Statistics in fMRI analysis

Shao-Fang Wang

Psych252 Winter 2019

science

Statistics in ~~fMRI analysis~~

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What is your research question?

How to collect data to answer the question?

How to analyze the data to answer the question?

- what are the characteristics of your data?

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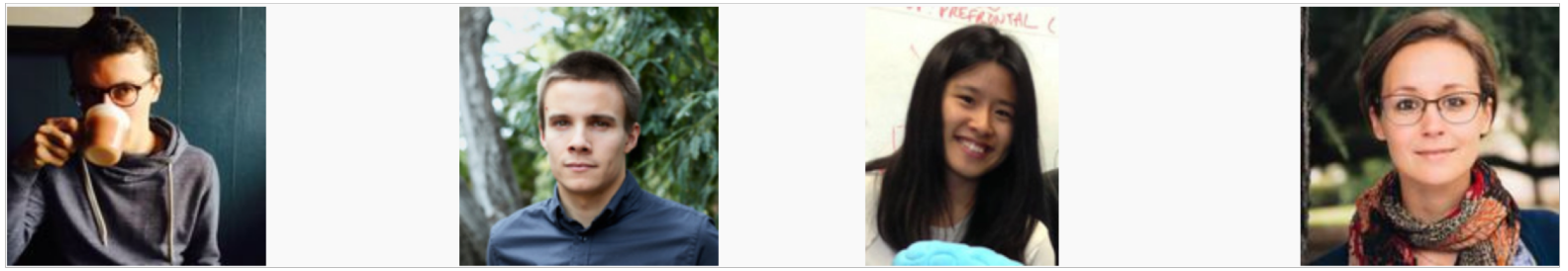

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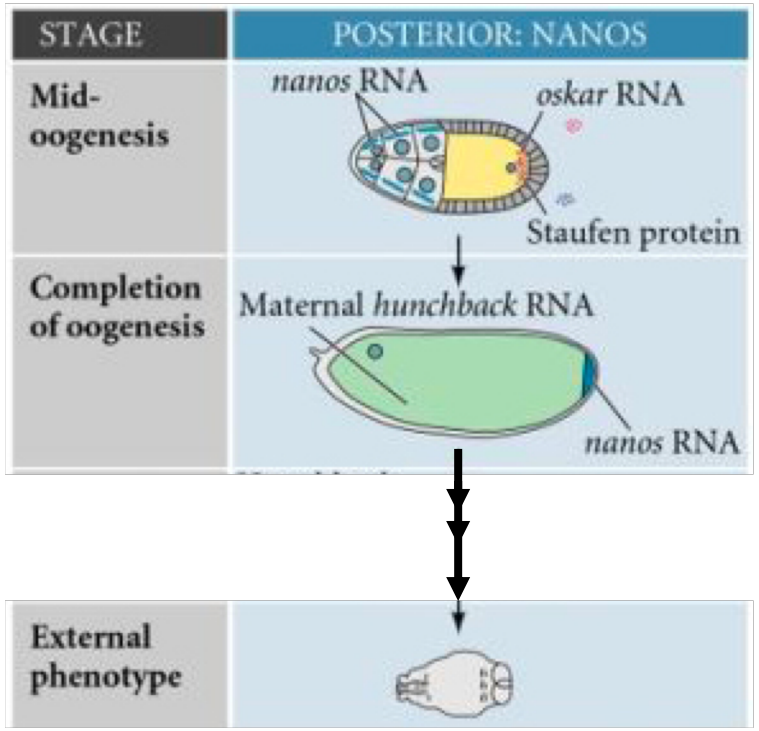
How proteins (dDcp1, dDcp2, and dGe-1) anchor oskar mRNA during oogenesis of Drosophila?



head tail

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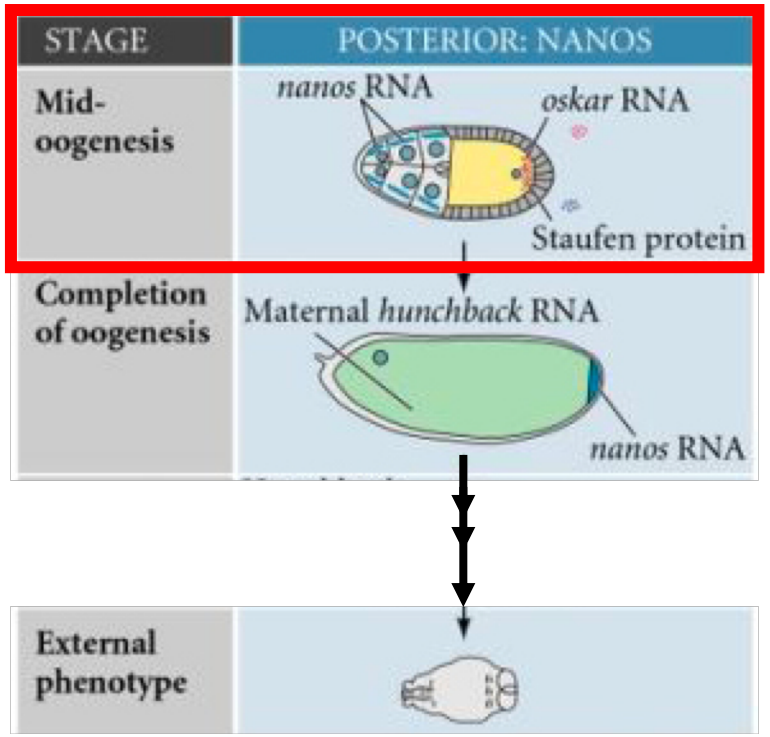
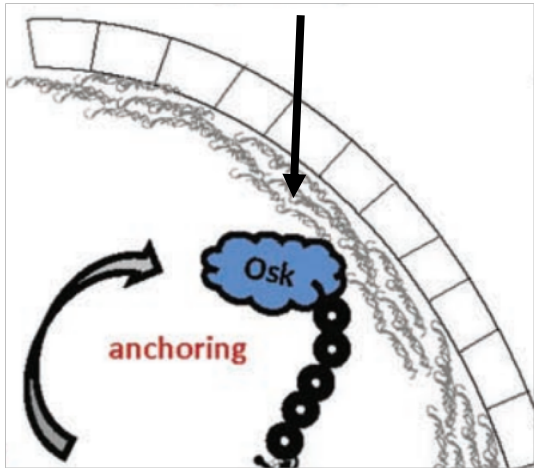


How do these proteins anchor oskar mRNA?



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Immunostaining the proteins and oskar mRNA

whole-mount *Drosophila* ovary immunostaining, co-IP, and P-element excision work

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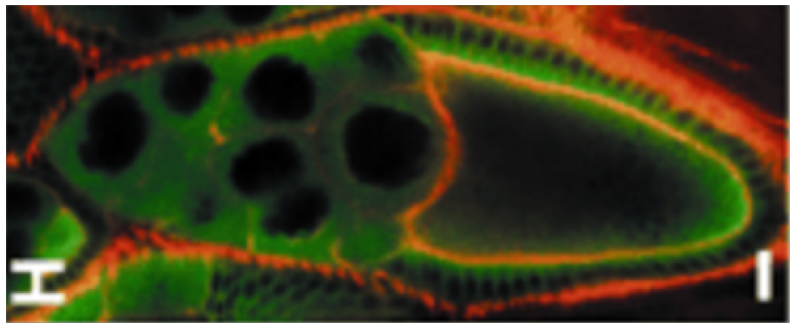
How to analyze the data to answer the question?

Just….look at it!



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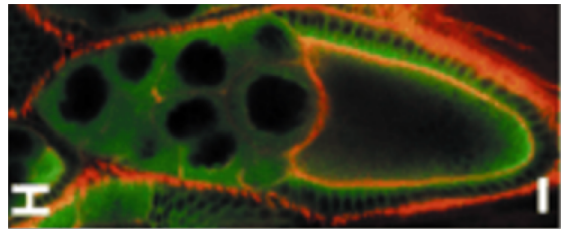
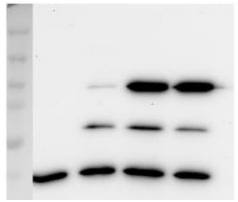


Just….look at it!

Repeat the experiments multiple times.

Using different methods to test the same hypothesis



Simple t-test!

What is your research question?

How do neural representations code spatial information in human brains?

How to collect data to answer the question?

Subjects navigate in virtual rooms. fMRI (BOLD signal)

How to analyze the data to answer the question?

- Not directly measuring neural response
- Very noisy (respiration, heart beat, head motion, other cognitive processing, machine noise, etc.)

First- and second- level statistical analyses and hypothesis testing

What about you?

What is your research question?

How to collect data to answer the question?

How to analyze the data to answer the question?

- what are the characteristics of your data?

P-values are overrated

Statistical analyses are really models

Models have assumptions

You need to test those assumptions

Evaluate how well your model fits the data

Then you can interpret parameters

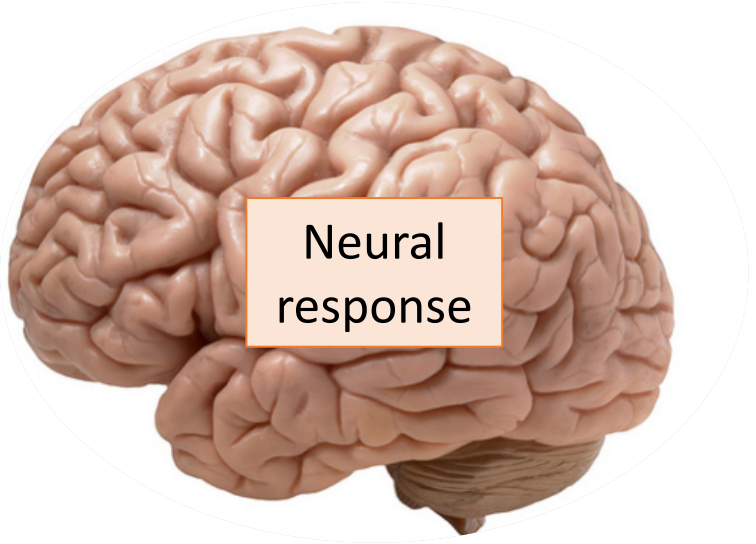
(well ok, here you might want to consider p-values)

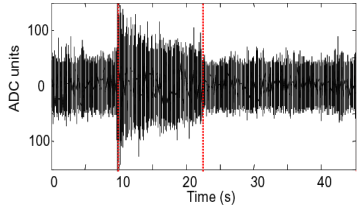
- fMRI data acquisition
- fMRI functional data preprocessing
  - Remove uninteresting variability from the data
  - Prepare the data for statistical analysis
- fMRI functional data secondary processing – Mona and Pam

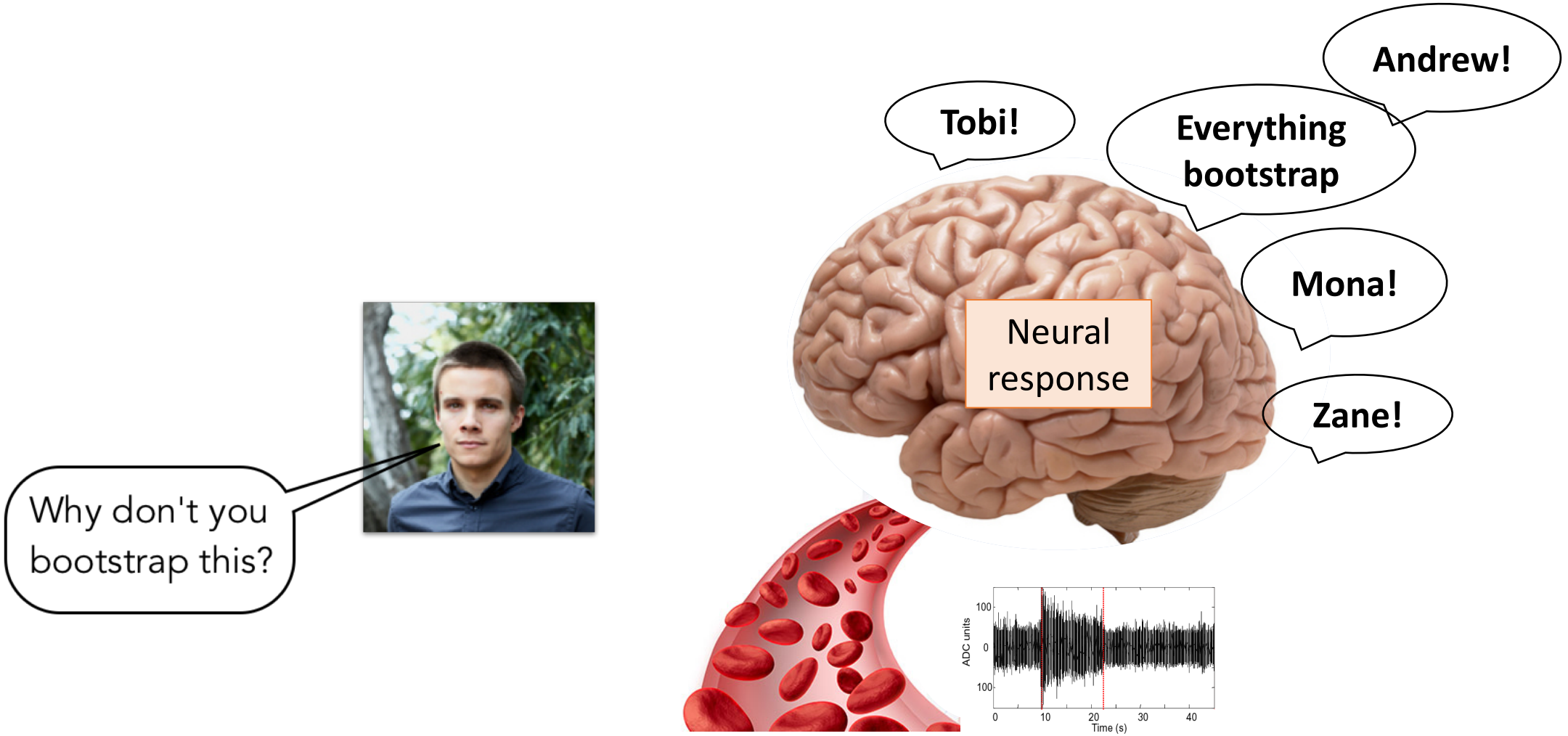
Some of the materials are from psych204B! Thanks Kalanit!

During a psych252 lecture…..

Why don't you bootstrap this?

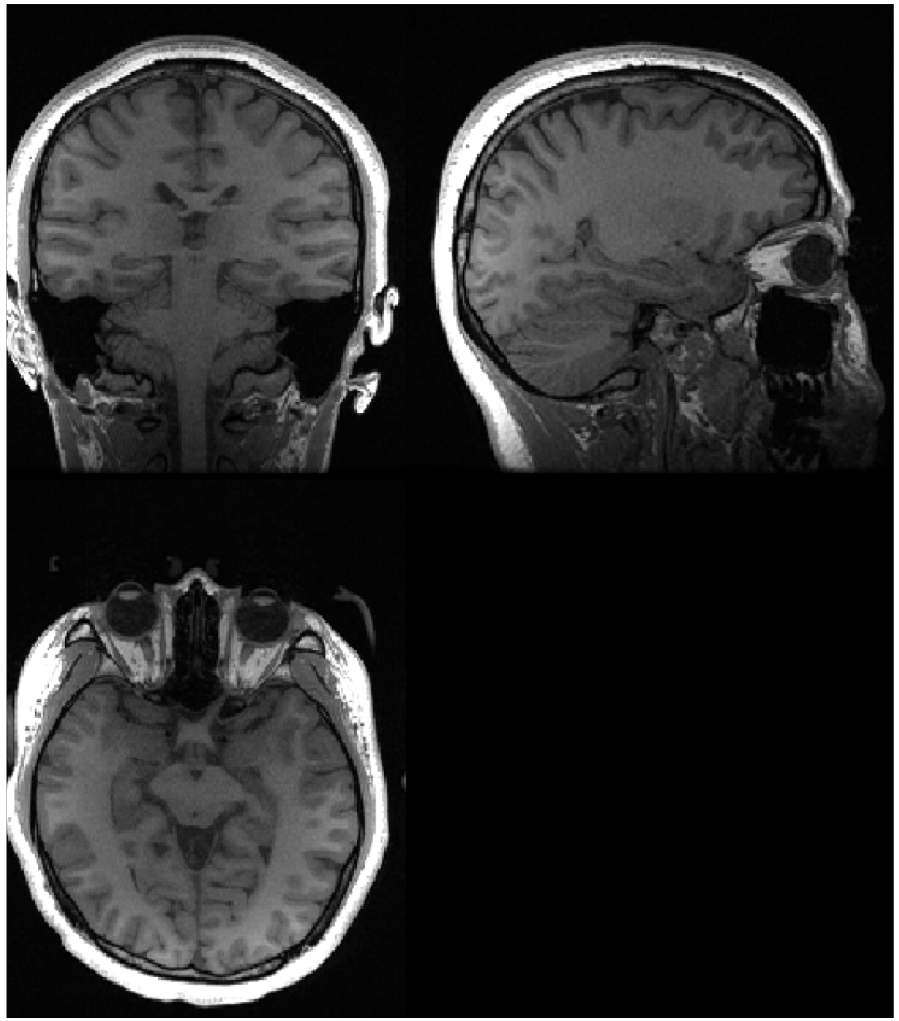




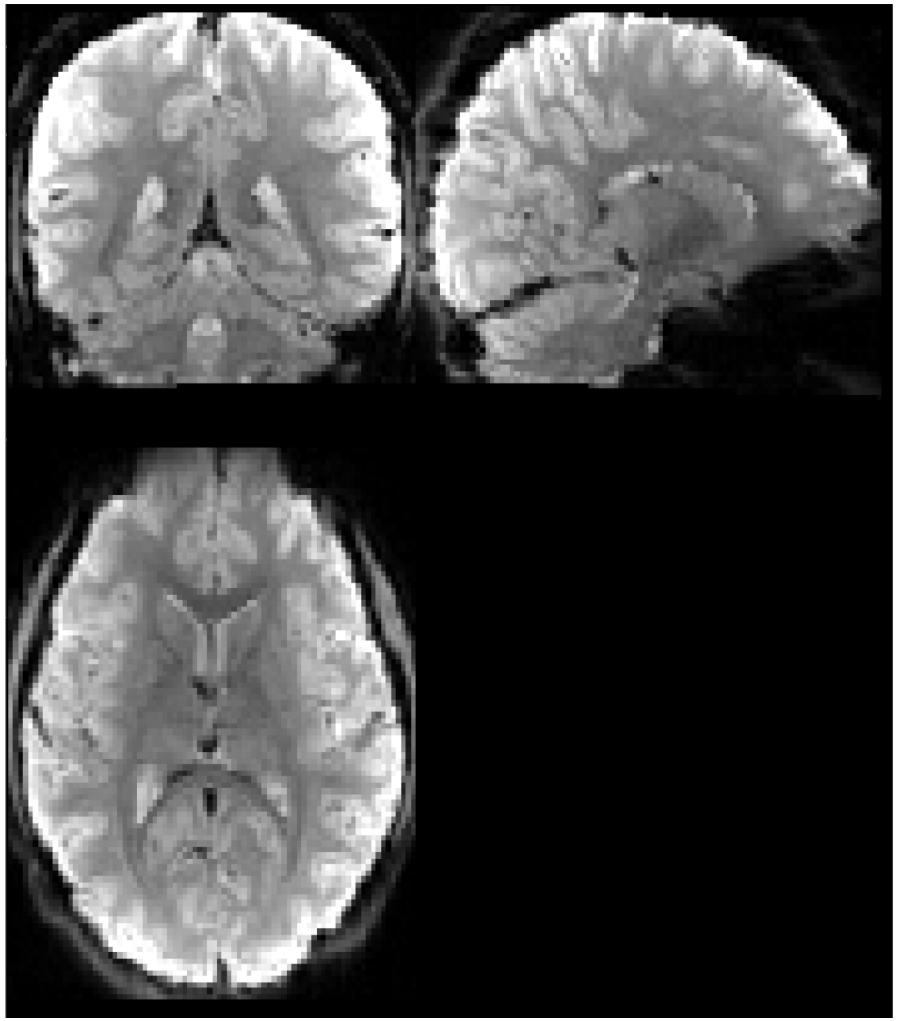

Why don't you bootstrap this?
Tobi!
Everything bootstrap
Andrew!
Mona!
Zane!
Neural response
ADC units
100
0
100
0
10
20
30
40
Time (s)

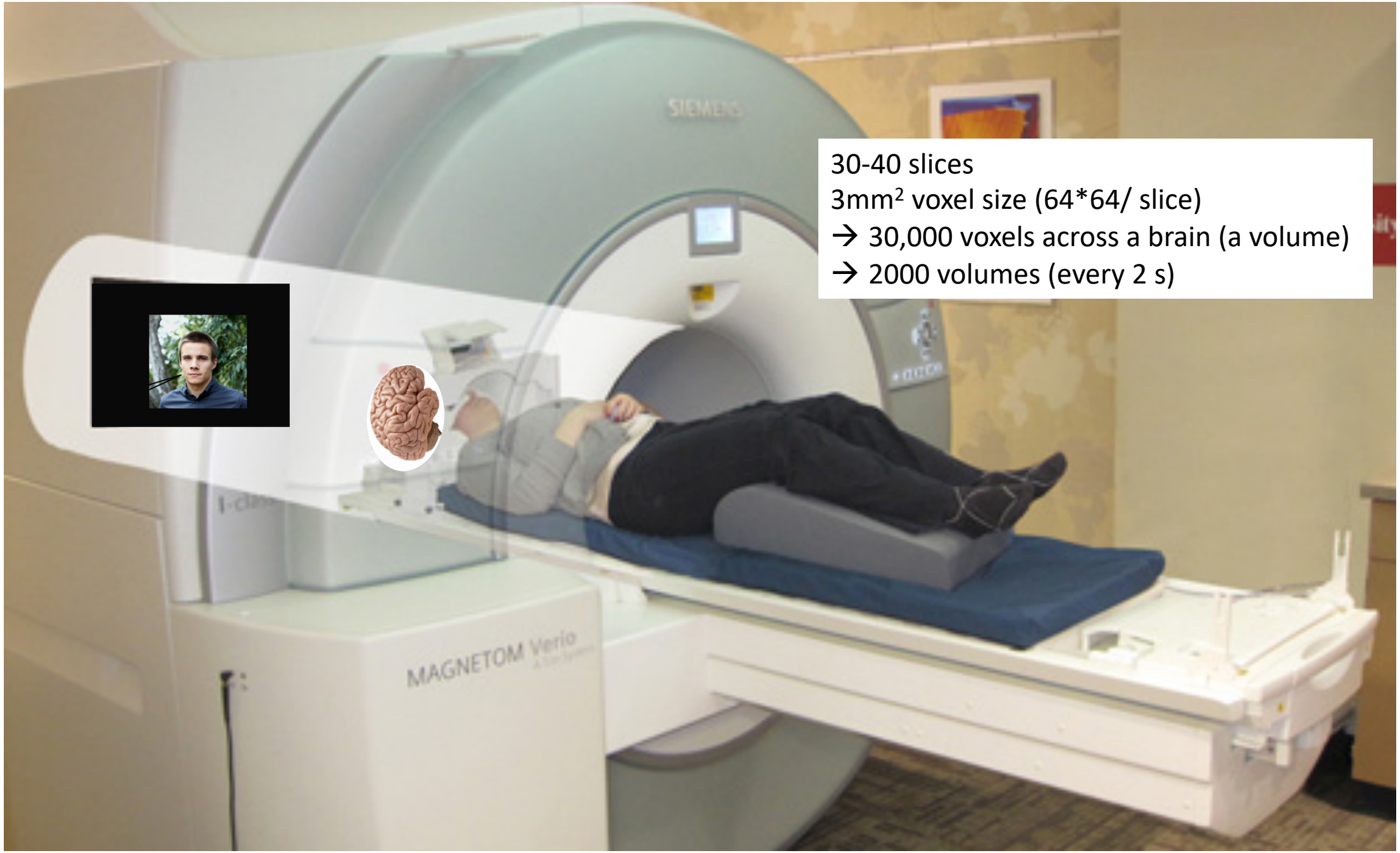
A strong magnetic field

Structural image



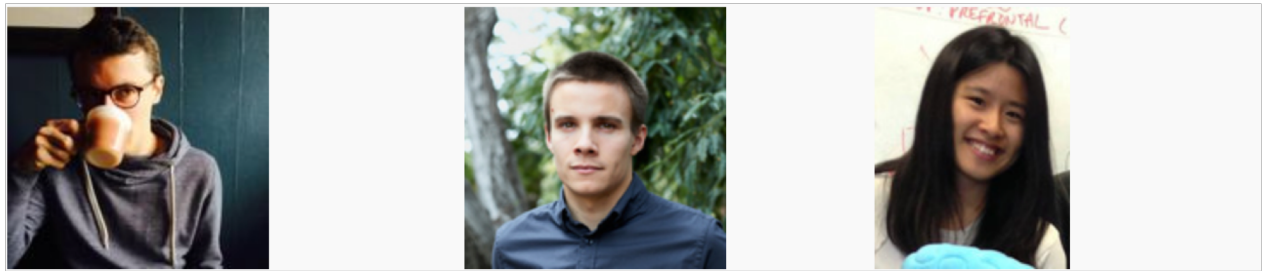
Functional image

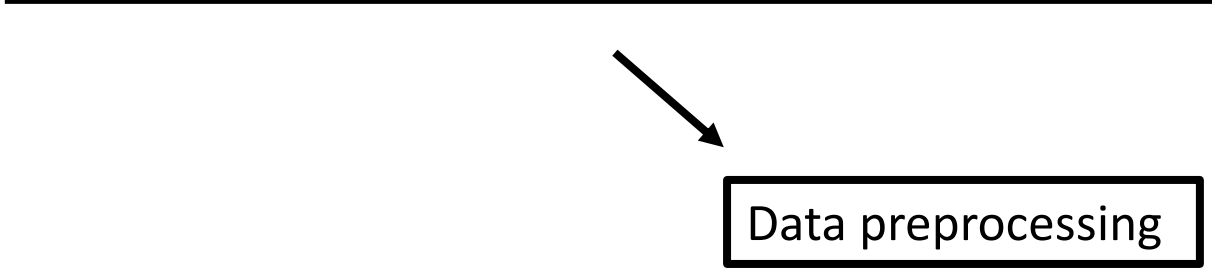




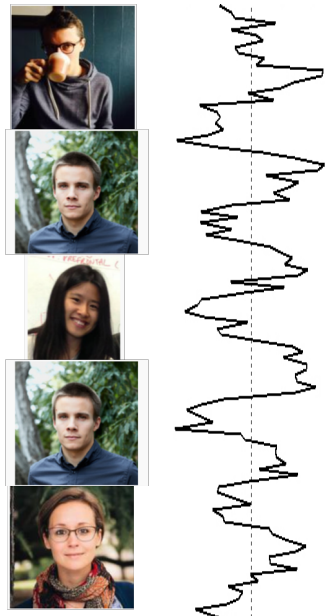
30-40 slices
3mm^2 voxel size (64*64/ slice)
→ 30,000 voxels across a brain (a volume)
→ 2000 volumes (every 2 s)

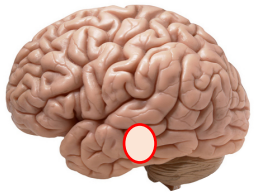
A very interesting experiment….





$$y(t) = \beta_1 g(t) + \beta_0 + \varepsilon$$





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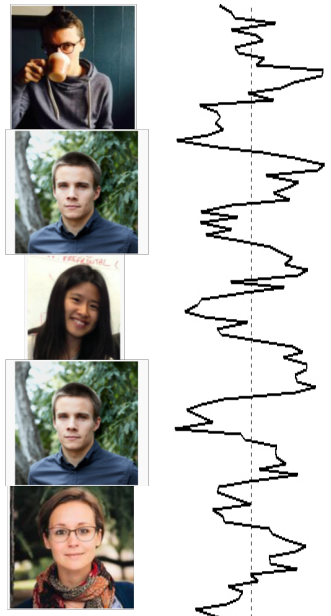
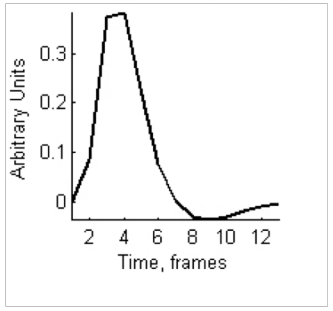
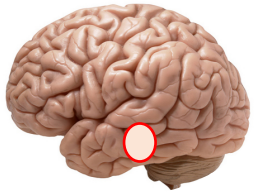


0
1
0
1
0





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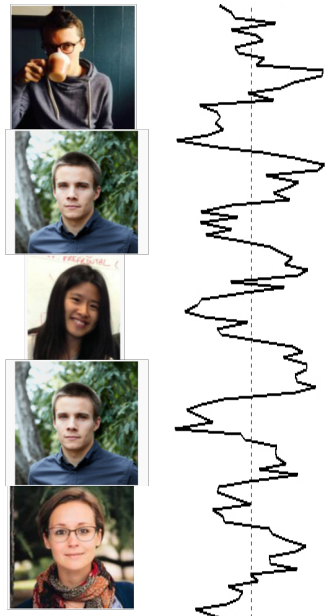

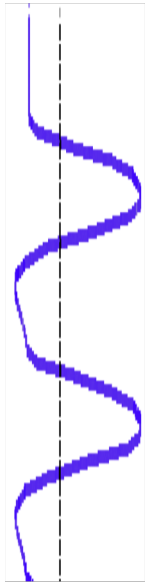

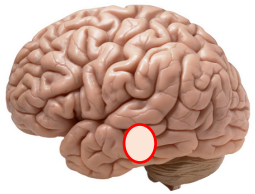

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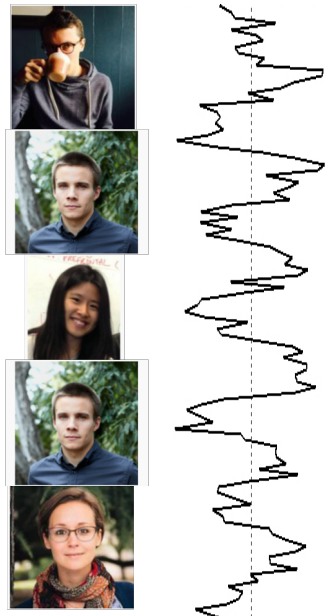
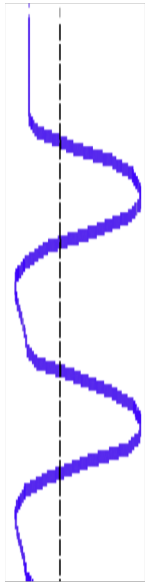
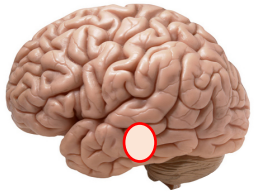
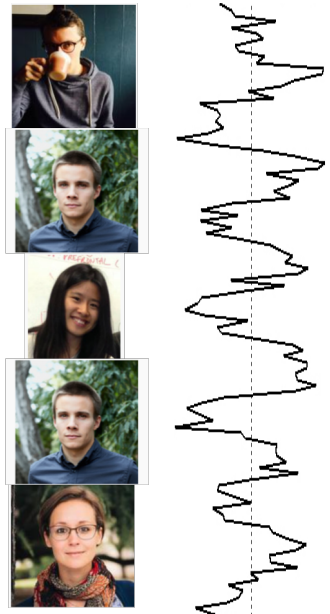


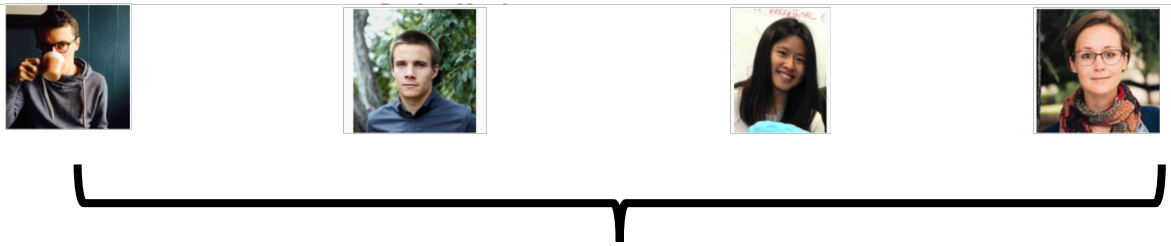


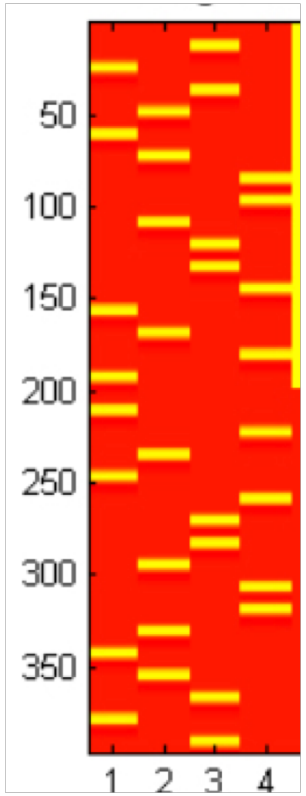
This is what you would like to estimate



$$y(t) = \beta_1 g_1(t) + \beta_2 g_2(t) + \beta_3 g_3(t) + \beta_4 g_4(t)$$







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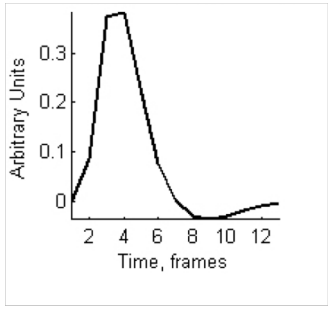

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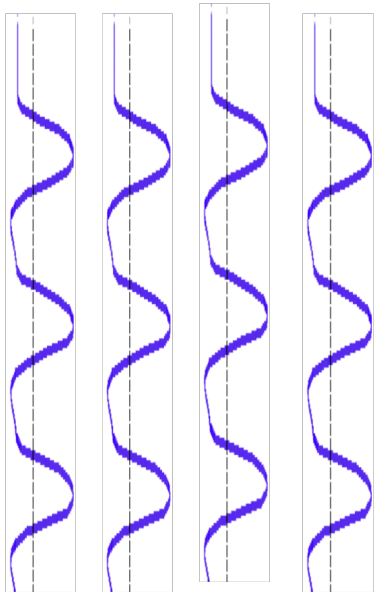

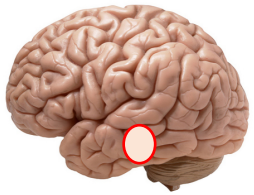

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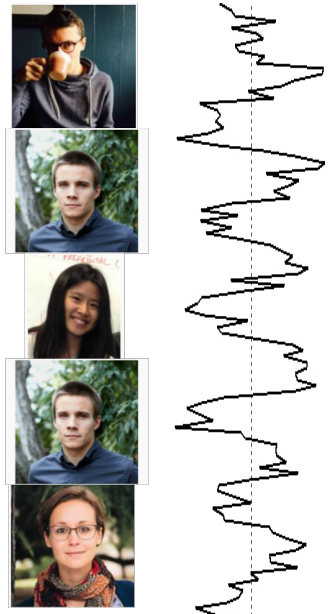
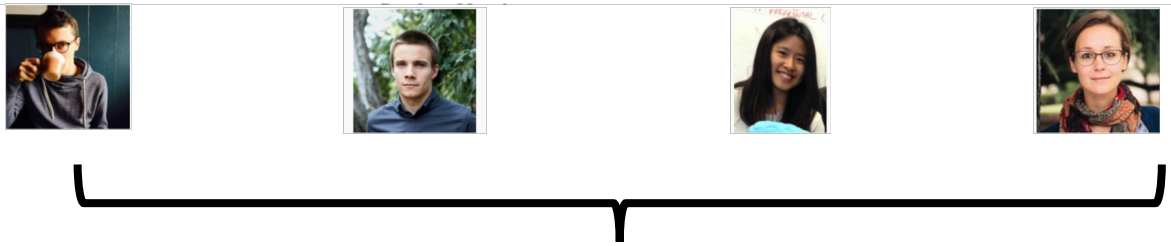
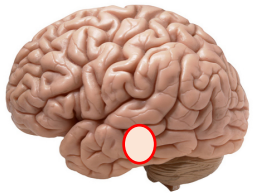
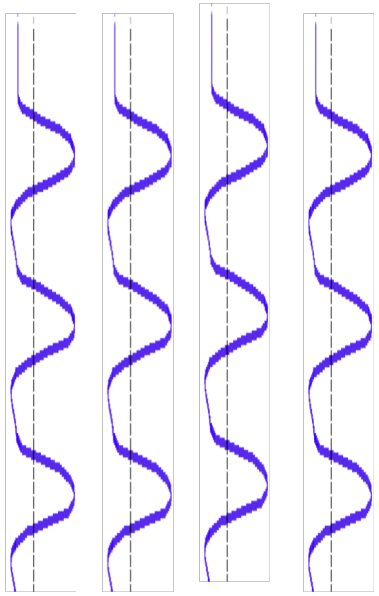




Use least square solutions to obtain the
4 beta estimates for every voxel



Weights to scale g(t)



4 Beta brains

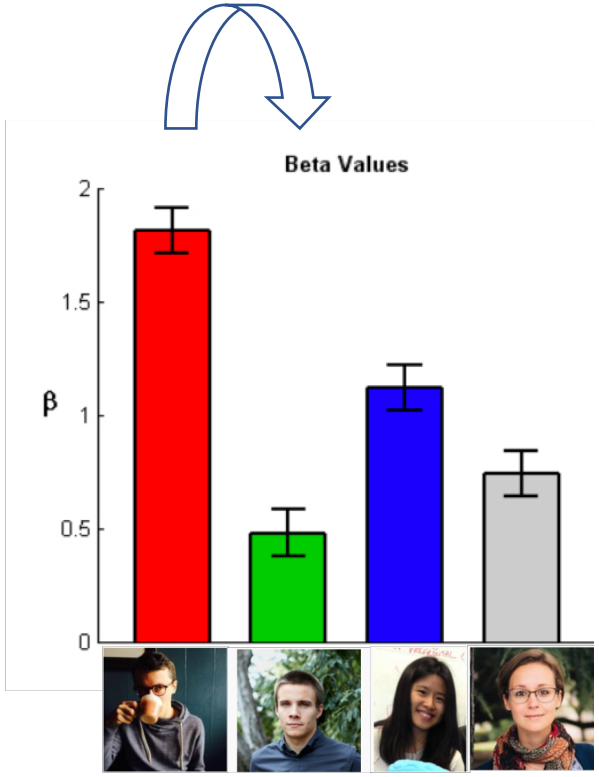
Subject 01

Detecting effect (group level analysis)

Usually we are more interested in comparing responses to different stimuli: Does stimulus A gives a bigger response than stimulus B?

$$y(t) = \beta_1 g_1(t) + \beta_2 g_2(t) + \beta_3 g_3(t) + \beta_4 g_4(t)$$

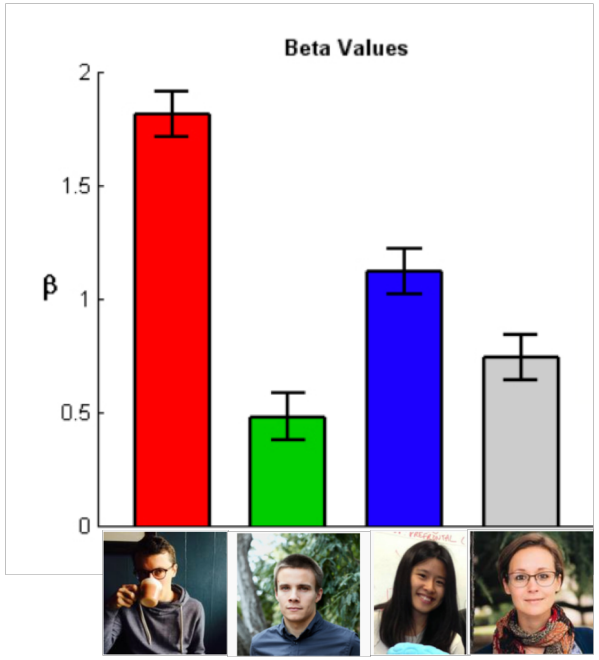
All subjects



Detecting effect

Usually we are more interested in comparing responses to different stimuli: Does stimulus A gives a bigger response than stimulus B?

We define our effect via contrasts:
C(1, -1, 0, 0)



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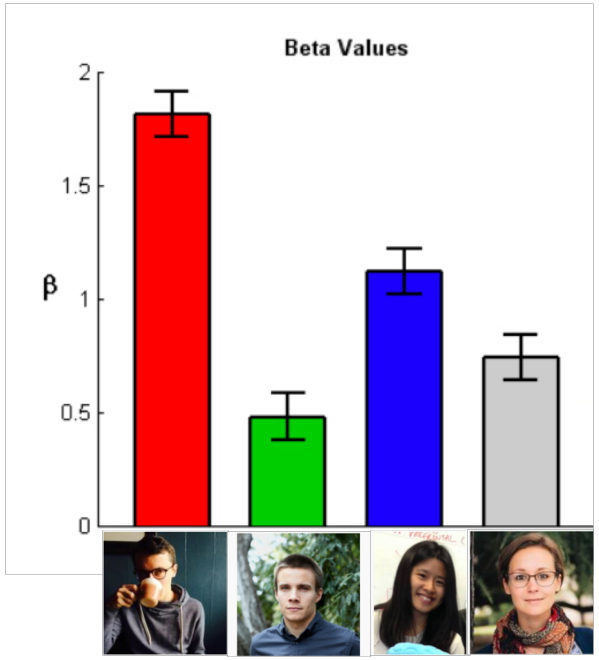
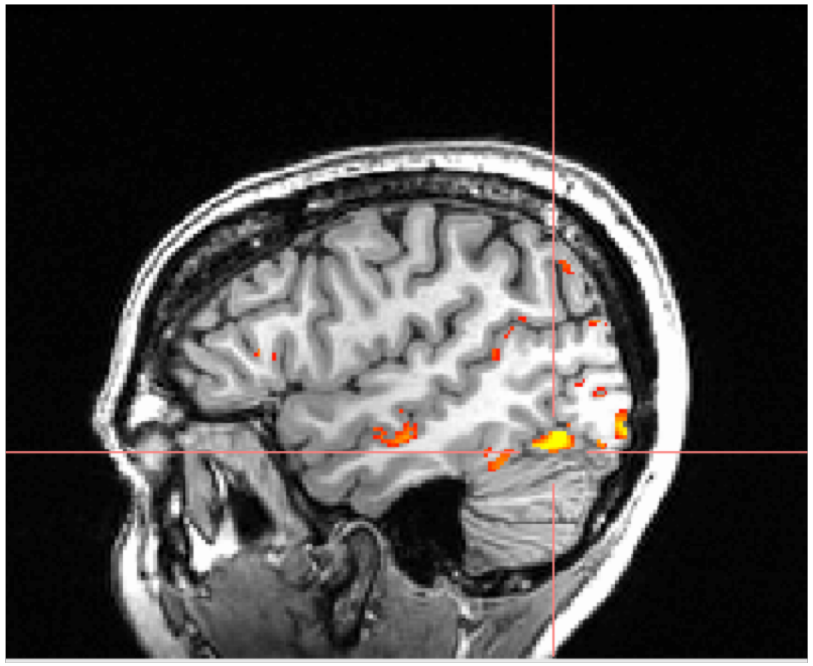


Calculate t-statistic
whether the effect differs from zero, using the ratio of the effect to its standard error

$$t = \frac{\beta_1 - \beta_2}{\sqrt{Var(c'\beta)}}$$



3 3.5 4 4.5 5 5.5 6 6.5 7 7.5 8

t value

Everything we have done so far is 1st-level analysis: obtain beta estimates for each condition. You obtain a set of beta estimates for each subject.

2nd-level analysis:
Single voxel – define the effect of interest for each subject using contrast and obtain t-statistic

Multiple voxels – do neural ”activity” patterns carry any information?

During retrieval….

How do neural representations code for different levels of spatial information in human?

Distinct representations v.s. Hierarchical representations for locations under the same global environment

How does stability of neural representations predict navigation duration?

If a subject successfully reinstated the representation for a specific location before navigation, did the subject navigate to the target location more efficiently?

Experimental design

ROOMS

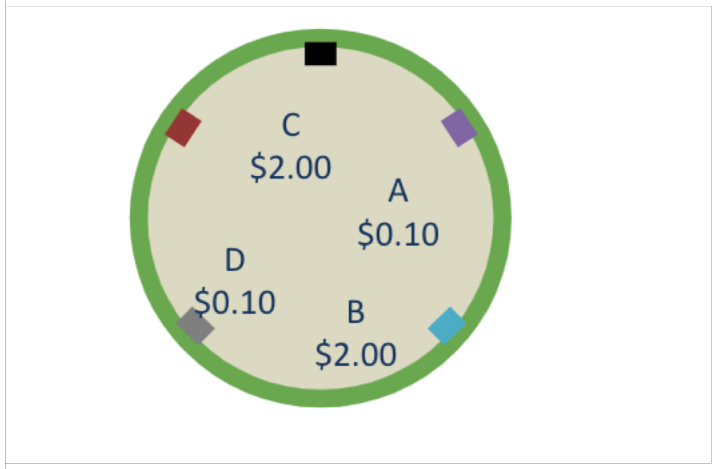
two virtual rooms (cube/cylinder; green/blue)

LOCATIONS

four hidden locations (A,B,C,D)

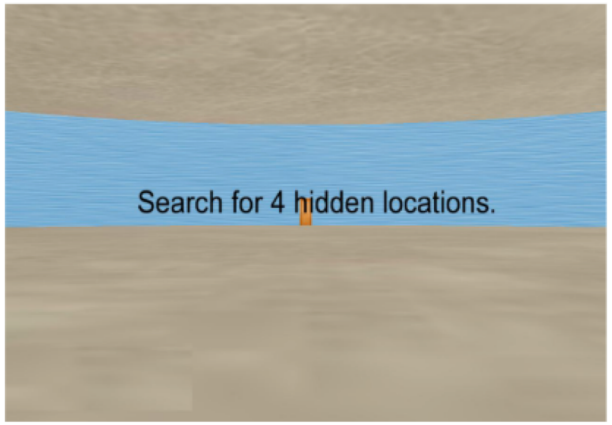
REWARDS

two rewards ($2.00/$0.10)



Day 1: Behavior (2.5 hr)

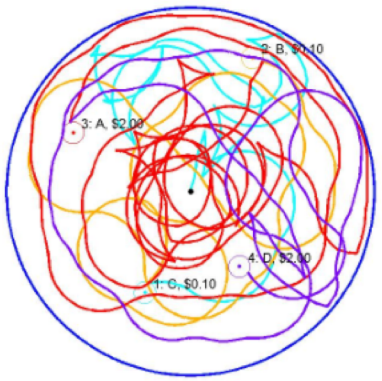
- Learn locations in one room (10 runs)
  - Free navigation. Limited time (3 min - 1 min) to find all locations in one room continuously.
  - If a location was not found within time limit, run ends and next run begins
- Test in one room
  - Navigate to cued locations
  - Each search starts from the center of the room
- Interleaved testing
  - Navigate to cued locations
  - Alternates between rooms



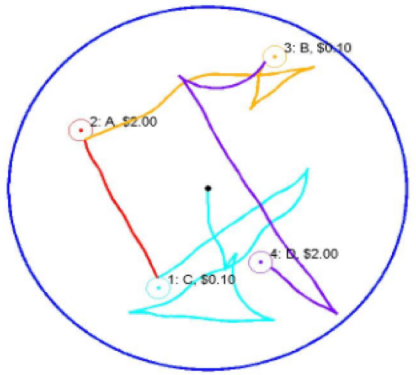
Day 1: Behavior

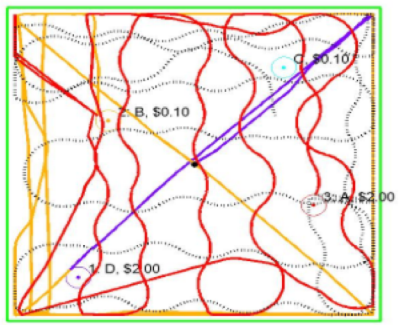
Learn locations in one room

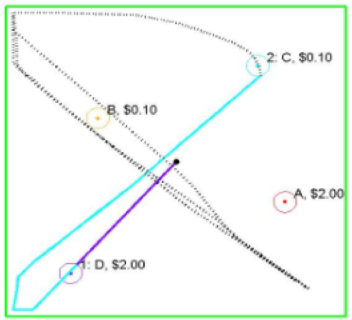
First learning block



Last learning block







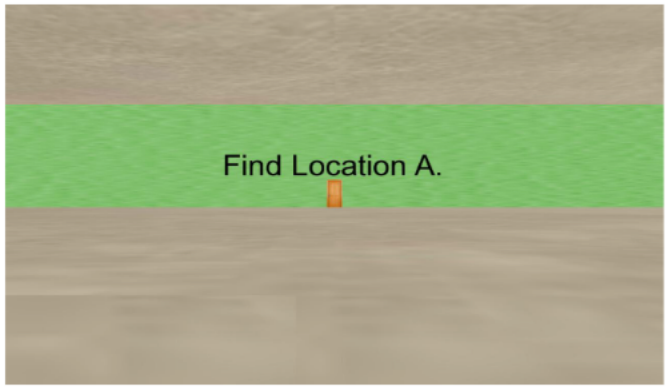
Day 2: fMRI scan (3.5 hr)

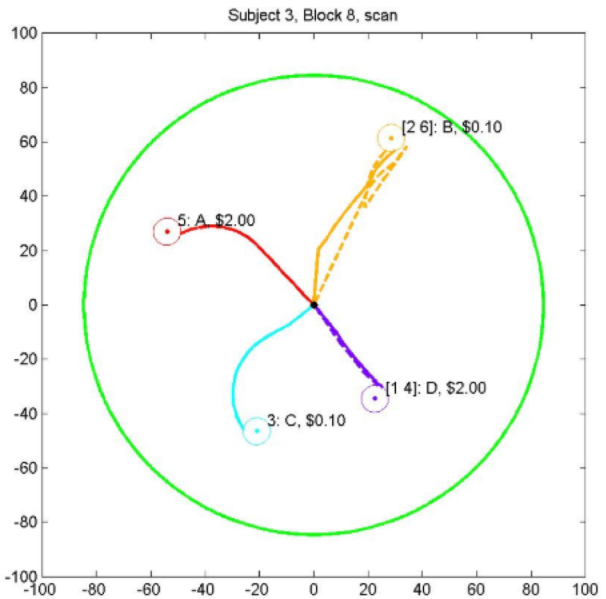
- Behavioral: Reminder learning and testing phases

- High-res fMRI Scan: Interleaved testing (~2hr)

  - Navigate to cued locations (30 sec)

  - Each search starts from the center of the room

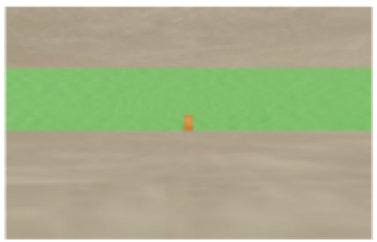




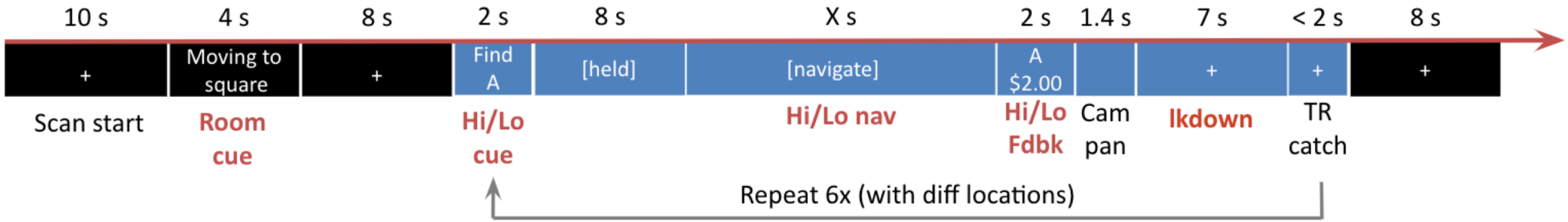
3 T MRI, GE Discovery MR750
High-resolution functional imaging
Repetition time = 2 s
Echo time = 32 ms
1.67 x 1.67 x 1.5mm

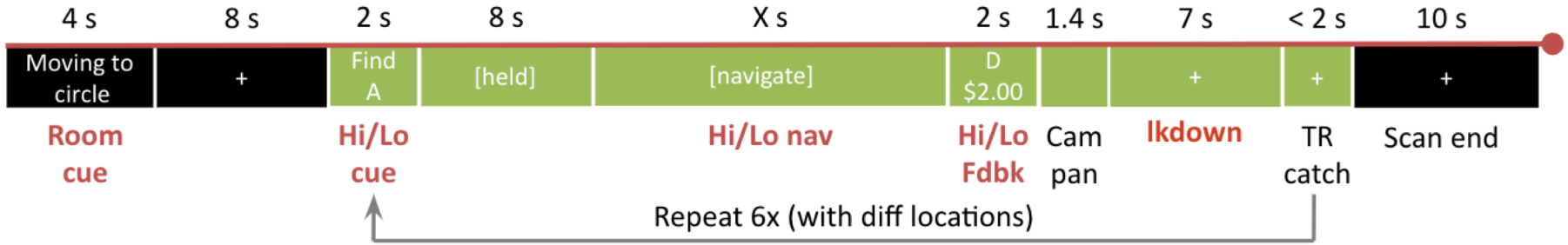
High-resolution anatomical imaging
Repetition time = 4.2s
Echo time = 66.05 ms
0.43 x 0.43 x 2.0 mm

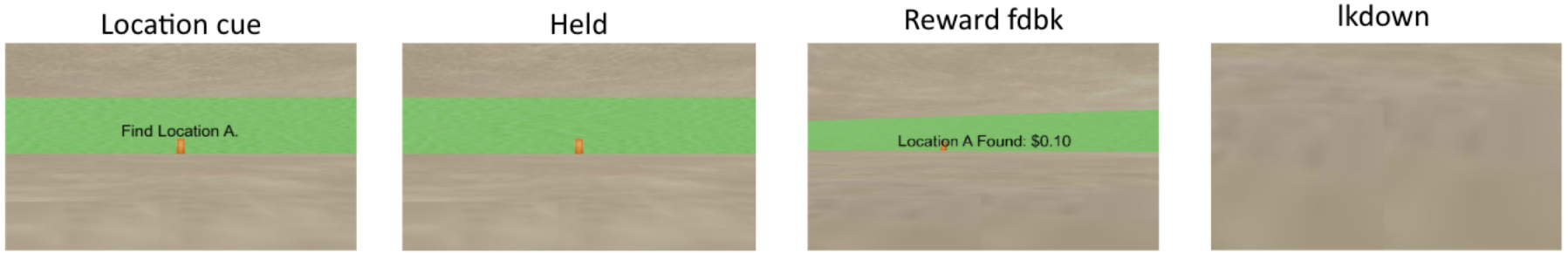
N: 15 (3 f, 12 m)
Age: 22.5 +- 1.9

Cue period 2s	Held 8s	Navigation Max 30 s	Feedback 2s	After feedback 7s
				

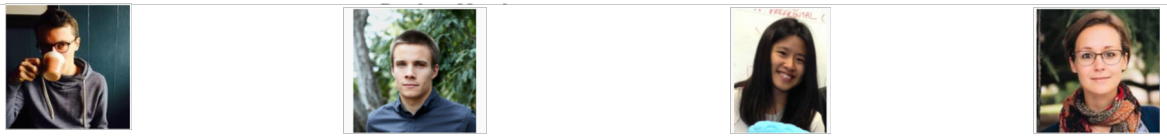
12 runs

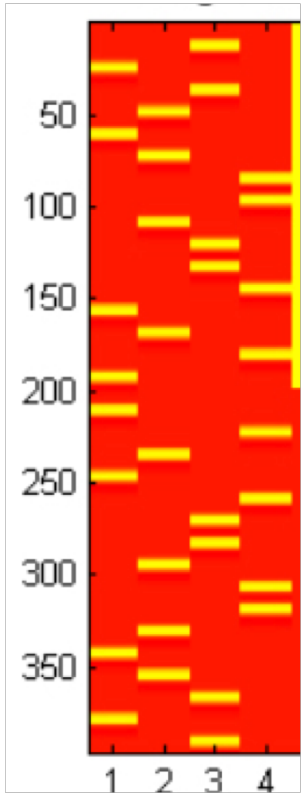

10 s
4 s
8 s
2 s
8 s
X s
2 s
1.4 s
7 s
< 2 s
8 s
+
Moving to square
+
Find A
[held]
[navigate]
A $2.00
+
+
+
Scan start
Room cue
Hi/Lo cue
Hi/Lo nav
Hi/Lo Fdbk
Cam pan
lkdown
TR catch
Repeat 6x (with diff locations)


4 s
8 s
2 s
8 s
X s
2 s
1.4 s
7 s
< 2 s
10 s
Moving to circle
+
Find A
[held]
[navigate]
D $2.00
+
+
+
Room cue
Hi/Lo cue
Hi/Lo nav
Hi/Lo Fdbk
Cam pan
lkdown
TR catch
Scan end
Repeat 6x (with diff locations)


Location cue
Held
Reward fdbk
lkdown
Find Location A.
Location A Found: $0.10

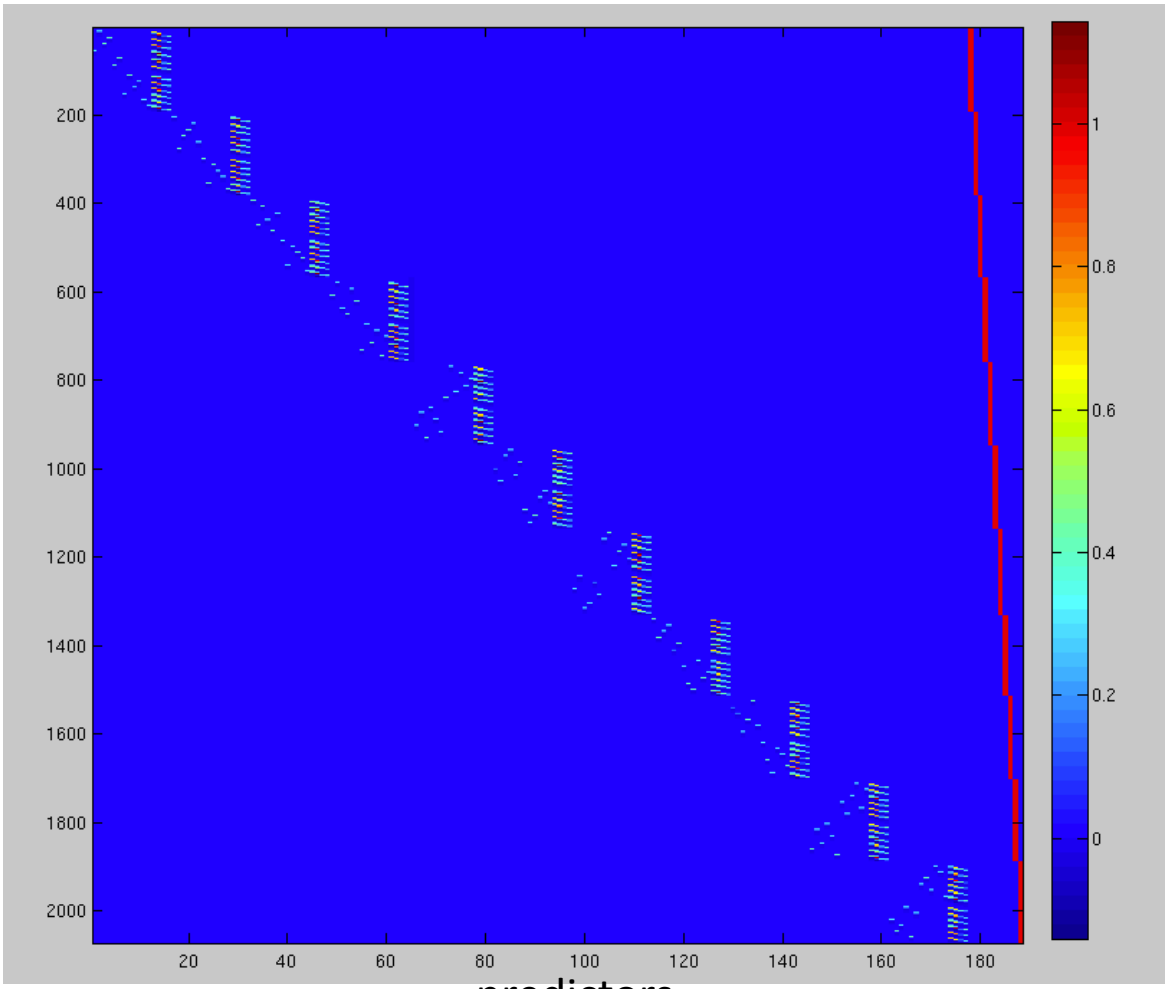
$$y(t) = \beta_1 g_1(t) + \beta_2 g_2(t) + \beta_3 g_3(t) + \beta_4 g_4(t)$$





My design matrix to obtain beta coefficients for every trial for every voxel in the brain

Loc_cue (2s)	held (4s)	Nav (nav durations)	Rwd fdbk (2s)	lkdown (2s)
• Success	• Success	• Success	• Cube (H/L) • Cyl (H/L)	• Success



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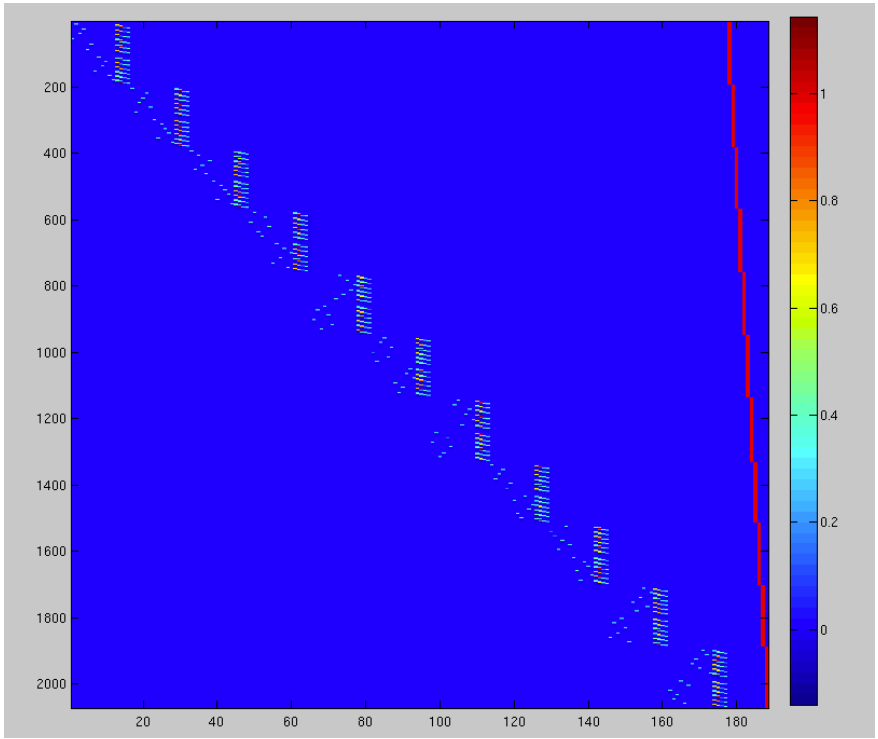
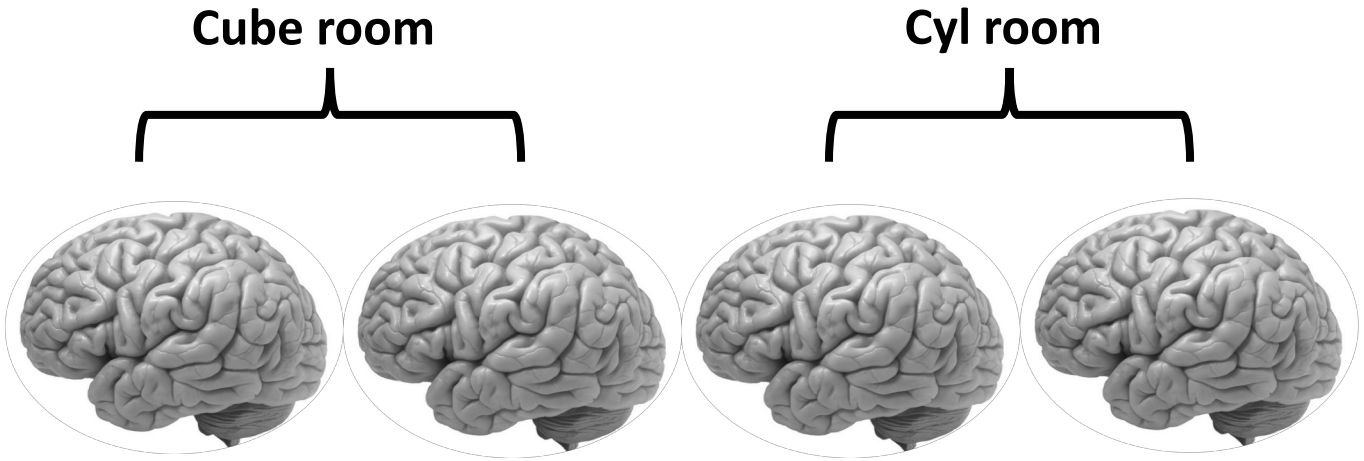
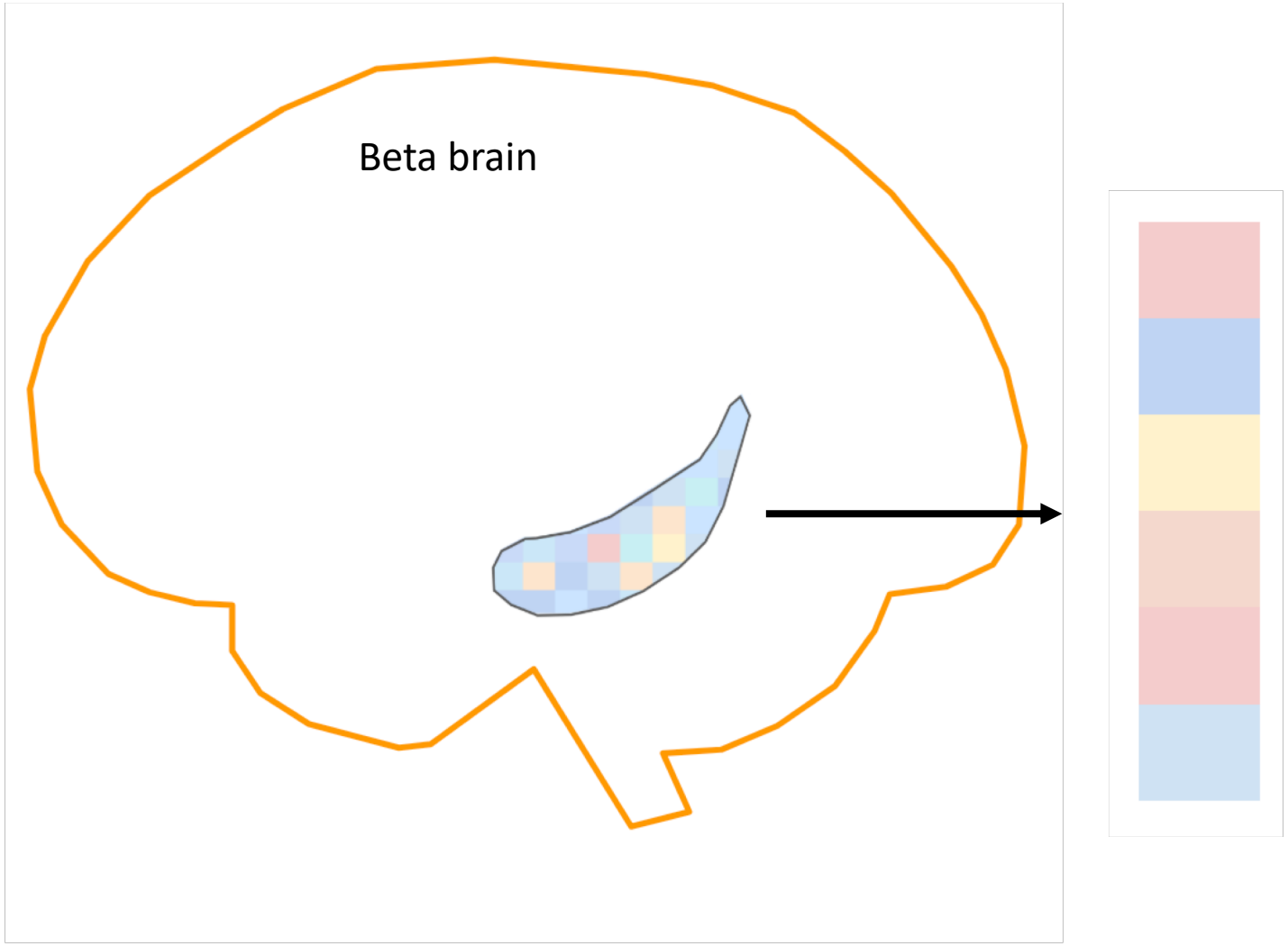
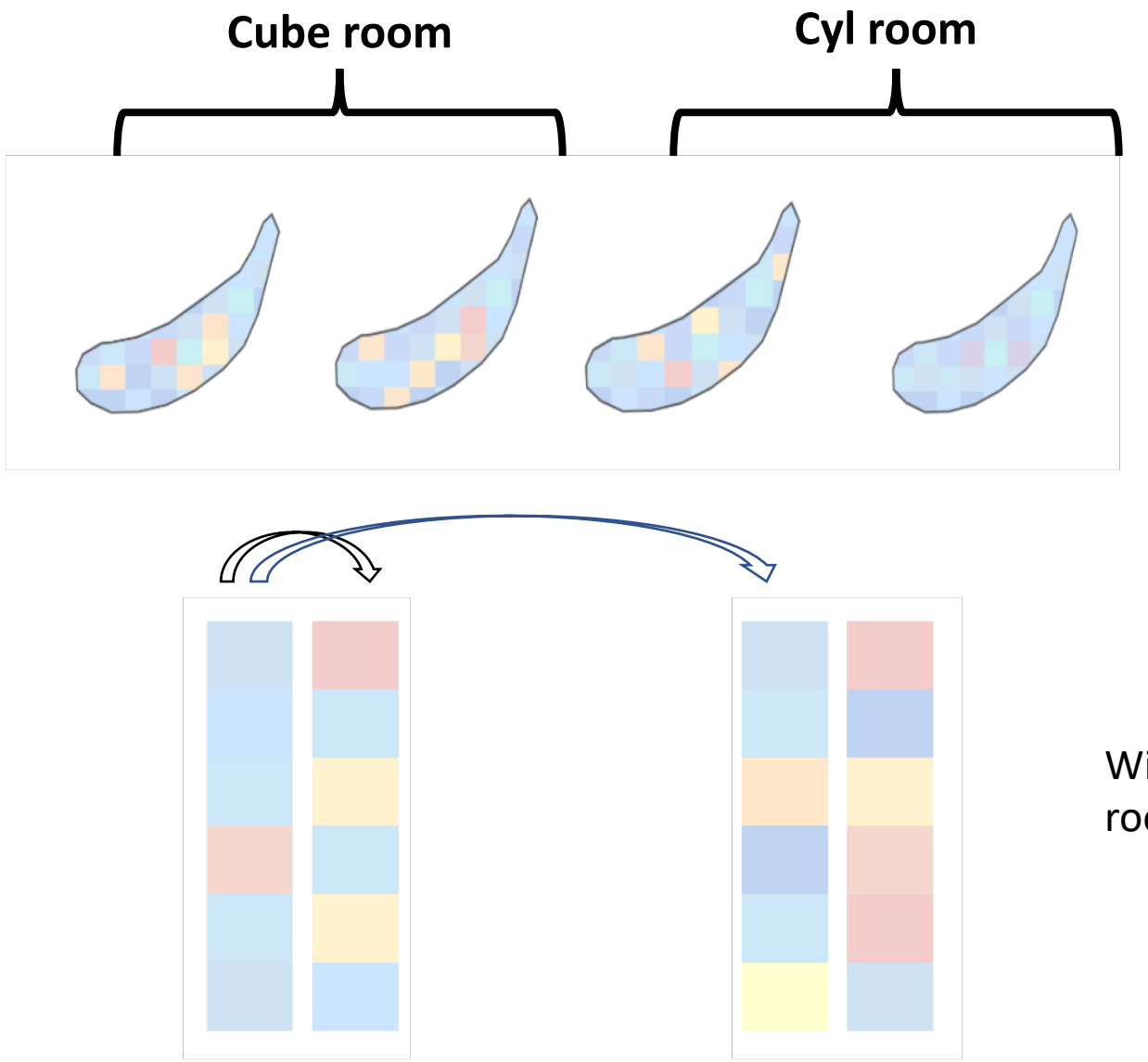


Beta brains

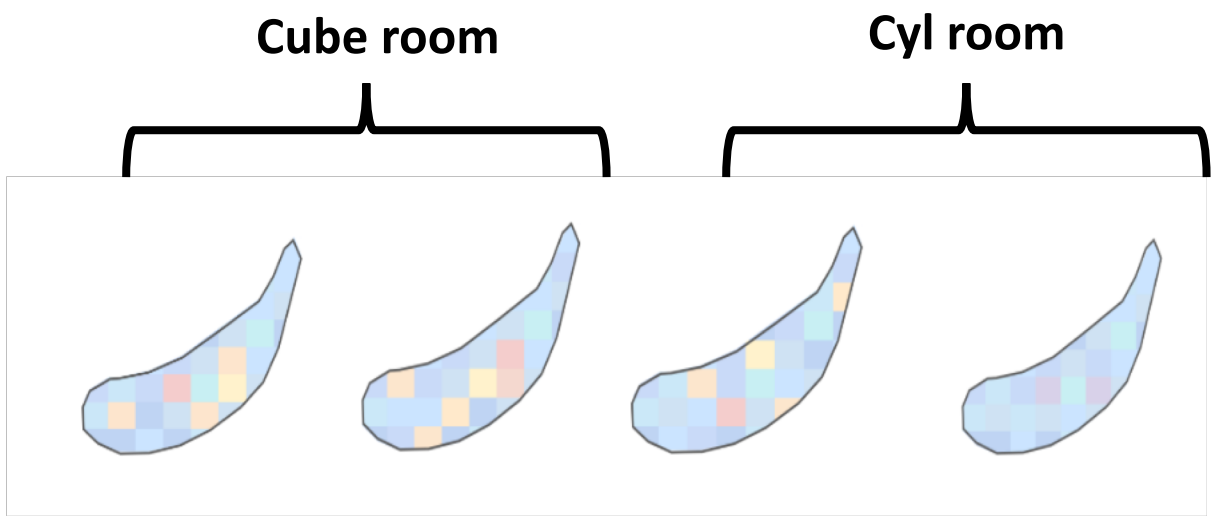


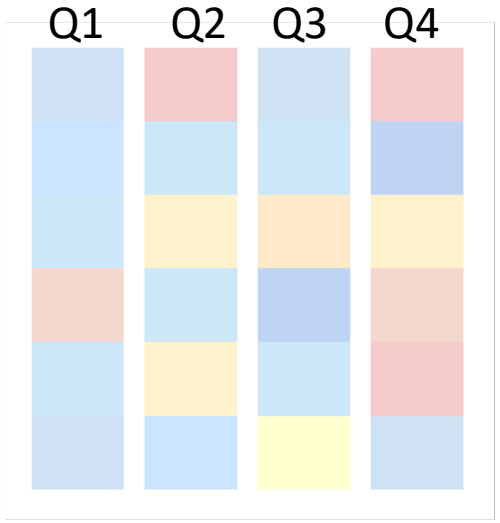
Region of interest (ROI) analysis + representation similarity analysis

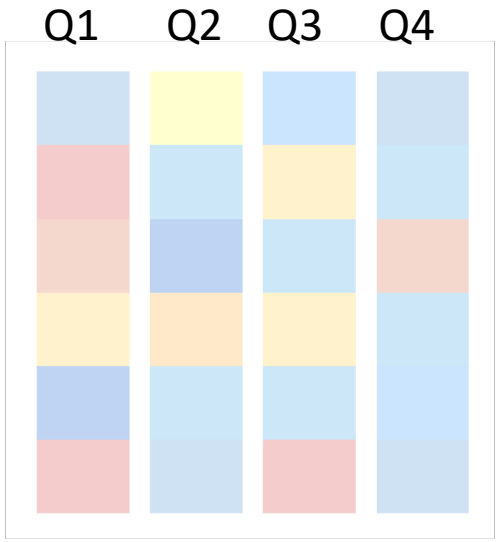


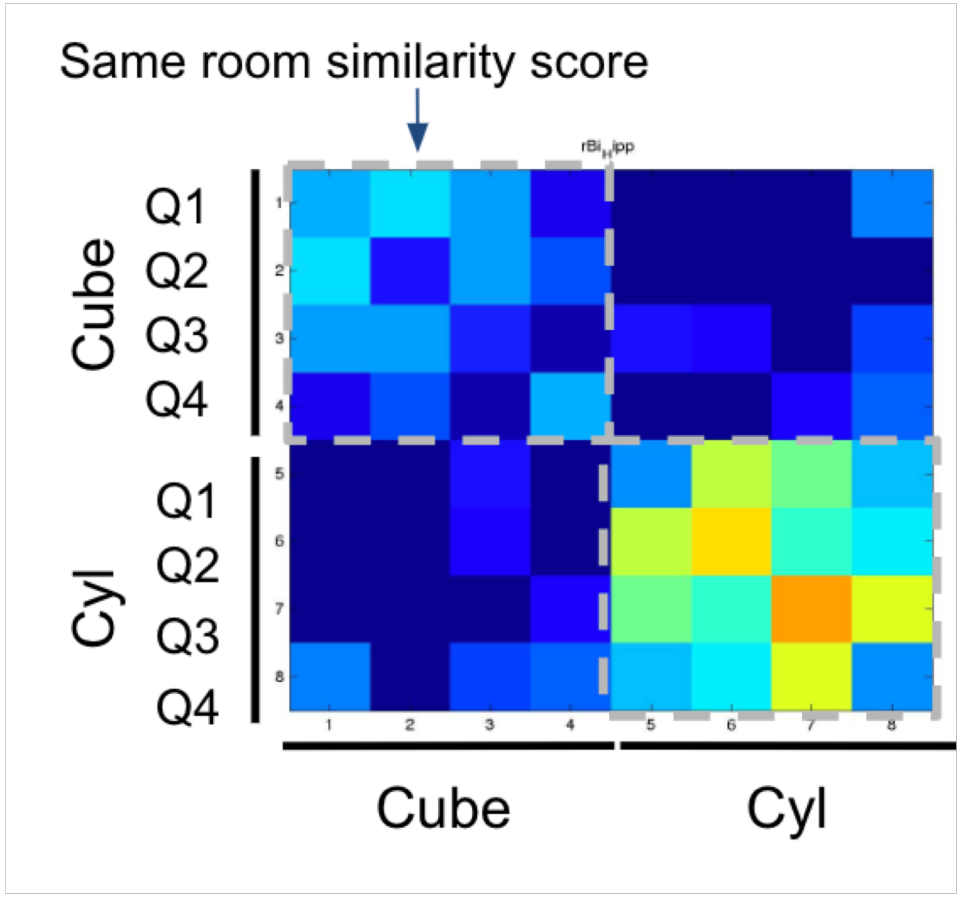


Within room and across rooms correlations

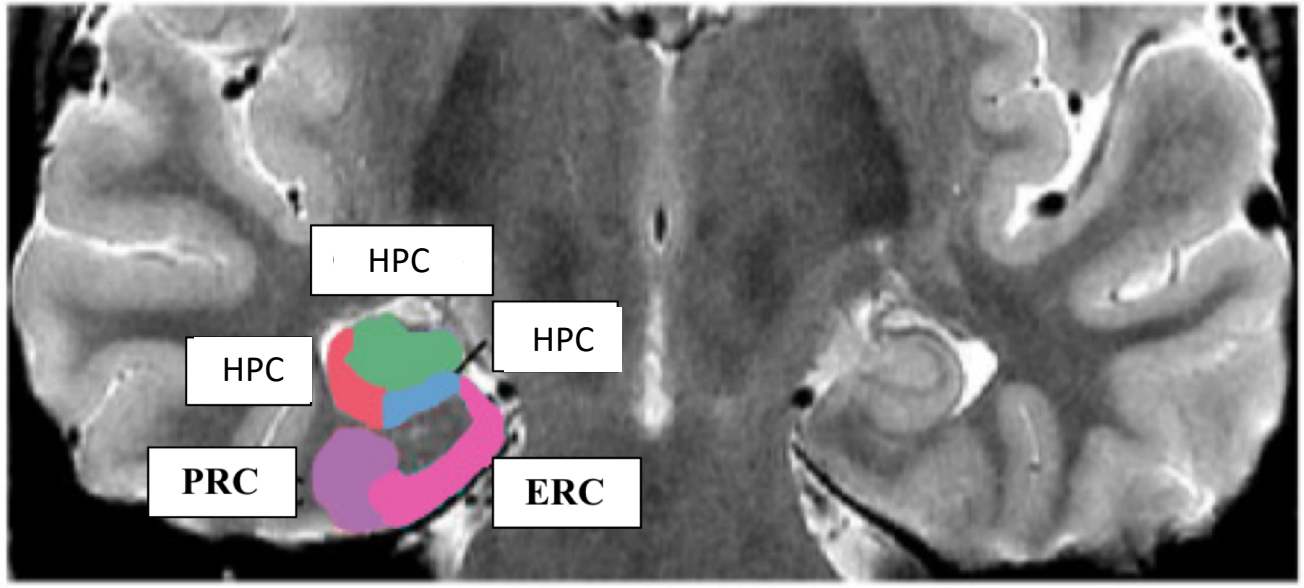

Cube room
Cyl room

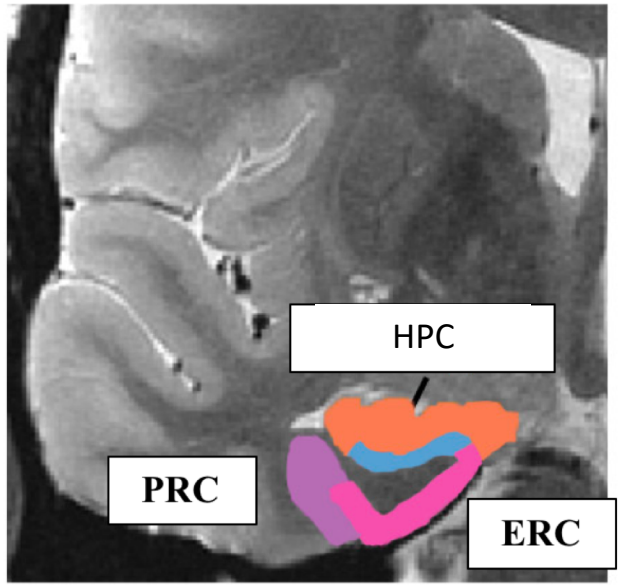

Q1
Q2
Q3
Q4


Q1
Q2
Q3
Q4

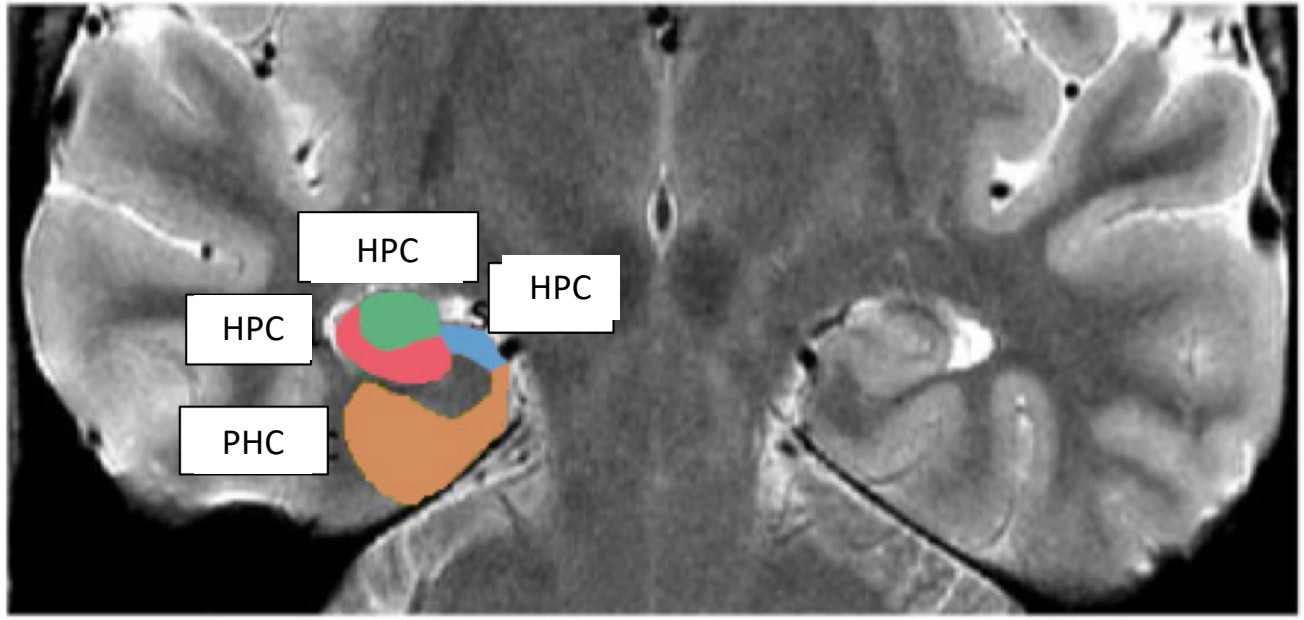

Same room similarity score
Cube
Q1
Q2
Q3
Q4
Cyl
Q1
Q2
Q3
Q4
1
2
3
4
5
6
7
8
Cube
Cyl

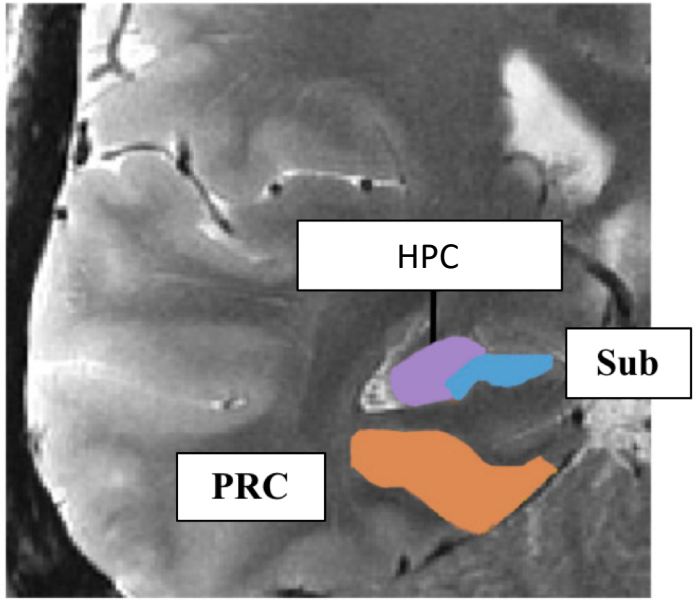
Anterior





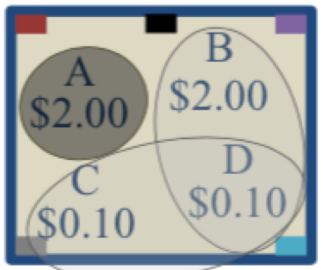
Posterior





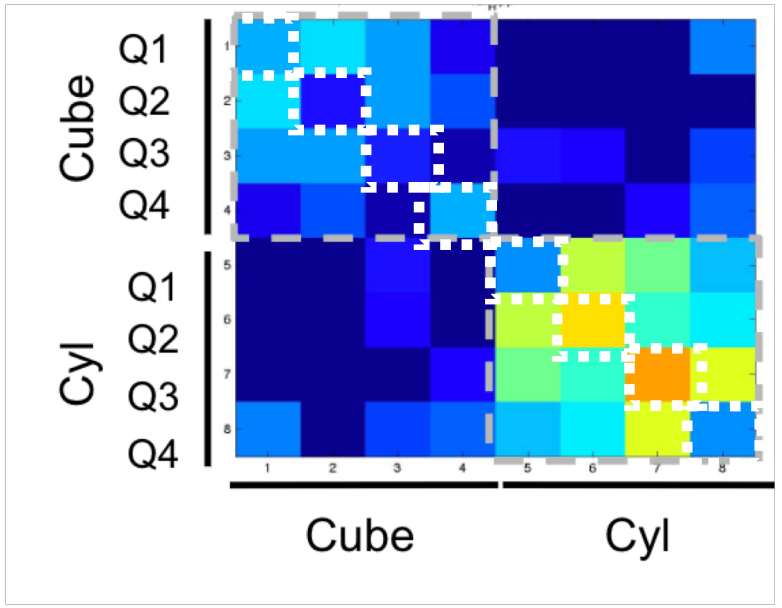
Reward fdbk

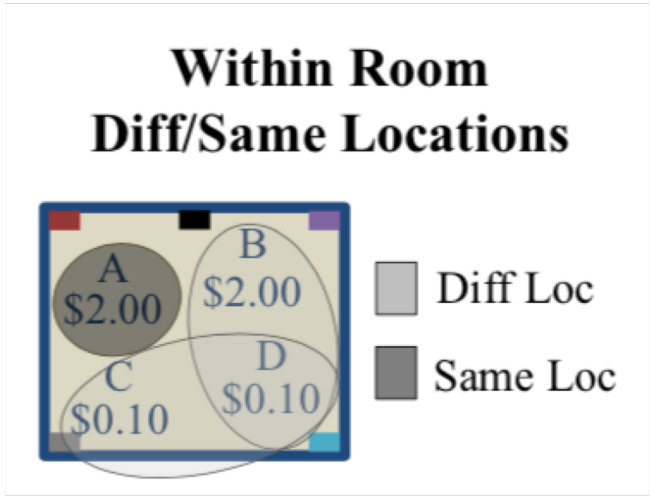
Within Room
Diff/Same Locations

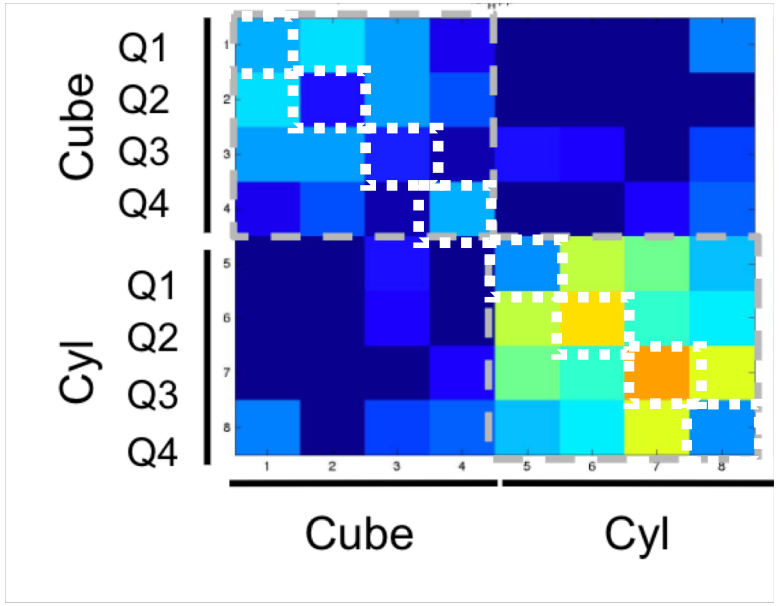


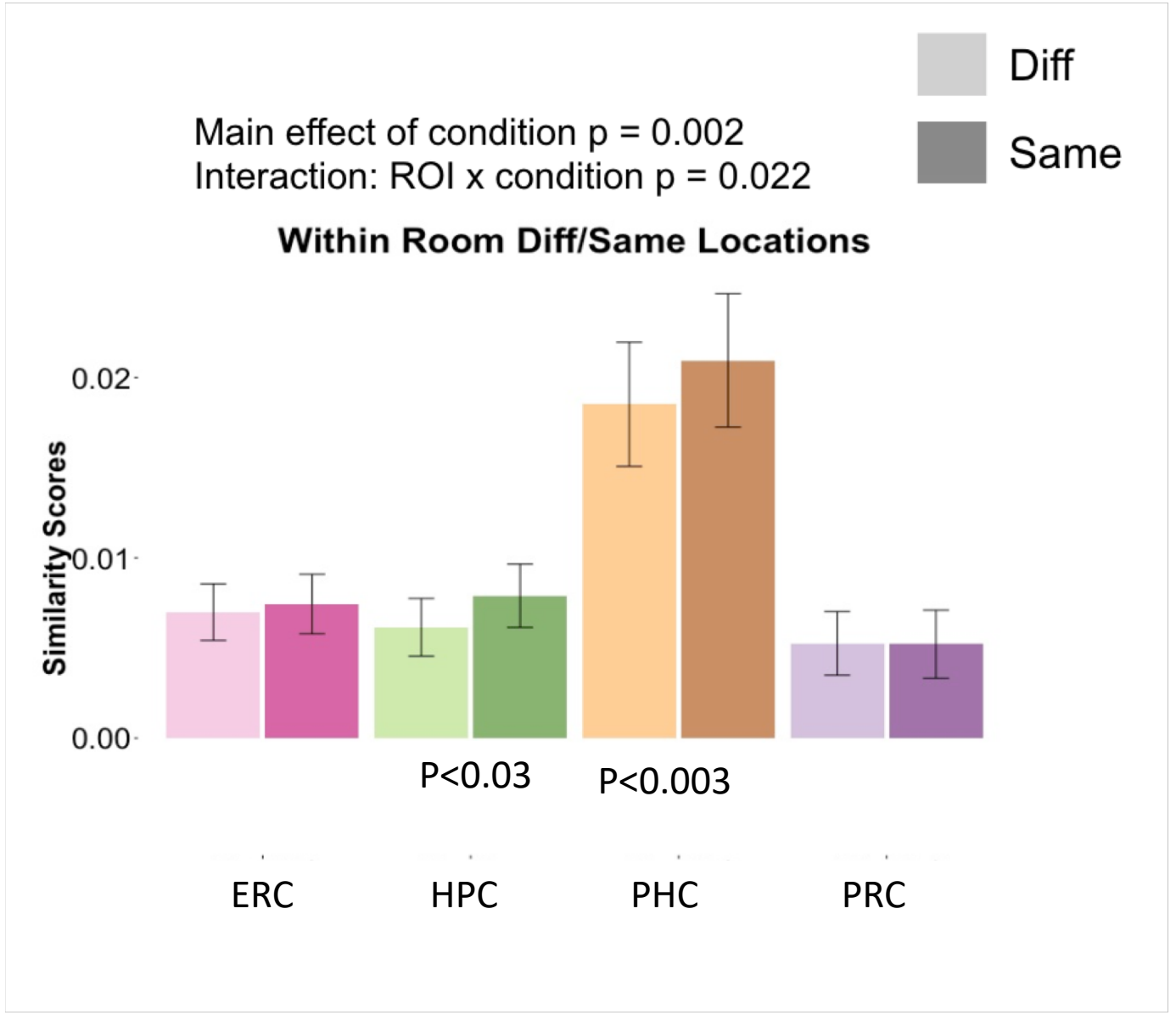
Diff Loc

Same Loc




Within Room
Diff/Same Locations
A
$2.00
B
$2.00
C
$0.10
D
$0.10
Diff Loc
Same Loc


Cube
Q1
Q2
Q3
Q4
Cyl
Q1
Q2
Q3
Q4
Cube
Cyl


Diff
Same
Main effect of condition p = 0.002
Interaction: ROI x condition p = 0.022
Within Room Diff/Same Locations
Similarity Scores
0.02
0.01
0.00
P<0.03
P<0.003
ERC
HPC
PHC
PRC

How does stability of neural representations predict navigation duration?

Location difference score (for each trial):
within room same location similarity score - within room different location similarity score

Log likelihood ratio test:

•Mixed-effect logistic regression
•How more likely the data are under the complete model than nuisance model

- Nav_dur ~ diff_score +(1|subID) +(0+diff_score|subID) vs. Nav_dur ~ (1|subID) +(0+diff_score|subID)

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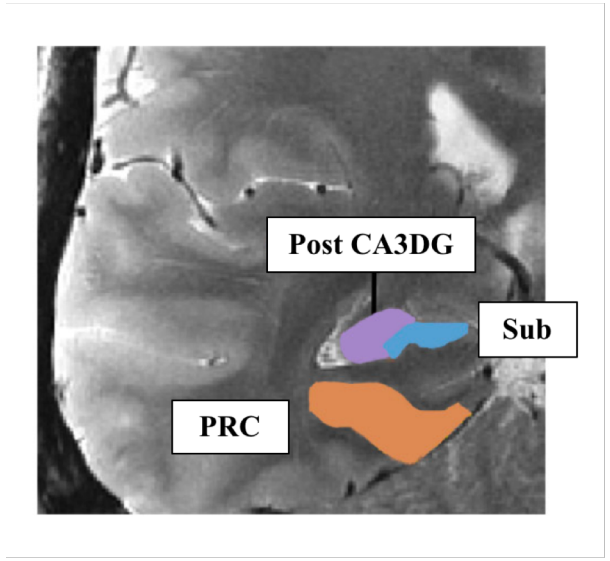
Likelihood Ratio Test Results

ROI	P-values
CA1	0.72
CA3DG	0.049
Ant CA3DG	0.44
Post CA3DG	0.0052
Sub	0.33



- When participants were situated in the virtual rooms (i.e., location cue period), navigation efficiency was predicted by strength of context-location representations in the posterior CA3DG
- HPC and PHC coded for location-specific information when participants arrived at goal locations
- Separate classification analyses and likelihood ratio test confirmed the pattern similarity findings