The basic fMRI study

all elements to consider

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National Institute of Mental Health

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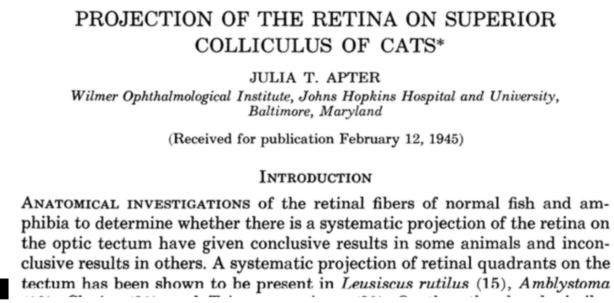
The basic fMRI study



PROJECTION OF THE RETINA ON SUPERIOR COLLICULUS OF CATS*

JULIA T. APTER

Wilmer Ophthalmological Institute, Johns Hopkins Hospital and University, Baltimore, Maryland

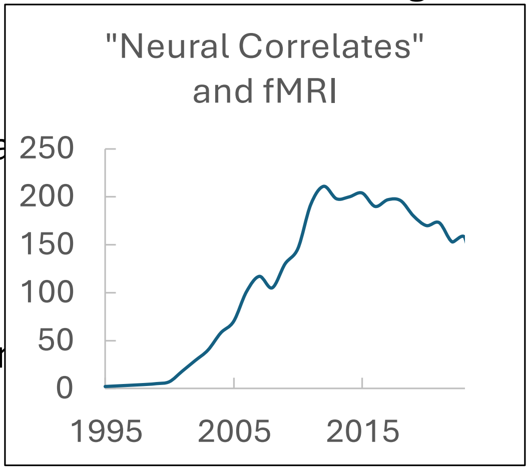
(Received for publication February 12, 1945)

INTRODUCTION

ANATOMICAL INVESTIGATIONS of the retinal fibers of normal fish and amphibia to determine whether there is a systematic projection of the retina on the optic tectum have given conclusive results in some animals and inconclusive results in others. A systematic projection of retinal quadrants on the tectum has been shown to be present in *Leusiscus rutilus* (15), *Amblystoma*

“Neural correlates” publications in 2001

- Neural correlates of driving.
- Neural correlates of conscious self-regulation of emotion.
- Neural correlates of change detection and change blindness.
- Neural correlates of attention and working memory deficits in HIV patients.
- Neural correlates of verbal memory encoding during semantic and structural processing tasks.
- Neural correlates of emotions in psychiatric patients in the light of functional neuroimaging findings.
- Neural correlates of traumatic memories in posttraumatic stress disorder: a functional MRI investigation.
- Neural correlates of dual task interference can be dissociated from those of study.
- Neural correlates of person familiarity. A functional magnetic resonance ima implications.
- Neural correlates of response inhibition for behavioral regulation in humans magnetic resonance imaging.
- Neural correlates of formal thought disorder in schizophrenia: preliminary fi magnetic resonance imaging study.



Goals of this talk

Learn the key phases of fMRI study design and analysis

Understand the types of decisions that researchers need to make in each phase

Not the goals of this talk

Learn best options for each phase of a study

Explain all fMRI study designs and analysis methods

Cannot cover details of all fMRI studies

Task fMRI: Each voxel fit to a predefined model

Visual temporal frequency preference shows a distinct cortical architecture using fMRI

Yuhui Chai [a,*], Daniel A. Handwerker [a], Sean Marrett [b], Javier Gonzalez-Castillo [a], Elisha P. Merriam [c], Andrew Hall [a], Peter J. Molfese [a], Peter A. Bandettini [a,b]

Task fMRI with <1mm^3 resolution

Topographical and laminar distribution of audiovisual processing within human planum temporale

Yuhui Chai [a,*], Tina T. Liu [b], Sean Marrett [c], Linqing Li [c], Arman Khojandi [a], Daniel A. Handwerker [a], Arjen Alink [d], Lars Muckli [e], Peter A. Bandettini [a,c]

Task & Rest with whole brain connectivity measures

Manifold learning for fMRI time-varying functional connectivity

Javier Gonzalez-Castillo[1]*, Isabel S. Fernandez[1], Ka Chun Lam[2], Daniel A. Handwerker[1], Francisco Pereira[2] and Peter A. Bandettini[1,3]

Resting fMRI: Correlations between predefined regions

Theta-burst TMS to the posterior superior temporal sulcus decreases resting-state fMRI connectivity across the face processing network

In Special Collection: CogNet

Daniel A. Handwerker, Geena Ianni, Benjamin Gutierrez, Vinai Roopchansingh, Javier Gonzalez-Castillo, Gang Chen, Peter A. Bandettini, Leslie G. Ungerleider, David Pitcher

Task fMRI with multi-voxel pattern analyses

A Unifying Model for Discordant and Concordant Results in Human Neuroimaging Studies of Facial Viewpoint Selectivity

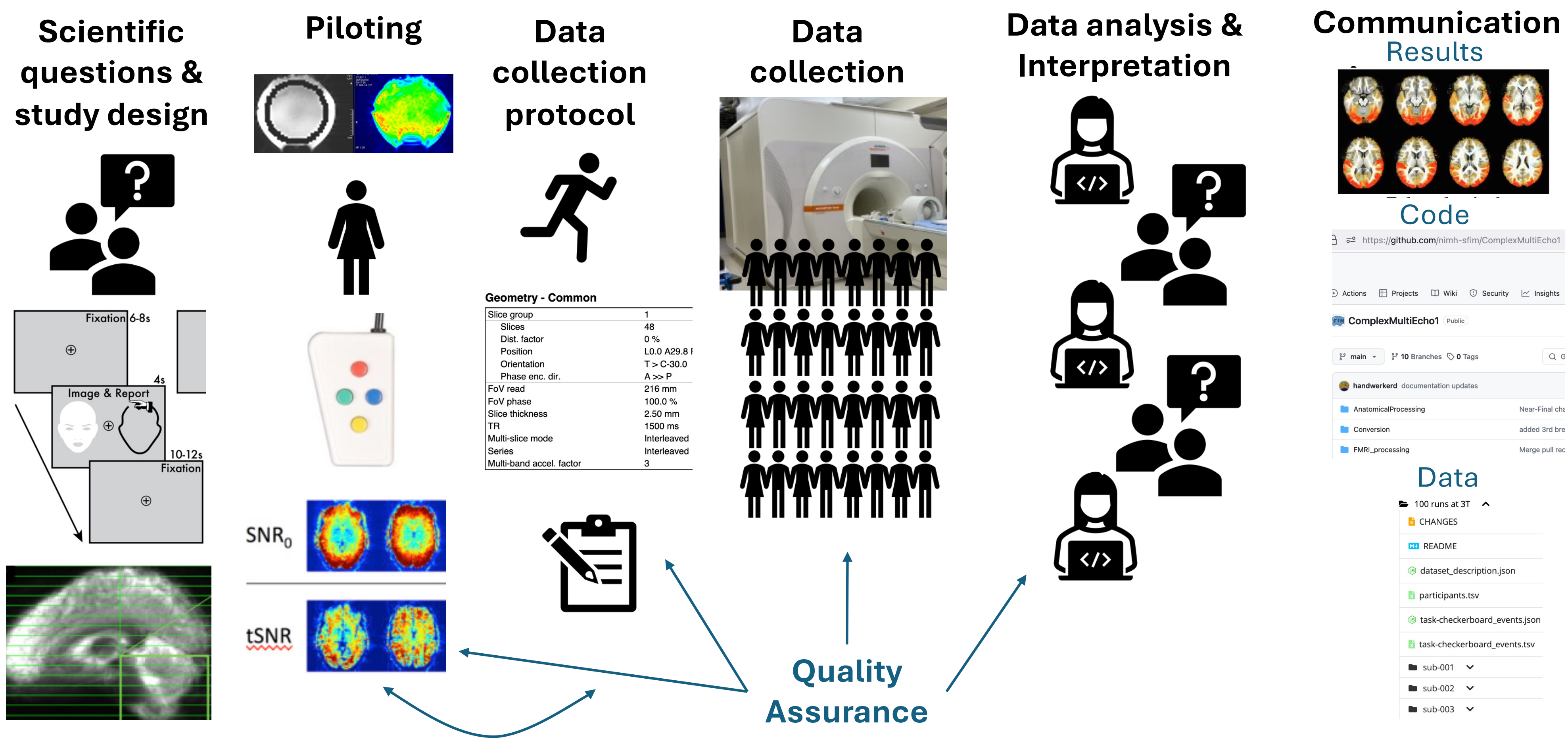
Cambria Revsine,[1,2] Javier Gonzalez-Castillo,[3] Elisha P. Merriam,[1] Peter A. Bandettini,[3,4] and Fernando M. Ramírez[1,3]

Movie viewing (naturalistic) fMRI with correlations across people

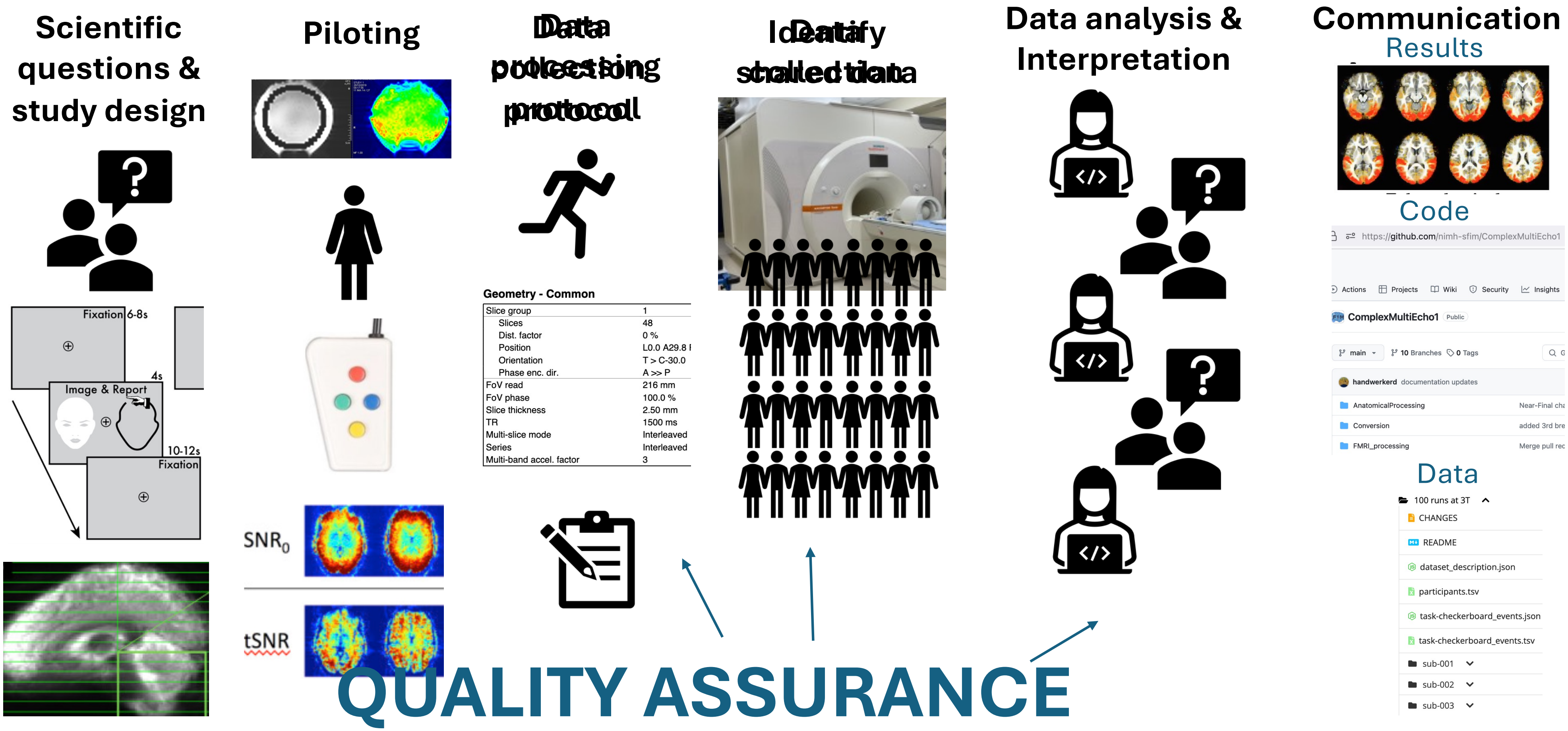
Idiosynchrony: From shared responses to individual differences during naturalistic neuroimaging

Emily S. Finn [a,*], Enrico Glerean [b], Arman Y. Khojandi [a], Dylan Nielson [c], Peter J. Molfese [a], Daniel A. Handwerker [a], Peter A. Bandettini [a]

The basic fMRI study



The basic fMRI study (existing data)



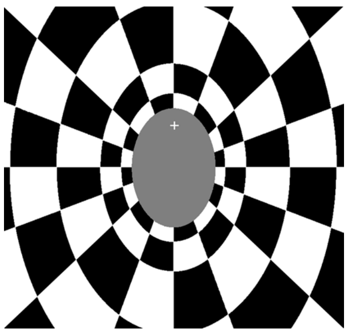
Scientific Questions & Study Design

What to collect?

- **What types of data have the potential to accurately and effectively answer your scientific question?**
- Task? Movie? Rest?
  - Task design, which movies, what type of “rest”
- Structural MRIs? Calibration measures?
- Simultaneous acquisitions: Pulse, Respiration, EEG, eye tracking, participant responses, ...
- Who to scan?
  - Lots of data from fewer people? A large population?
    Across populations? Within-person changes?

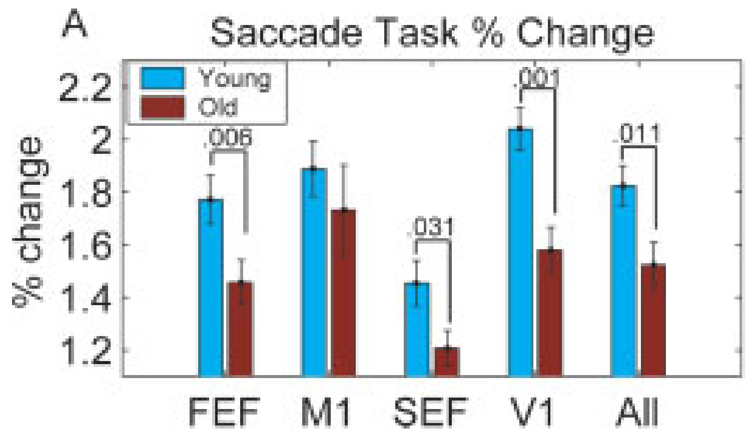
Don’t neglect peripheral measurements!

A breathless cautionary tale



Present a 200ms flickering checkerboard every 18-24s

Volunteers press a button and move their eyes



Handwerker, Gazzaley, et al 2007

The unpublished part

- Stimuli presented for 3s, 6s & 12s durations
- A non-trivial # of volunteers held their breath for the stimulus duration
- No respiration data →
  Visually appealing results →
  Misinterpreted results

See also: Birn, Murphy, et al, NeuroImage 2009

Scientific Questions & Study Design
Study Level Questions

- Number of participants & amount of data / participants
  - Looking for individual-level effects?
  - Looking for consistent group effects?
  - Looking for behavioral/fMRI response variation across participants?
  - Looking for diagnostic or treatment relevant markers?

- Power analyses are important
- Power analyses can be over-emphasized and over-simplified
  - Making sure each dataset is high quality will improve results more than increasing sampling size or focusing on statical thresholding methods.

Scientific Questions & Study Design
fMRI acquisition parameters

- No universally best parameters
- Never copy parameters from another study without understanding why they made their choices
- The question drives the study design. What matters?
  - Brain coverage
  - Dropout
  - Distortion
  - Temporal Signal-To-Noise Ratio (TSNR)
  - Head motion sensitivity

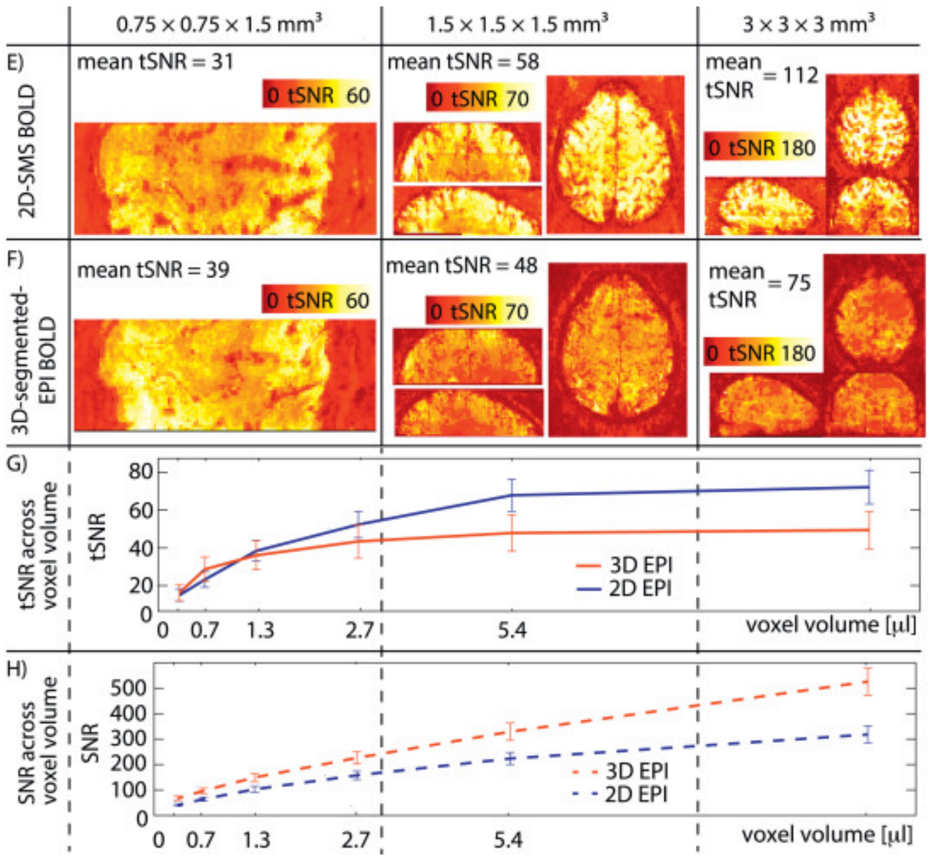
Scientific Questions & Study Design

fMRI acquisition parameters

TR (speed of scanning)

- Finer temporal resolution
- More volumes over the same time
- More noise per volume
- Acceleration to get faster TRs potentially makes more artifacts
- Possibly less brain coverage and larger voxels

Scientific Questions & Study Design
fMRI acquisition parameters



- Smaller voxels can give more spatial precision
- More noise
- Slower

Huber, NeuroImage 2018

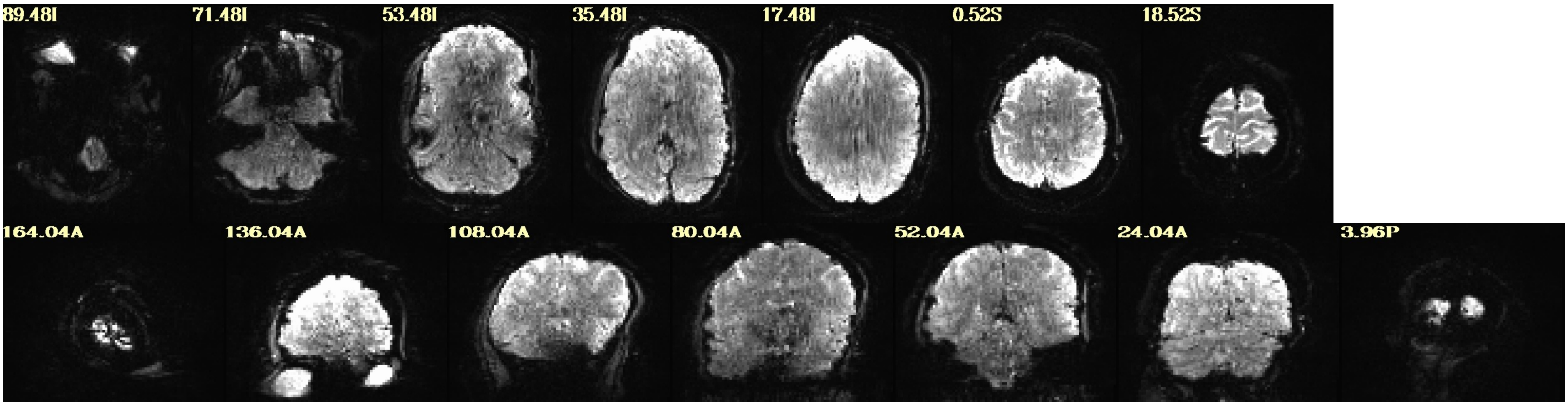
Scientific Questions & Study Design
Other fMRI acquisition parameters

- Acceleration methods
- Multi-echo fMRI
- Non-BOLD contrasts
- 2D vs 3D
- Flip angle

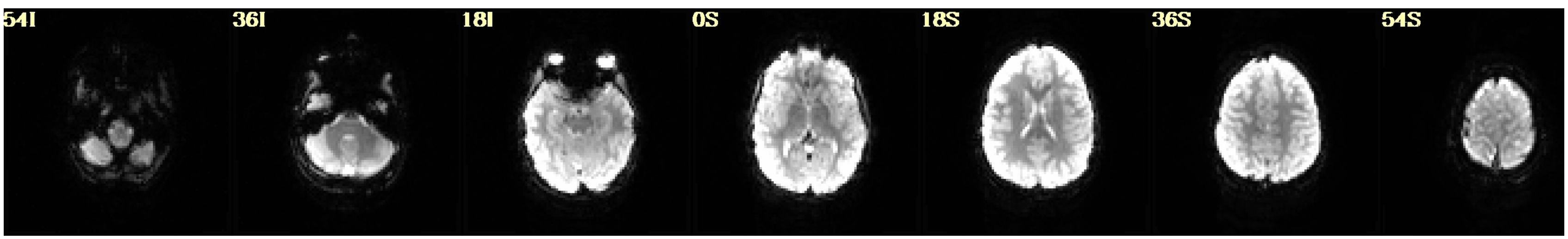
A (mildly provocative) case study

There is no such thing as ”gold standard data”

Arbitrary volunteer from the original Human Connectome Project



Arbitrary volunteer from ABIDE



A (mildly provocative) case study

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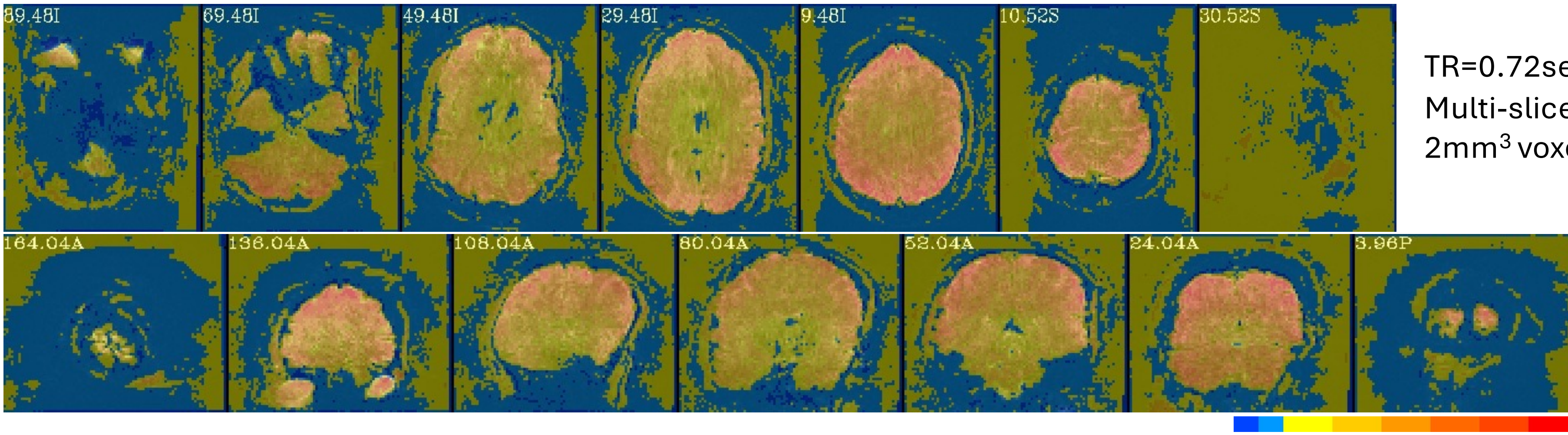
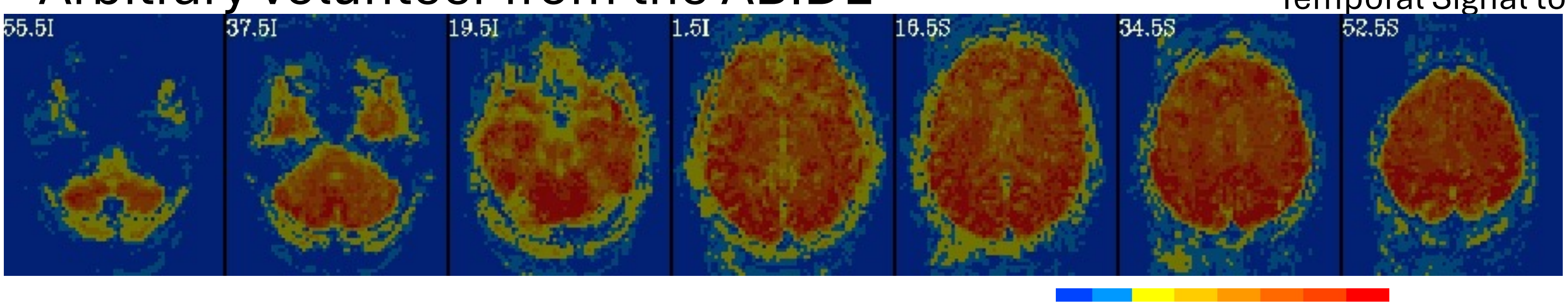


TR=0.72sec
Multi-slice accel=8
$2mm^3$ voxels

Arbitrary volunteer from the ABIDE



TR=2.5sec
In-slice accel=3
~$3mm^3$ voxels

Context and applications matter

- Successful Research using HCP data
  - ROIs that average across multiple small voxels
  - Correlation or task studies that summarize data across time
  - Averages across the large population
- HCP weaknesses
  - Studies that fully take advantage of the short TR **and** smallish voxel size
  - Brain-wide association studies that require robust signal in individuals' data
- **Note:** This is a broad & not completely fair generalization.
- **Take home message**
  - Great data for one application, might not be great for all applications
  - Identify and view data quality metrics relevant to your application

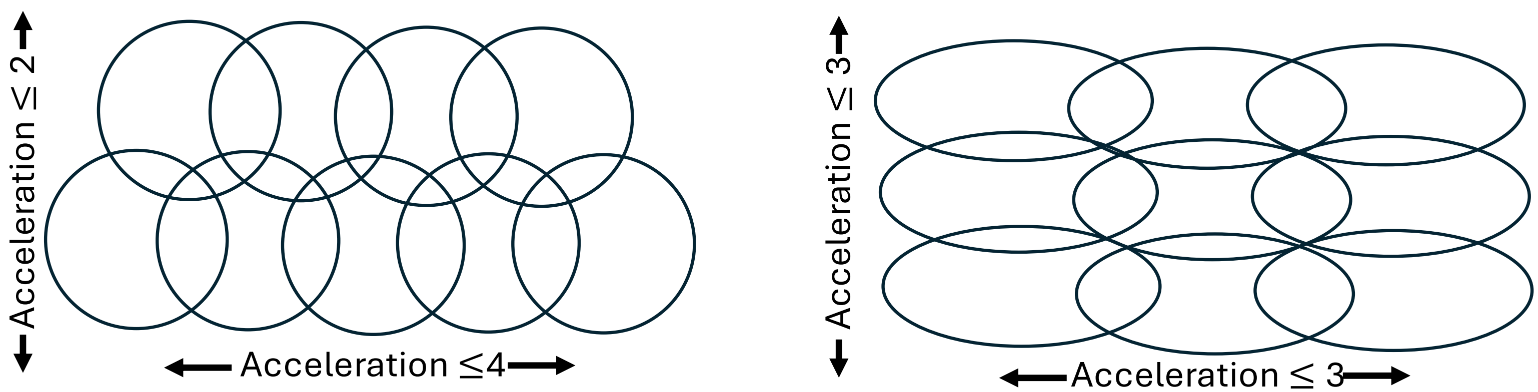
Piloting

- Comparing options for potential study designs
- Collecting data to make sure design decisions are working as expected
- Making sure acquisition workflow works with real people
- Decide how to log key information, store, and process data
- Start to make a Quality Assurance (QA) workflow

Piloting

- Do not use scanning parameters just because they worked for someone else
- Do not use scanning parameters just because they worked for someone else
- If you’re **not an expert** in MRI physics, things you did not consider might affect data quality.

Alternate geometries for a 9-channel head coil



- If you **are an expert** in MRI physics, you’re even more likely to collect pilot data

Data Collection Protocol

- Checklists and workflows for both regulations, safely, and experimental needs
- What to save?
- Ways to organize data in ways that facilitate future sharing
  - Consistent structure across individuals both for: data, information explaining the data, scanning notes, & results
  - Making analysis workflows that your future self will understand
- Quality Assurance steps to run during and soon after each acquisition

Questions for a study protocol

Priority	Context & Examples
General	
Which voxels have usable data?	Voxel-wise data quality & coverage*
Are locations of voxels accurately defined?	Distortion & alignment to anatomy & templates*
Define context	Scientific questions & study priorities affect what is or is not good quality data
During study planning	
QC measures to support study goals	Particularly for study-specific QC priorities, this is a good time to seek expert advice
Operation procedures to decrease acquisition errors	Good procedures are critical for making sure data are accessible and consistently documented
Additional measures to collect	Experimenter notes, behavior logs, respiratory & cardiac traces
Organization & sharing QC measures	Inaccessible information is not useful
Piloting acquisition & processing	Evaluate and improve a QC protocol as part of study piloting
During Acquisition	
Real-time monitoring of severe image distortions, head motion, task non-compliance	Observing problems during acquisition can give time to recollect data or fix problems for the current or future scans
Monitor peripheral measures	Respiration, cardiac, eye tracking
Soon after acquisition or download	
Expected data are all present and properly documented	Missing, duplicated, or corrupted files, incomplete runs.* For MRI data, behavioral logs, and peripheral measurements
Data consistency & documented parameters match data	Consistent MRI field of view, contrast, orientation, number of runs, & run lengths match documentation*+
Documentation on QC during acquisition or pre-sharing exists	No documentation means there are undocumented problems
Data plausibly useful for study goals	Regions of interest should have full coverage. No substantive temporal artifacts that affect connectivity measures
Atypical brain structures, acquisition artifacts, drop out, and distortion	May still be fine` , but might require altered processing. AFNI's instacorr can be useful for assessment
During and after processing	
Scripts ran properly	Expected logs, QC metrics, & outputs created*
Appropriate voxels retained or removed	Voxels with good SNR in brain are within mask and voxels outside of brain are removed.*
Voxels lost to dropout or field of view	Check that similar voxels are retained across the population+
Consistent measures of temporal signal-to-noise and intrinsic spatial smoothness across population	Sessions with non-trivially lower TSNR or different smoothness can be a warning sign of other problems*
Automatically removed data	Number of censored volumed and DOF lost from noise regression, temporal filtering, & censoring*
Artifacts like ghosting, phase wrapping, or leakage	Instacorr is useful for checking if the temporal signal from an article is folding over into other brain regions
Partially-thresholded activation maps	Are areas with the largest model fits in anatomically plausible patterns inside the brain?*
Task correlated head motion or breathing	Not commonly checked and can bias results.* (AFNI automatically checks motion, but not breathing.)
Skull properly masked for anatomical & functional data	Can cause problems with alignment. Part of report from AFNI's SSwarper
Intensity inhomogeneity	Brighter signal on the surface can be expected, but can cause problems with masking and alignment*
Good anatomical to functional alignment & alignment across days/runs	Can be a serious hidden problem if one just looks at group maps.+
Left & right hemispheres flipped between anatomical & functional data	More common than it should be & requires excluding data unless the true left/right can be determined*
Good anatomical to anatomical alignment across participants	Often correctable and causes problems if not corrected+
Group coverage across population	A summation of aligned functional masks highlights brain areas missing in part of the population+
Processed peripheral data are good	Plausible behavioral timing files, good peak detection in respiratory & cardiac traces

Questions
Not a
checklist

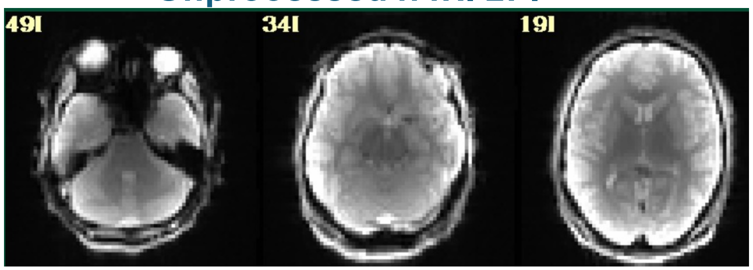
Teves et al "The art and science of using quality control to understand and improve fMRI data" Front. Neurosci. (2023) https://doi.org/10.3389/fnins.2023.1100544

Data Collection!

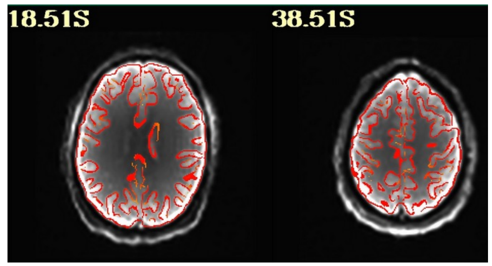
- If planning was done well,
  then data collection follows a script
- Pay attention to when you go off-script
  and if the plan needs to change
- QA soon after each acquisition
  - Identify fixable problems before a lot of data are collected
  - Identify data anomalies or unexpected variations that might skew or hide key results
- **All datasets have problems**
  - Not checking → Incorrect or misleading interpretations of results
  - Checking → **Fewer** unknown problems

AFNI automatic QC Report after processing data

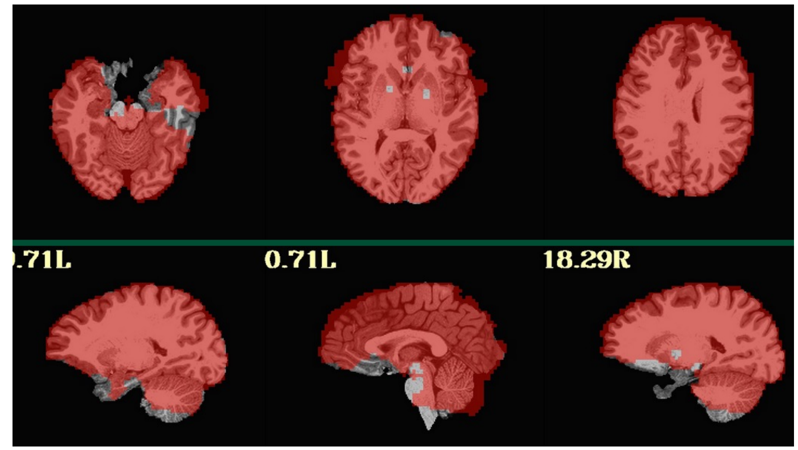
Unprocessed fMRI EPI



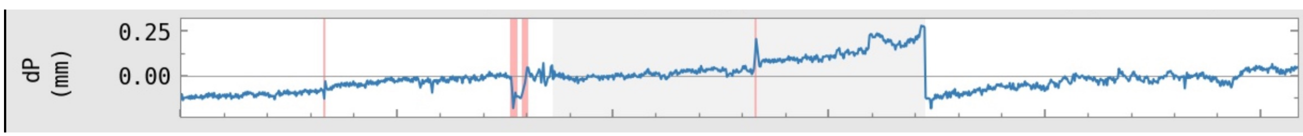
EPI to anatomical alignment



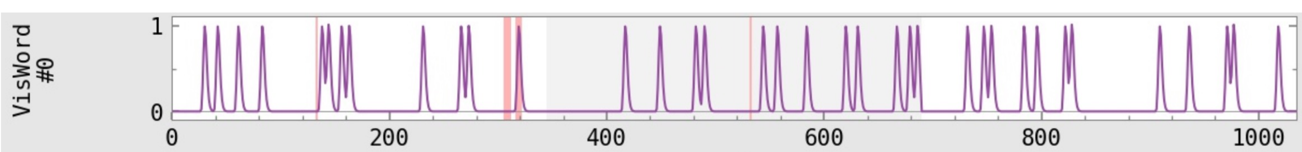
Brain regions without fMRI data



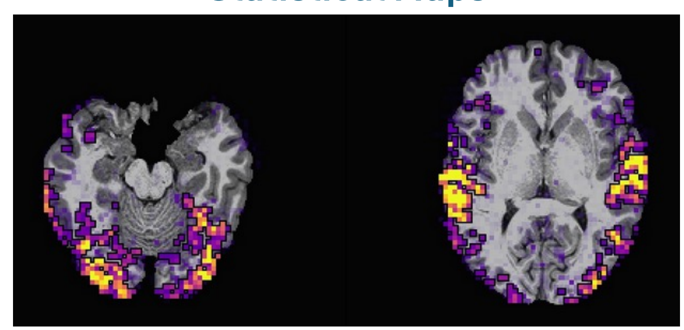
Head motion & censored volumes



Modeled task timing and censored volumes

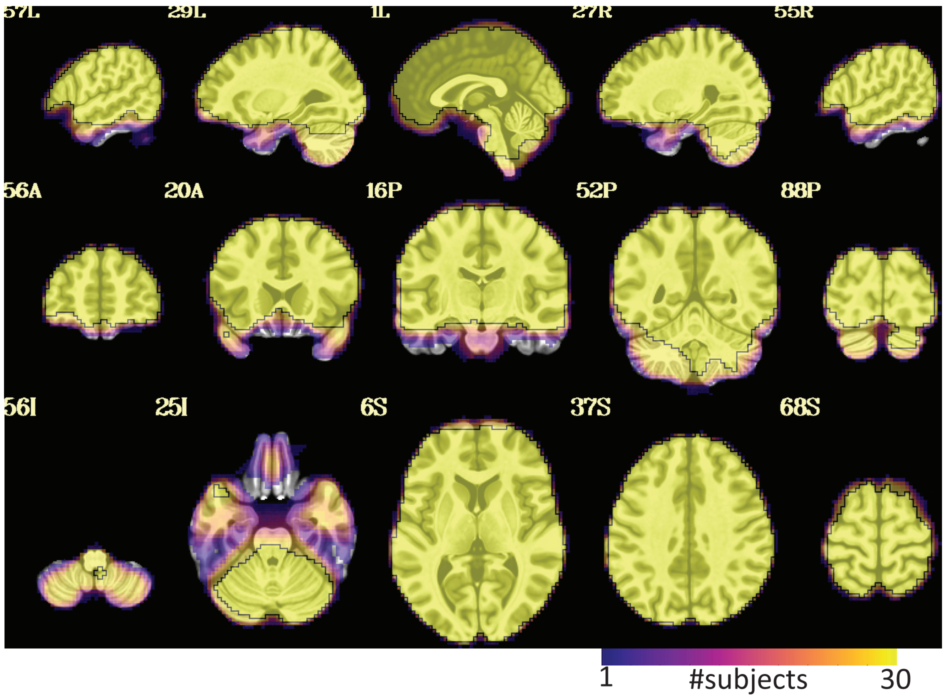


Statistical Maps

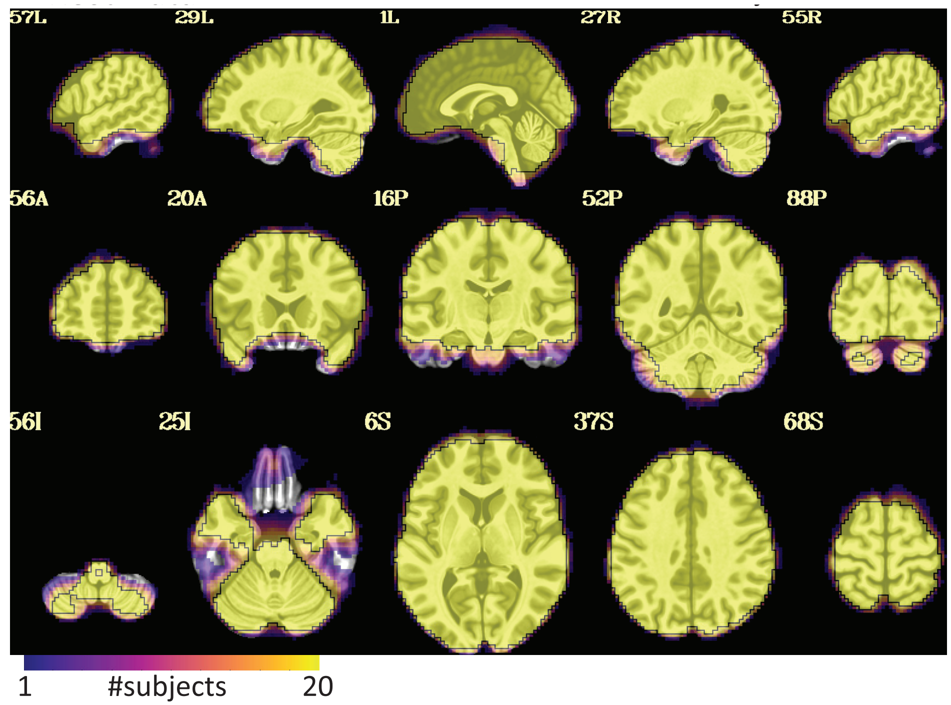


QA: Full study coverage map

Task data



Rest data



Coverage differs between studies: “Sufficient” coverage is study-specific

Teves et al. Front. Neurosci. (2023) https://doi.org/10.3389/fnins.2023.1100544

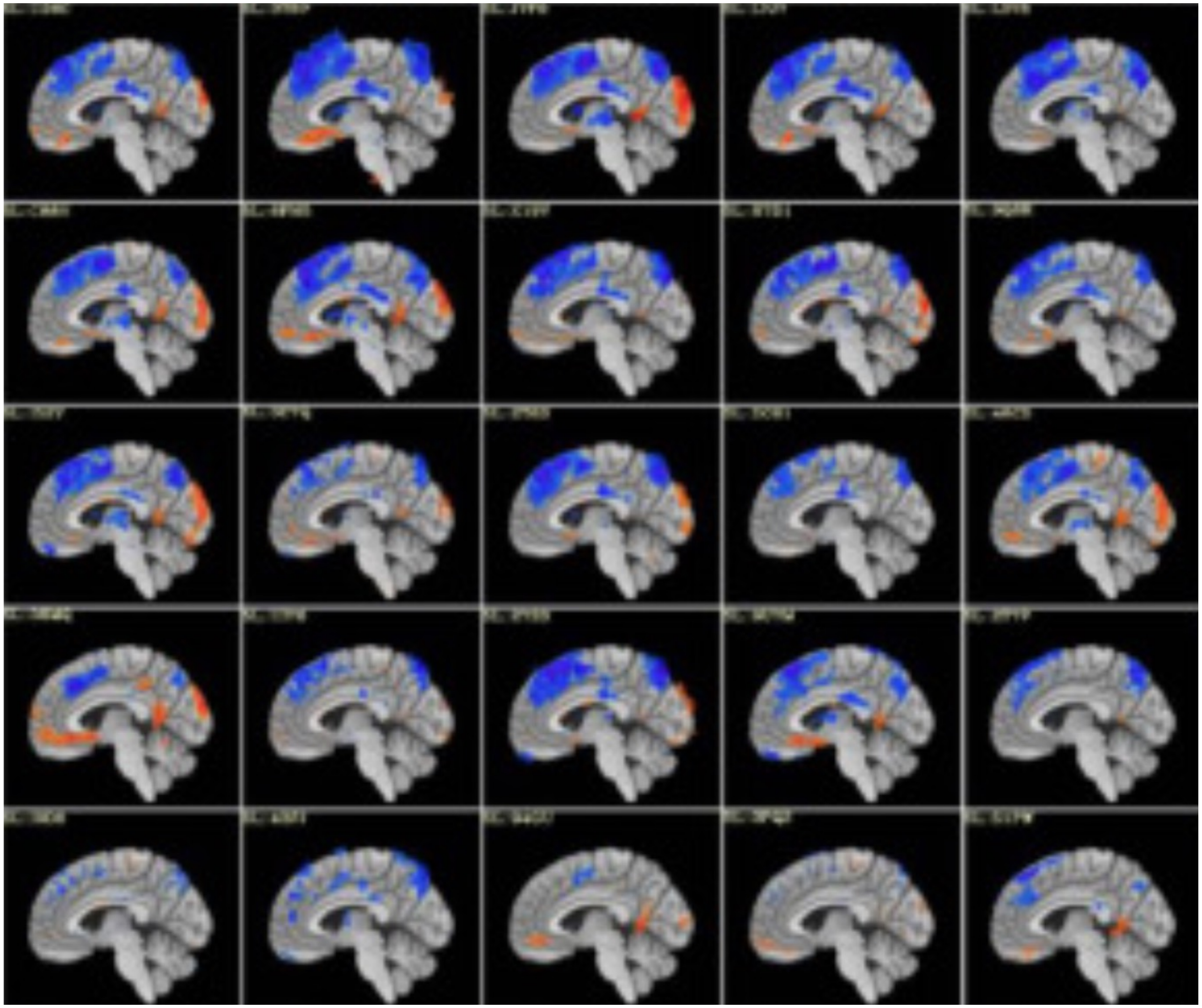
Analysis and interpretation

Cannot cover even a fraction of fMRI analysis methods

- Make sure analysis scripts fail in clear ways
- Save intermediate processing data
- Look at your data!
- Track provenance (how processed data were created)

Communication

Show as much data as possible



Taylor et al
“Highlight results, don’t hide them…”
NeuroImage 2023

Communication

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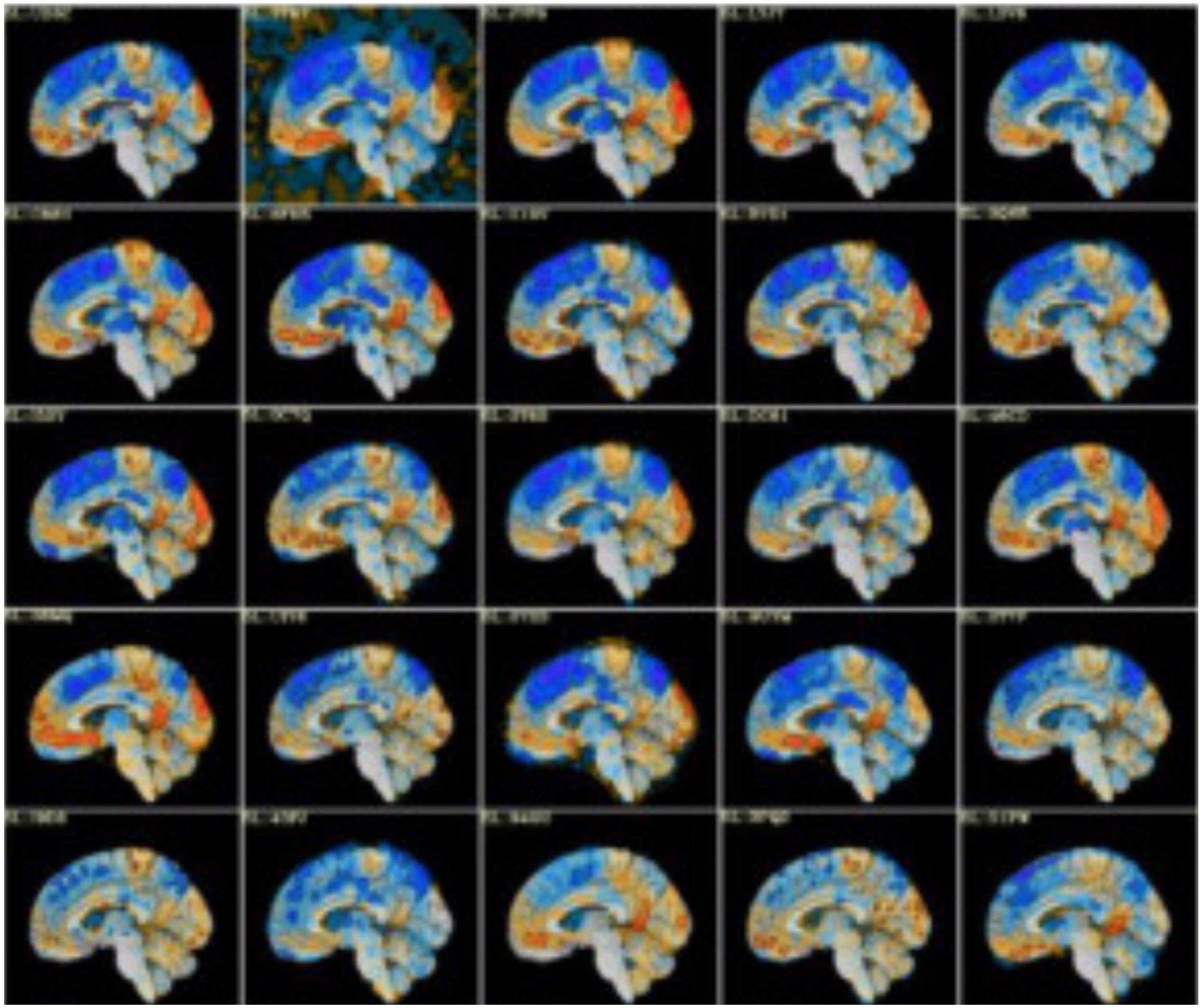

Taylor et al
“Highlight results, don’t hide them…”
NeuroImage 2023

Communication

- It is easier to share code and data if it’s set up with sharing in mind
  - Write code that you can share with your future self
- If you share data, share quality assessment measures!

Take home messages

- Make time to think through choices at every step of a study
- Quality Assessment is a critical part of every study
- No one is an expert in every step of every neuroimaging study
  - Behavioral psychology
  - Clinical Medicine
  - Neuroanatomy
  - MRI physics
  - Statistics
  - Software Development
  - Scientific Communication
- Learning what you don’t know and who to ask is almost as important and what you do know.