What Can and Can't* Be Done with FMRI

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*As yet, anyhoo (AFAIK)

Pics from Nepal

Bespoken by PAB


Start with a few controversial points

What Can't Be Done (IMHO)

- Determine *what* a brain region is doing (decode)
  - *e.g.*, what information is received and how it transforms it and then what gets sent to where
- Determine directionality of information flow
  - *Might* be possible with shorter TRs
- Determine if a brain region is critical for a task
  - *e.g.*, if it were lesioned, could the task still be done?
- Determine mix of excitatory and inhibitory neural activity
  - Both consume energy hence oxygen, hence BOLD
- Micro to Macro scaling issues (as usual)


Back to the main line of what FMRI can do

Characteristics of FMRI

- Signal measured by FMRI is more-or-less proportional to blood oxygen level in the veins inside each imaging voxel
- Blood oxygenation = an OK proxy for neural activity immediately upstream from the veins
  - **Coming from a 3-5 second interval centered about 5-7 seconds in the past**
- BOLD FMRI is a *great* tool for localizing brain activity ***in space*** (within 3 mm, say; maybe better)
- FMRI is a *crude* tool for measuring brain activity ***in time*** (should get better in the future)

A Rough Analogy

- Suppose the brain is a piece of software
  - Each "part" of the brain is some sort of subroutine
- **FMRI measures "activity"** → measuring how much a subroutine is invoked when the software does various user-initiated tasks
- **Brain decoding problem** → figure out what each subroutine does based on the correspondence between software inputs and how much the subroutine gets invoked
  - **Resting state FMRI** → decipher an operating system from how often subroutines are co-invoked

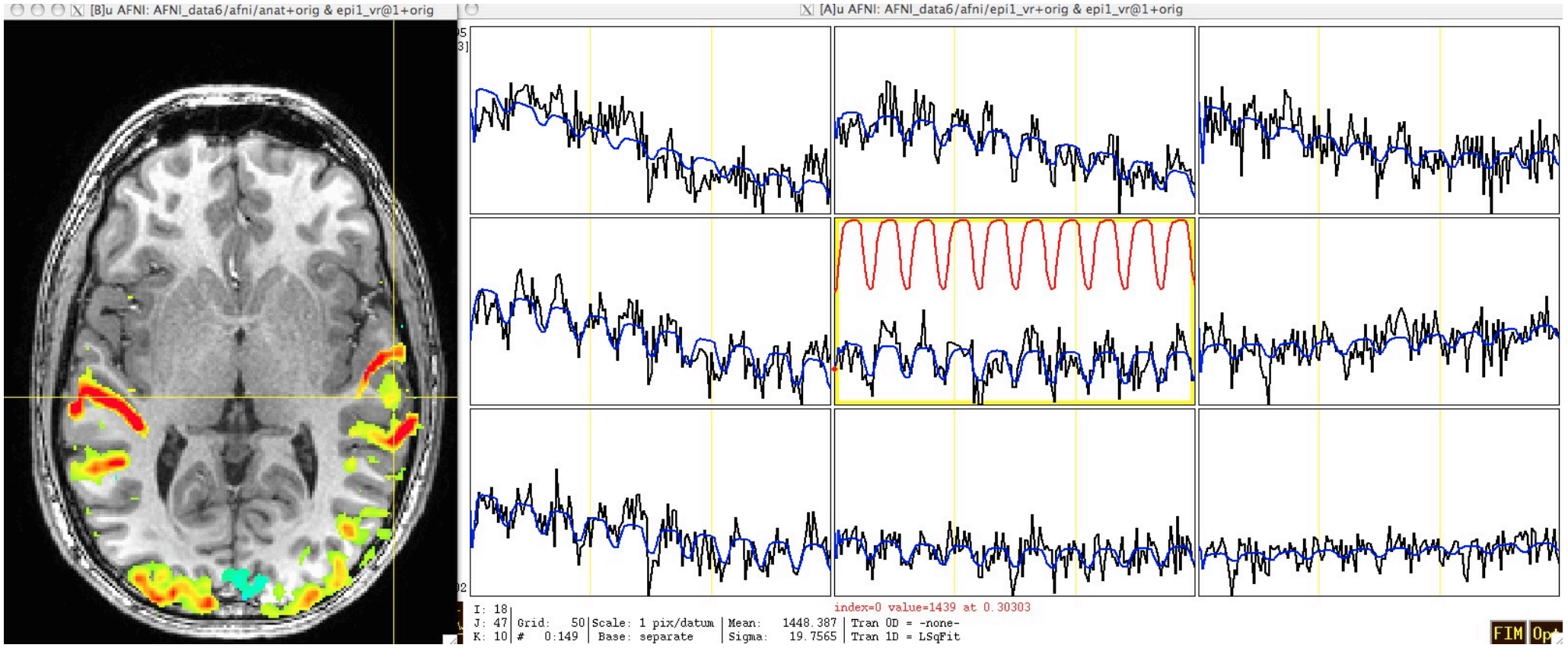
Annoyances in FMRI

- Can only measure ***changes*** in brain activity
  - Must contrast 2 (or more) mental conditions
  - Can't tell inhibition from excitation (both take energy)
- MRI signal changes affected by many things:
  - Hematocrit; Caffeine; NSAIDs (etc.); CO_2 level ; Heartbeat; Breathing; Blood inflow; Geometry of draining veins; Spatially varying hemodynamics; Nonlinearities in BOLD; *Subject head movement!*
- Signal changes are weak ➔ average across multiple trials to get decent voxel statistics
- Time blurring ➔ very hard to see sequencing of activity in the brain (not helped by long TRs)

Task Based FMRI

- To find out information about brain processing of *short* (1-30 seconds) stimuli or tasks
- Locations in brain that are more or less active in different tasks (*brain mapping*)
  - and correlations between activation fluctuations (e.g., PPI, DCM, SEM, …)
- Dependence of neural activation strength (BOLD effect) on task parameters (pain level; face type; drug dose; …)
- Dependence of neural activation on subject parameters (age; disease severity; genotype; …)

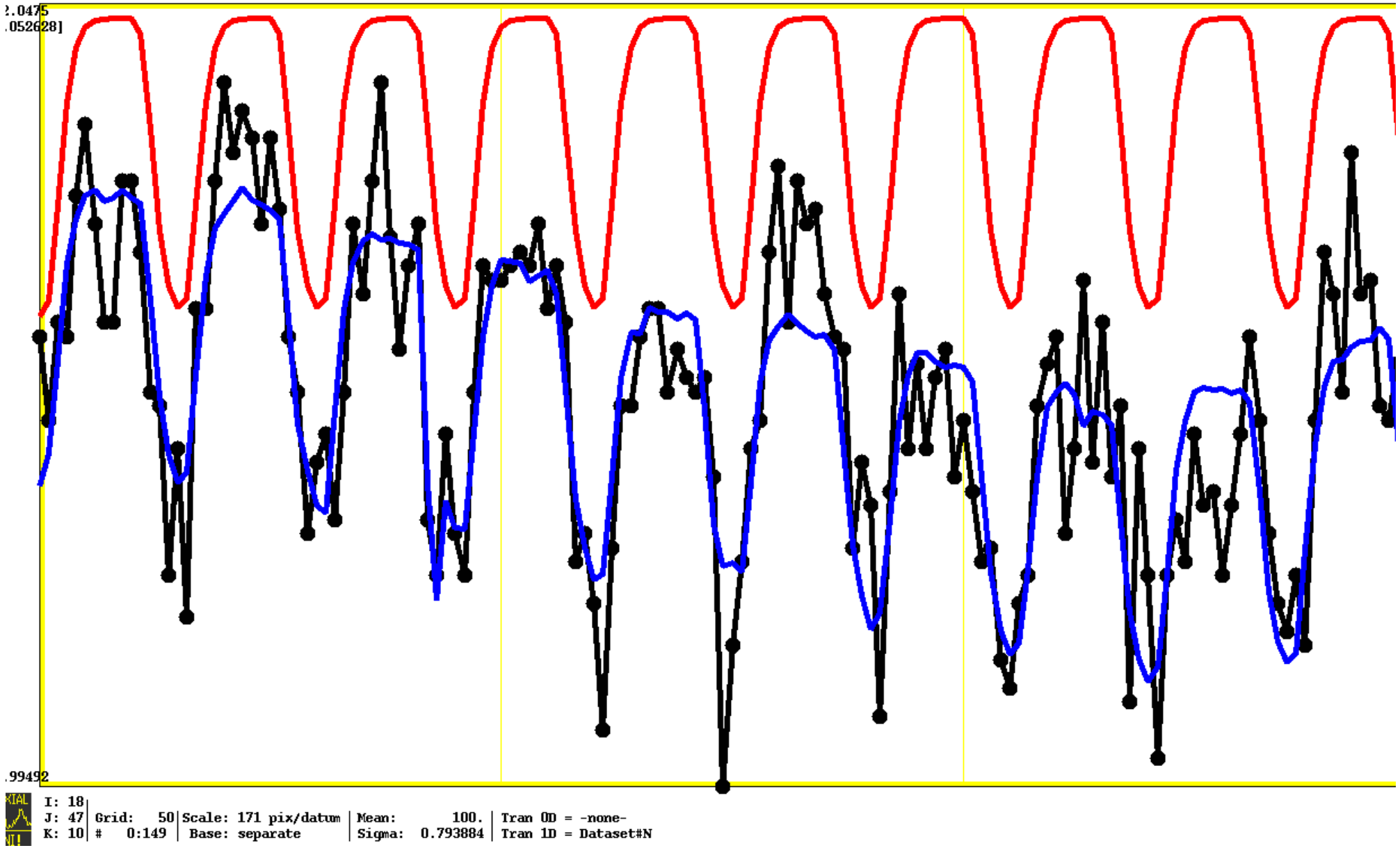
Some FMRI Data



- **Left** = decent looking single subject activation map
  - From 300 s of data (150 time points)
- **Right** = data time series that gives activation map
  - This is ***good*** data [strong activation, little head movement]

Blowups Happen

(central voxel time series)



Type of Stimuli or Tasks

- Short visual or auditory (sound) inputs
  - Faces / Houses ; Musical tones ; Words
- Decisions
  - Same face? Tones up or down? Animal? Gambling / Financial? Social?
- You may not care about actual task
  - You might care about the **CONTEXT** in which the task appears
  - e.g., Faces: task is **MALE** or **FEMALE** but context is **angry** or **fearful** face

Variety of Tasks: 1 Week in 2014

3 of 91 articles added to Scopus with "FMRI" in abstract/title

✧FMRI evidence for abnormal resting-state functional connectivity in euthymic bipolar disorder patients. P Favre *et al*. J Affective Disorders **20**: 182-189 (2014).

- Inter-group seed-based connectivity analyses on BP patients during "normal" periods

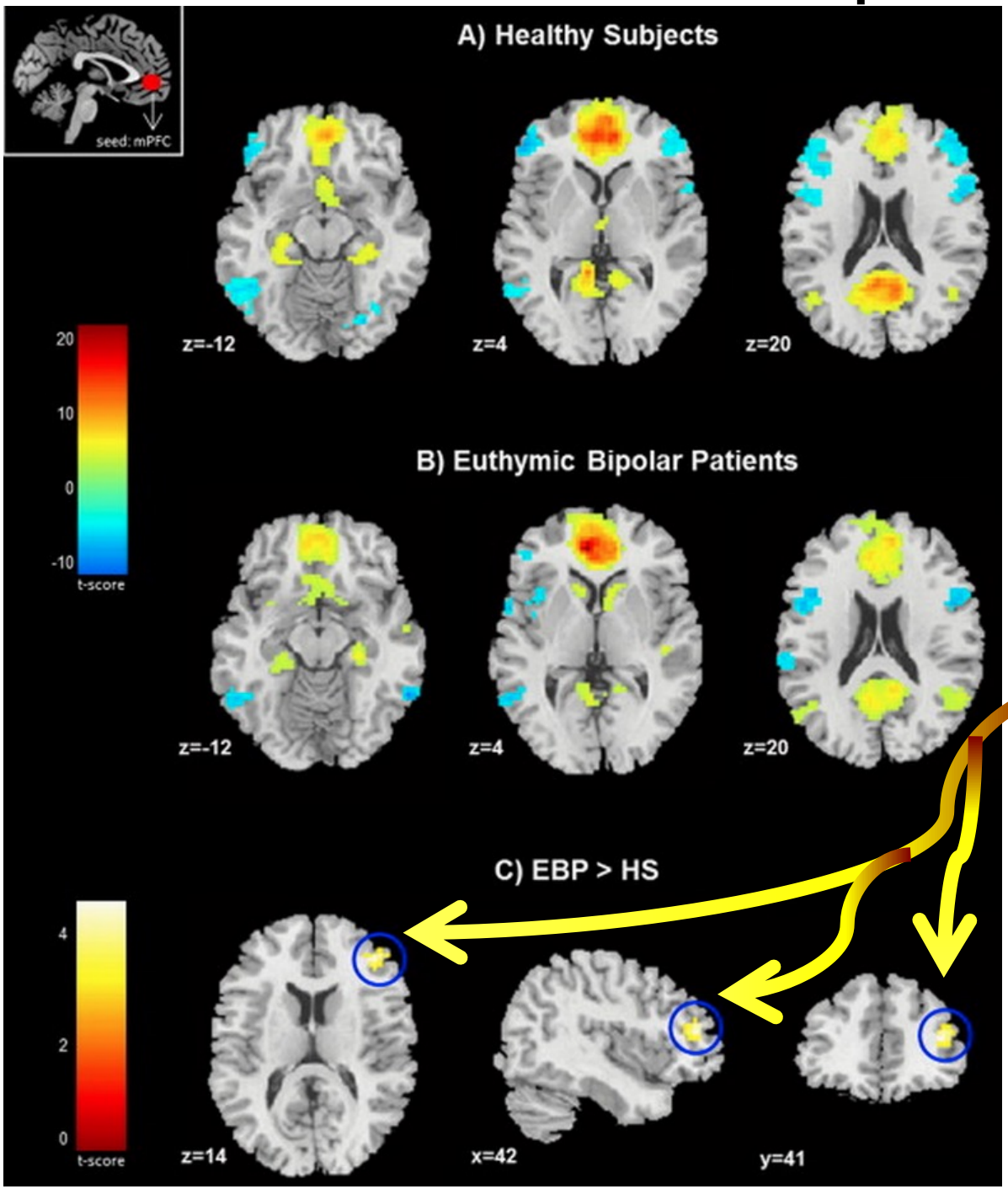
✧Discovering the structure of mathematical reasoning. J Anderson *et al*. NeuroImage **97**: 163-177 (2014).

- Brain pattern analysis and modeling; breaks problems solving in 5 phases, with distinct activation patterns

✧Sweet lies: Neural, visual, and behavioral measures reveal a lack of self-control conflict during food choice in weight-concerned women. LN van der Lann, *et al.* Frontiers in Behavioral Neuroscience **8**: art num 184 (2014).

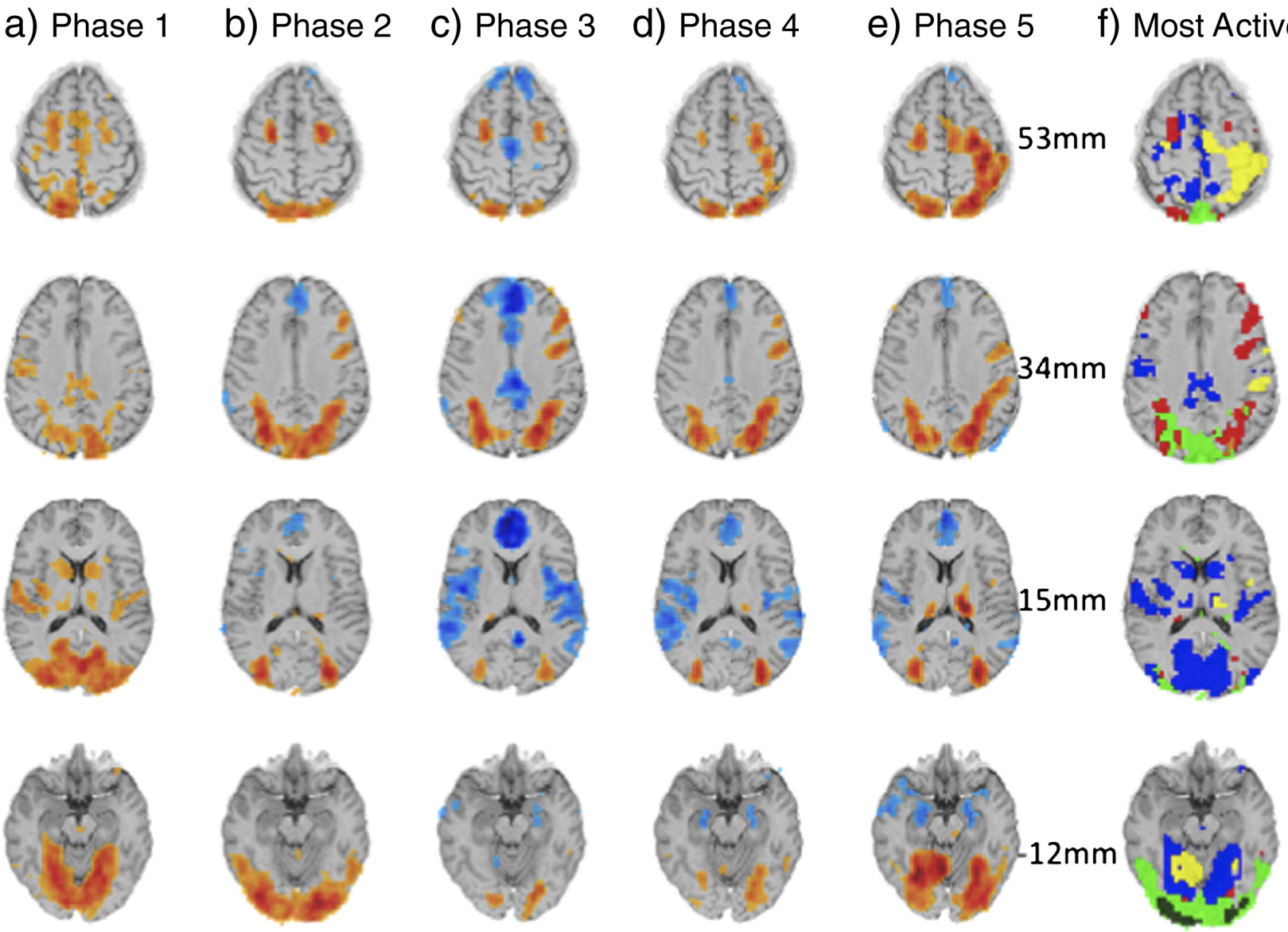
- Choosing between high- and low-calorie foods, with matched and mis-matched tastiness ratings

RS-FMRI in Bipolar Patients



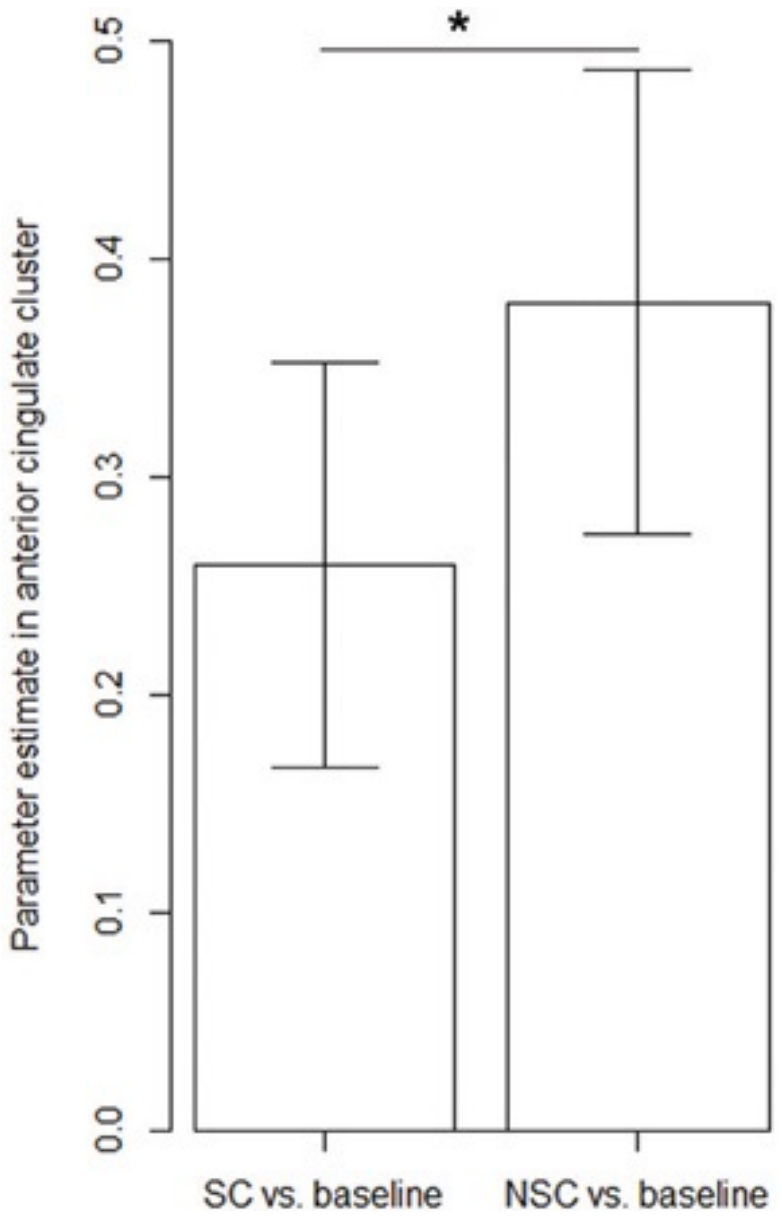
- Correlation seed in medial pre-frontal cortex (mPFC)
- 20 subjects in each group (EBP and HS)
- mPFC-dlPFC negative in HS but not in EBP
- mPFC-right amygdala more correlated in EBP than in HS

Math is Fun!

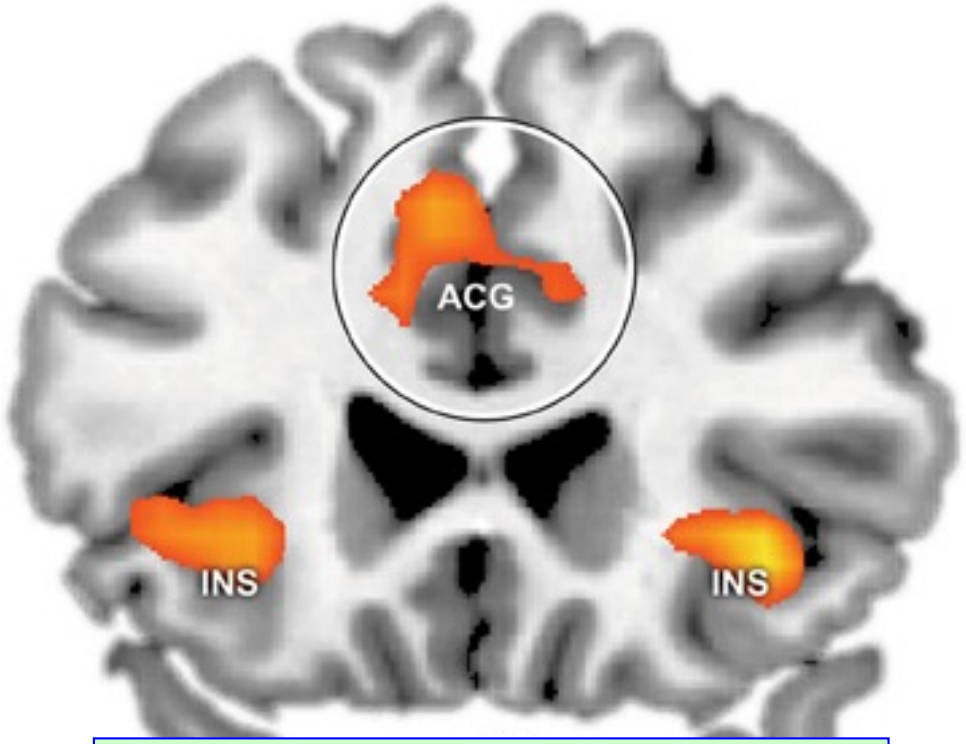


Define	Encode	Compute	Transform	Respond
Blue	Green	Red	Orange	Yellow

But is Self Control fun?



More activation in tastiness matched (NSC) vs. tastiness contrasted (SC) trials!

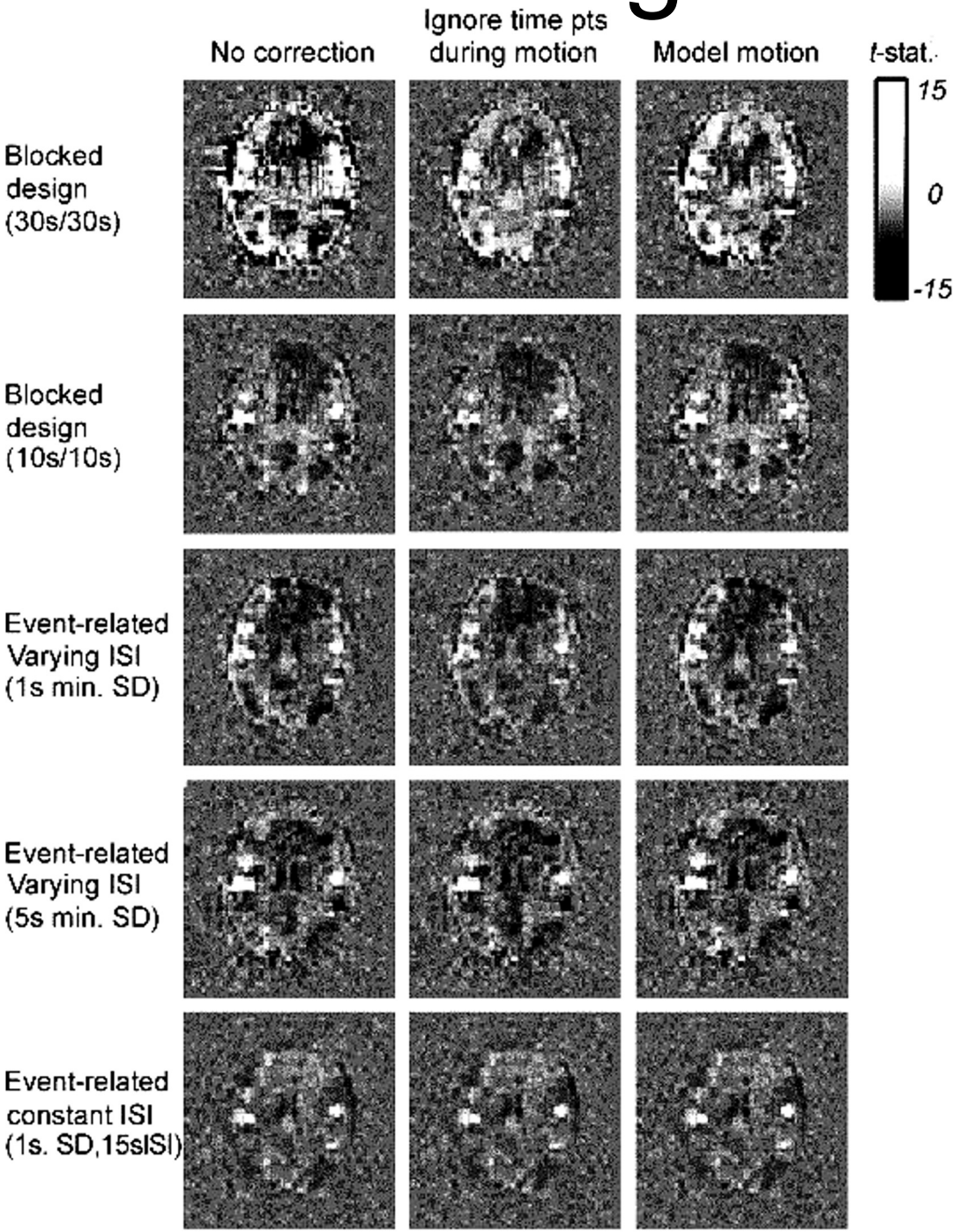


However, they don't show the SC > NSC results, except in a suppl table

Hard Tasks for FMRI

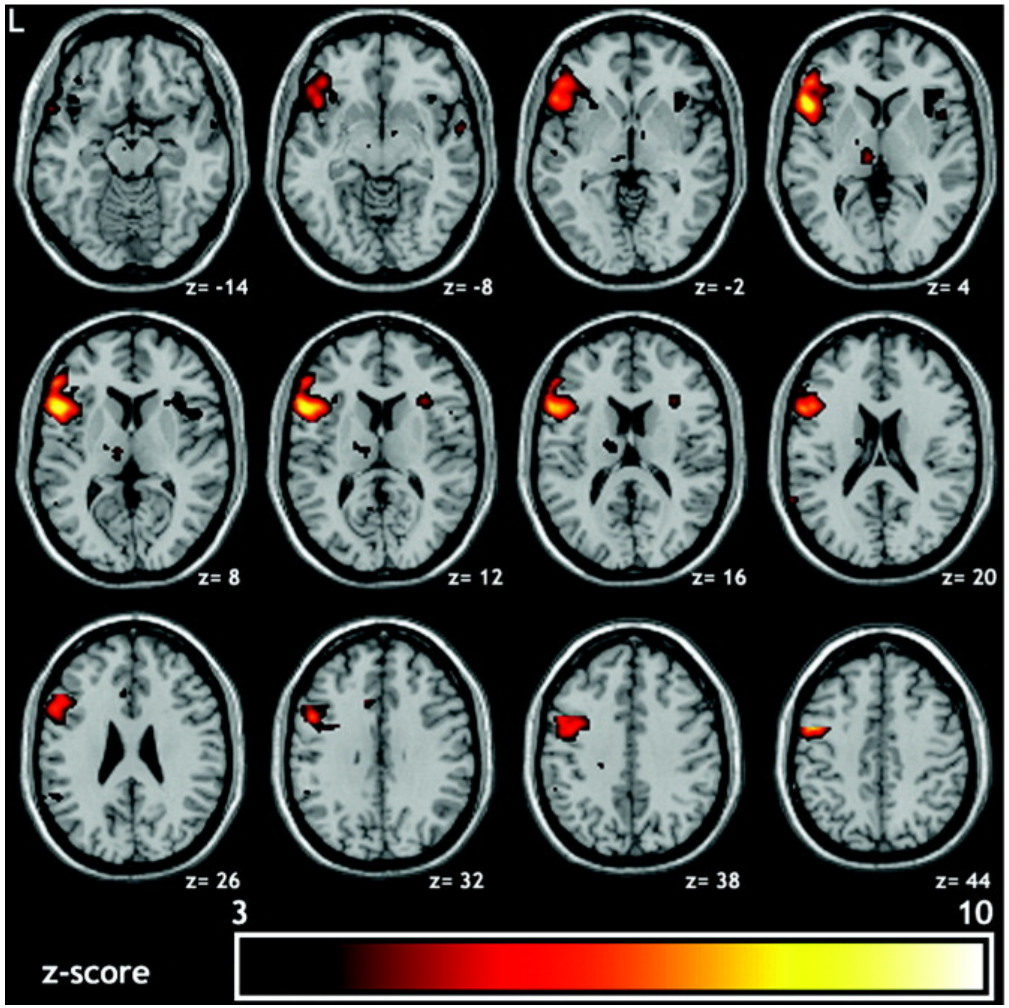
- Anything requiring subject to speak or move
  - One word or sound can be OK
  - Requires censoring out MRI volumes during subject speech — jaw motion is bad for images
- Anything that uses subtle sounds (*e.g.*, music)
  - Scanner is ***very*** loud
  - One solution: silent period between scans
- Very long duration tasks (*e.g.*, learning; drugs)
  - Hard to tell long activation changes from MRI signal drifting up or down (e.g., head drift)
  - Not impossible, but requires special analyses

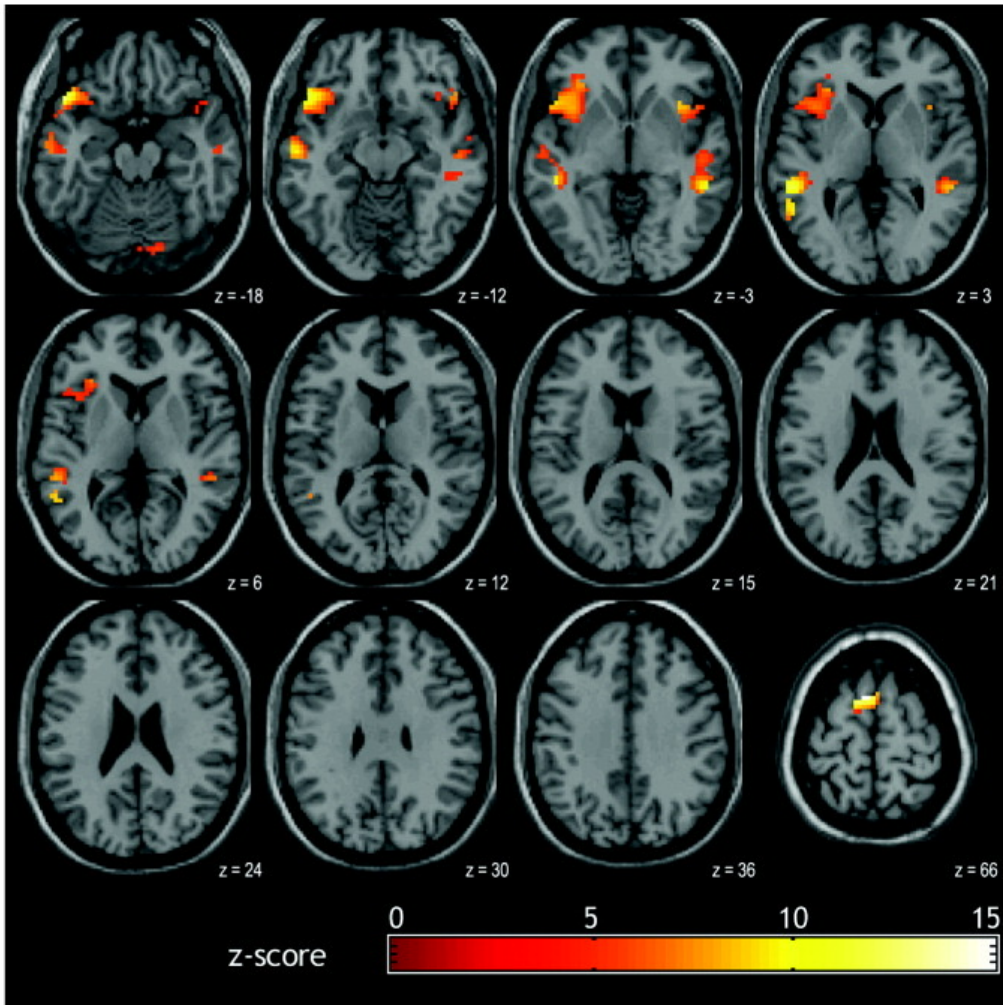
Strategies for Speech - 1



- Single word speech
- Standard BOLD-weighted FMRI
- Different experimental timings and processing ideas

Strategies for Speech - 2





- Continuous speech tasks: sentence generation vs. simple syllable repetition '***pa-ta-ka***'
- **Left** = ASL imaging **Right** = BOLD imaging

Group Studies

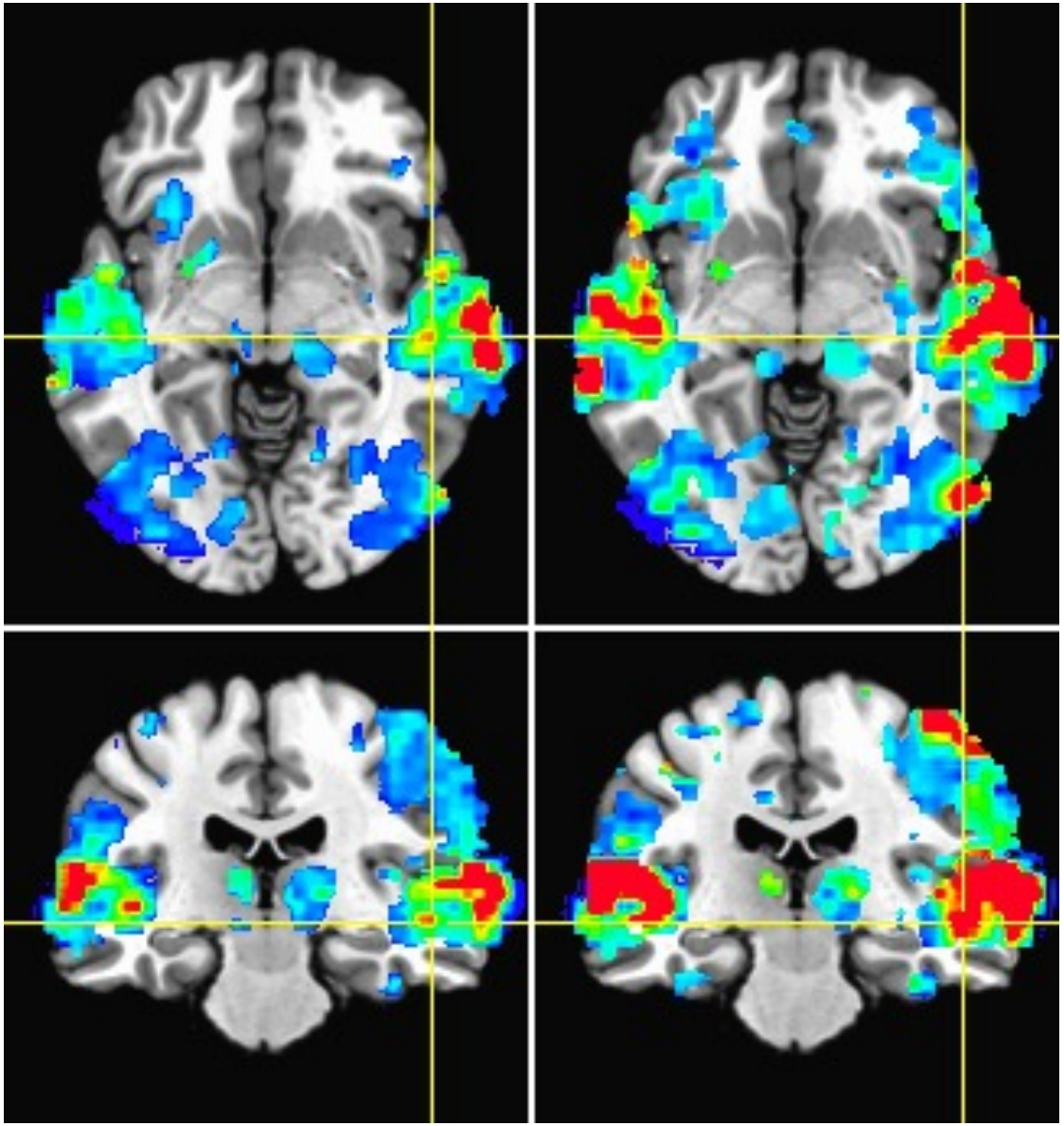
- Most FMRI studies look at groups of subjects
- To make collective statements about
  - All of humanity (1 pretty sizeable group)
  - Differences between groups (e.g., patients and controls; young and old; mono- and bi-lingual)
- Effectively are averaging across subjects within a group (and subtracting between groups)
  - Differences within a pre-selected group are taken to be "noise" (AKA signal changes we don't understand)

➔ Cannot apply most FMRI research results to individuals

Groups of Subjects

- Can look for differences in
  - Activation magnitude (% signal change)
  - Size of activation regions (AKA ***blobs***)
  - Inter-regional activation correlations
    - e.g., “connection” of amygdala with something
  - Correlation of activation/correlations with subject covariates (age; IQ; drug abuse, …)
- Confounds:
  - MRI "noise" level may differ between groups
  - Circularity in reasoning

Inter-Subject Variability



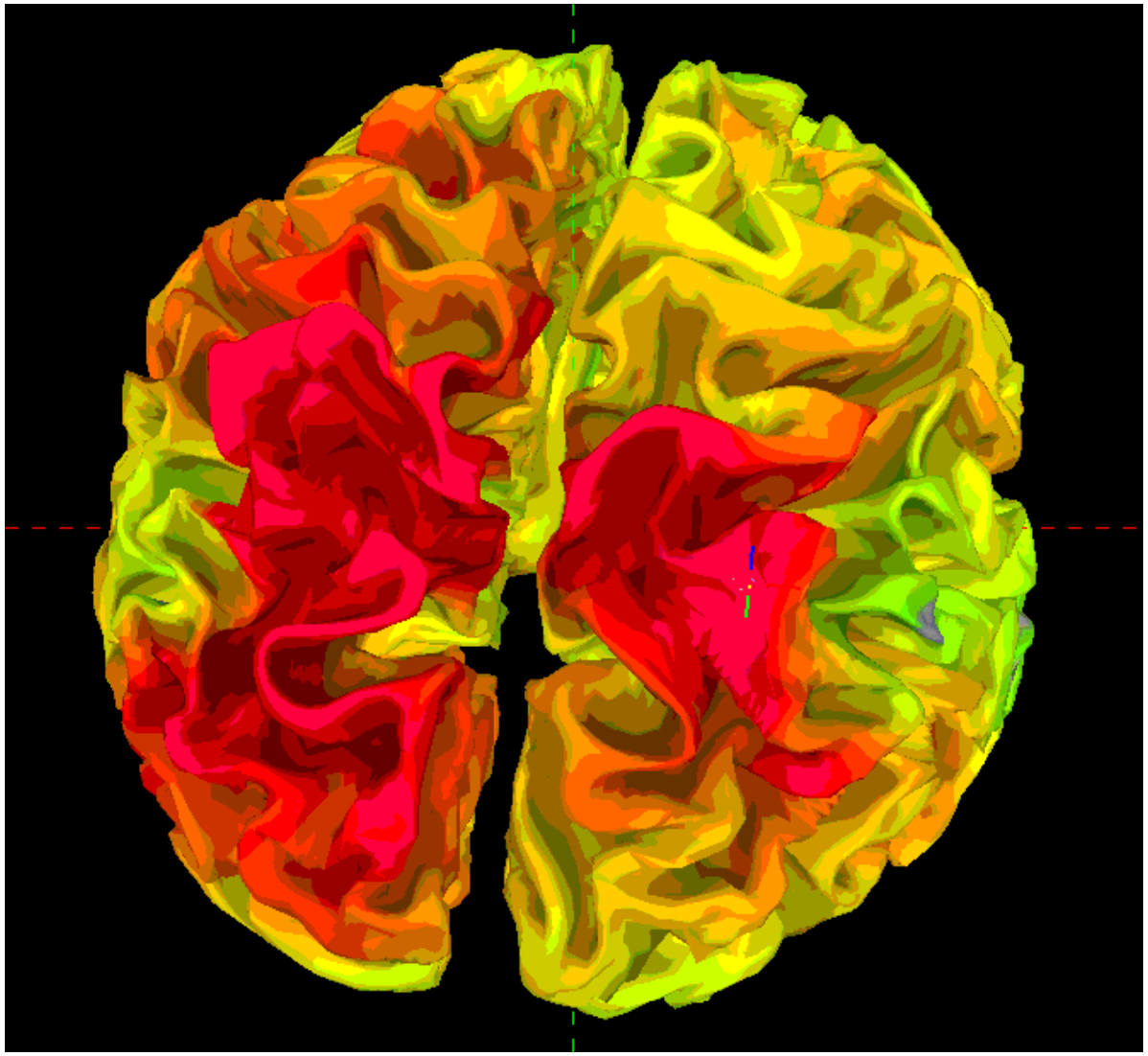
Left=GLSQ Right=OLSQ

- Individual maps from 17 subjects
  - Time = subject
- These subjects are all supposed to be "the same"
- Activation blobs are common, but strength (relative to noise) varies – a lot

FMRI "Connectivity"

- Looking for MRI signal fluctuations that are correlated (vary up and down at same times) in different spatial locations
  - Lots of annoyances in the data, of course!
- Can be based on task FMRI or based on "resting" FMRI — can be done by anyone
- Hot new-ish word in USA: **Connectome**
- Data analysis methods are more variable than for task-based FMRI brain mapping
  - Interpretation of correlations is obscure
  - Methodology is newer
  - Not "tied down" to task/function timing

Resting State Correlations



- Correlation of FMRI time series from a seed location vs. all other locations
- Seed is moving around
- Long range correlations

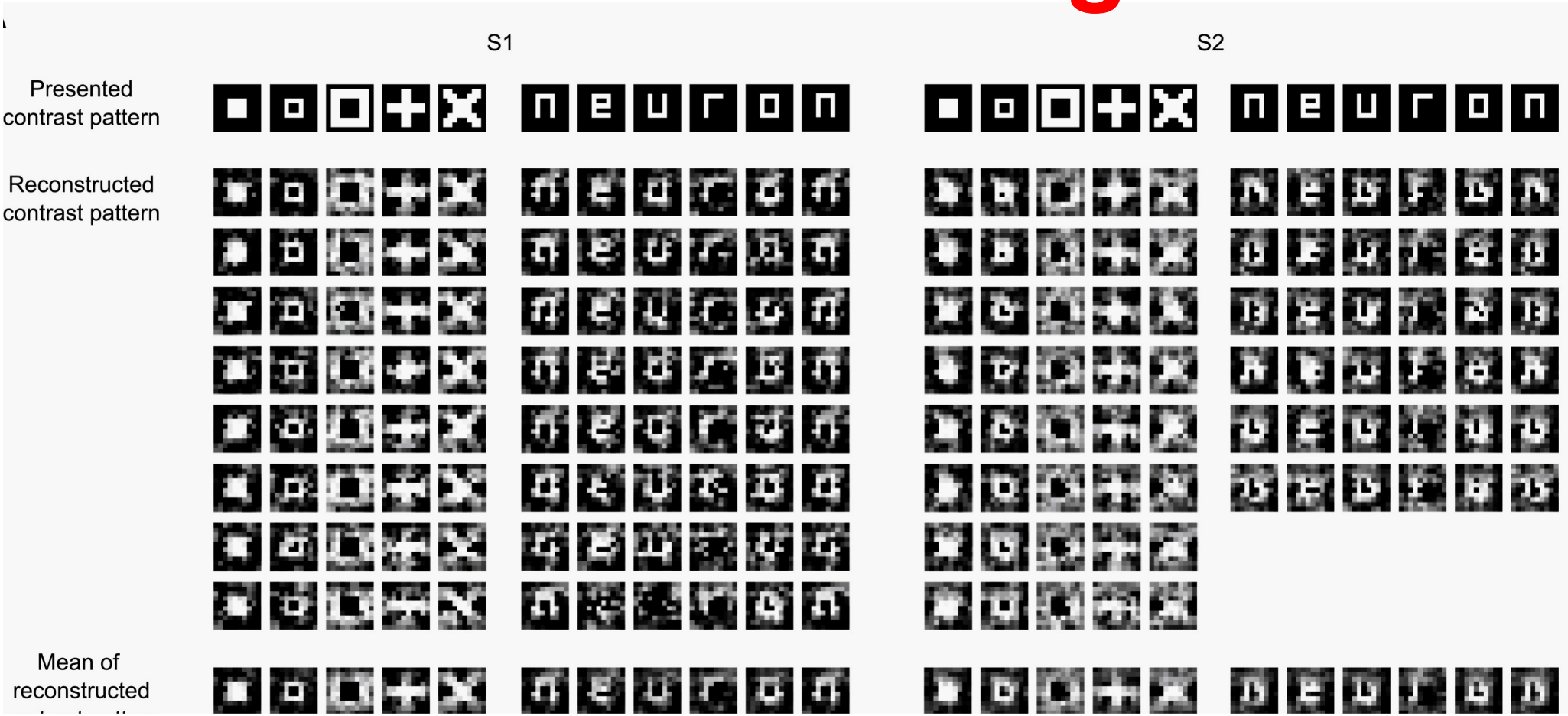
Individual Subjects in FMRI

- Things that work
  - Pre-surgical planning
  - "Brain reading" (lots of caveats here!)
- Things that are (very) controversial
  - Lie detection (or general “mind reading”)
  - Biofeedback for chronic pain, drug cravings
    - Slowness of hemodynamics is one issue
- Things we wish we could do
  - Distinguish sub-groups of patients to help in prescribing drugs (e.g., for depression)
  - Diagnose Alzheimer's dementia (e.g.)

Brain "Reading"

- Trying to find out what the brain is doing from the FMRI data at a given time
  - Is the subject looking at a face or at an elephant?
- Multi-Voxel Pattern Analysis = **MVPA**
- Training data: Build up spatial patterns of brain data for different categories of brain functions
- Then apply patterns to new brain data to estimate what subject is doing ***at each TR***
- What can be "read" with MVPA?
  - 80+% accuracy for some discriminations
  - Inter-subject patterns? Generic categories?

Brain "Reading"



- Reconstruction of what subject was looking at (10 x 10 binary patterns)

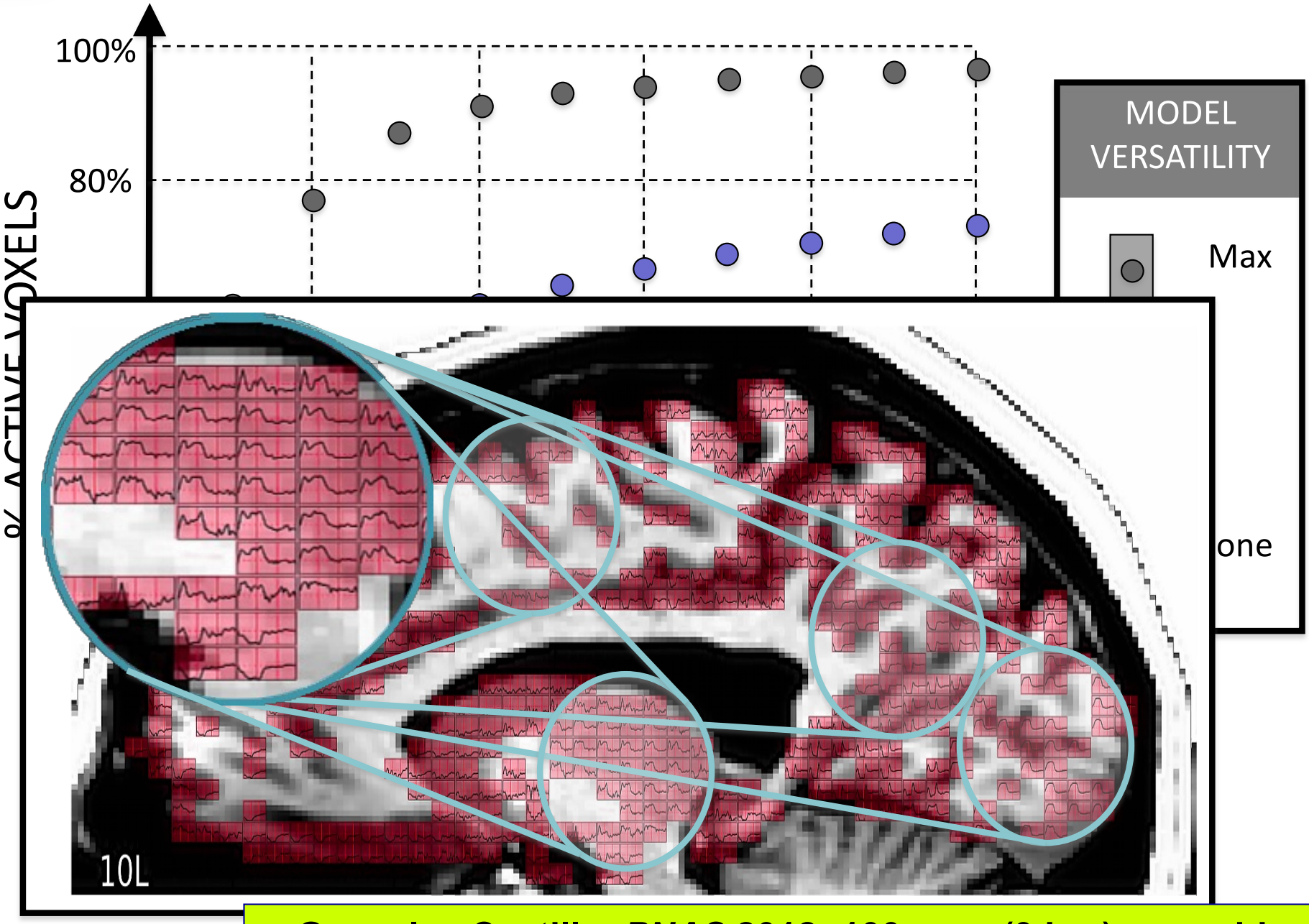
Brain "Reading"

- Has been applied to patients in "minimally conscious" state to assess level of awareness and attention
- Instruct patient to think of physical activity (tennis playing) to answer a question **YES** and to think of walking around in their house to answer a question **NO**
- A fraction of patients not otherwise able to communicate were able to respond correctly in this way to questions about their lives
- Studies to date are limited in scope

Confusions & Distinctions

- Brain vs. Mind
  - Neuroscience vs. Cognitive science
- Mass level vs. Micro-circuitry
  - Connecting blobs to cell-level actions?
- Excitation & Inhibition both consume energy
  - What does “active” mean?
- Active vs. Necessary (e.g., lesion studies)
- Modulated here? Or there?
- MVPA vs. Specificity
- Resting State: “Function” vs. Physiology

PUSHING THE SENSITIVITY LIMITS OF FMRI



Gonzalez-Castillo, *PNAS* 2012; 100 runs (9 hrs) per subject

ThThThat's All, Folks