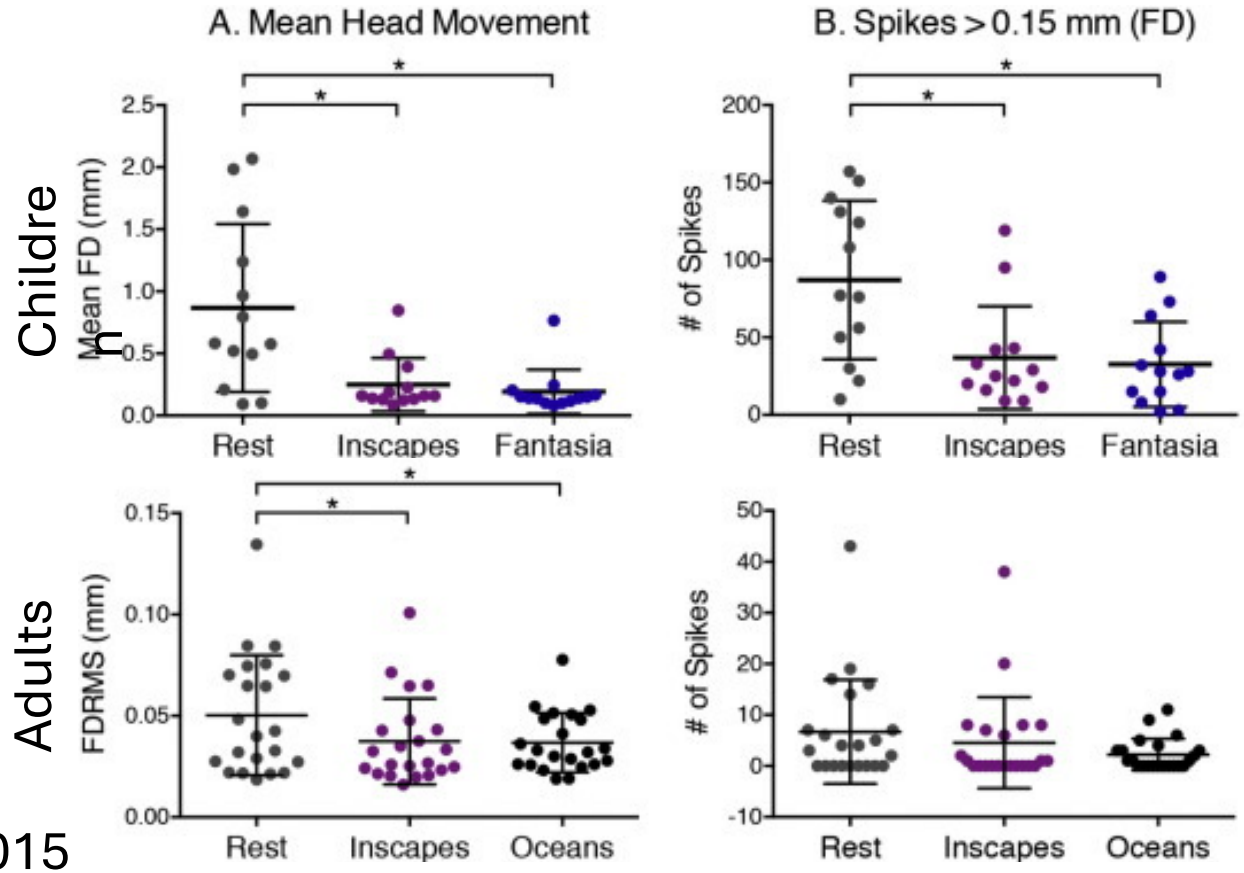
Experimental design affects head motion



Huijbers, Van Dijk, et al 2017

Task design & head movement

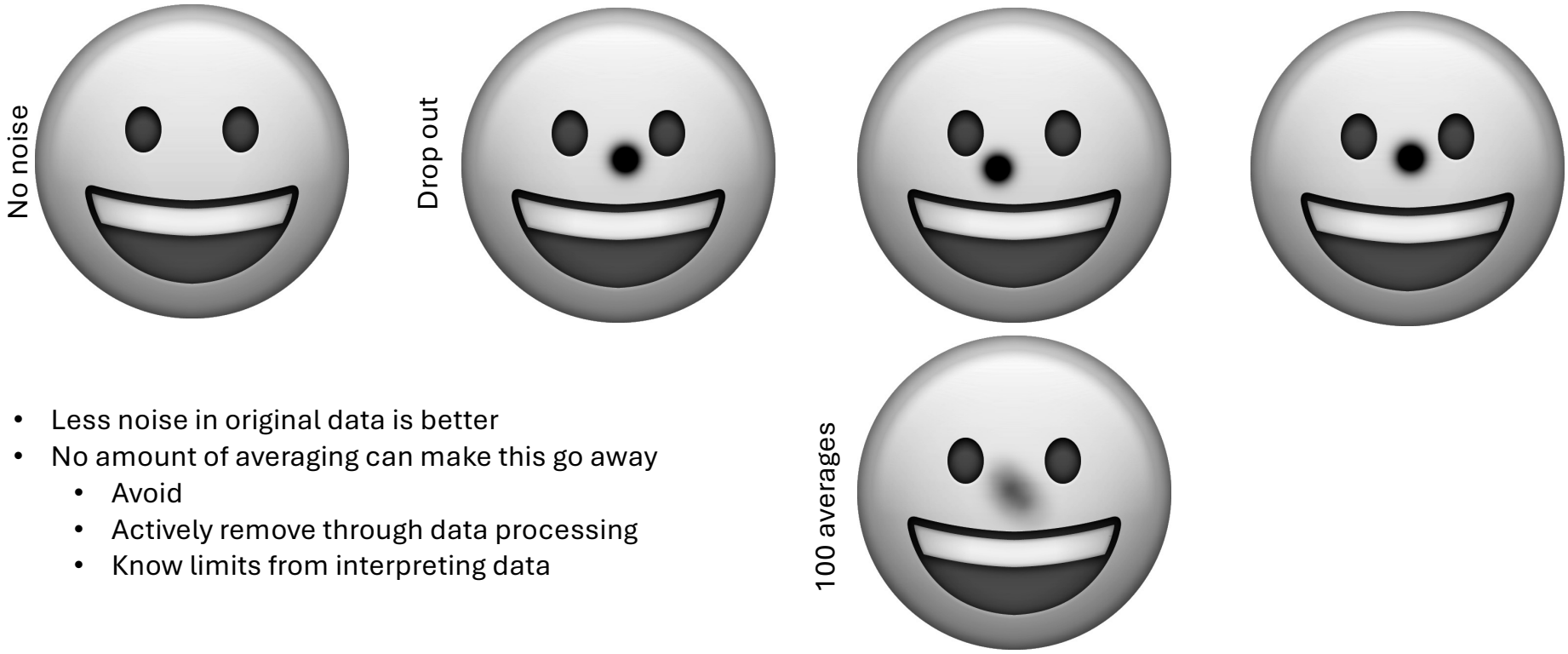
Experimental design affects head motion



Vanderwal, Kelly, et al 2015

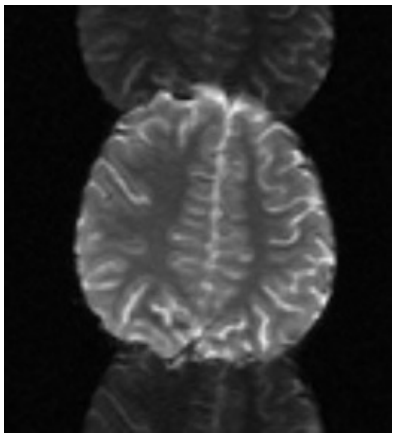
How to think about noise reduction or removal

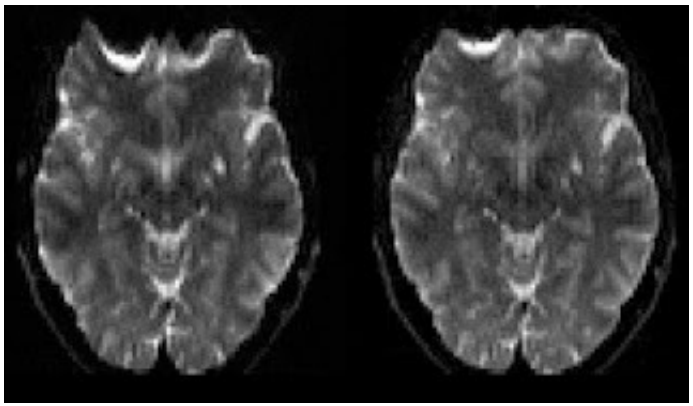
Structured non-random noise



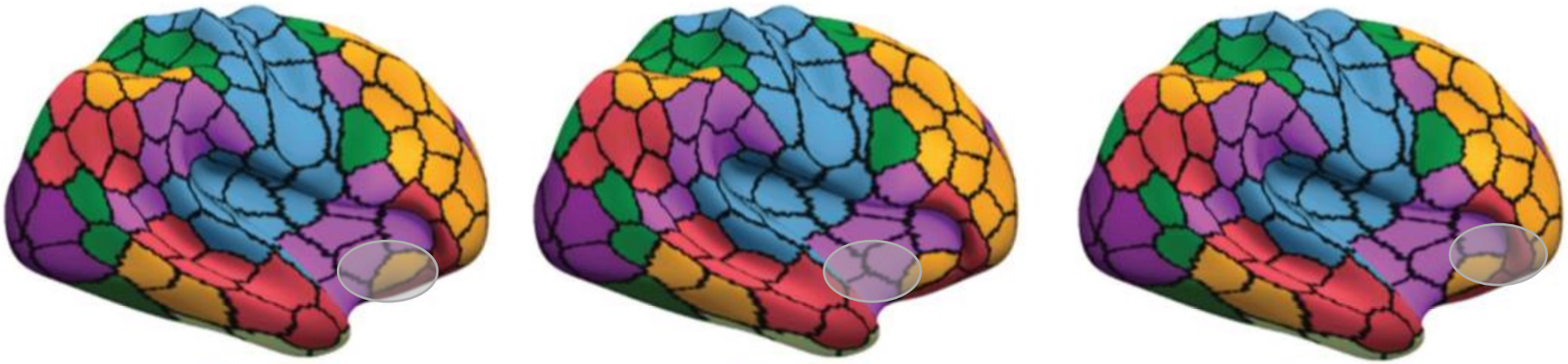
- Less noise in original data is better
- No amount of averaging can make this go away
  - Avoid
  - Actively remove through data processing
  - Know limits from interpreting data

Structured non-random noise





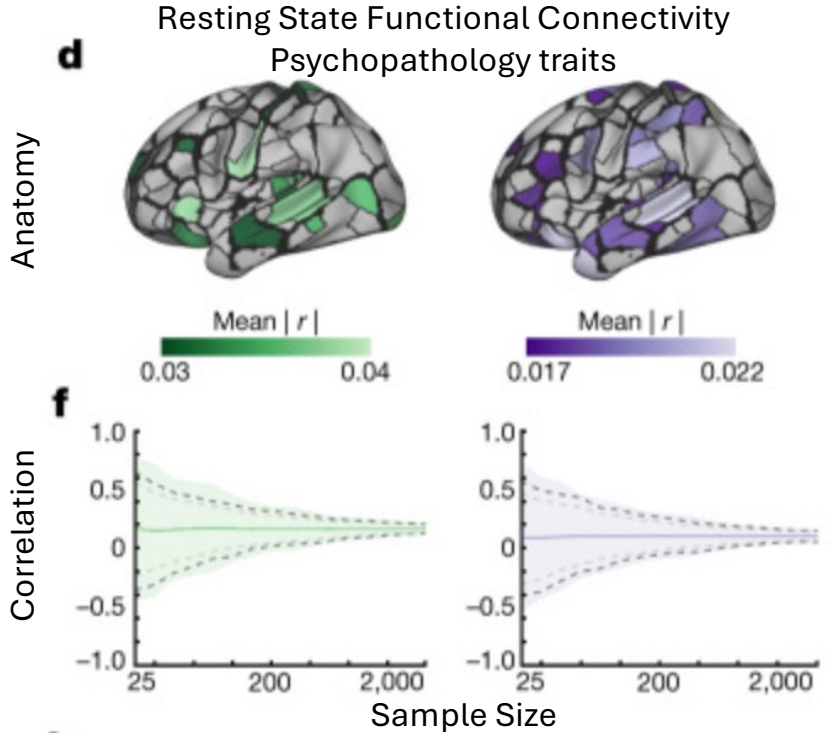
Signal dropout and regions-of-interest



If dropout regions affect different regions-of-interest then ROIs are representing different cortical brain areas

This noise is completely hidden once data are converted into ROI-averaged time series

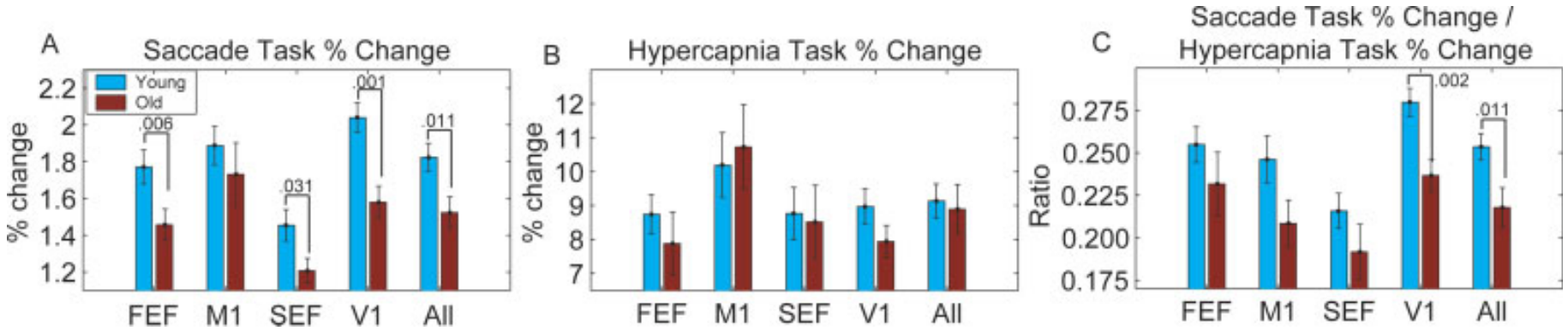
How much unreliability is variation in dropout noise?



A large number of individuals are needed to get stable trait predictions

Marek at al Nature 2022

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.

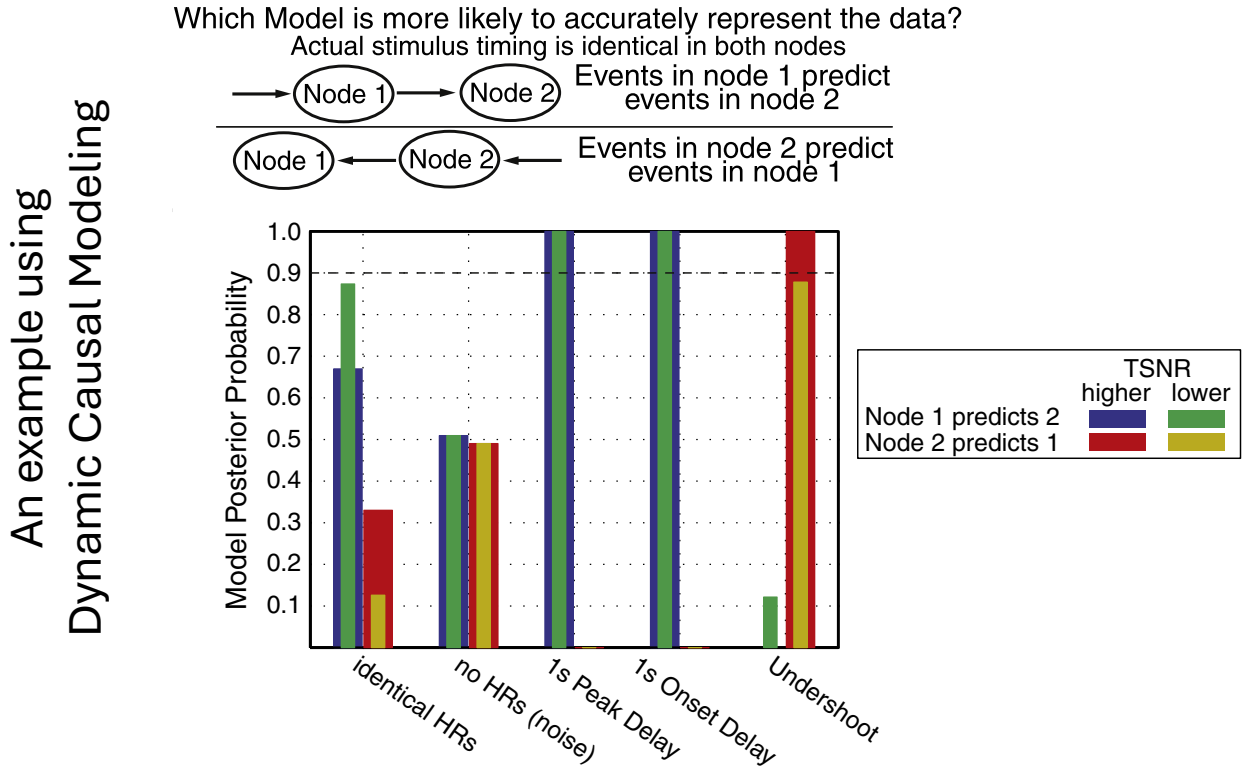
Separate measures of simple tasks, enriched gas breathing, baseline CBF, standard deviation of resting scans can provide calibration or simply sanity checks

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

Handwerker et al, Human Brain Mapping 2007

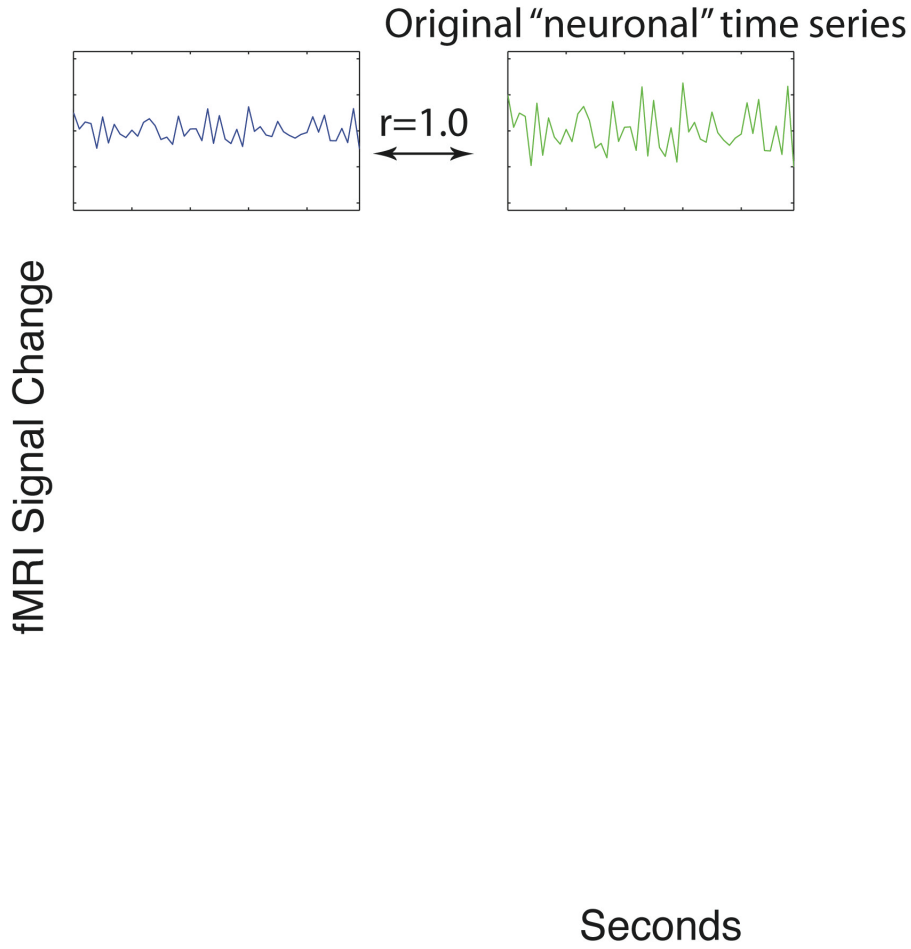
Modeling the order of neural events with fMRI is fundamentally problematic

An example using Dynamic Causal Modeling



Handwerker et al *NeuroImage* 2012

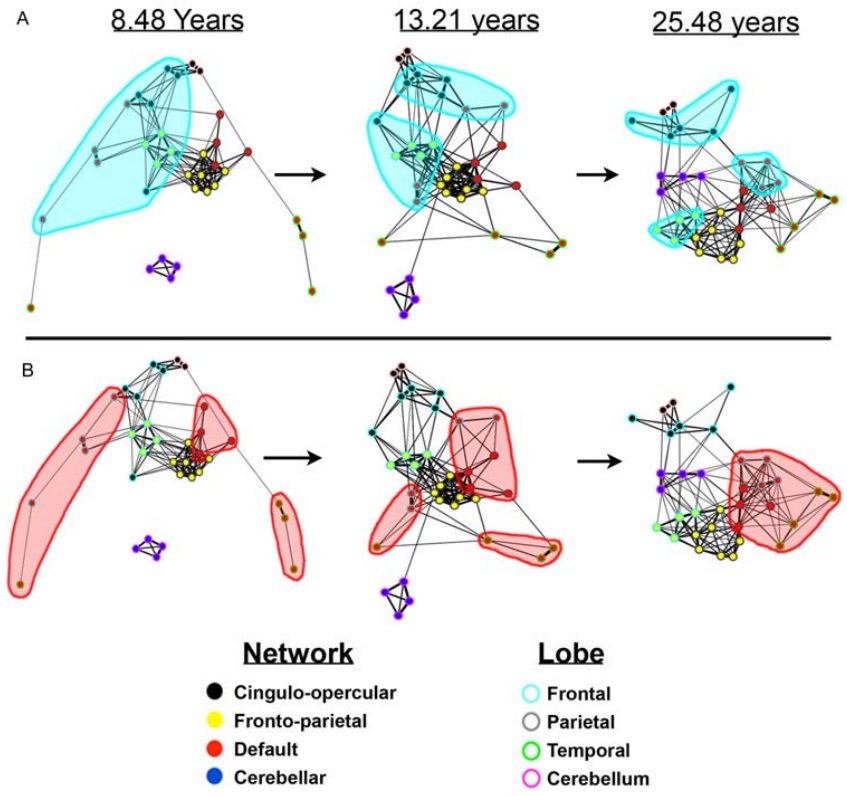
Signal & noise are correlated for functional connectivity



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

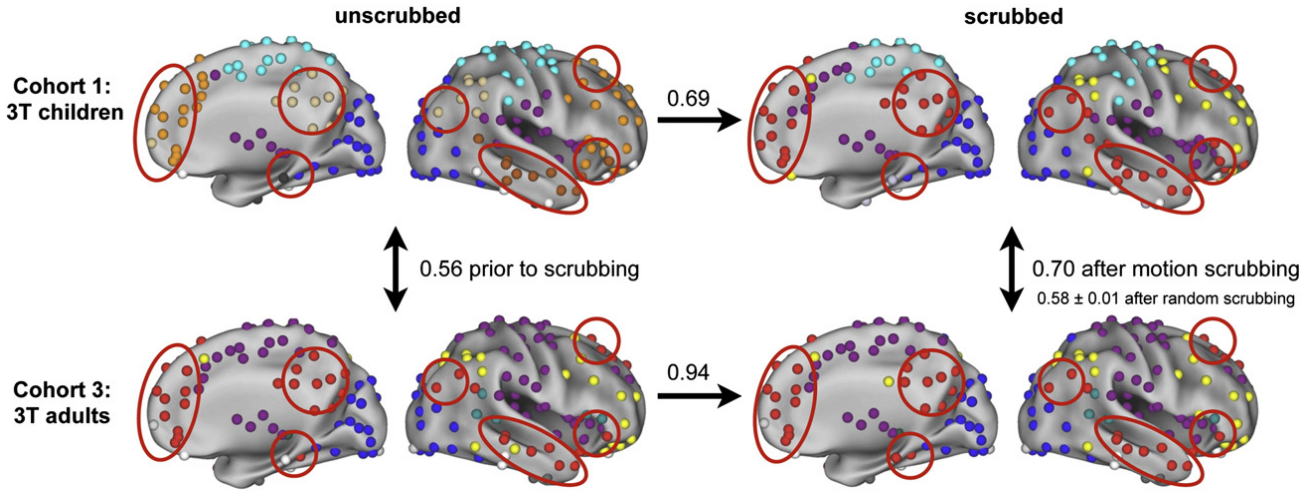
Connectivity-based fMRI
Common noise across regions can contaminate results

Functional Brain Networks Develop from a “Local to Distributed” Organization



Fair... Petersen, PLoS Comp Bio 2009

Noise from head motion drove the network result



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

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

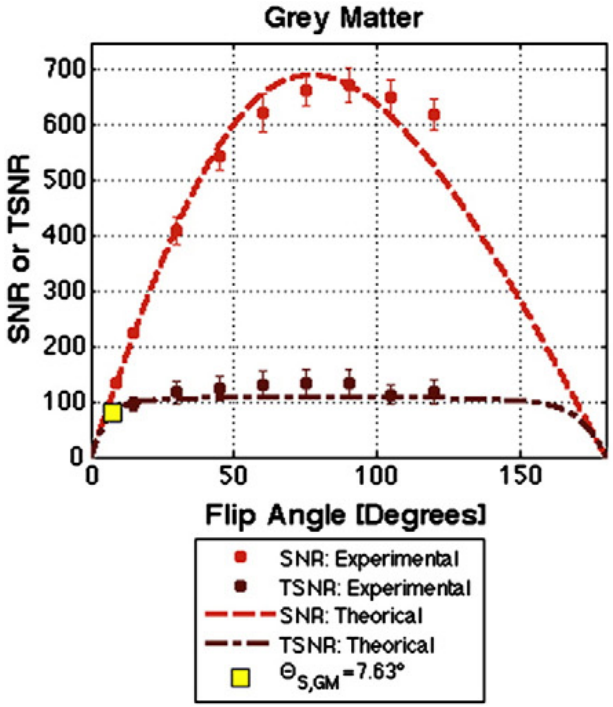
General acquisition goals

- 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

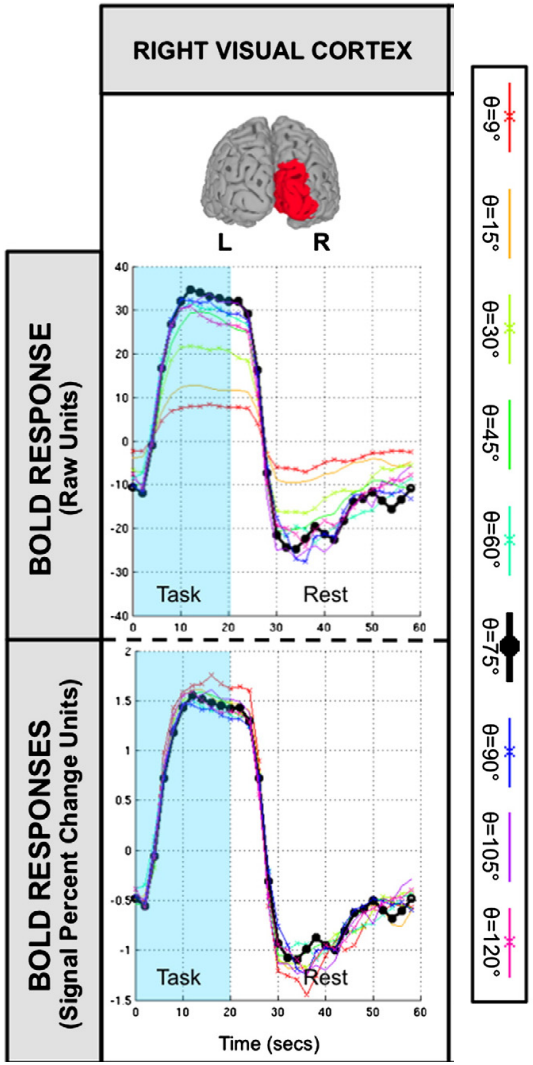
- The optimal acquisition options aren’t always obvious.

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

Optimal flip angle?



Gonzalez-Castillo, Roopchansingh, et al 2011



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

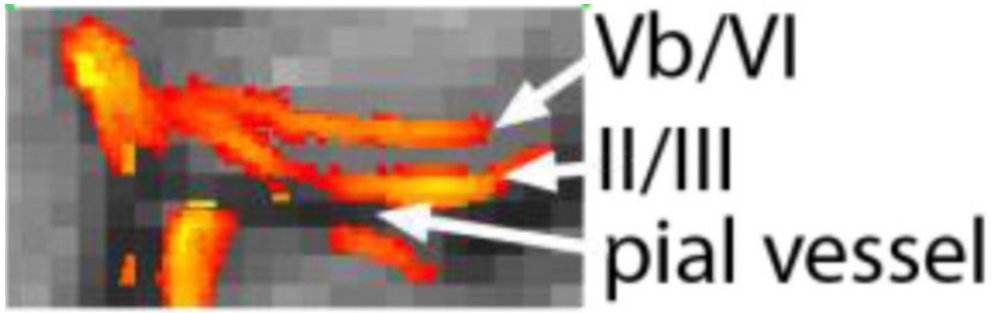
λ is amount of physiological noise

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

Selecting the right voxel size

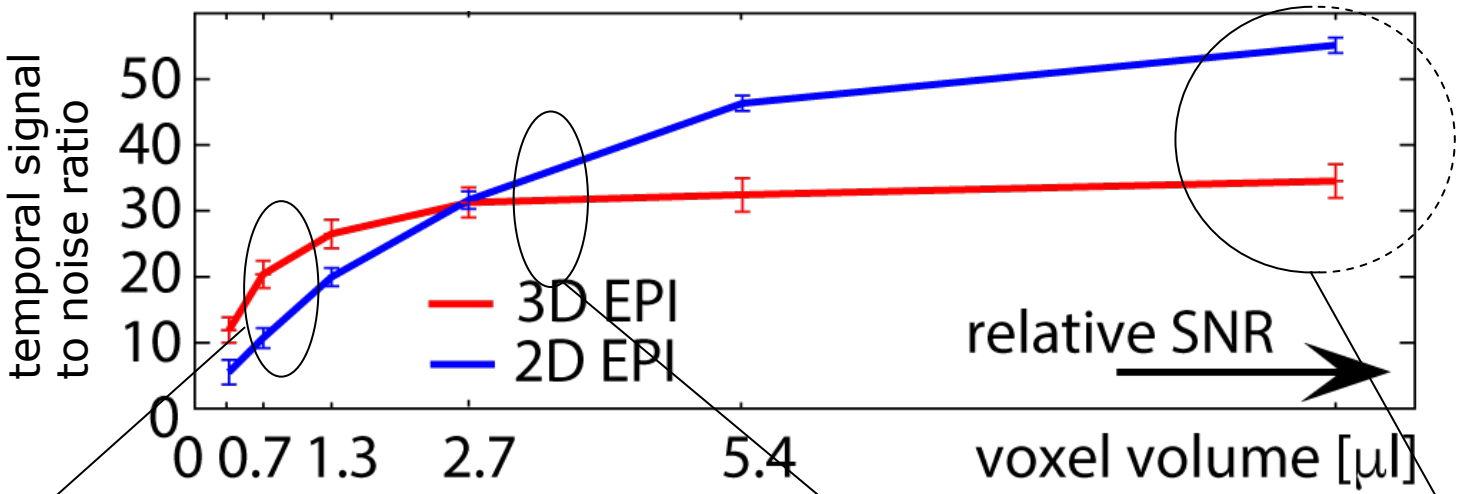
- Smaller -> Lower SNR
- Smaller -> More anatomical specificity -> Higher TSNR of interest

$3x3x3mm^3$ voxels = 27 mm^3
$1x1x1mm^3$ voxels = 1 mm^3



Huber, Tse et al NeuroImage (2018)
VASO imaging with spatial smoothing

The “best” pulse sequence interacts with voxel size & SNR

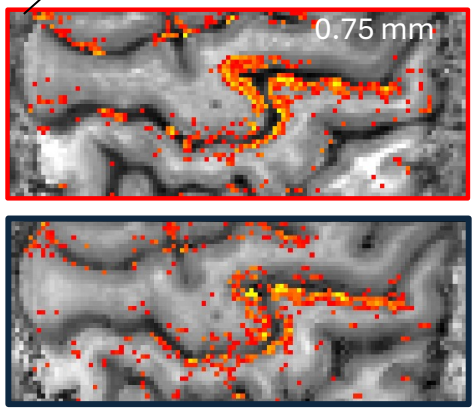


Huber et al., NeuroImage, 2016

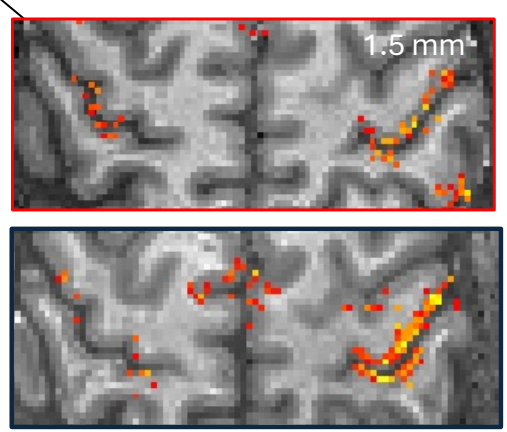
SMS wins in physiological noise dominated regime

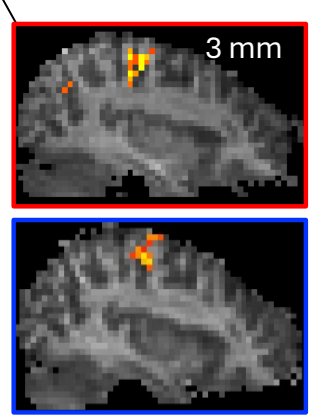
3D EPI

2D SMS

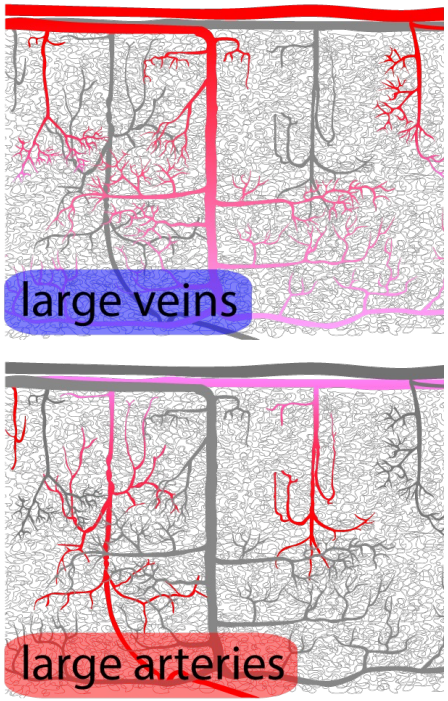


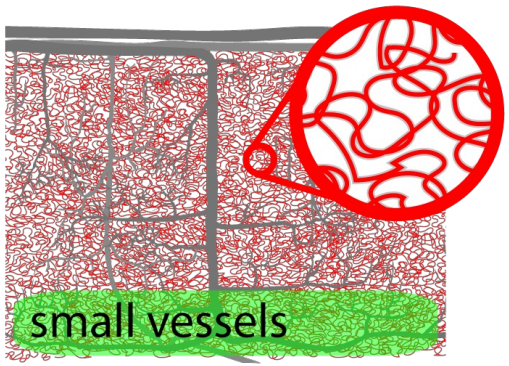
SMS is challenged in thermal noise dominated regime]

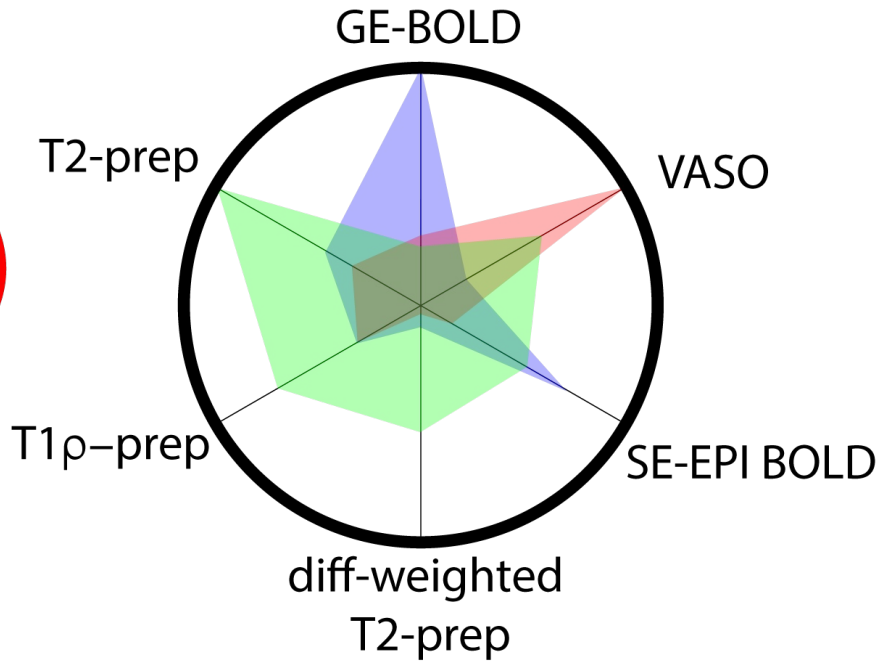




Pulse sequence sensitivies



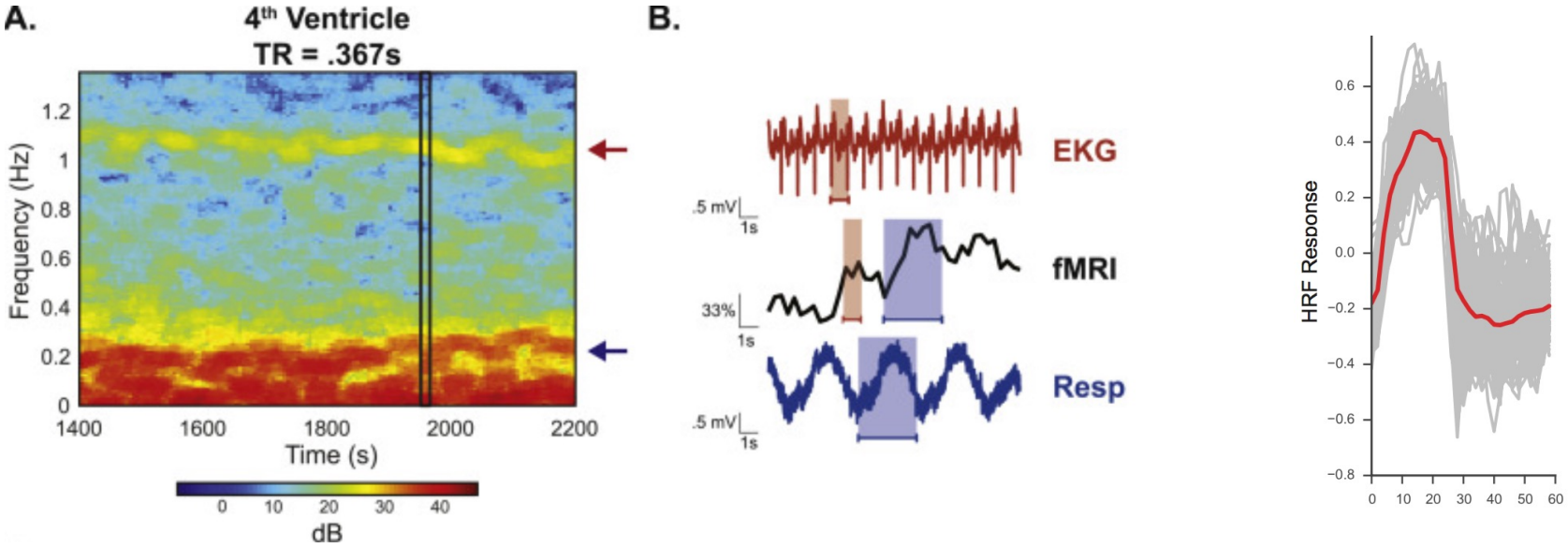




Images from Laurentius Huber
graphical depiction of review articles [Uludağ and Blinder 2017] and [Huber et al., 2017]
drawn based on Duvernoy, 1981 Brain Res

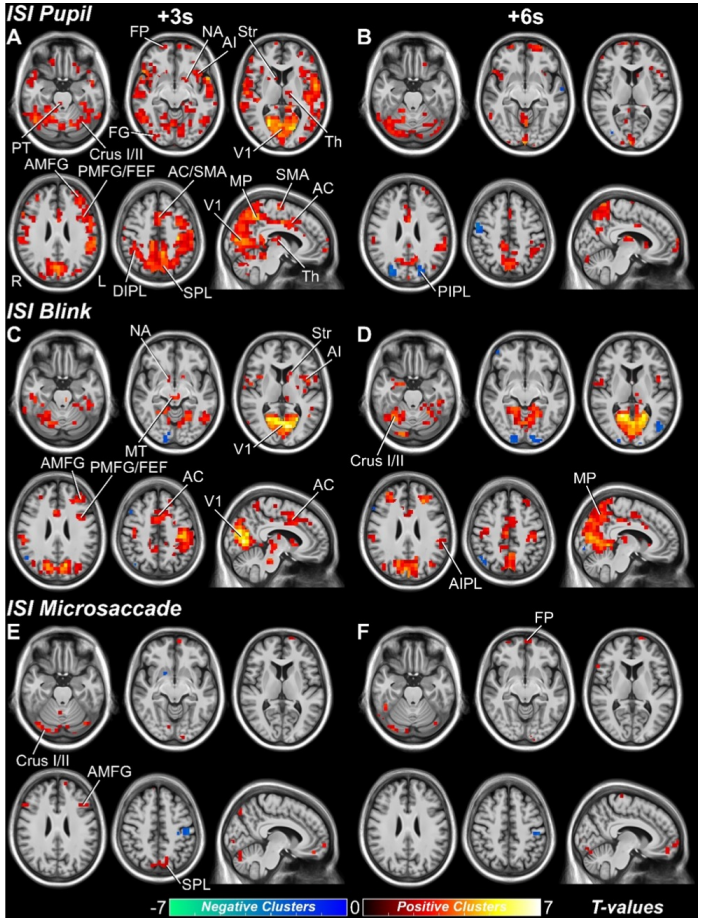
Temporal Sampling Rate (TR)

- Shorter -> lower SNR, but better temporal resolution & possibly higher TSNR
- Shorter -> Better filtering of high frequency artifacts
  - TR needs to be shorter than sometimes assumed
  - (if not removed using other methods)
- Partially limited by the speed of the hemodynamic response
  - See Polimeni & Lewis *Prog in Neurobiology* 2021 for examples of fast task modeling



Agrawal, Brown, Lewis. *NeuroImage* 2020

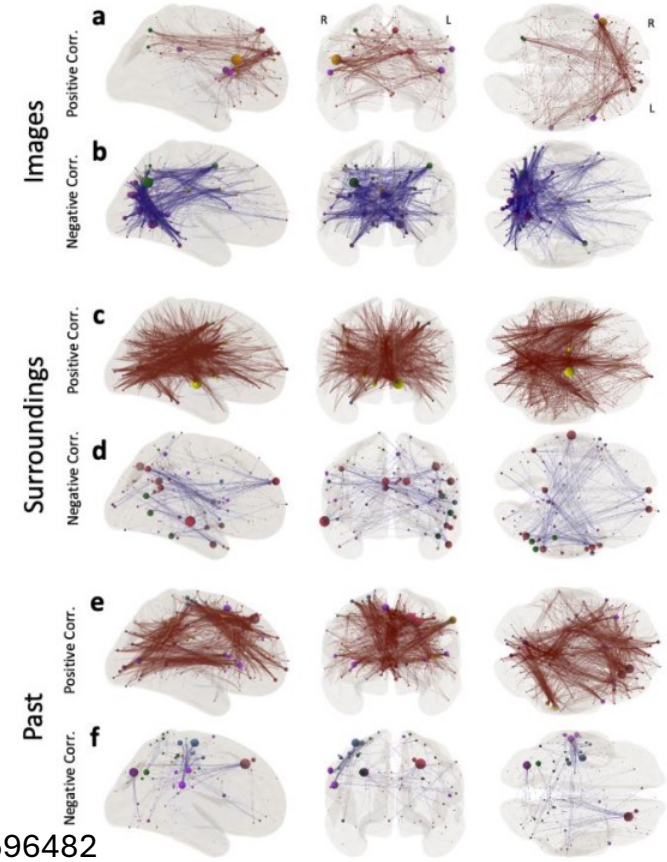
Using peripheral measures: Eye tracking



There are distinct activity maps depending if a person's pupil dialated, they blinked, or has a microsaccade during the interstimulus interval of a task

Kronemer et al, Nature Communications 2022

Peripheral measures
Feedback on internal thoughts during “rest”



For the same rest runs, connectivity maps vary based on whether people report they were thinking about images, their surroundings, or past events

Gonzalez-Castillo, bioRxiv, 2024
https://doi.org/10.1101/2024.06.05.596482

Take home messages

- There are some things that are noise in every fMRI study
- The difference between signal and noise is often study specific
- Even for things that are always noise, their importance can vary
- Clearly defining your desired signal and possible sources of noise can help improve study designs and analyses