Part 2: Task-Based Functional MRI

Cajal Course on Aging Cognition

Workshop: Approaches to functional and structural neuroimaging analysis

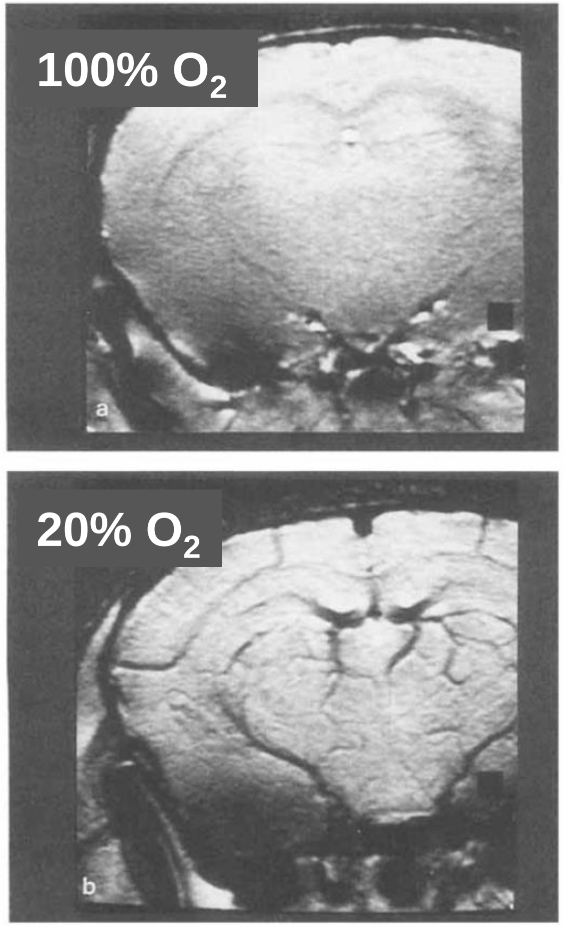
Materials: https://github.com/jennyrieck/workshops/tree/master/2021_Cajal_NeuroImaging

27 Sep 2021

Jenny Rieck

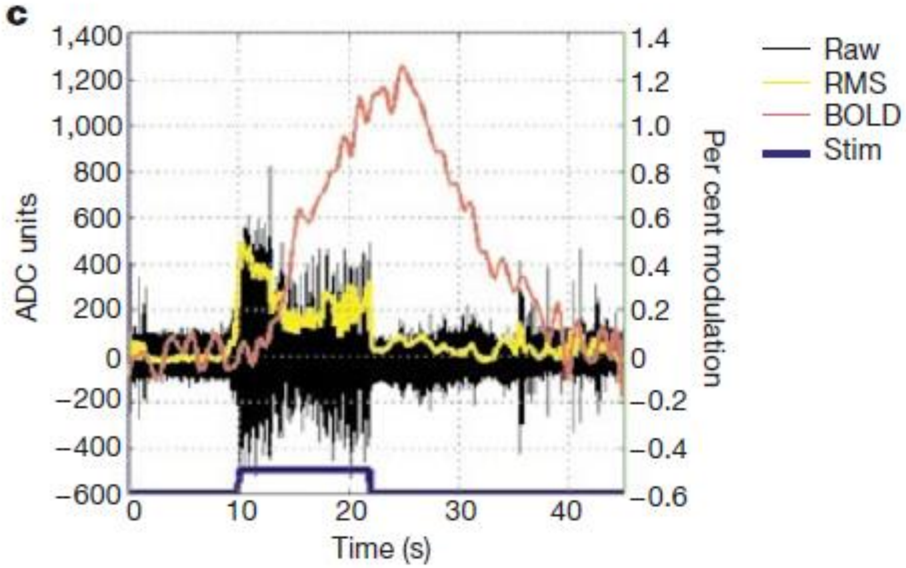
Blood oxygen level dependent (BOLD) signal

BOLD allows us to measure oxygen in the brain



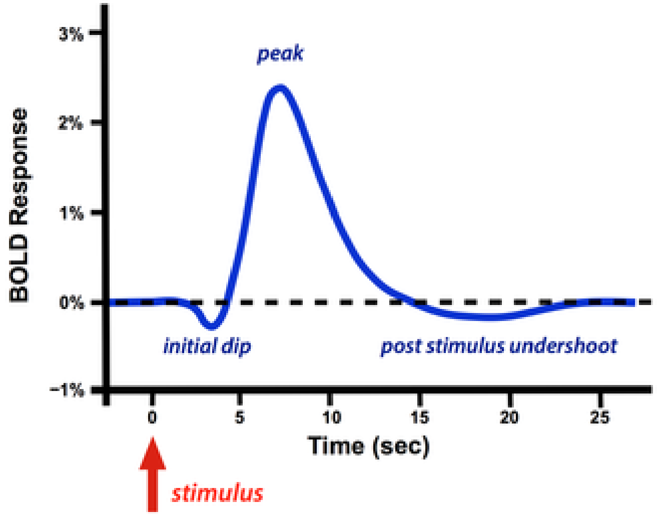
Ogawa, 1990, *Mag Res Med*

BOLD is linked to direct measures of neural activity



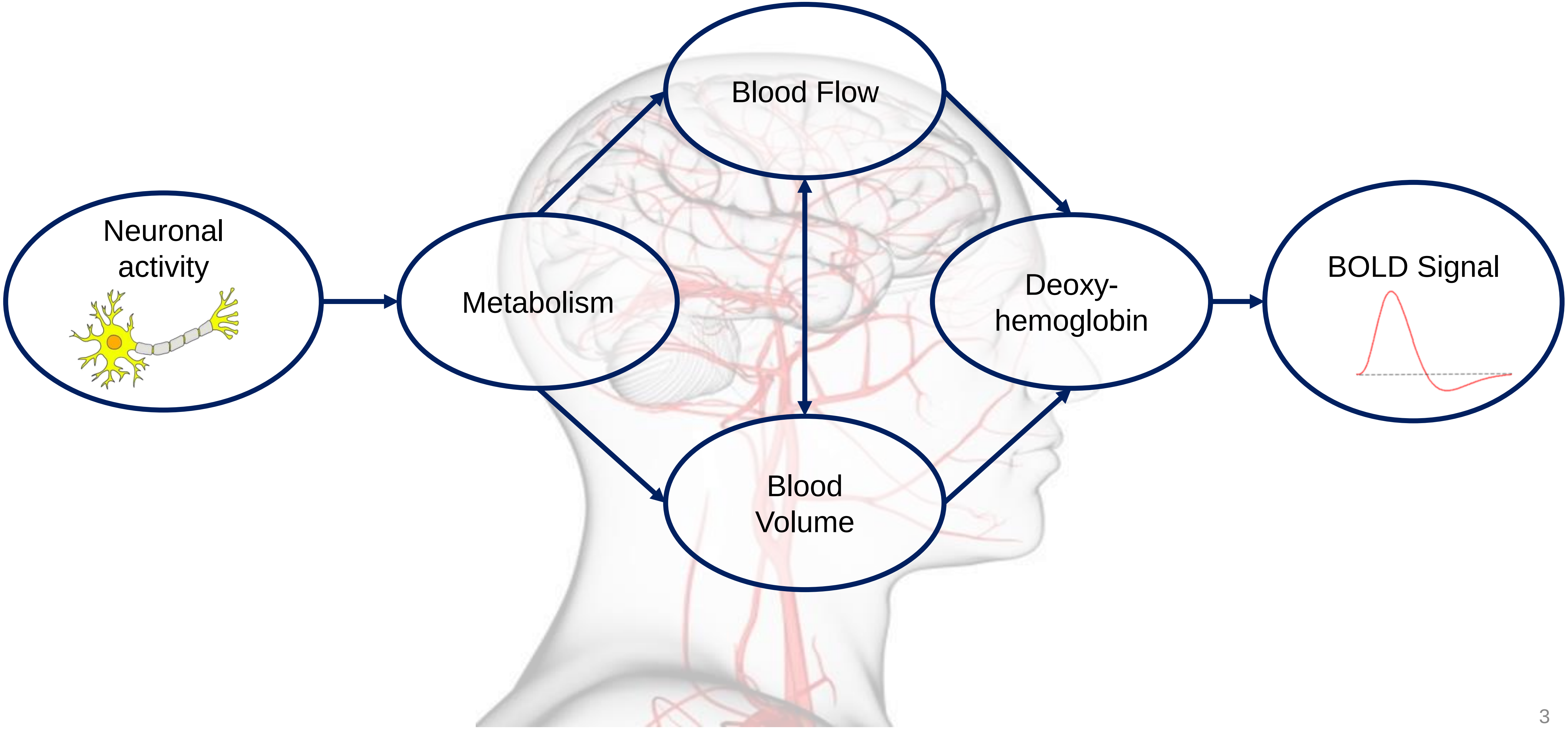
Logothetis, 2001, *Nature*

Hemodynamic response function (HRF) models the BOLD response



BOLD response is delayed, slow to peak, and continues after neural firing

BOLD is an indirect measure of activity



Considerations with BOLD fMRI

- Collecting many brain volumes over time to map brain function to specific cognitive processes
- Hemodynamic response function is slow and limits temporal resolution
- BOLD data are noisy, many trials of the experiment
- Movement over time can cause artifacts

Typical task-based fMRI workflow

1. Pre-process data to deal with noise and artifacts
2. Model expected functional activity corresponding to experimental conditions (design matrix)
3. Predict functional activity in each voxel (most often with multiple regression)
4. Compare functional activity across conditions, groups, or as a function of between-person predictors (e.g., age)

fMRI Preprocessing

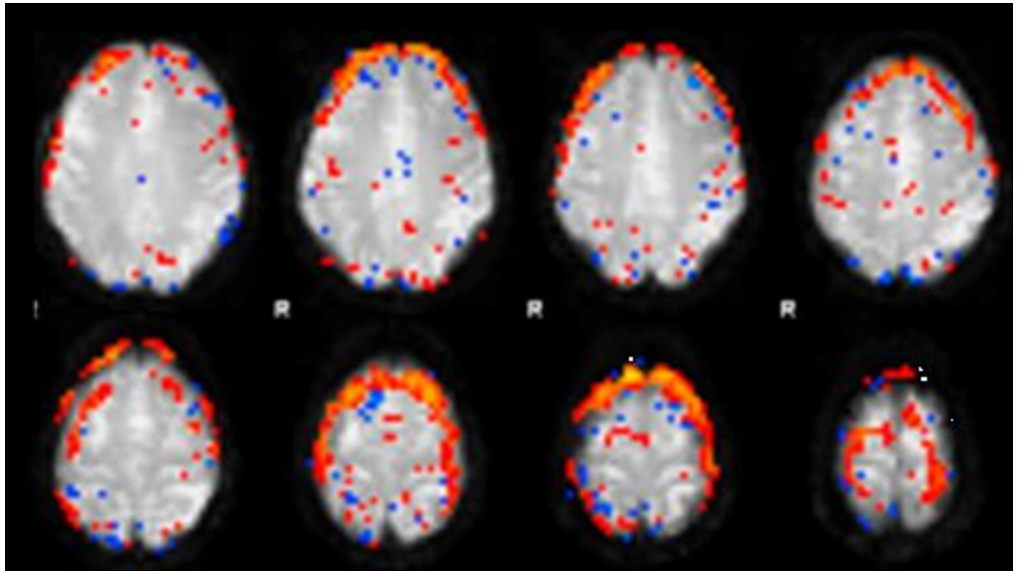
Preprocessing steps

- Conventional preprocessing steps
  - Motion correction
  - Slice timing correction*
  - Temporal filtering (high pass filter)
  - Spatial Smoothing
  - Warp to common space

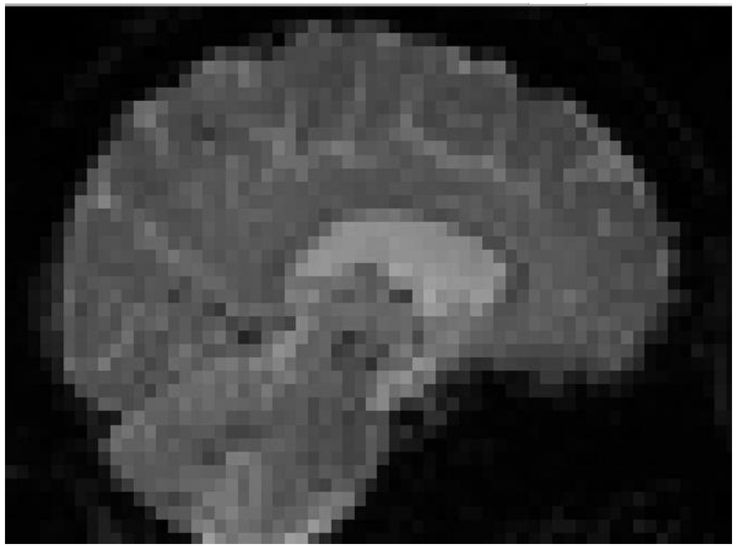
- Additional noise reduction steps (important for rest)
  - Nuisance regression
  - Temporal filtering (low pass)
  - Volume censoring
  - ICA-based denoising
  - Physiological noise regression

Motion correction

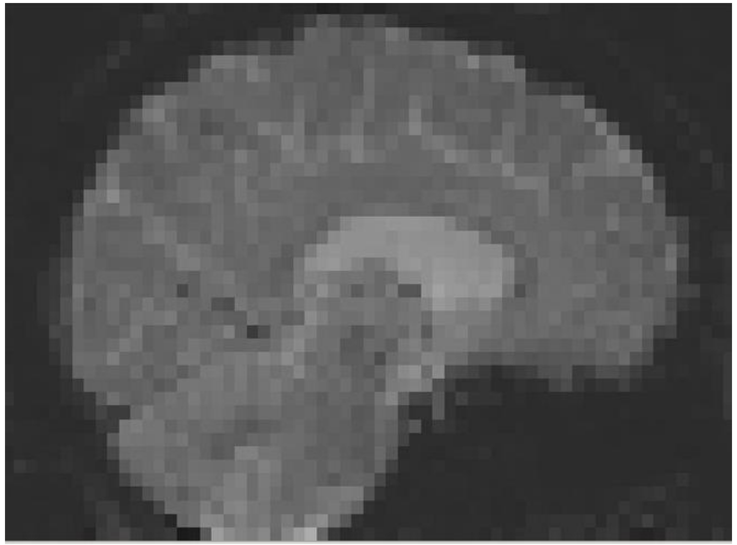
- Motion can lead to “ringing” artifacts
- Corrected with rigid frame-to-frame registration of brain volumes across timeseries



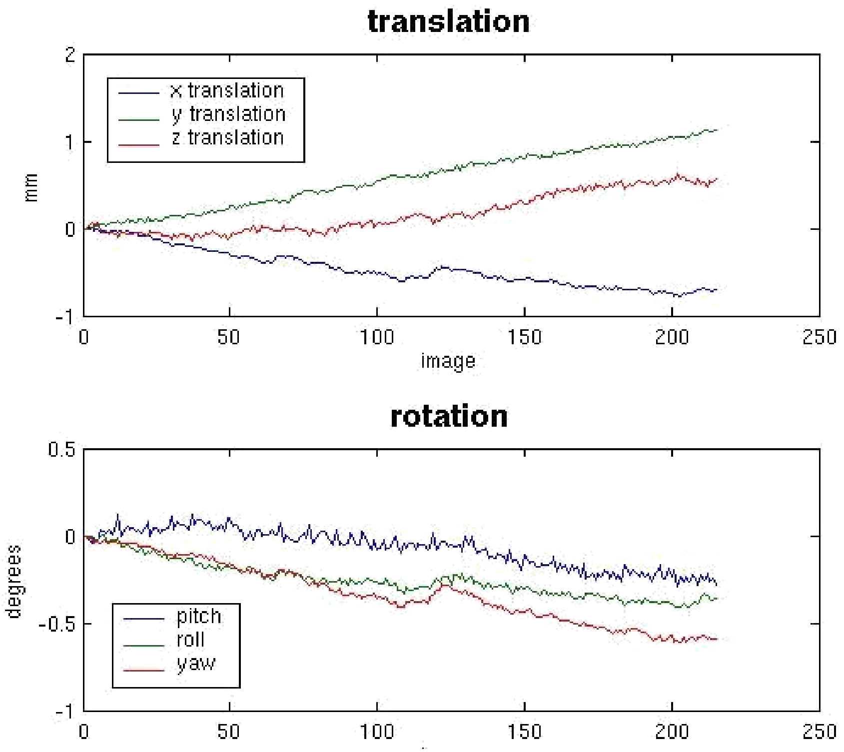
77 year old, unprocessed



77 year old with motion correction

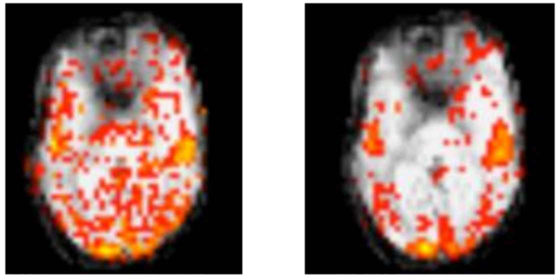


Additional motion correction



Compute composite motion estimates (e.g., mean frame displacement)

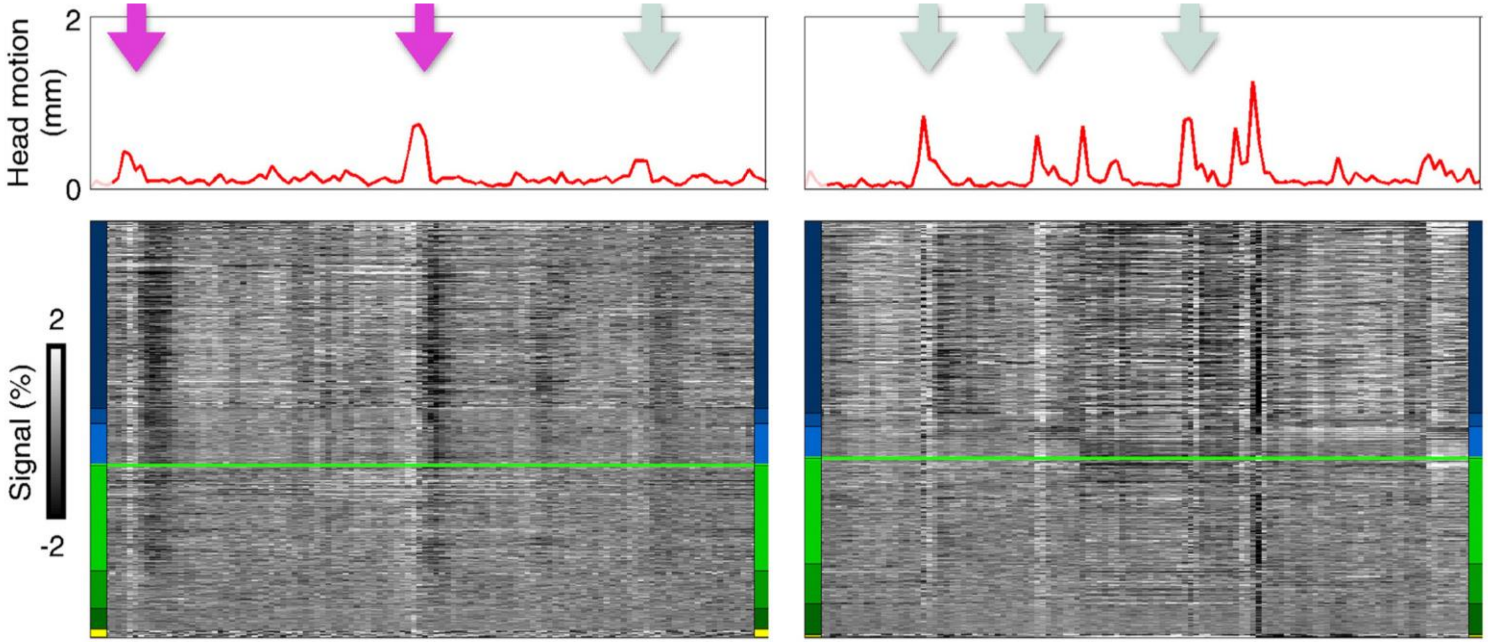
Motion parameters as nuisance regressors in statistical models



Without motion parameter EVs

With motion parameter EVs

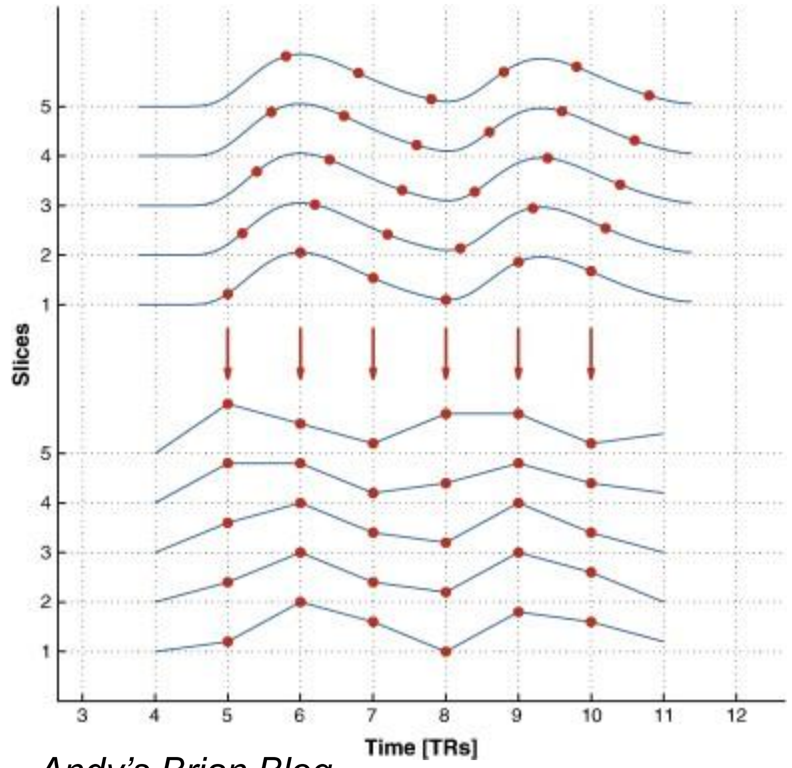
Flag volumes with high movement



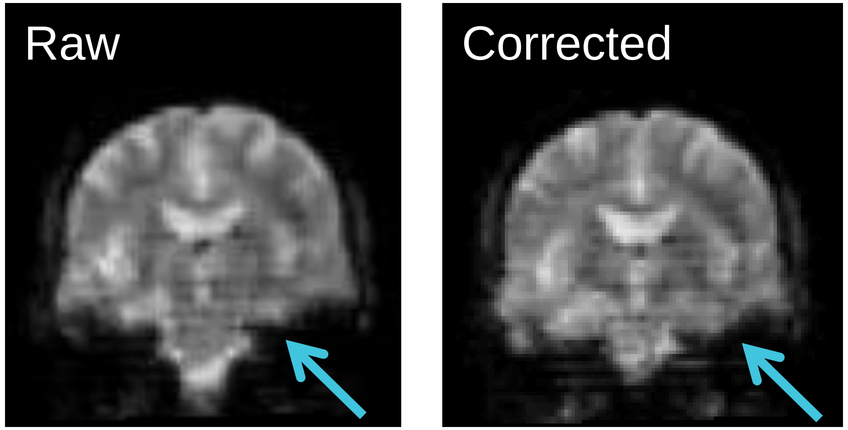
Power, 2017, *NeuroImage*

Slice timing correction

- Brain volume collection is not instantaneous
- Slice timing correction “shifts” data acquired at each slice via interpolation
- Less needed with newer acquisition sequences that collect full volume in shorter time

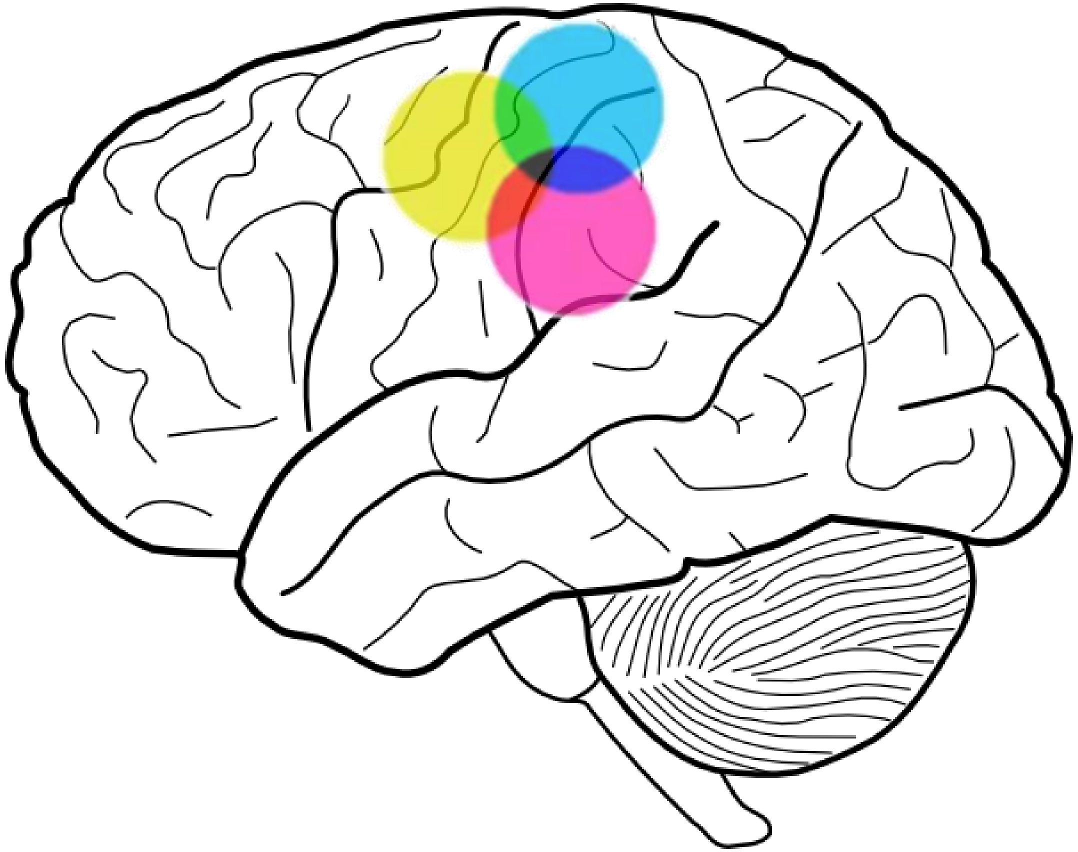


Andy’s Brian Blog

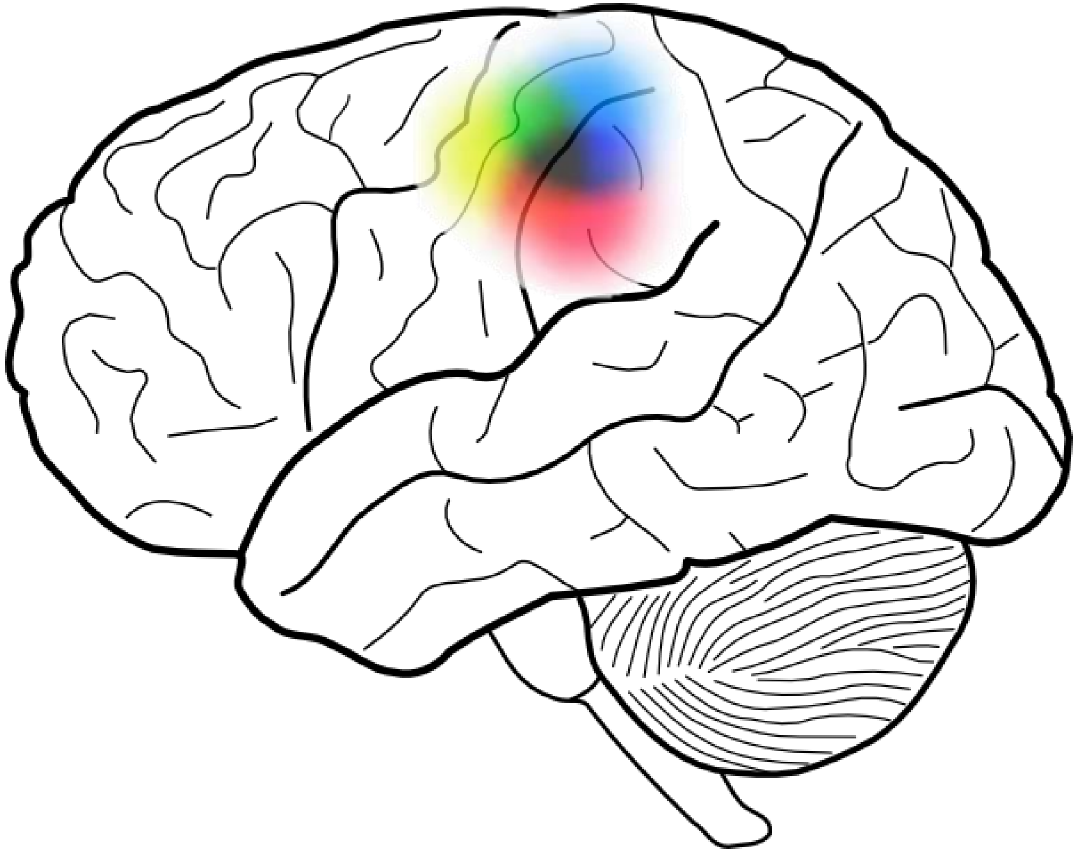


Slice timing corrections may exacerbate movement-related artifacts

Spatial smoothing



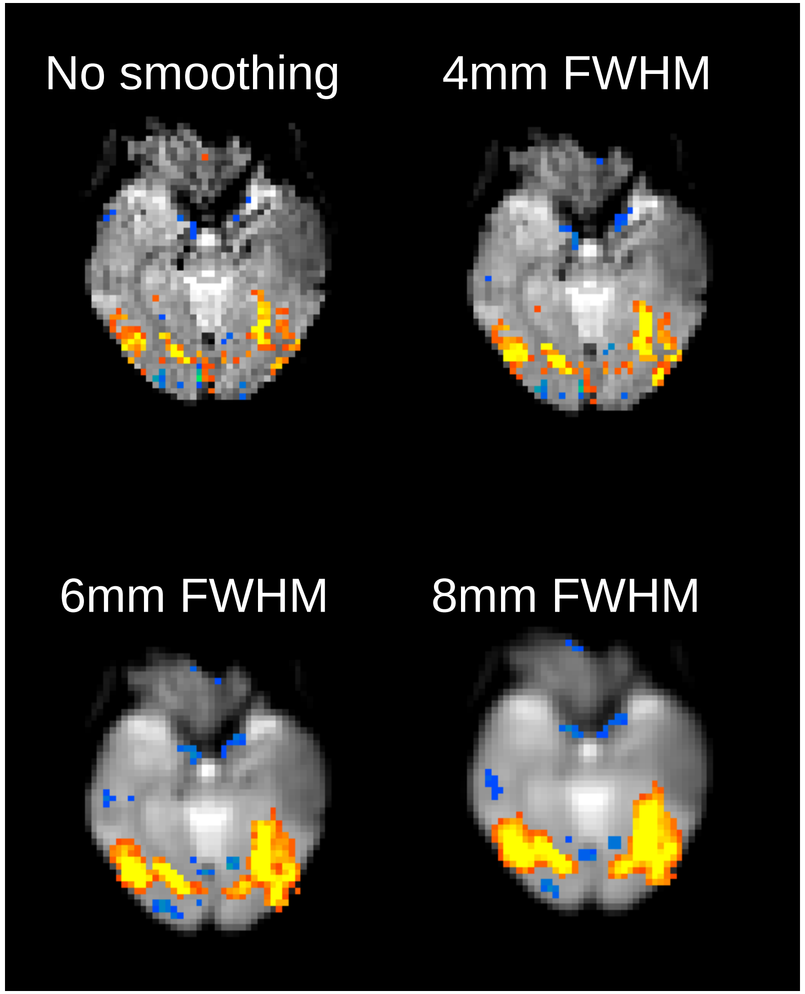
Individual differences in neuroanatomy may result in slightly different areas of activity underlying the same functional representation



Spatial smoothing with a Gaussian filter averages signal from adjacent voxels

Spatial smoothing

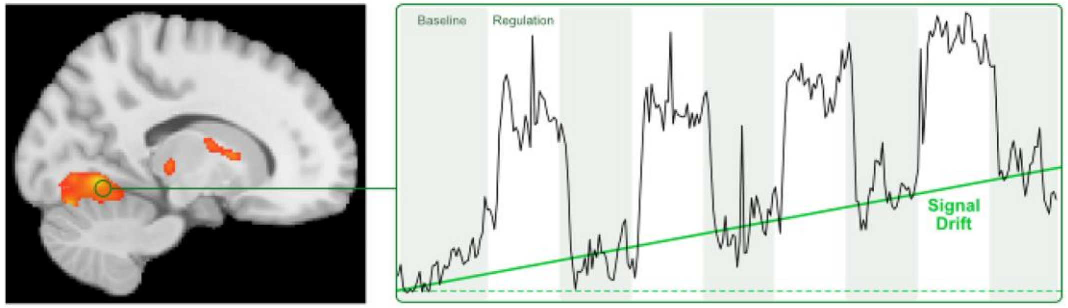
- Benefits
  - Improves SNR and increases sensitivity*
  - Normalizes error distributions
  - Accommodates anatomical/functional variations between subjects
- Drawbacks
  - Reduces spatial resolution of the data
  - Merging of separate clusters
  - Type I errors if smoothing kernel is set too large



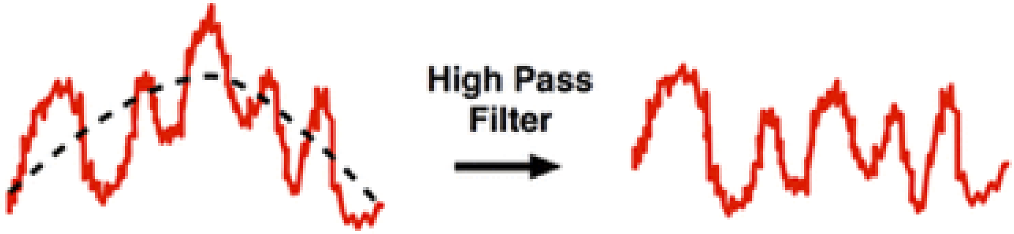
Brain Voyager

Detrending/temporal filtering

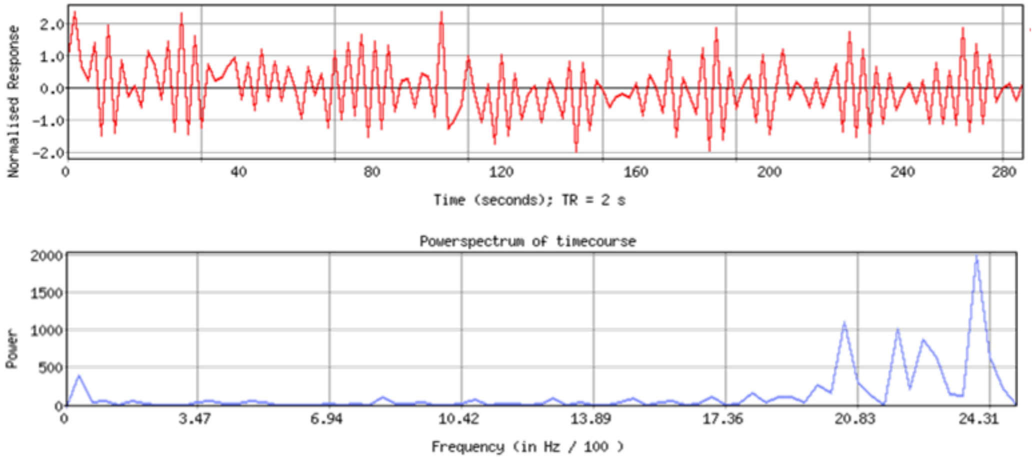
- High pass filter to remove low frequency noise

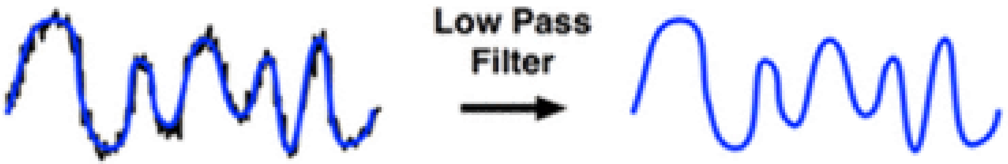


Kopel, 2019, *NeuroImage*



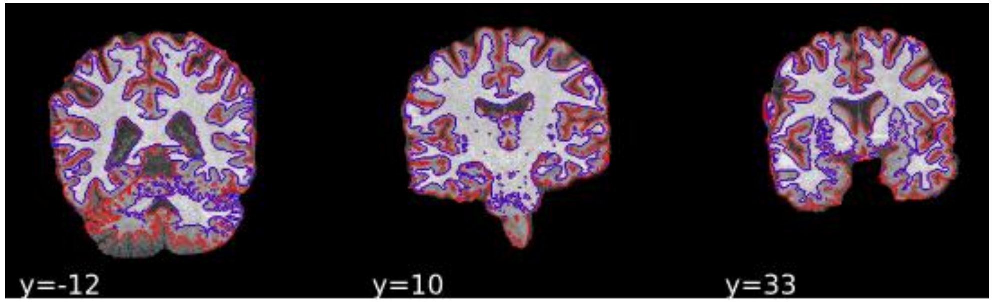
- Low pass filter to remove high frequency noise





Warp to a standard space

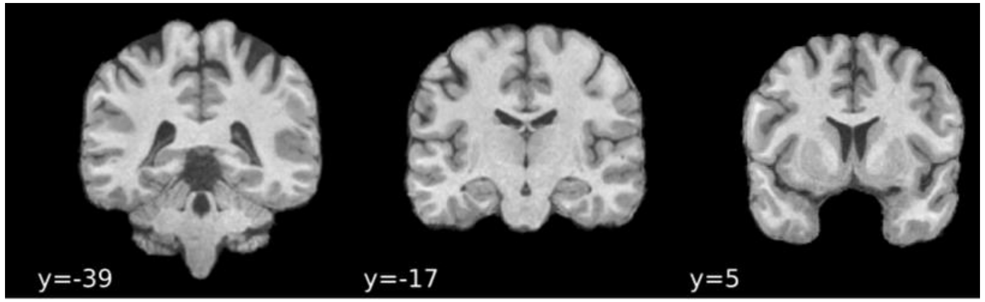
Segment anatomical T1 image



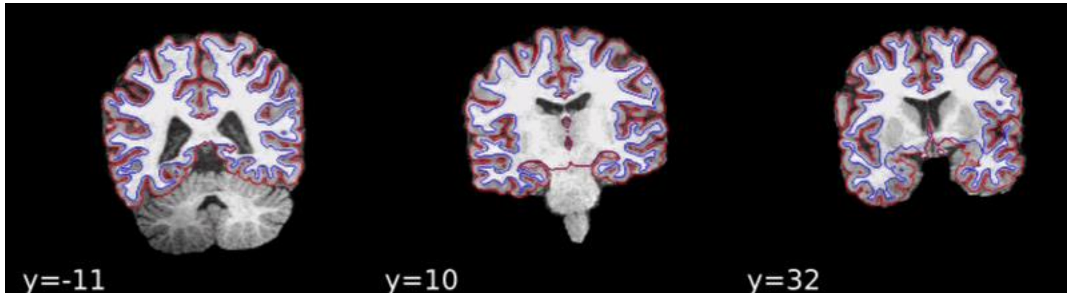
Affine registration

Rigid registration

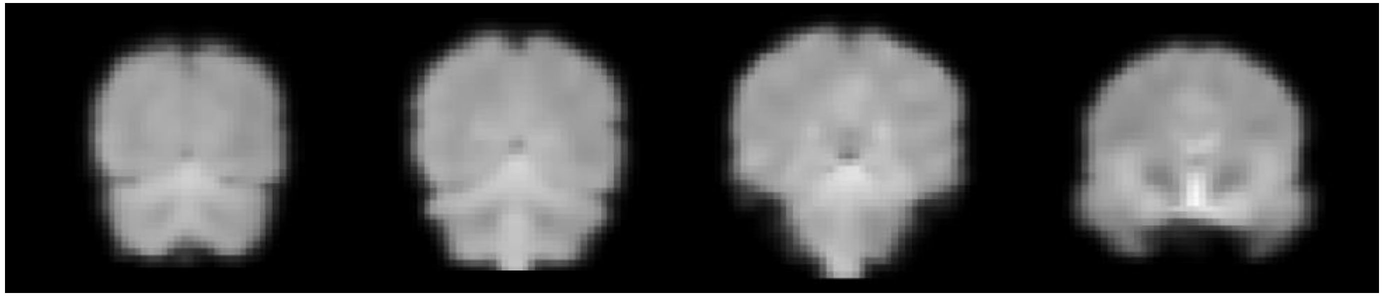
Warp anatomical T1 to template space (e.g., MNI)



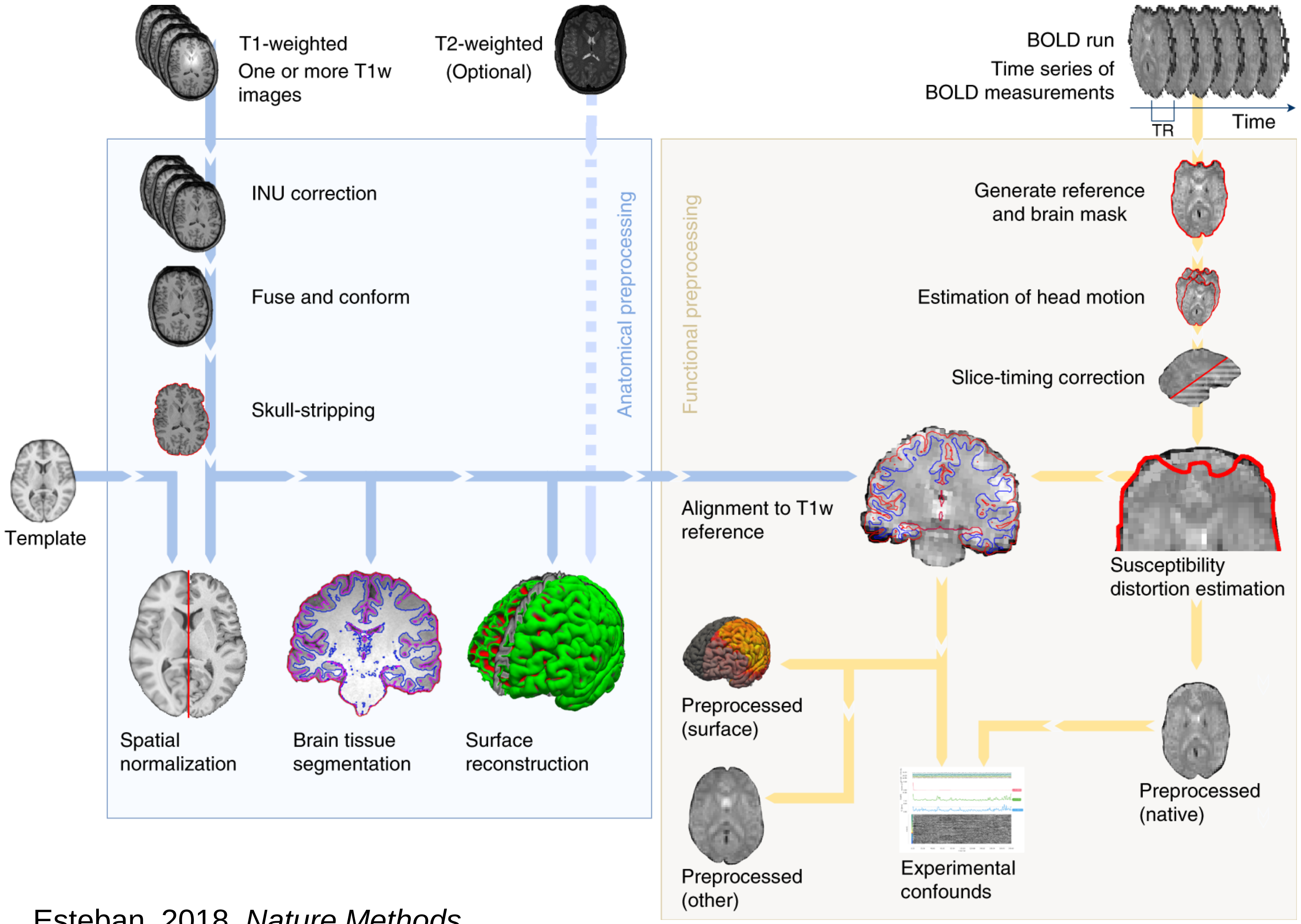
Co-register anatomical T1 and BOLD volumes



Apply transformation matrix to BOLD volumes



Automated tools for preprocessing: fmriprep



fmriprep

Combines tools across software packages

[Visual QC reports]()

Minimal user input

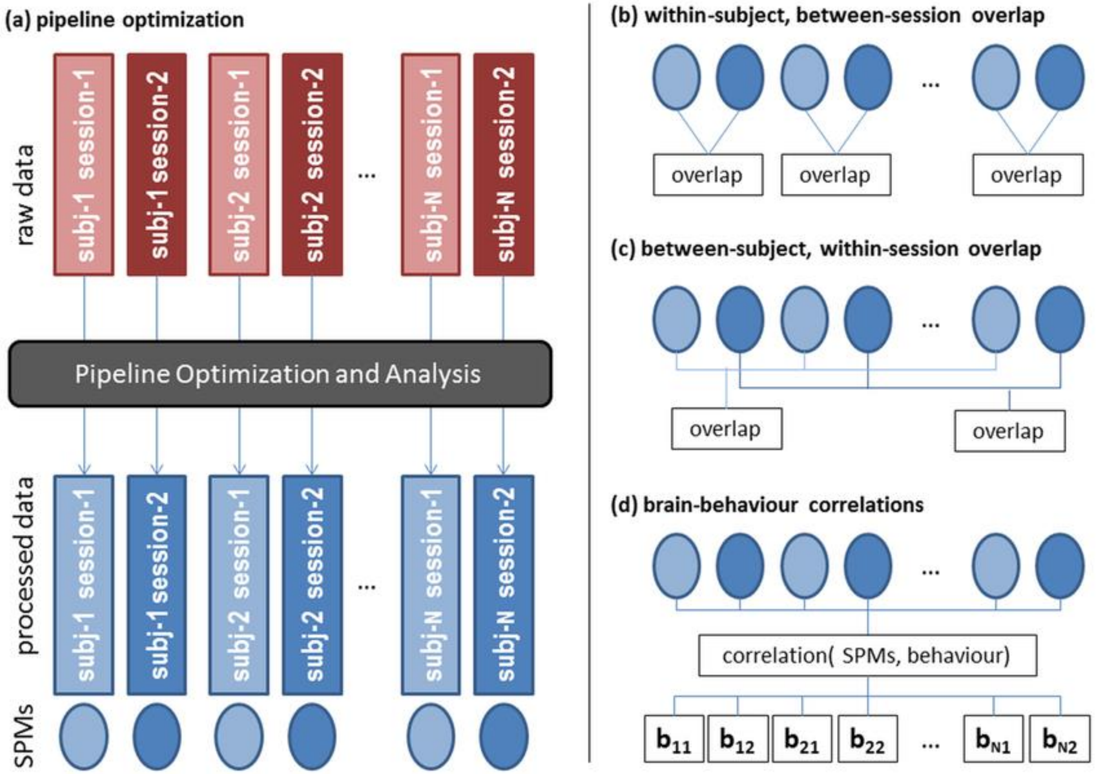
BIDS format

Esteban, 2018, *Nature Methods*

Automated tools for preprocessing: OPPNI

PIPELINE STEPS	CHOICES
1. Estimate minimum-displacement brain volume	ON
2. Rigid-body motion correction	**OFF / ON**
3. Censoring of outlier brain volumes	**OFF / ON**
4. Physiological correction; external physiological measures (RETROICOR)	**OFF / ON**
5. Slice-timing correction	**OFF / ON**
6. Spatial smoothing	6mm FWHM
7. Subject-specific non-neuronal tissue m	
8. Temporal detrending	
9. Motion parameter regression	
10. Global signal regression using Prin	
11. Including task design as a regresso	
12. Physiological correction; multivaria	
13. Analysis model: univariate (GNB) or m	

doi:10.1371/journal.pone.0131520.t001



OPPNI

Turns preprocessing options ON/OFF

Finds “optimal” pipeline via cross validation and task design

Churchill, 2015, *PLoS ONE*

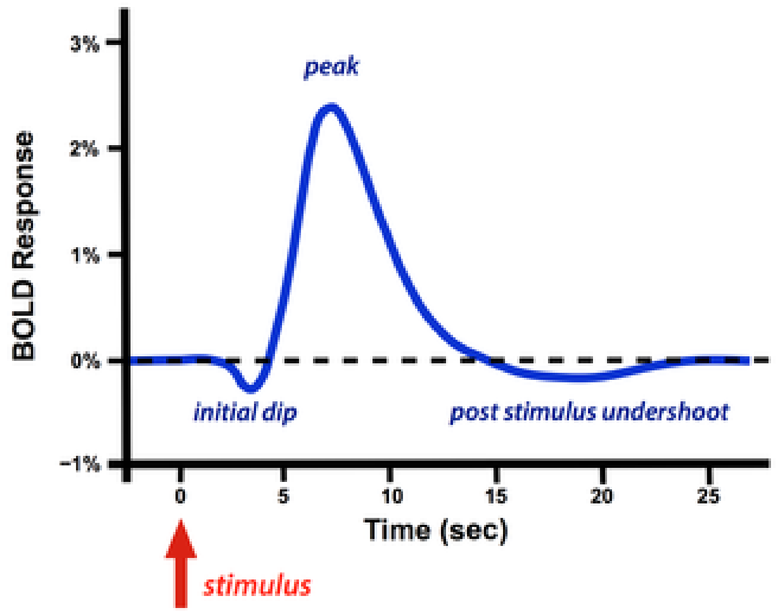
fMRI Analysis (first level)

Typical task-based fMRI analysis steps

1. Pre-process data to deal with noise and artifacts
2. Model expected functional activity corresponding to experimental conditions (design matrix)
3. Predict functional activity in each voxel (most often with multiple regression)
4. Compare functional activity across conditions, groups, or as a function of between-person predictors (e.g., age)

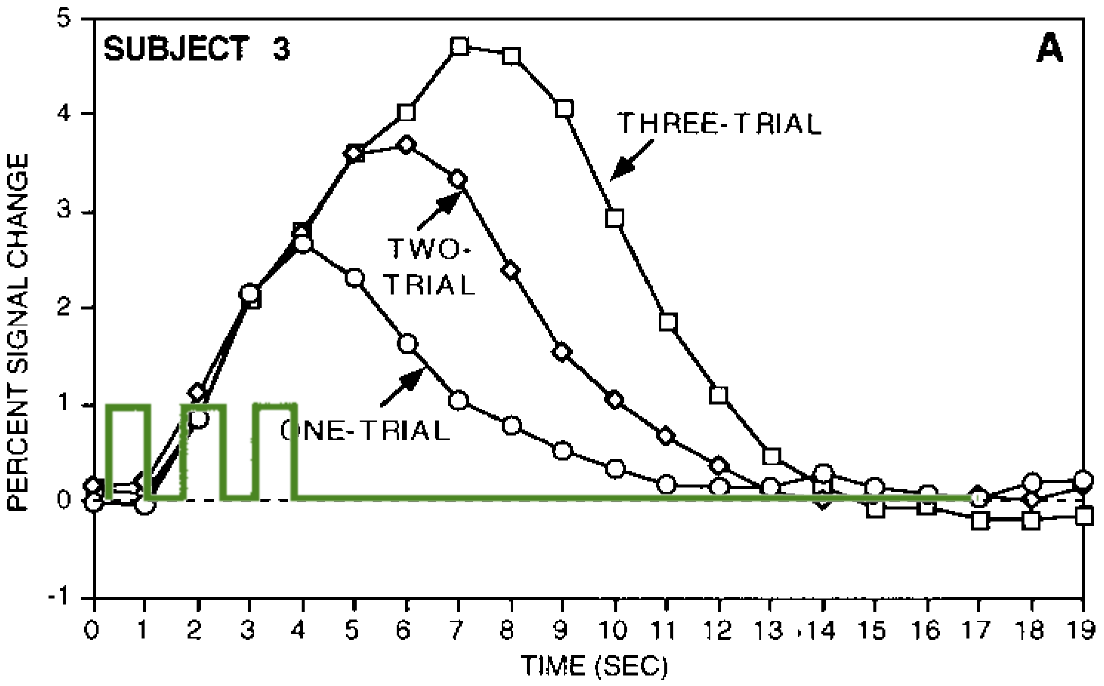
Modeling expected BOLD response

BOLD signal follows an expected shape (HRF)



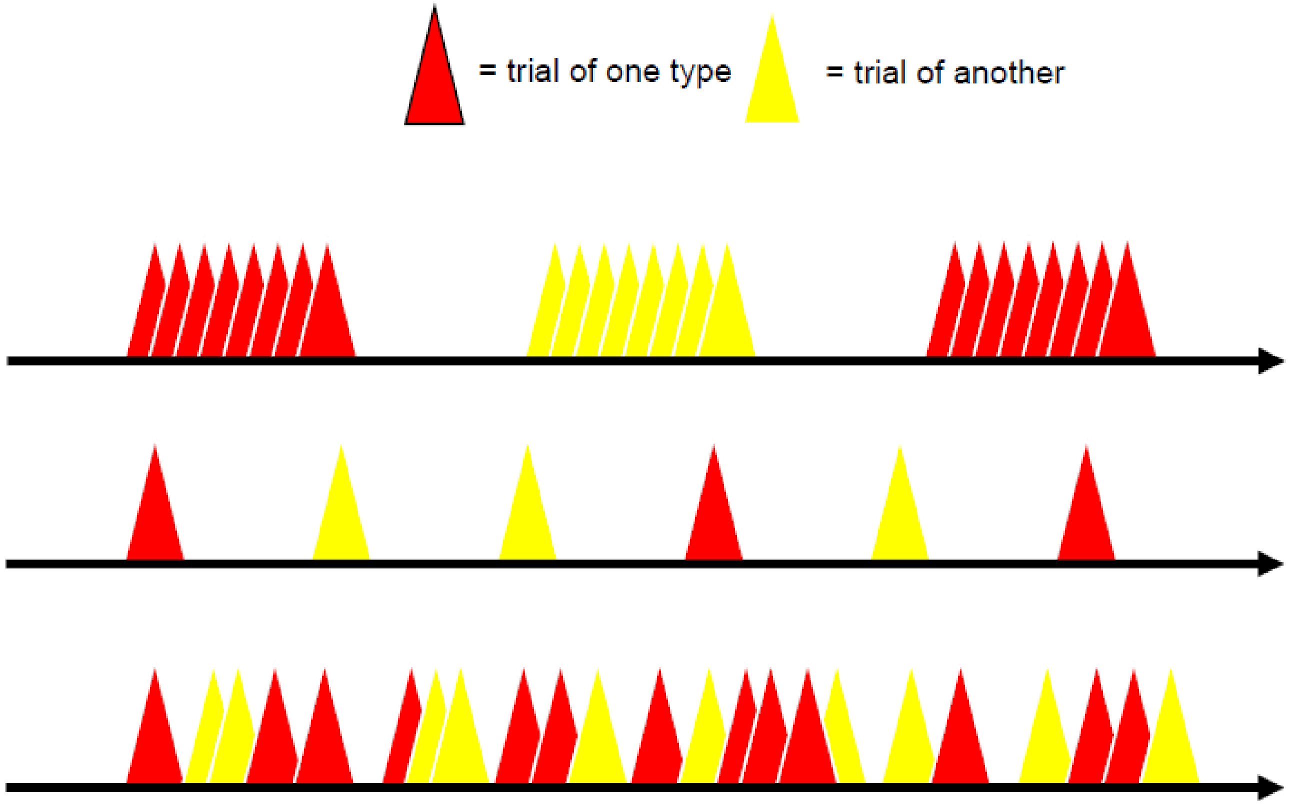
initial dip (~1-2s) → peak (4-8s) → undershoot → return to baseline (~20s)

BOLD signal is additive across trials



Dale & Buckner, 1997, *Hum Brain Mapp*

Types of fMRI experimental designs



Block design

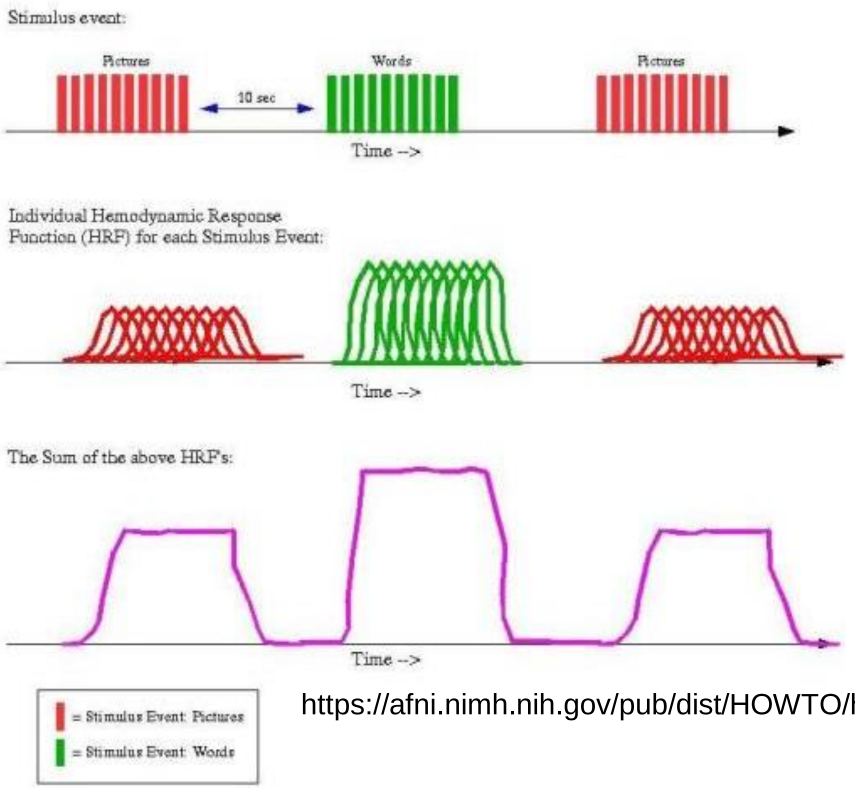
Slow event-related

Rapid event-related

An efficient design requires less scan time for sufficient power

Block design

- Typically, 15-30s blocks per condition
- Same block length for all conditions, block order randomized



https://afni.nimh.nih.gov/pub/dist/HOWTO/howto/

Pros:

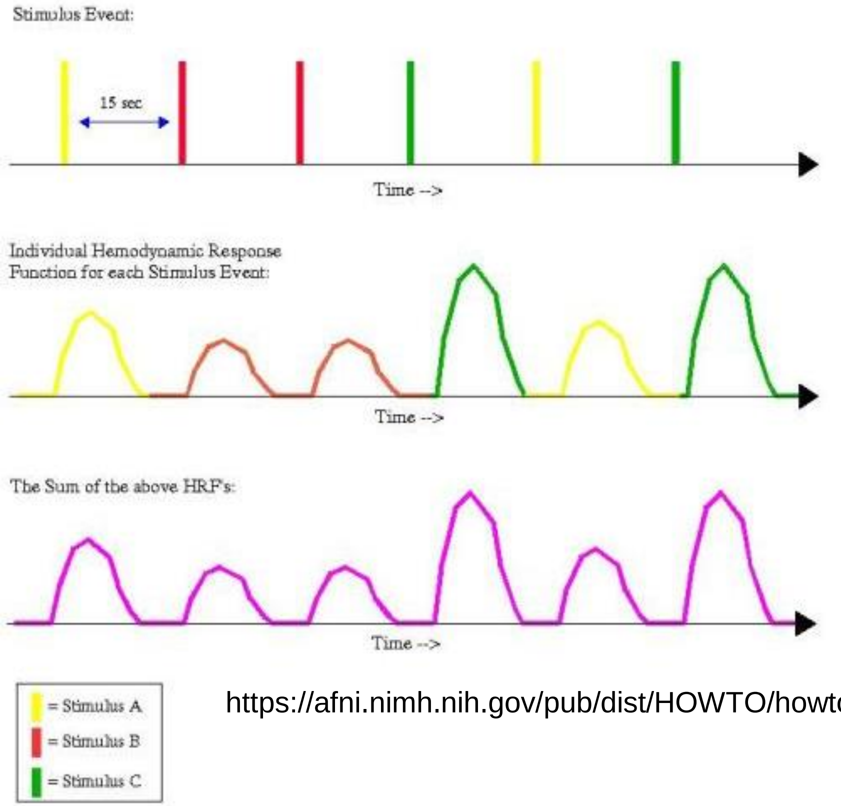
- High signal detection power
- Widely used
- Accurate HRF not as critical
- Experimental flexibility (e.g., parametric, multi-factorial designs)

Cons:

- Cannot look at single trials
- Long blocks may correlate with low-frequency noise
- Strength of BOLD signal can decrease over time

Slow event-related design

- Trials far enough apart to allow HRF to reach baseline after each trial
- At least 12-15s inter-trial interval recommended



https://afni.nimh.nih.gov/pub/dist/HOWTO/howto/

Pros:

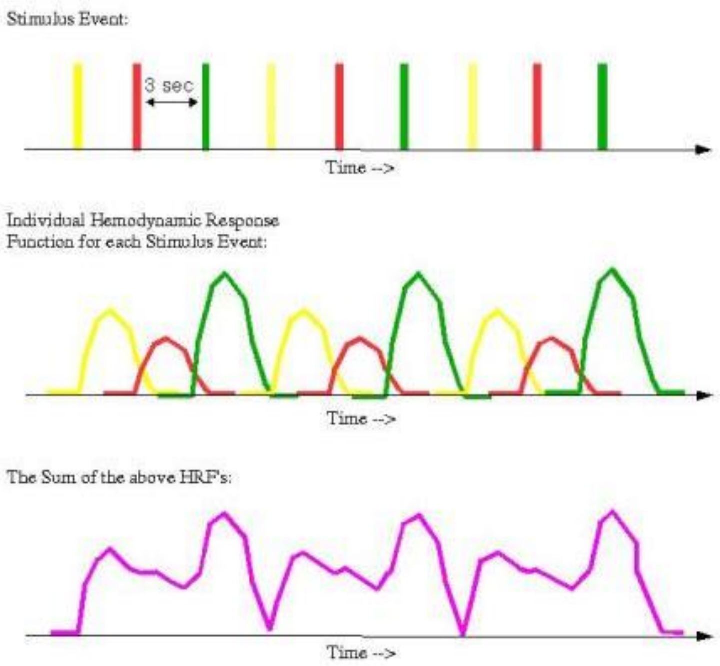
- Accurately model HRF for individual trials
- Examine differences in time course of BOLD response
- Post-hoc sorting of trials (e.g., remembered vs forgotten)

Cons:

- Reduced signal detection (~1% change)
- Either long scan time or fewer trials per condition (inefficient design)
- Participants can get bored
- Does not work with certain tasks (i.e., inhibition tasks like go/no-go)

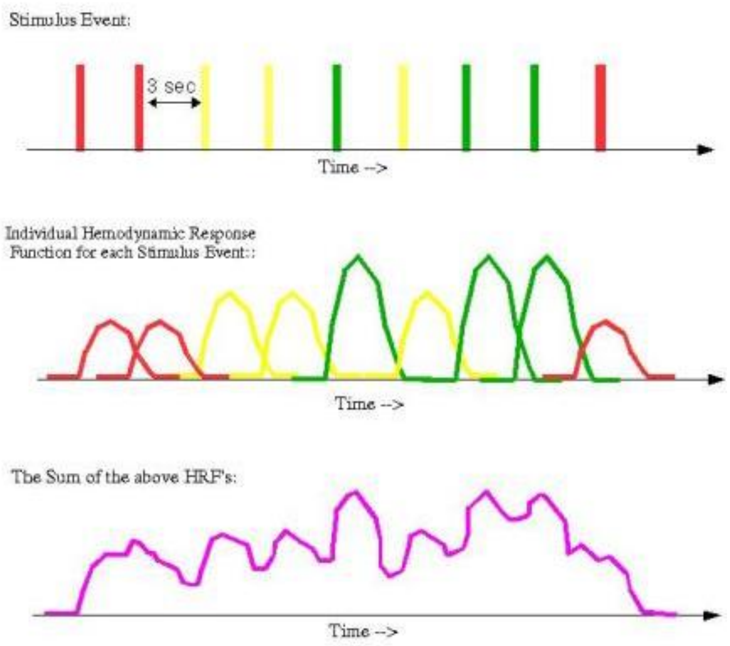
Rapid event-related design

Fixed inter-trial interval,
Non-randomized stimuli order

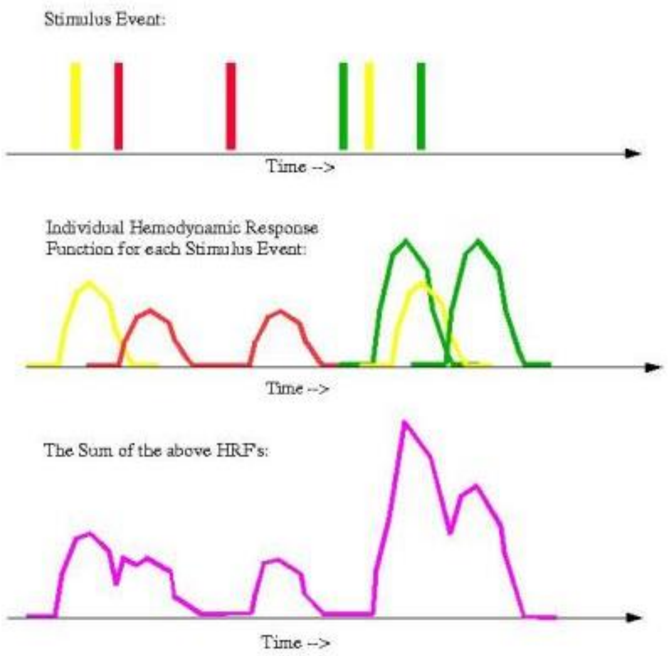


Source condition of the observed HRF is ambiguous

Fixed inter-trial interval,
Randomized stimuli order



“Jittered” inter-trial interval,
Randomized stimuli order



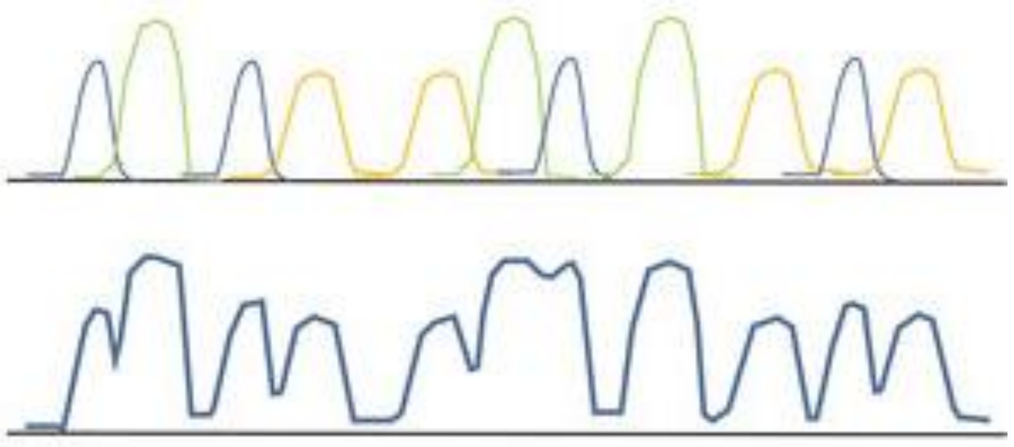
Randomization provides more degrees of freedom to deconvolve overlapping HRFs

Rapid event-related design

- Randomization (trial order, inter-trial interval) is crucial

Pros:

- Efficient design (many trials in less time)
- Model HRF for individual trials
- Post-hoc trial sorting (e.g., remembered vs. forgotten)



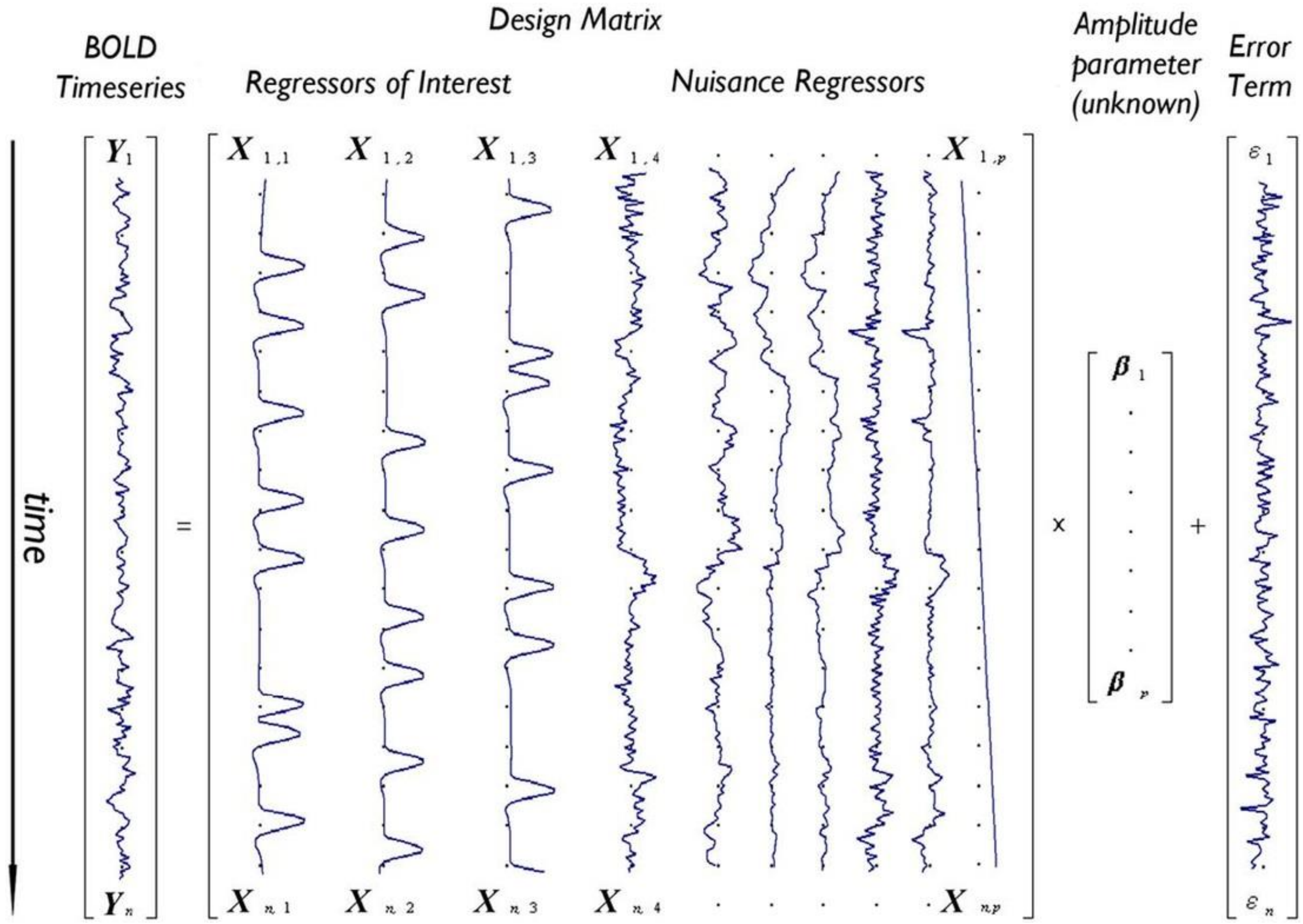
Event-related design

Cons:

- Reduced signal detection (~1% change expected)
- Dependent on accurate HRF modeling (may differ by brain region or population)

Predicting functional activity

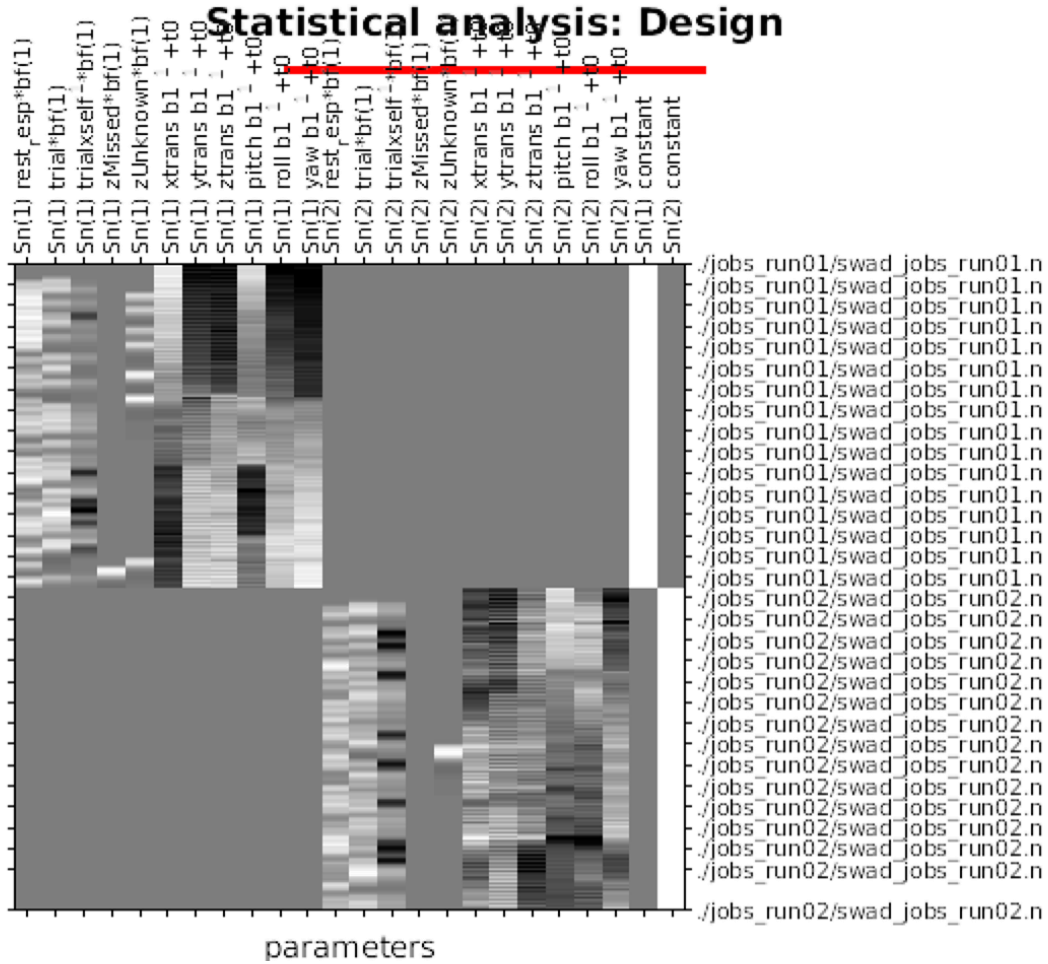
- Model each voxels activity with multiple regression (GLM)
    - Task design
    - Nuisance covariates
- Whole brain map (beta-weights) for each regressor (estimate of BOLD amplitude for specific conditions)



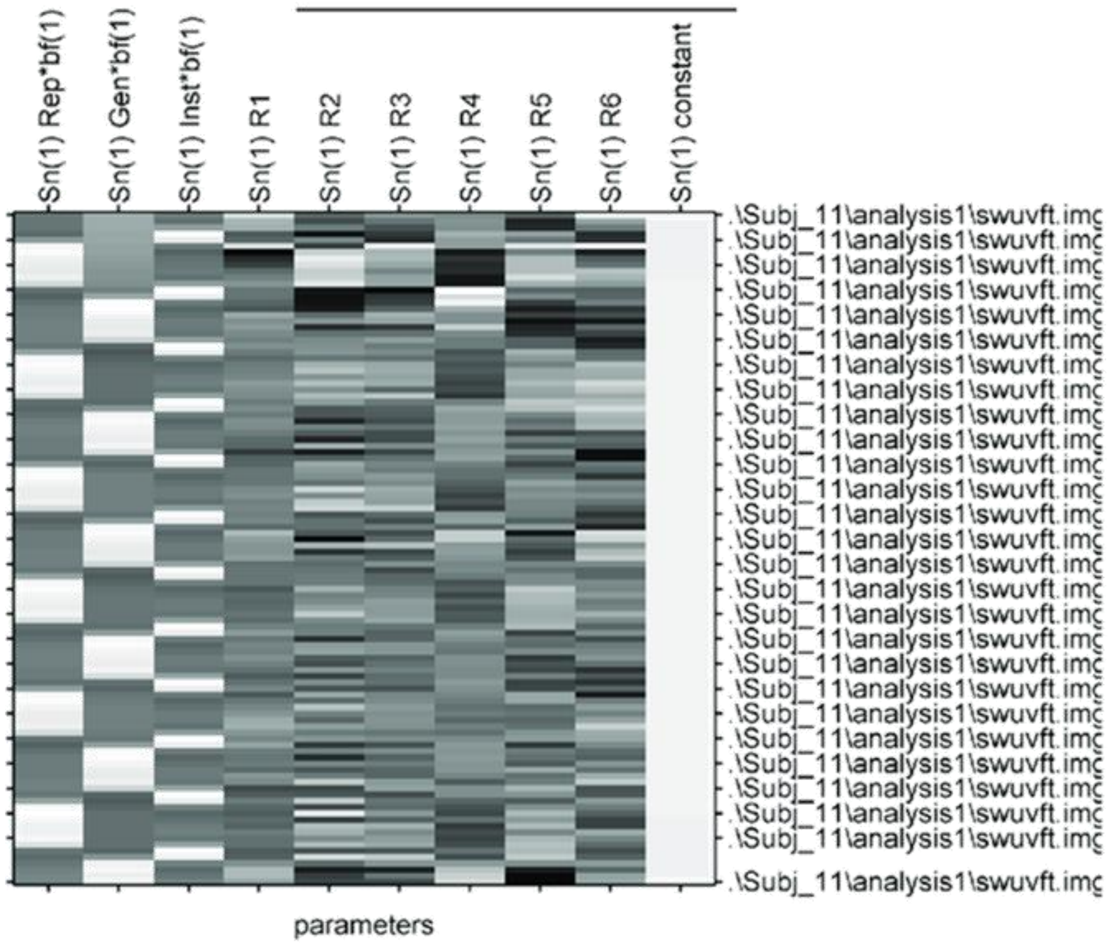
Monti, 2011, *Front Hum Neurosci*

Predictors can be visualized with a design matrix

Time (each row a volume)



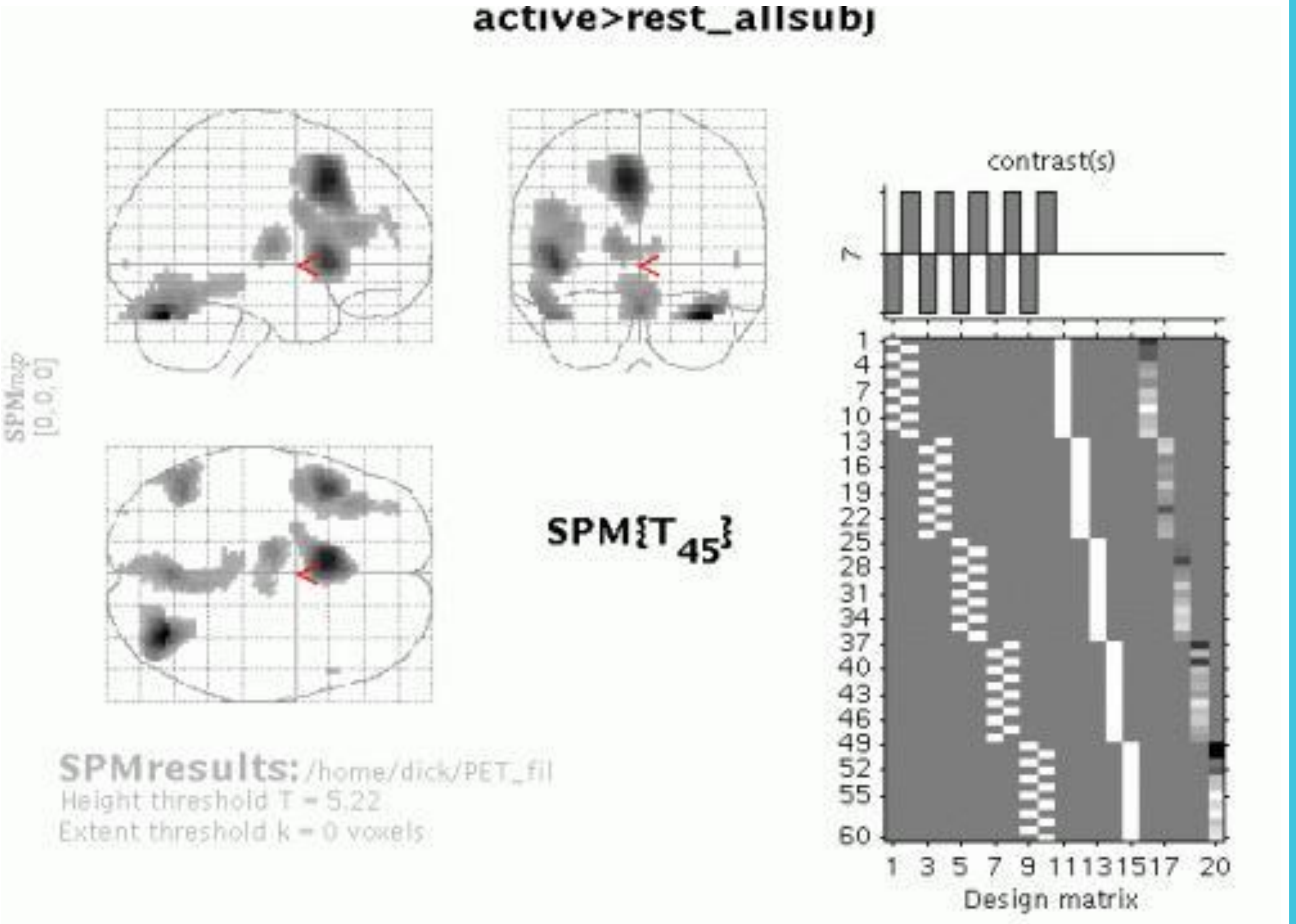
Event-related design (2 scan sessions) + 6 motion parameters



Block-design design (1 run) + 6 motion parameters

Contrasts to examine changes in activity

- Statistical tests to compute differences in functional activity associated with predictors
- t-contrast to test difference between 2 conditions (signed)
- F-contrast to test variance explained by set (2+) predictors (unsigned)



Active vs. rest blocks t-test across 5 runs

[-1 1 -1 1 -1 1 -1 1 -1 1]

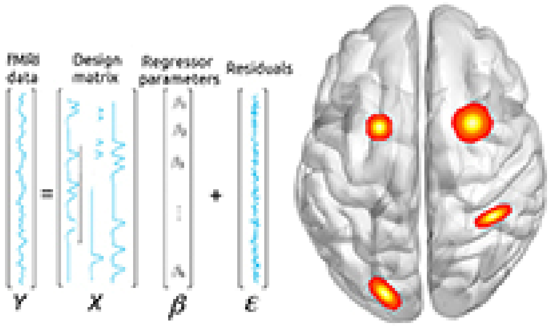
fMRI Analysis (second level)

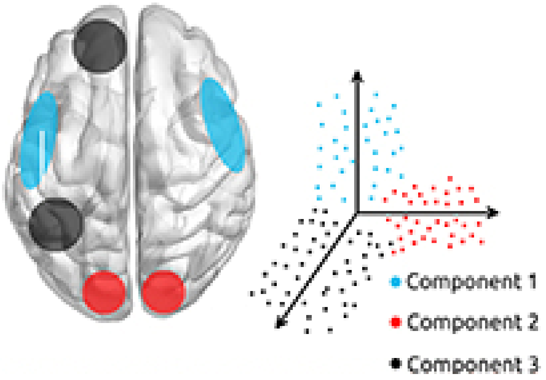
Typical task-based fMRI analysis steps

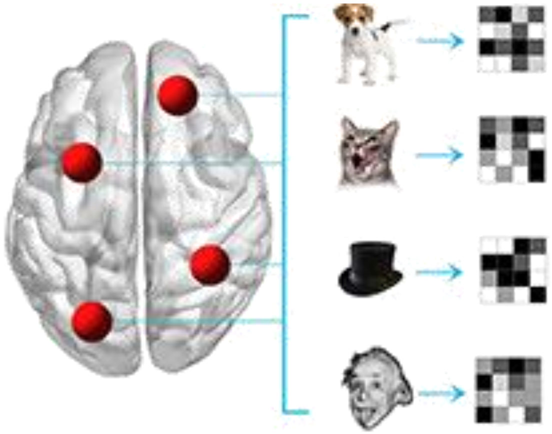
1. Pre-process data to deal with noise and artifacts
2. Model expected functional activity corresponding to experimental conditions (design matrix)
3. Predict functional activity in each voxel (most often with multiple regression)
4. Compare functional activity across conditions, groups, or as a function of between-person predictors (e.g., age)

Analysis approaches

- Voxel-level univariate approaches
  - GLM-based (ANOVA, multiple regression)
- Multivariate approaches
  - Partial least squares
  - Representational spaces
    - Multivoxel pattern analysis (MVPA)/decoders
    - Representational similarity analysis



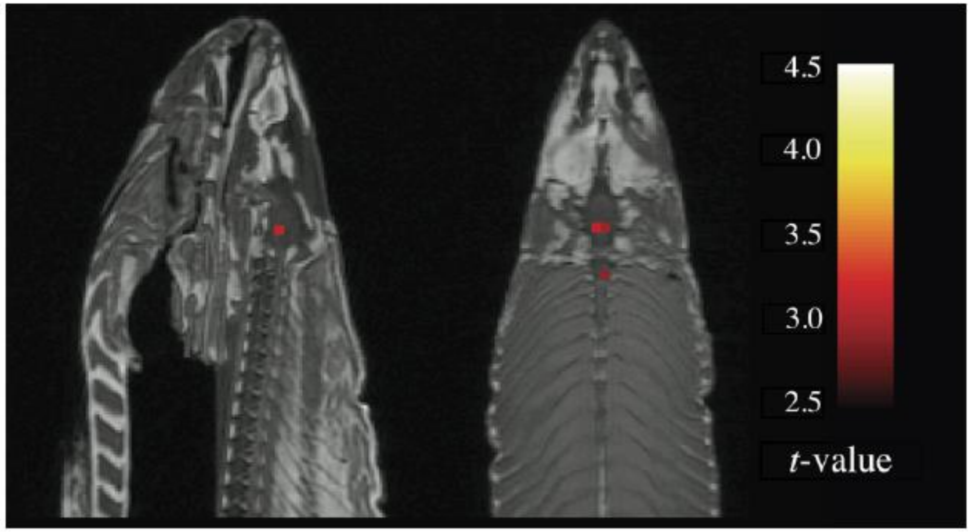




GLM-based univariate approaches

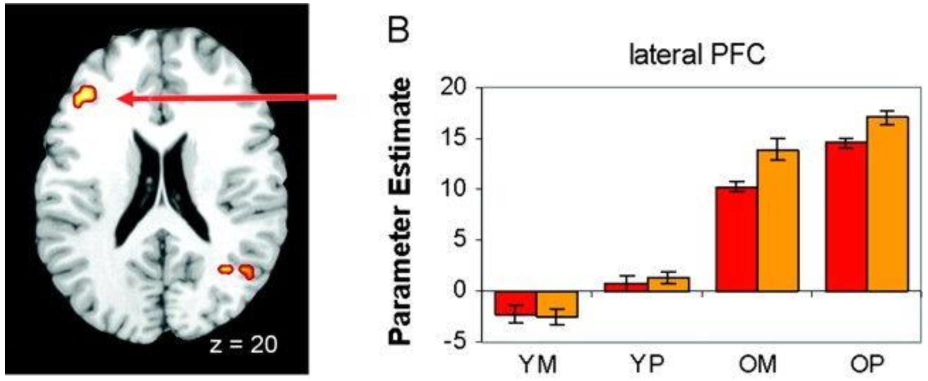
- Compute a statistical test (e.g., regression, ANOVA) for each voxel (or region of interest) in a brain map
- Beware of Type II (false positive) errors
  - Typical brain is ~30k – 100k separate voxels, which may yield ~1.5k – 5k false positives with typical p < .05 threshold
- Cluster-based multiple comparison corrections balance Type I and Type II error

Dead salmon with "significant" activation

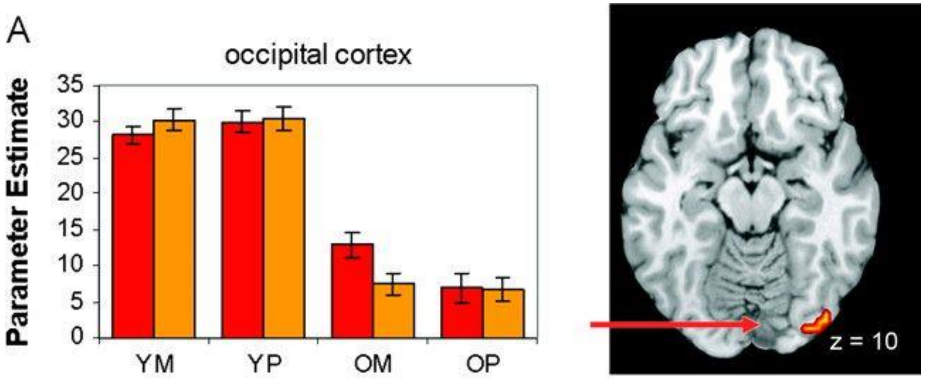


Bennett, 2009, *NeuroImage*

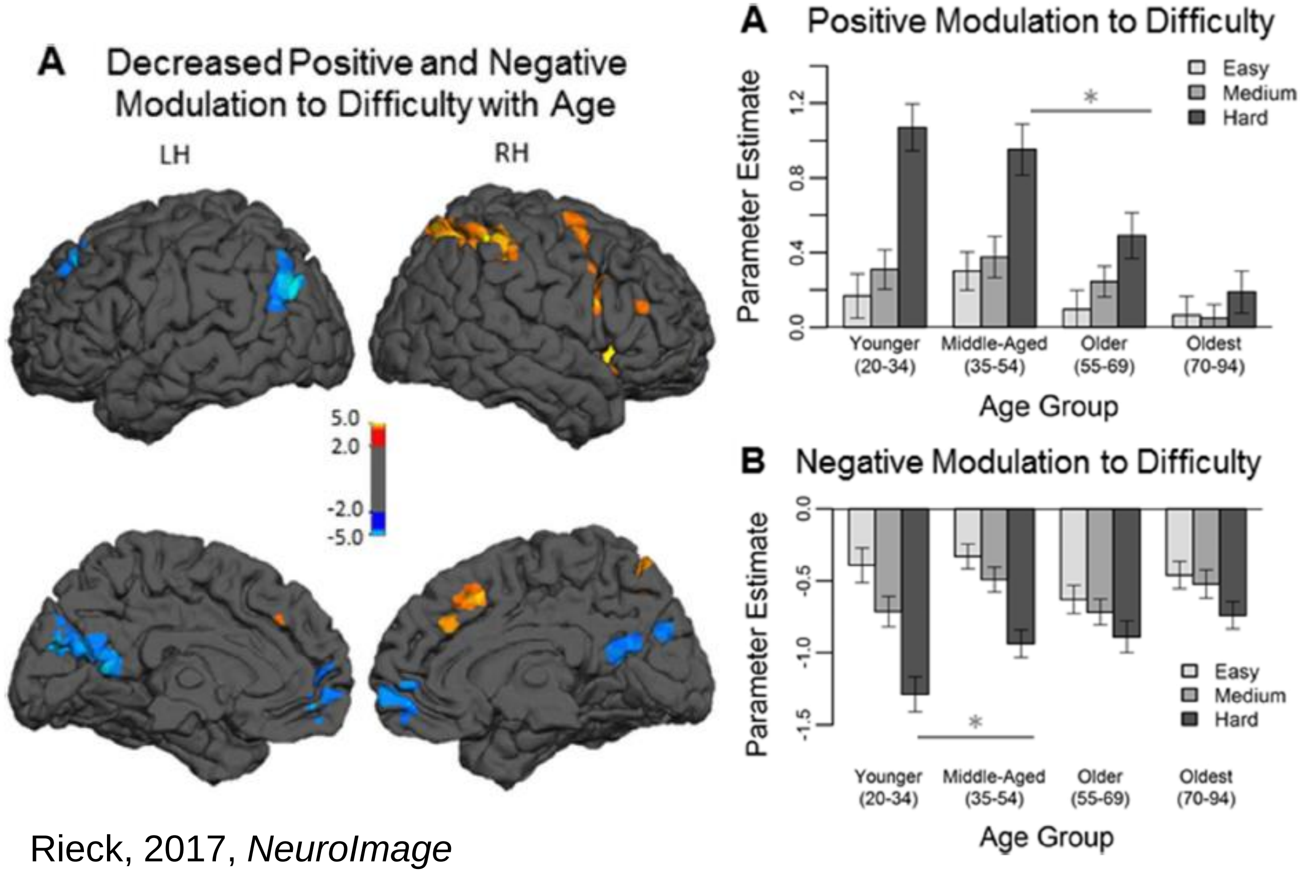
Effects of age on amplitude of fMRI activity



Older adults show greater activity in anterior cortex and less activity in posterior cortex



Davis, 2007, *Cereb Cortex*

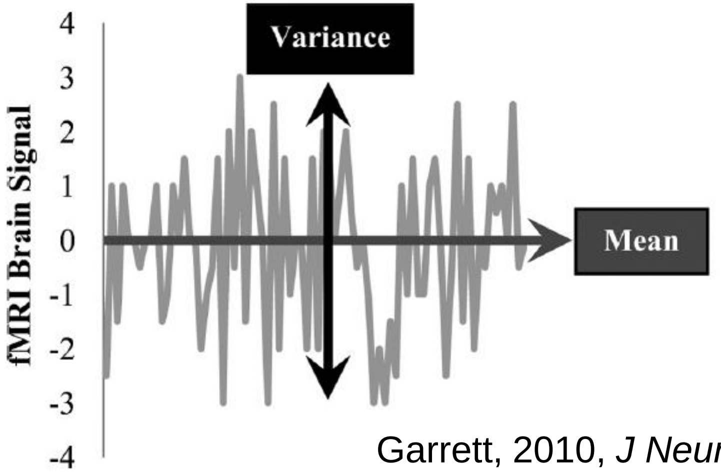


Rieck, 2017, *NeuroImage*

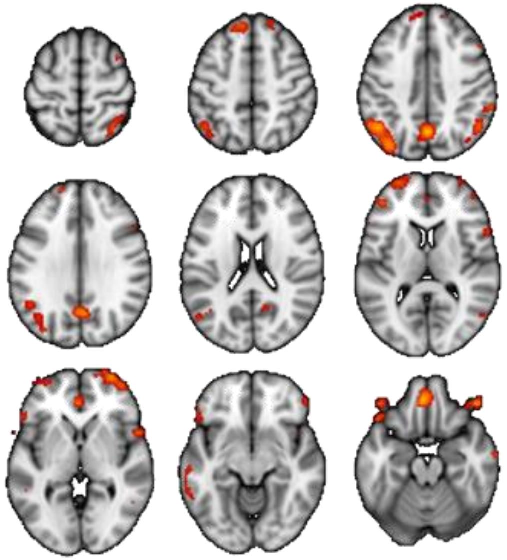
Older adults show less changes in functional activity across difficulty levels

More than amplitude: BOLD variability

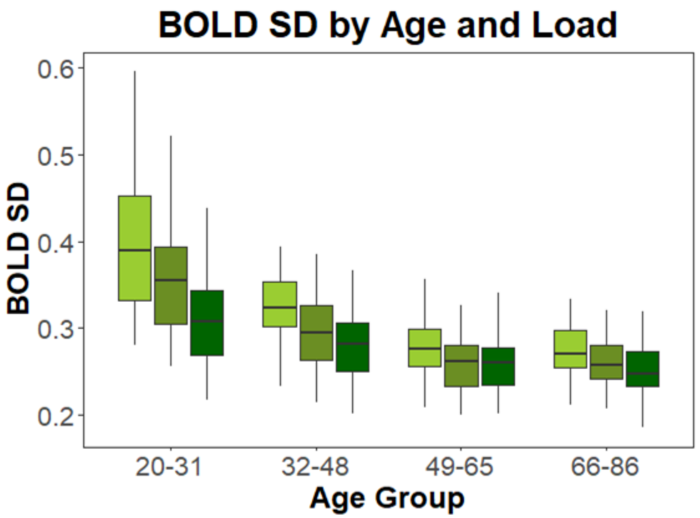
- BOLD variability measures moment-to-moment fluctuations in BOLD signal
- Sensitive to individual differences in cognition and aging



Garrett, 2010, *J Neurosci*



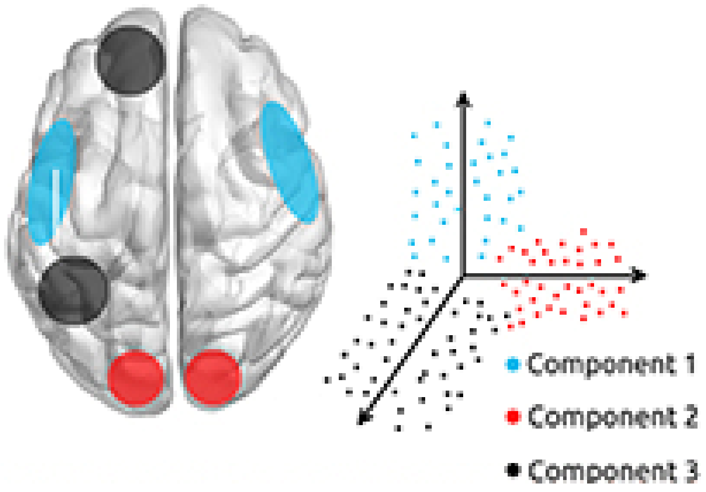
In older age, BOLD variability is decreased and shows less modulation to cognitive load



Rieck, under review, *Neurobio Aging*

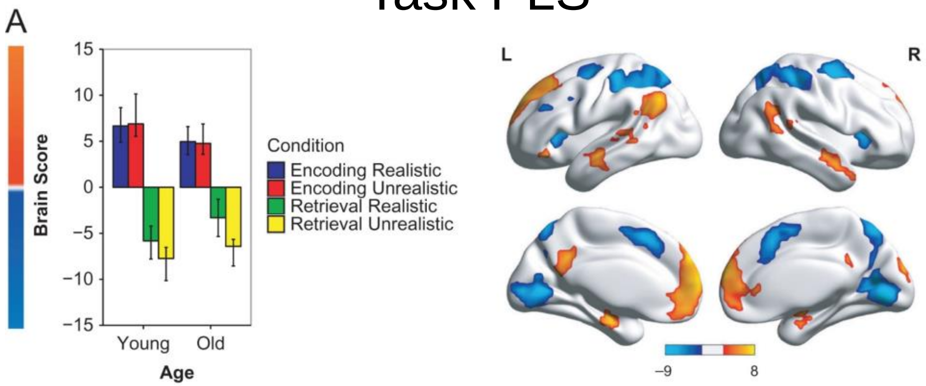
Partial least squares (PLS) analysis

- Multivariate data-driven approach to analyzing patterns of functional activity associated with different task conditions, participant groups, and/or covariates
- Singular value decomposition to derive “latent variables” (aka components, factors)
- Inference testing based on non-parametric resampling

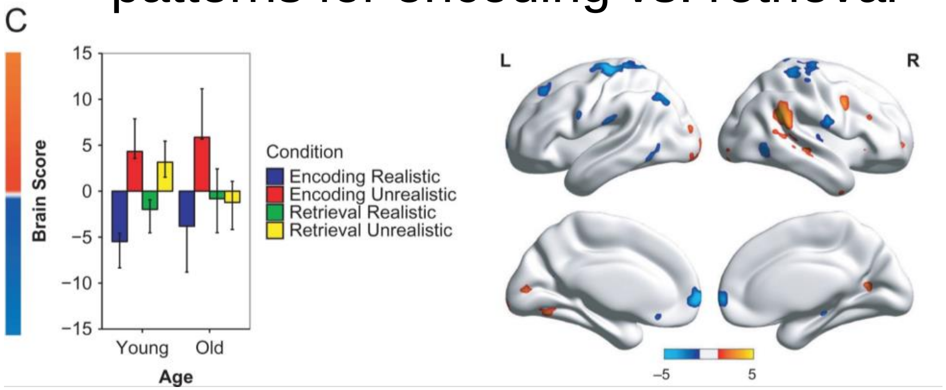


Using partial least squares in aging

Task PLS



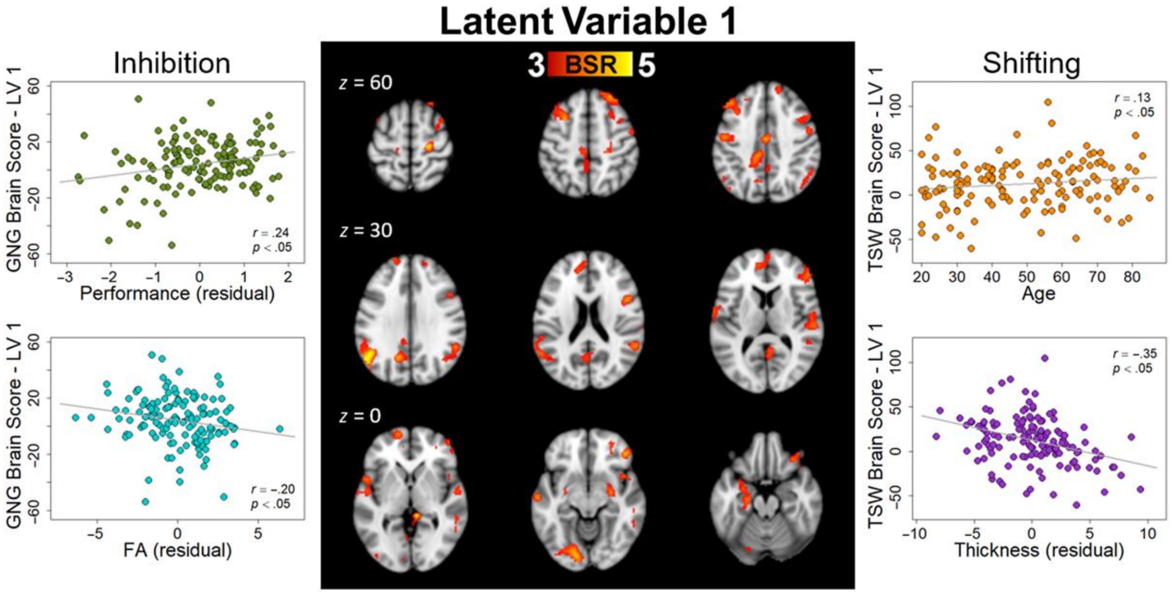
Both young and older adults show robust patterns for encoding vs. retrieval



Older adults do not show separable patterns during retrieval of realistic vs. unrealistic items

Amer, 2019, *Cereb Cortex*

Behavioral PLS

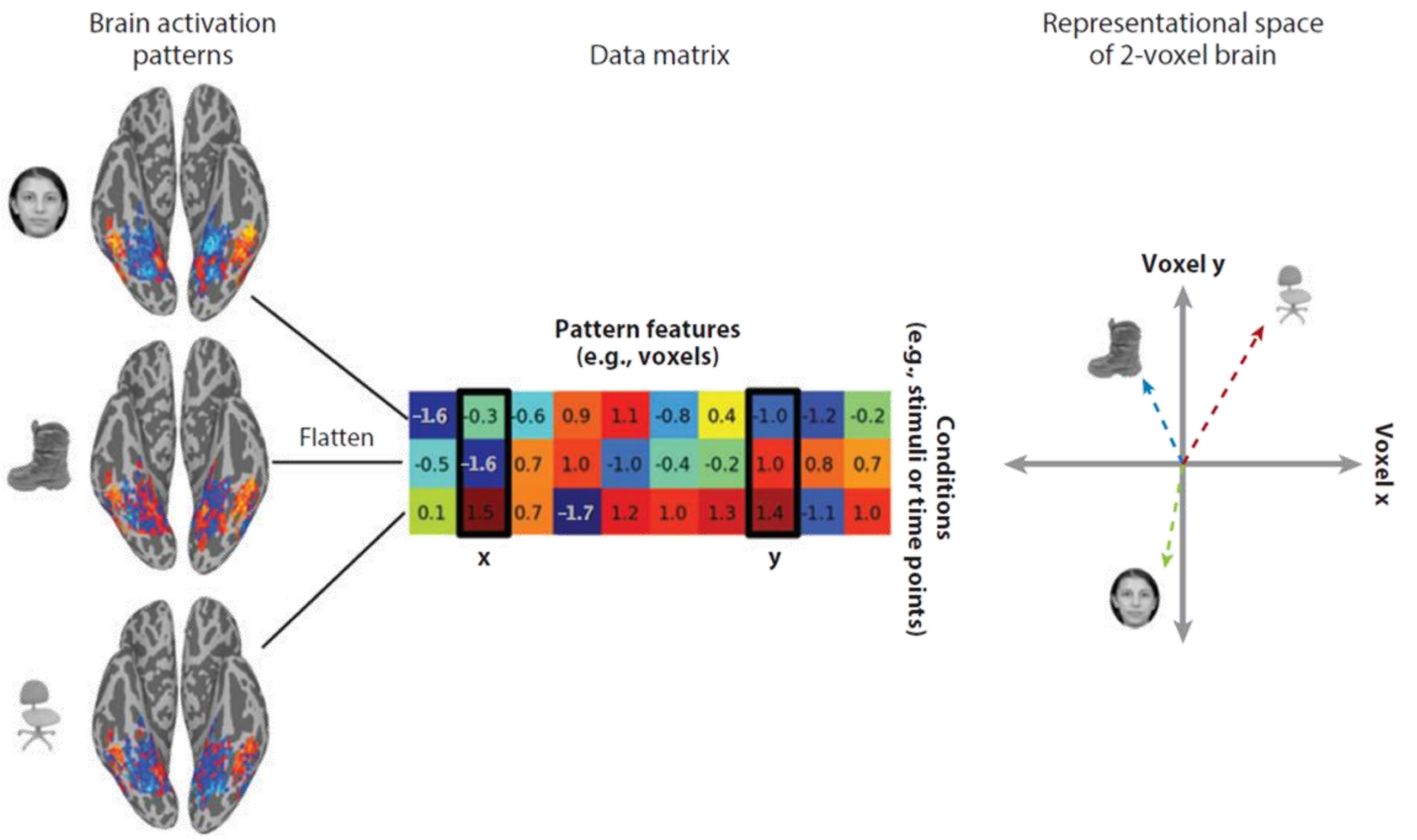


Patterns of default mode activity show differential relationships with age, performance, and brain structure based on cognitive control domain

Rieck, 2021, *J Cog Neurosci*

Representational spaces

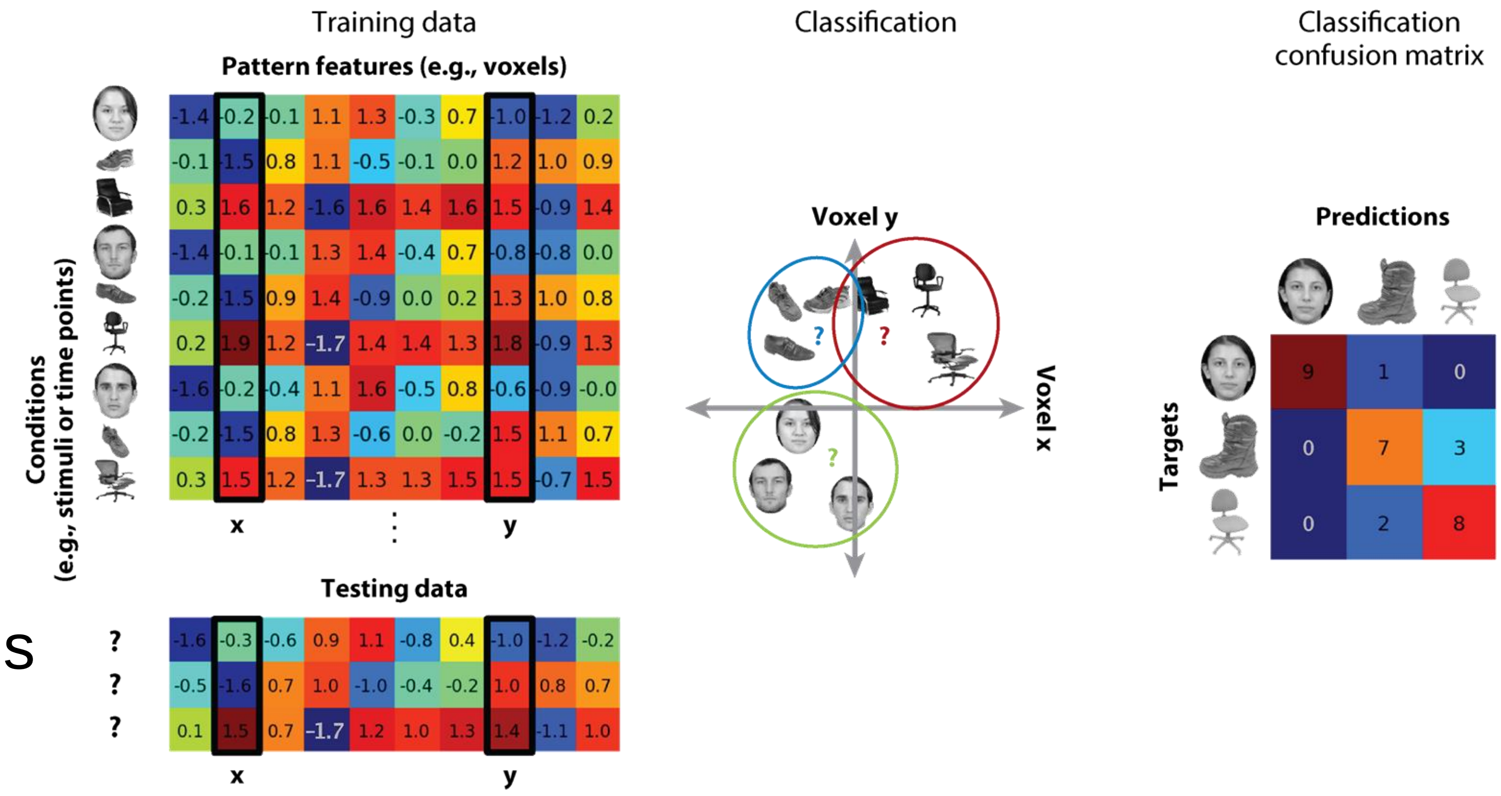
- Distributed patterns of functional activity associated with each stimulus analyzed as vectors within a high dimensional space



Haxby, 2014, *Ann Rev Neurosci*

Multivariate pattern analysis (MVPA)

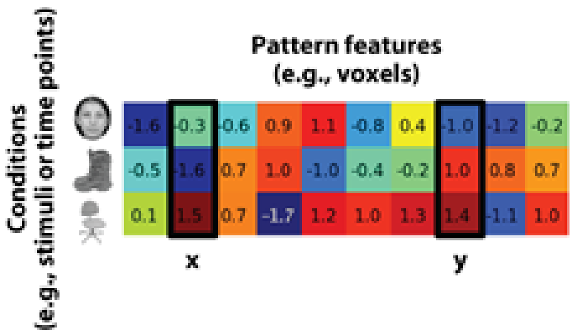
- Use the representational space to predict task condition
- Generally based on ML/ classifier algorithms:
  - Support vector machine
  - Neural networks
  - Linear discriminant analysis
- Involves training and test sets

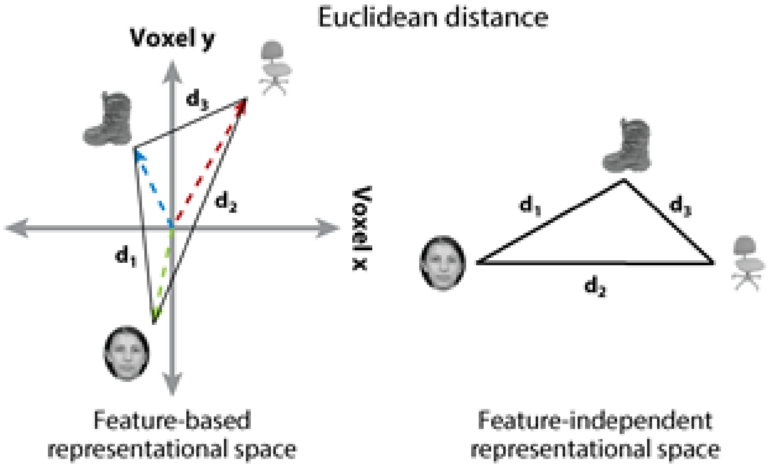


Haxby, 2014, *Ann Rev Neurosci*

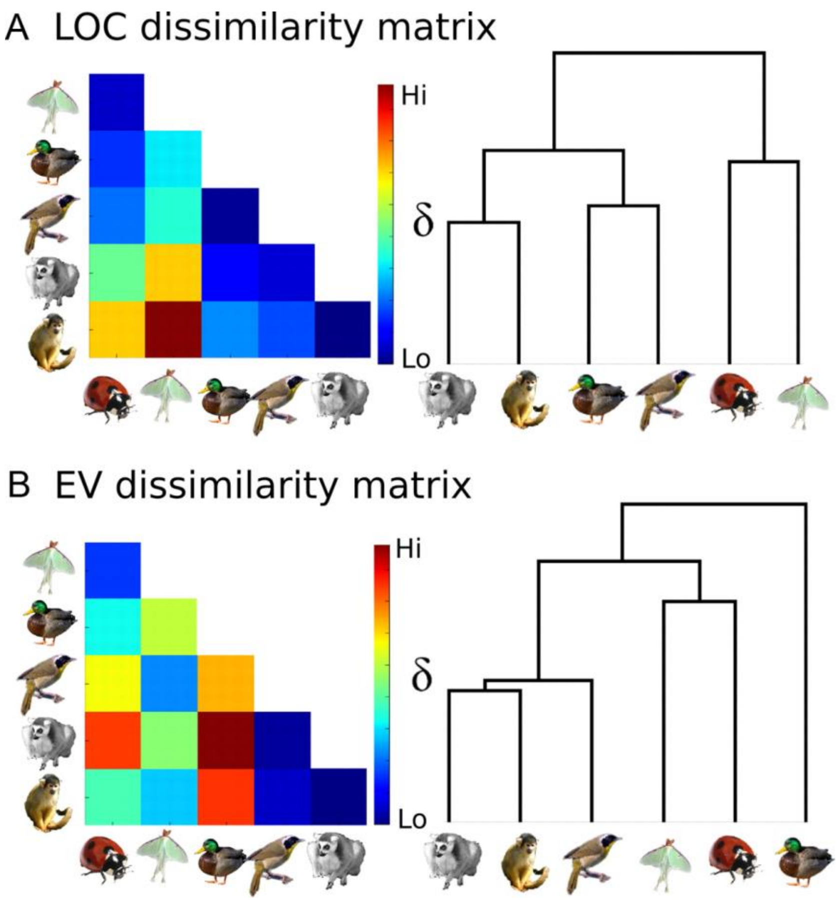
Representational similarity analysis (RSA)

- Use the representational space to examines similarity (and dissimilarity) of patterns of functional activity
- Compute distances between vectors to create dissimilarity matrix





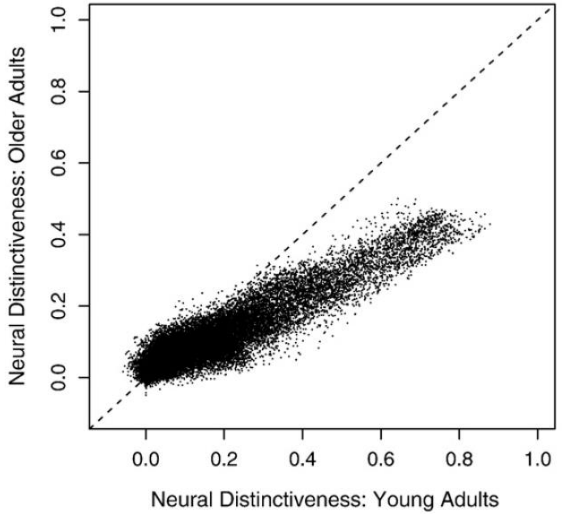
Haxby, 2014, *Ann Rev Neurosci*

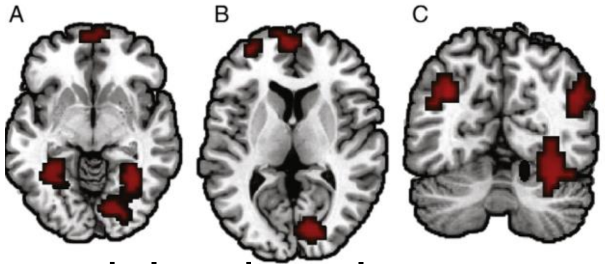


Connolly, 2012, *J Neurosci*

Representational analyses in aging

Multivariate pattern analysis

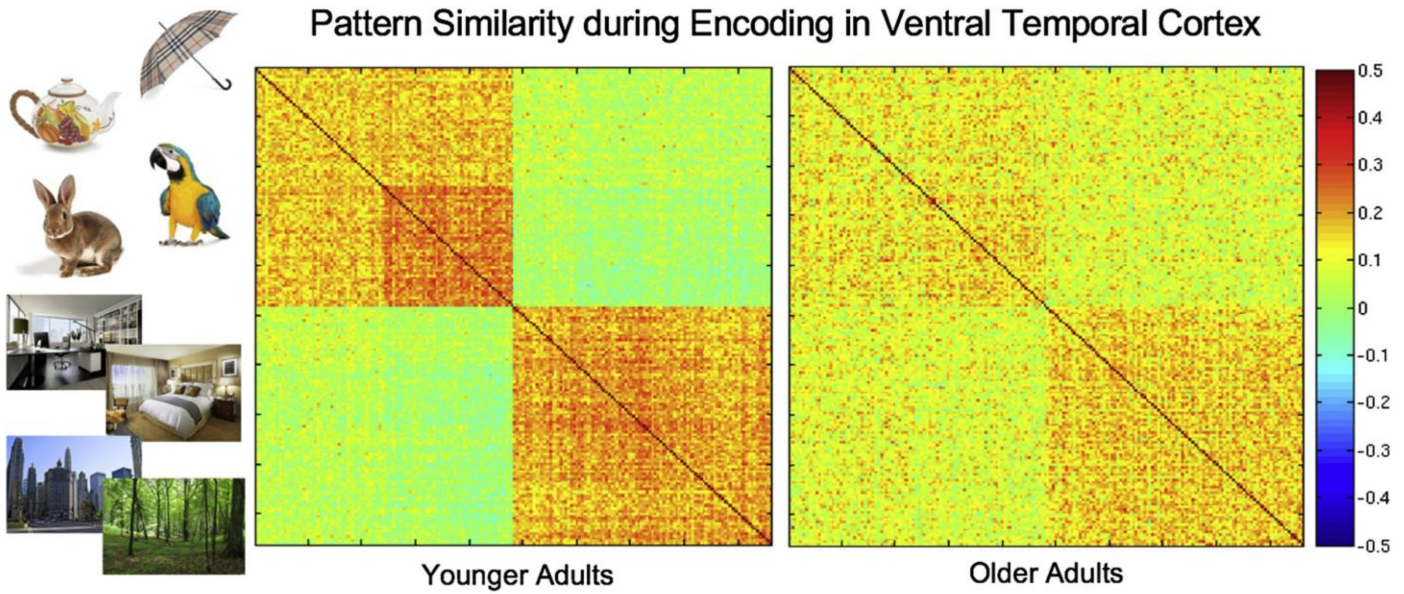




Older adults show less neural distinctiveness for decoding faces vs. houses across the brain

Carp, 2011, *NeuroImage*

Representational Similarity Analysis

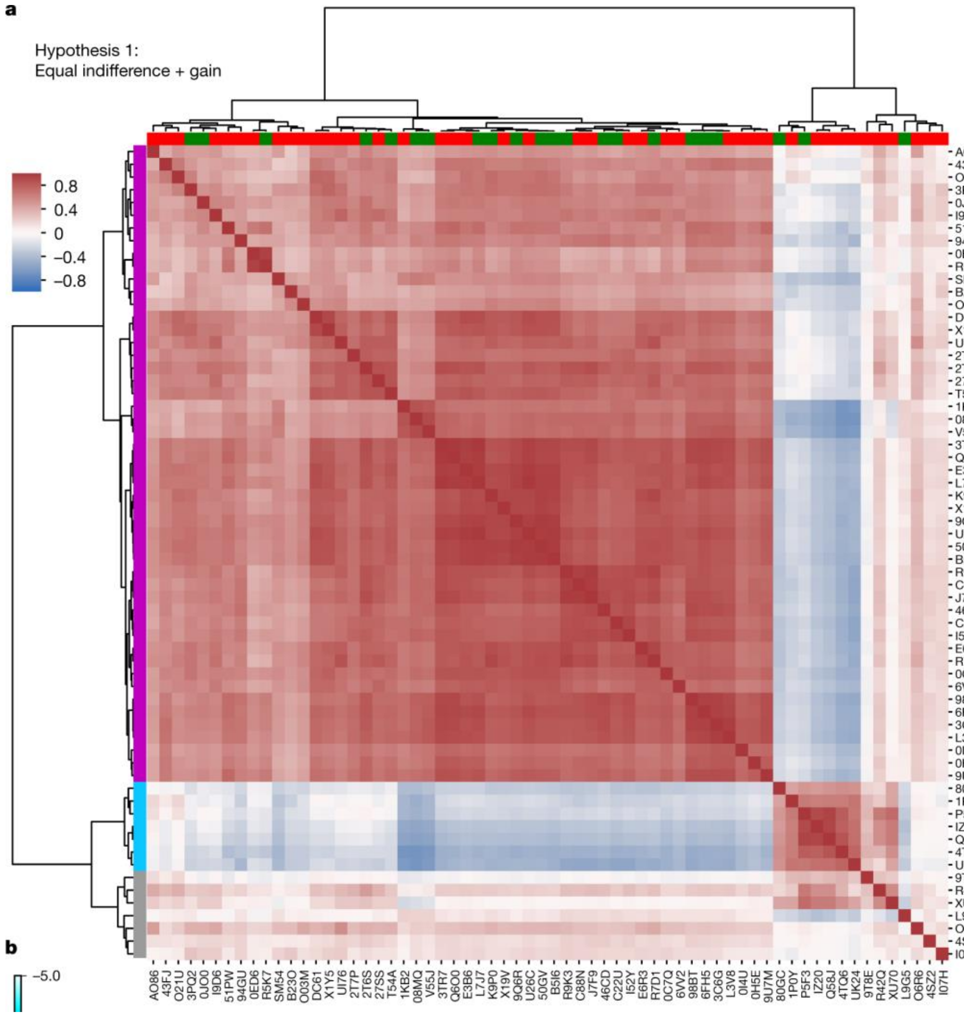


Older adults show greater similarity in neural representations underlying different stimulus categories (items vs. scenes)

Trelle, 2019, *Neurobio Aging*

Which approach is best?

- Depends on your research question!
- Considerations:
  - Complexity of task design
  - Hypothesis driven vs. exploratory?
- Using different approaches can offer complementary views of the data
  - see the NARPS project



Botvinik-Nezer, 2020, *Nature*

Open datasets with task fMRI

- Human Connectome Project (HCP) – Aging: https://www.humanconnectome.org/study/hcp-lifespan-aging
- Nathan Kline/Rockland: http://fcon_1000.projects.nitrc.org/indi/enhanced/
- Cambridge-Center for Aging and Neuroscience (Cam-CAN): https://camcan-archive.mrc-cbu.cam.ac.uk/
- UK Biobank: https://www.ukbiobank.ac.uk/
- www.openneuro.org

Resources

- FSL courses: https://open.win.ox.ac.uk/pages/fslcourse/website/
- Andy's brain blog/book: https://andysbrainblog.blogspot.com/ https://andysbrainbook.readthedocs.io/en/latest/
- Neurosynth for meta-analysis: https://neurosynth.org/
- Partial least squares toolbox: https://www.rotman-baycrest.on.ca/index.php?section=84
- Software specific forums/mailing lists
- https://neurostars.org/