2017.07.27 政大 fMRI進階工作坊
Psychophysiologic interaction analysis

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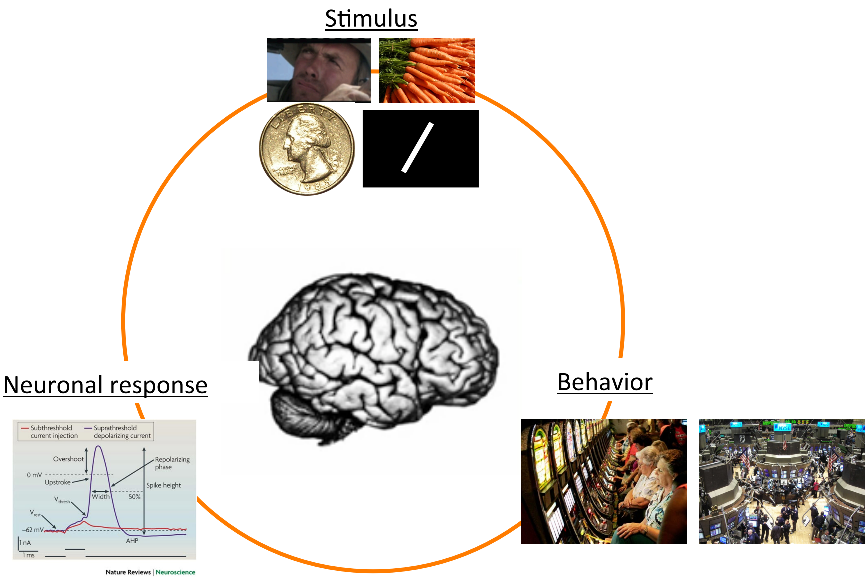
Outline

- Overview on functional connectivity
- Psycho-Physiologic Interaction (PPI) analysis
  - What is it?
  - What can it address?
- Connectivity dynamics

0. A brief introduction to cognitive neuroscience

系統/認知神經科學 (Systems/cognitive neuroscience)

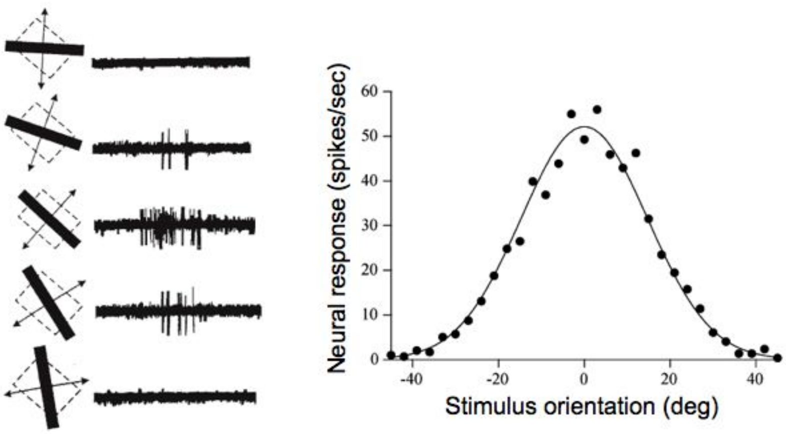


Neurophysiology
Measuring activity of single neurons (1960)

https://www.youtube.com/watch?v=IOHayh06LJ4

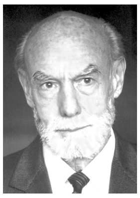
Measuring activity of single neurons

透過紀錄神經元活動，瞭解神經系統如何處理訊息



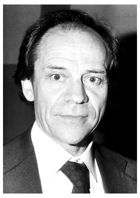
Nobel laureates in physiology or medicine
Neurophysiologists

1981



R Sperry

D Hubel



T Wiesel

2004

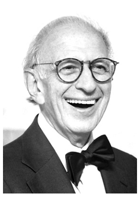
R Axel

L Buck

2000

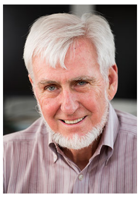
A Carlson

P Greengard



E Kandel

2014



J O'keefe

M-B Moser

E Moser

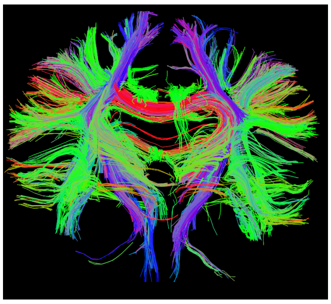
What is a network?

- Neurons or brain regions that are anatomically and/or functionally connected

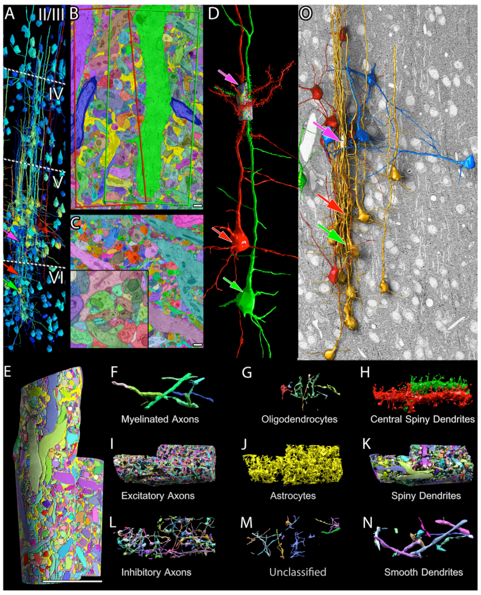
Anatomical/Structural connectivity

Def – Based on "structures"

Diffusion tensor imaging (DTI)



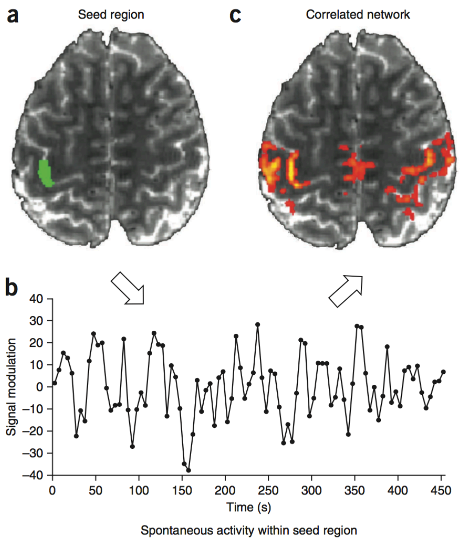
http://www.martinos.org/neurorecovery/technology.htm



Kasthuri et al., 2015, Cell

Functional connectivity

Based on brain "activity"



This will be today's focus!

Buckner et al. (2013, Nat Rev Neurosci)

Relation between structural and functional connectivity:

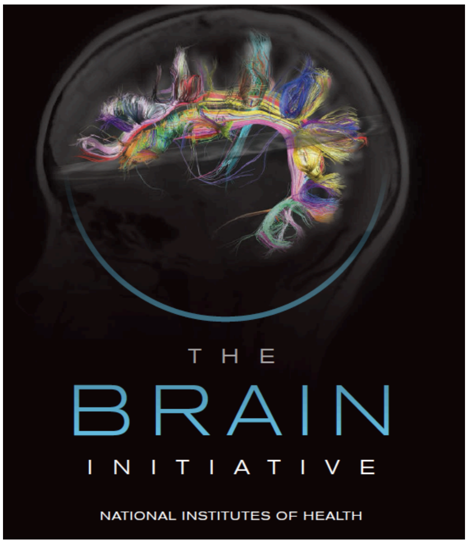
Functional connectivity is not a simple proxy for
static anatomic connectivity

Buckner et al. (2013, Nat Rev Neurosci)

Why is understanding brain dynamics important?

Its role in understanding behavior

Brain **R**esearch through **A**dvancing **I**nnovative **N**eurotechnologies (BRAIN) Initiative



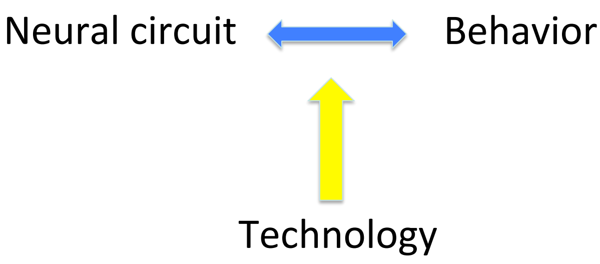
http://www.braininitiative.nih.gov

BRAIN Initiative: April, 2013

"To understand the circuits and patterns of neural activity that gives rise to mental experience and behavior"

(6:00-7:30)
http://www.braininitiative.nih.gov

Creating a dynamic picture of brain function



"Accelerate the development and application of new technologies to construct a dynamic picture of brain function that integrates neuronal and circuit activity over time and space"

http://www.braininitiative.nih.gov

BRAIN Initiative: 6 research areas

1. Mapping neural circuits
2. Recording neuronal dynamics
3. Manipulating circuit activity
4. Studying and measuring behavior
5. Modeling: theory, modeling, and statistics
6. Human neuroscience and neurotechnology

http://www.braininitiative.nih.gov

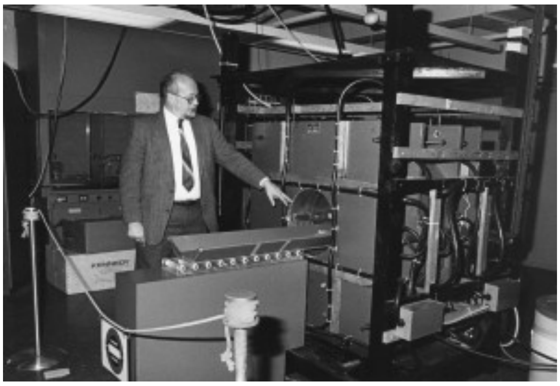
What is the level/scale of the measurements of brain activity I will be talking about?

The birth of magnetic resonance imaging (MRI)

2003

P Lauterbur

P Mansfield



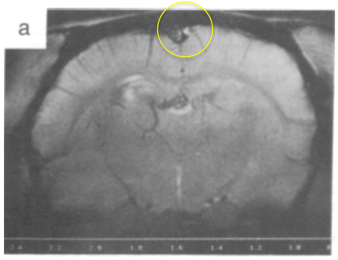
Functional magnetic resonance imaging (fMRI)

- Blood oxygen level dependent (BOLD) signal (a proxy of local neural activity)
- Spatial resolution: 1mm – 3mm
- Temporal resolution: on the order of seconds

Functional magnetic resonance imaging (fMRI)

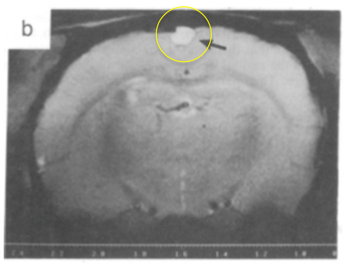
- Ogawa et al. (1990)
- Manipulation: the amount of oxygen the animal breathed
- Find Blood oxygen level dependent (BOLD) signal

100% O_2



Strong BOLD contrast

90% O_2/10% CO_2

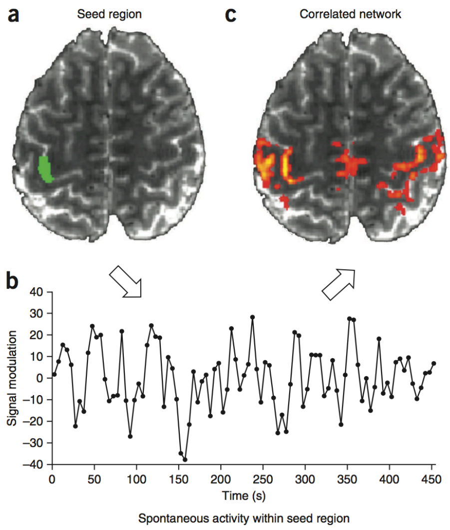


Weak BOLD contrast

I. Brain networks and resting-state fMRI

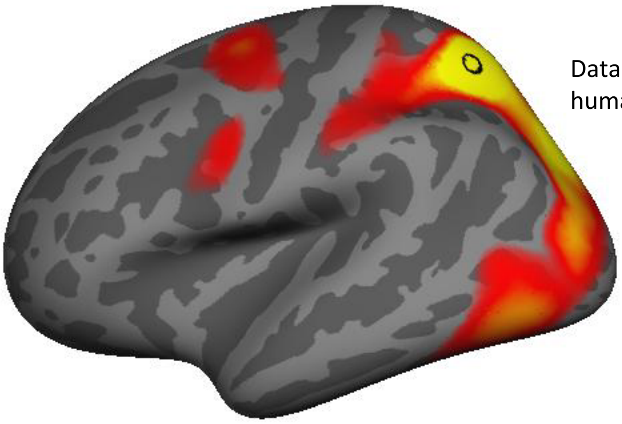
Resting state fMRI

- Subjects are scanned without being asked to perform tasks



Resting state functional connectivity

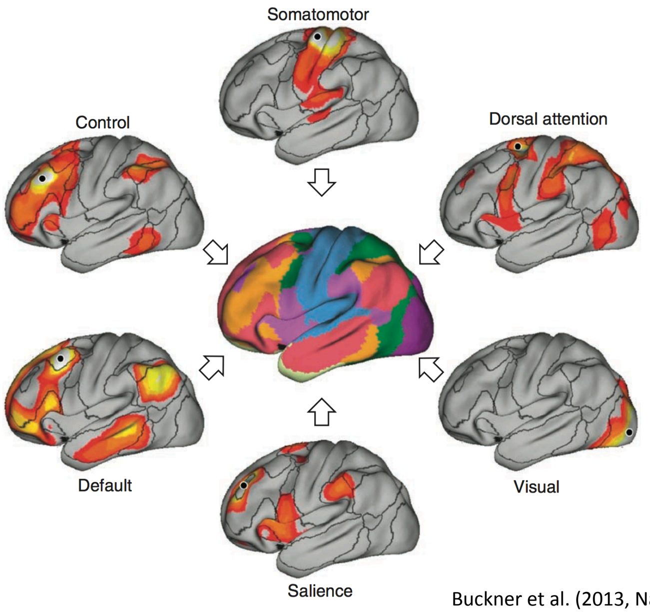
- Focus of the field: to identify networks based on functional connectivity (coactivation patterns) between regions



Data from 1000 human subjects

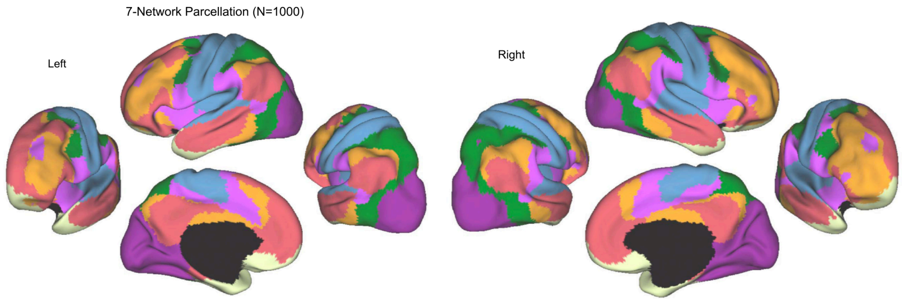
Buckner et al. (2013, Nat Rev Neurosci)

Large-scale brain networks



Buckner et al. (2013, Nat Rev Neurosci)

Network parcellation



Yeo et al. (2011, J Neurophysiol)

Default-mode network

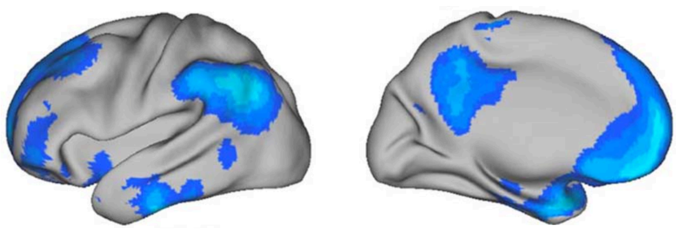
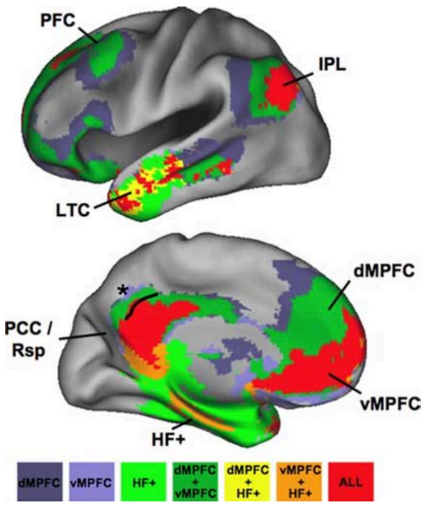


TABLE 1. Core regions associated with the brain's default network

REGION	ABREV	INCLUDED BRAIN AREAS
Ventral medial prefrontal cortex	vMPFC	24, 10 m/10 r/10 p, 32ac
Posterior cingulate/retosplenial cortex	PCC/Rsp	29/30, 23/31
Inferior parietal lobule	IPL	39, 40
Lateral temporal cortex†	LTC	21
Dorsal medial prefrontal cortex	dMPFC	24, 32ac, 10p, 9
Hippocampal formation††	HF+	Hippocampus proper,EC, PH

from Buckner et al. (2008)

“Hubs” in the default-mode network



- Hub: a region that connects (co-vary) with all other regions
- Hubs in default-mode network: vmPFC, PCC, IPL

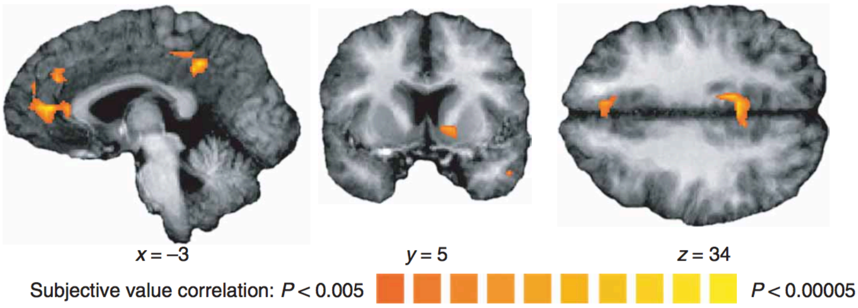
from Buckner et al. (2008)

II. Brain networks and cognition

Default-mode network

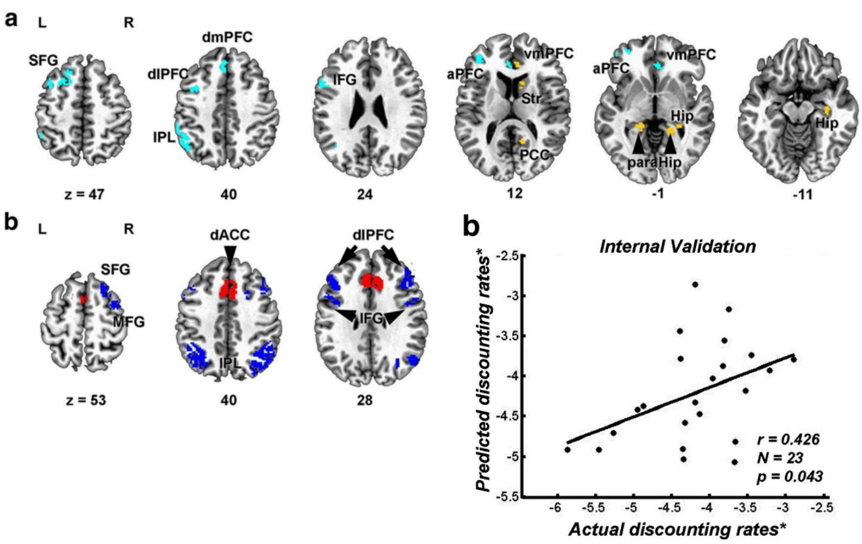
Default-mode network and decision making

$1000 now or $10,000 in 6 months



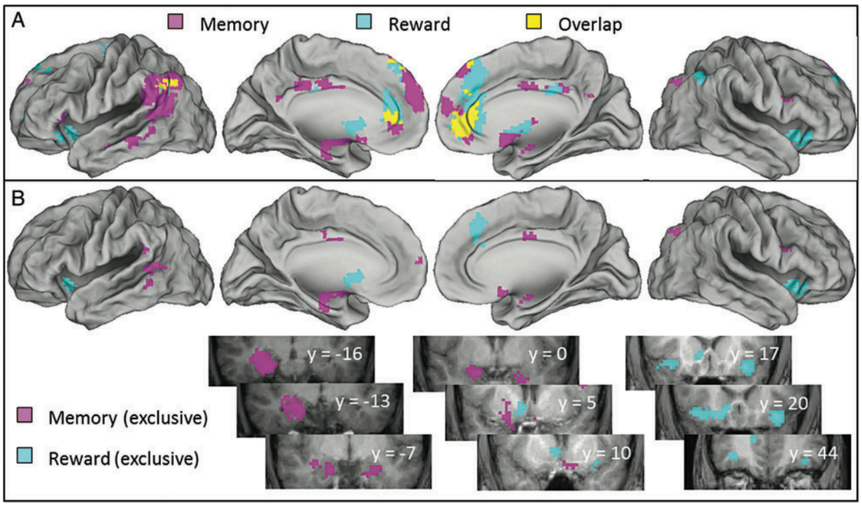
Kable & Glimcher (2007)

Resting-state connectivity and impulsivity



Li et al. (2013, J Neurosci)

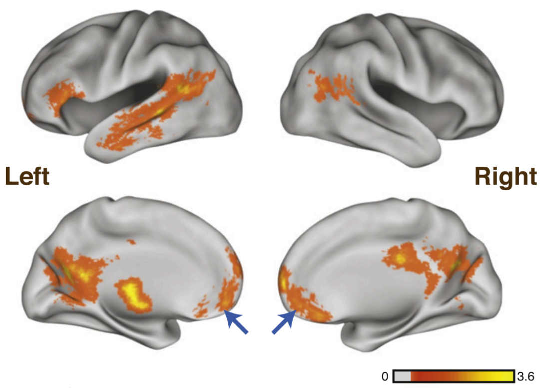
Memory, reward, and default-mode network



Elward et al. (2014, Cereb Cortex)

Moral judgment and default-mode network

Expected number of lives to be saved



Shenhav & Greene (2010, Neuron)

III. Understanding network dynamics

A. resting-state (task-independent)

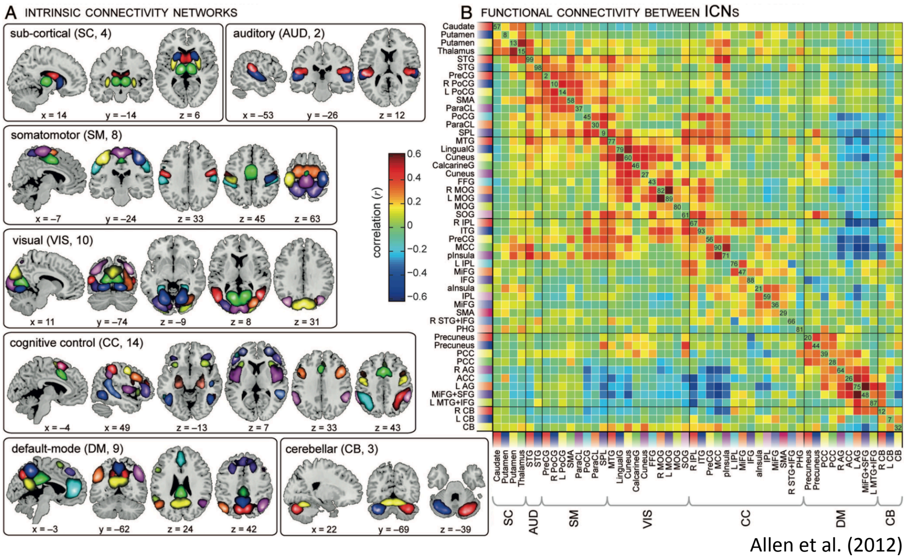
Resting-state network dynamics

- Does functional connectivity change over time?
- Past resting-state fMRI identifies networks but did not consider such possibility
- Dynamics can potentially be prominent in the resting state, during which mental activity is unconstrained

Allen et al. (2012)

Tracking dynamics

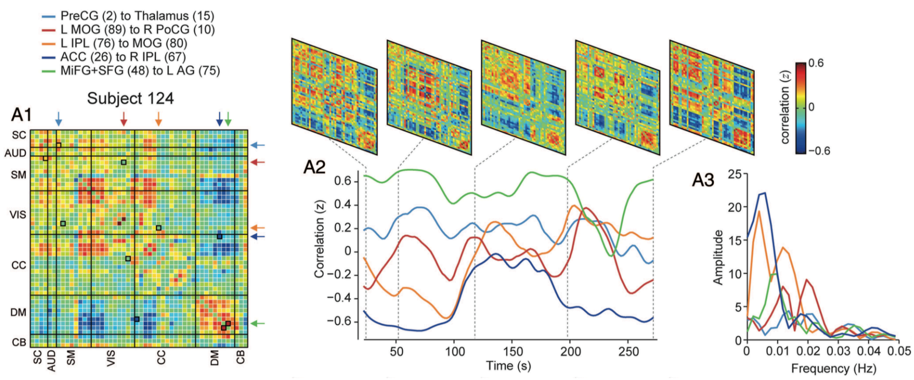
- Identifying network components



Allen et al. (2012)

Tracking dynamics of connectivity

- Functional connectivity can change over time

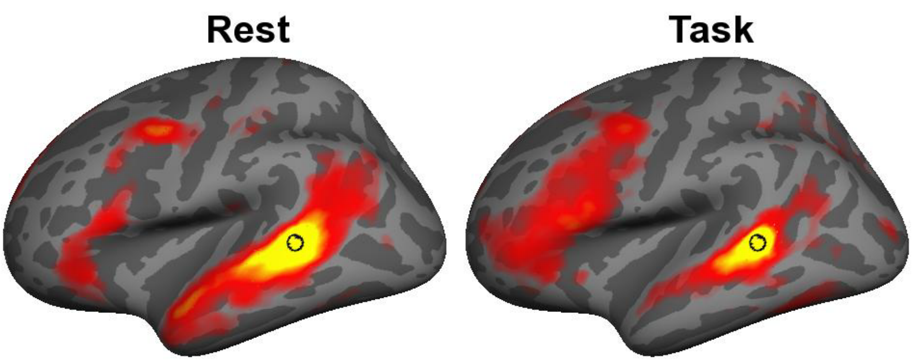


Allen et al. (2012)

III.B. Task-dependent network dynamics

- Does task-related functional connectivity change over time?

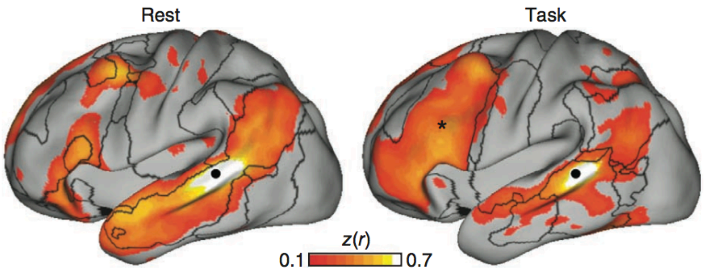
Task-dependent functional connectivity



Buckner et al. (2013, Nat Rev Neurosci)

Task-dependent functional connectivity

Change in connectivity when comparing task with rest



Buckner et al. (2013, Nat Rev Neurosci)

Psychophysiologic Interaction (PPI) analysis

A tool to investigate task-dependent functional connectivity

Psycho-Physiologic Interaction (PPI)

Goal

- To identify regions in the brain whose time course are correlated with a 'seed' region and the extent of correlation is modulated by some task-related manipulation in the experiment

- example: Hare et al. (2009, Science)

Tasty, bad for health

Or

Not tasty, good for health

Psycho-Physiologic Interaction (PPI)

Example: Hare et al. (2009)

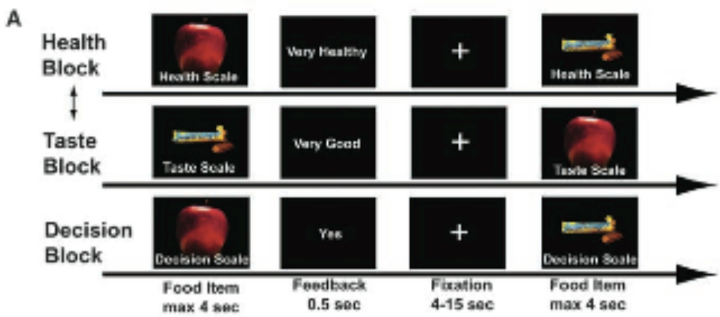
- How do people exercise self-control when choosing among food to eat?

- What are the neural mechanisms for *exercising* self-control during decision making?

Psycho-Physiologic Interaction (PPI)

Example: Hare et al. (2009)

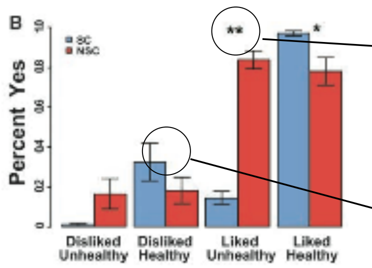
- 3 types of trials: Health rating, Taste rating, and food decision trials



Psycho-Physiologic Interaction (PPI)

Example: Hare et al. (2009)

- Divide subjects into self-control (SC) and non self control (NSC) groups

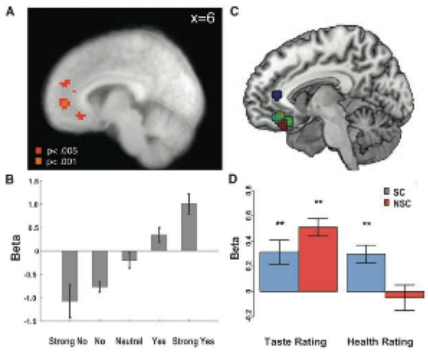


- The percentage of saying 'yes' to liked but unhealthy food was significantly smaller in SC group than NSC group
- The percentage of saying 'yes' to unliked but healthy food was marginally greater in SC group than NSC group

Psycho-Physiologic Interaction (PPI)

Example: Hare et al. (2009)

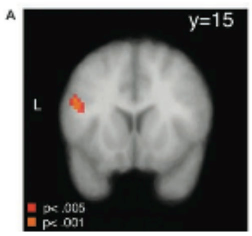
- Activity in ventro-medial prefrontal cortex (vmPFC) correlated with subjective value of food (irrespective of its taste and health)



- NSC' s taste rating is more corrleated with vmPFC activity than SC' s; SC' s health rating is more correlated with vmPFC activity than NSC' s

Psycho-Physiologic Interaction (PPI)

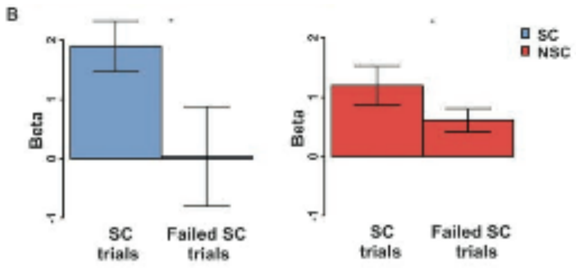
How might the brain exercise self control?



1. Activity in dorsolateral prefrontal cortex (DLPFC) was greater in successful self-control trials in SC group than in NSC group

Psycho-Physiologic Interaction (PPI)

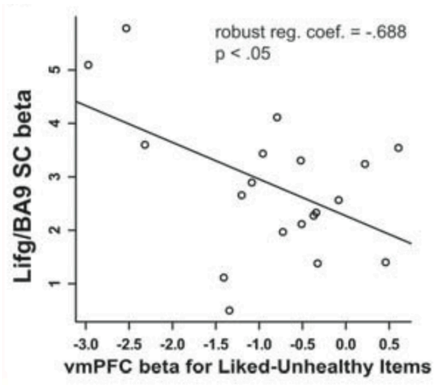
2. Both groups showed greater activity in SC trials than failed SC trials



Could DLPFC be responsible for exercising self control??

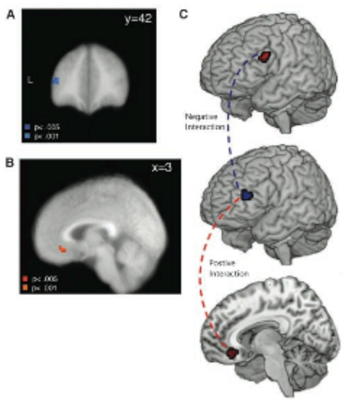
Psycho-Physiologic Interaction (PPI)

3. In trials where liked-but-unhealthy trials were avoided, vmPFC activity negatively correlated with DLPFC activity in SC groups



Psycho-Physiologic Interaction (PPI)

PPI analysis



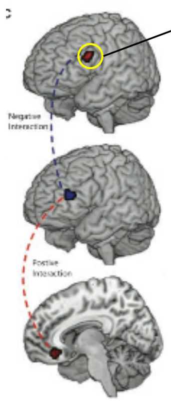
- Looking at the SC group:
  - Decreased functional connectivity during unhealthy trials between DLPFC and IFG (seed: DLPFC)
  - Increased functional connectivity during unhealthy trials between IFG and vmPFC (seed: IFG)
  - No PPI effect on NSC group

Neural mechanism: DLPFC exercise self-control to vmPFC through IFG

Psycho-Physiologic Interaction (PPI)

Example: Hare et al. (2009)

PPI procedure



1. Extract the BOLD time course of the seed regions
2. Estimate the time course of neuronal activity of seed using deconvolution
3. Construct GLM for PPI analysis

Psycho-Physiologic Interaction (PPI)

PPI GLM

$$y = \beta_{psych} x_{psych} + \beta_{physio} x_{physio} + \beta_{PPI} \left[x_{psych} \cdot x_{physio} \right] + \ldots$$

- Psychological regressor (psych): some task regressor (e.g. trials in which subjects made successful self-control; 1 for successful self-control, 0 otherwise)

- Physiological regressor (physio): time course of neuronal activity Of the seed region

- PPI regressor: interaction between psych and physio

Psycho-Physiologic Interaction (PPI)

Why deconvolution?

$$y = \beta_{psych} x_{psych} + \beta_{physio} x_{physio} + \beta_{PPI} \left[x_{psych} \cdot x_{physio} \right] + \ldots$$

$$H\left[X_{psych} \cdot x_{physio} \right] \neq \left[H(x_{psych}) \right] \cdot x_{BOLD}$$

It is critical to deconvolve the BOLD time series (x_{BOLD}) to neuronal activity x_{physio}

Psycho-Physiologic Interaction (PPI)

Discussion PPI

- PPI can address task-related changes in functional connectivity between 2 regions

- Beware of efficiency of your PPI GLM (especially check the correlation between psych and physio regressors

- It is a model-based approach (GLM) to understand functional connectivity, but could definitely be more informative than simply correlating time course between 2 regions

- The results of PPI are often complementary to the main results; they are typically not the main results of the experiment

Task-related, time-dependent connectivity and the dynamics of decision making

memory retrieval

learning

Something …

Sharing experiences in functional connectivity analysis

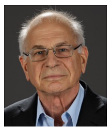
I. Individual differences ⟺ connectivity profile

II. Within-trial dynamical interactions

III. characterizing connectivity time-series

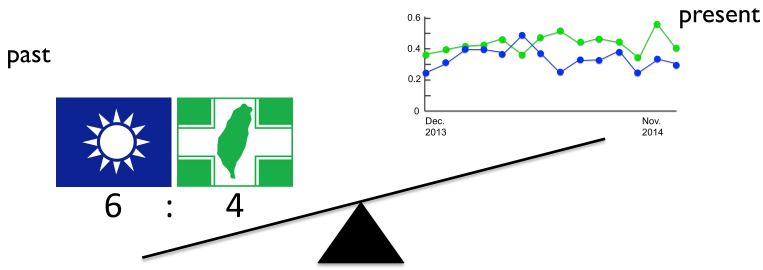
I. Interested in – Individual differences ⟺ connectivity profile

Issue:
Probabilistic/statistical inference



Ting et al. (2015, J Neurosci), Yang & Wu (in prep)

How people *weight* past and present information will determine his/her prediction

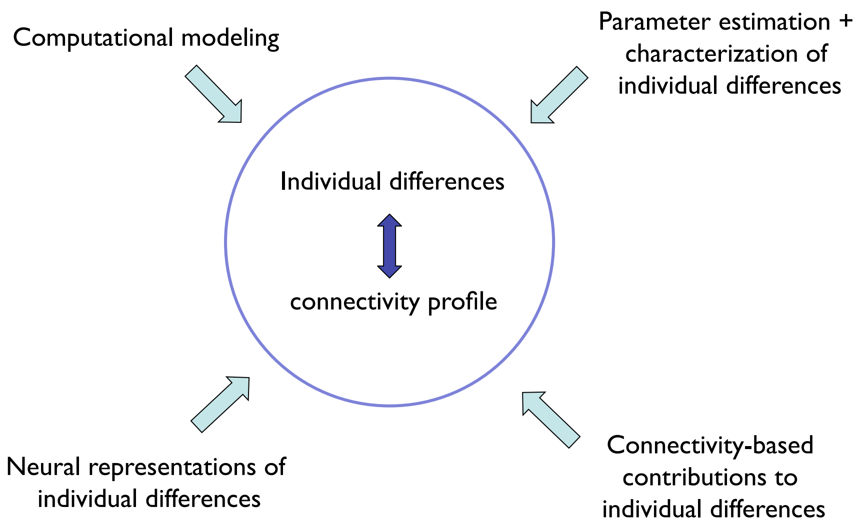


Prediction:  will win

What are the statistical properties of information that contribute to suboptimal inference?

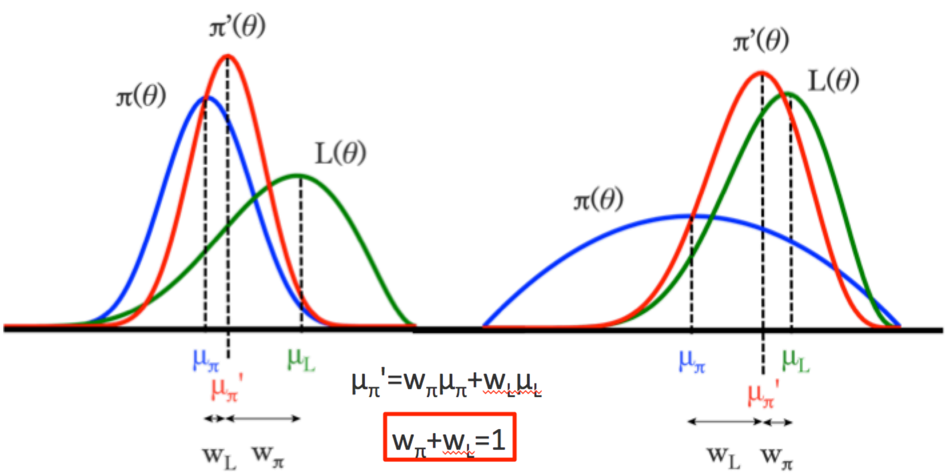
How can we characterize the boundary of rational inference at the neural-mechanistic level?

Framework + approach



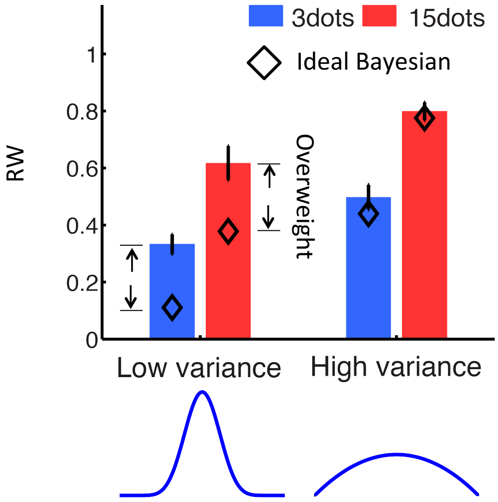
I. Computational model: Bayesian decision theory

- Infer weights assigned to different sources of information from choice behavior



2. Identify statistical properties contributing to suboptimal inference

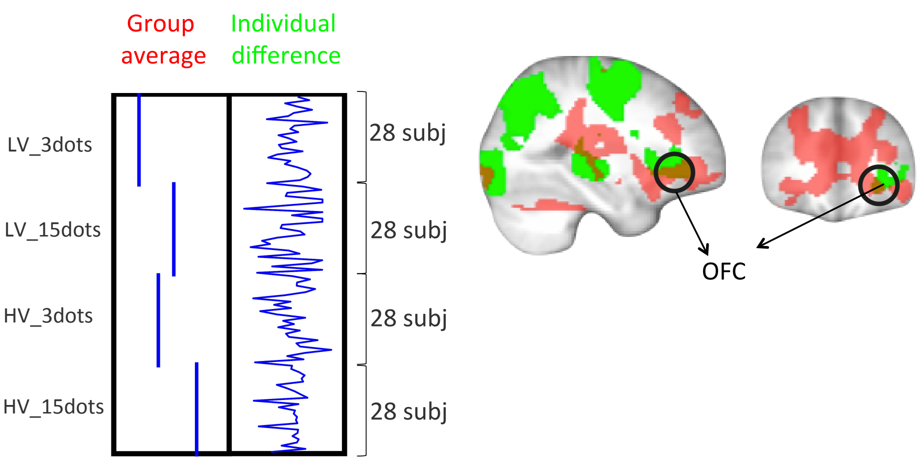
- By comparing actual with model-predicted behavior



- Failure to take into account *variance* of prior information

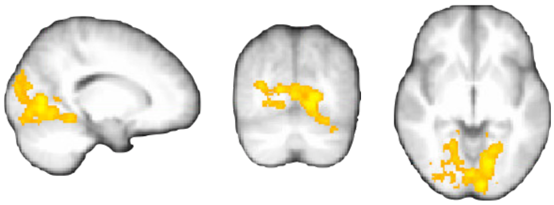
3A. Identify computational substrates for probabilistic inference

OFC represents individual differences in subjective weight inferred from choice behavior



3B. Identify representations for statistical properties contributing to suboptimal inference

The ventral visual pathway represents prior uncertainty

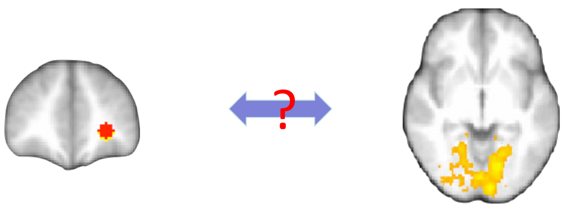


x= -16 y= -70 z= -4

p<0.05 (corrected)

- Higher activity for larger prior uncertainty

Why is it that humans are suboptimal?
What might be the neural-mechanistic interpretation?

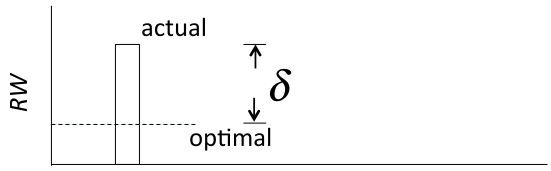


Conjecture:

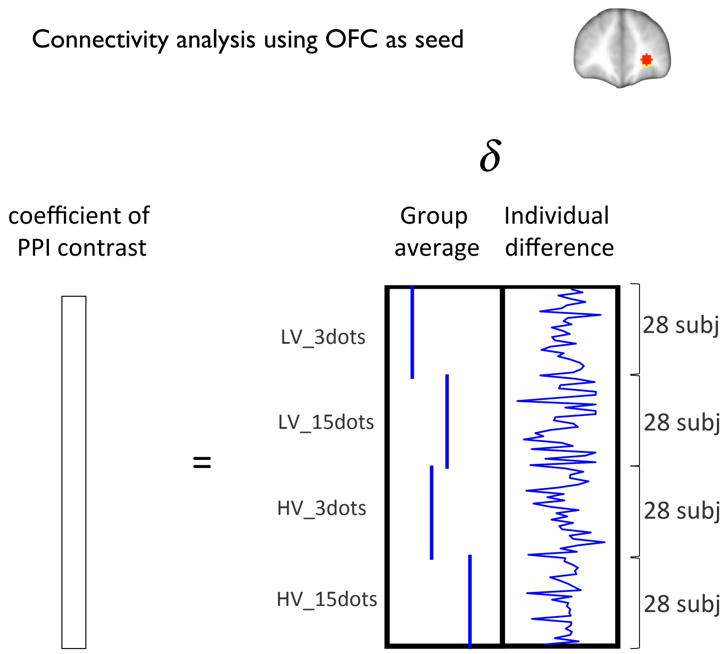
Is suboptimal inference associated with efficiency in information communication between OFC and ventral visual pathway?

Behavioral index for suboptimal inference:

Deviation from optimality δ



Connectivity analysis using OFC as seed

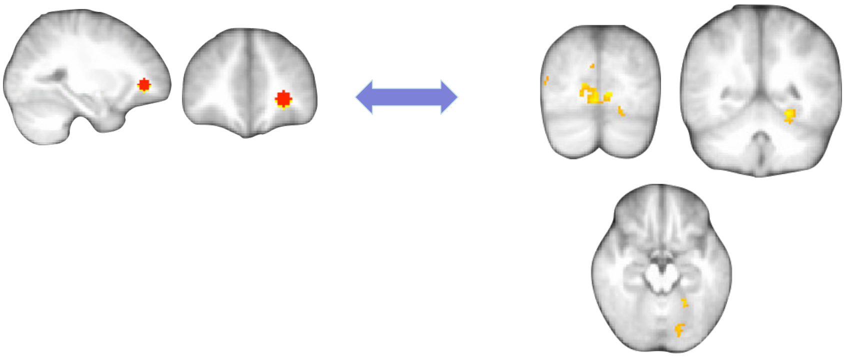


Connectivity between OFC and ventral visual pathway is correlated with deviation from optimality

The more prior info is ignored, the weaker the functional connectivity

OFC

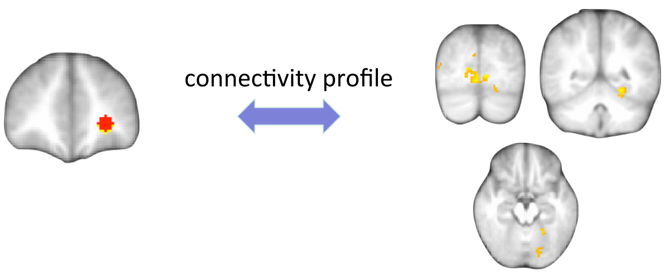
Ventral visual pathway
(Conjunction map: PPI + Prior Uncertainty)



Characterizing the boundary of rational inference

- Identify statistical properties that lead to suboptimal inference

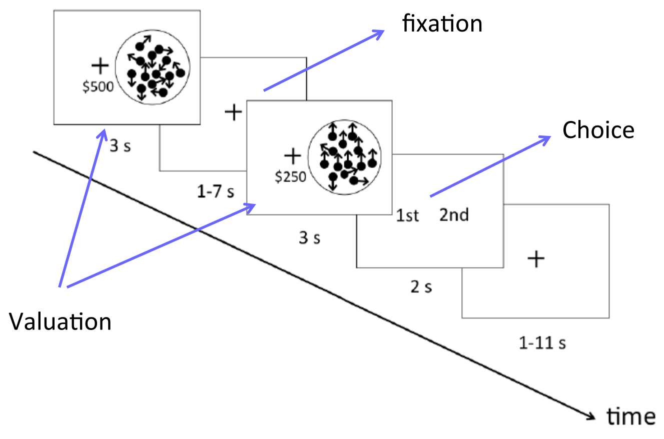
  - Identify neural properties that are associated with suboptimal inference



II. Interested in –
Within-trial dynamical interactions

Wu, Delgado, Maloney (2015, Front Neurosci)

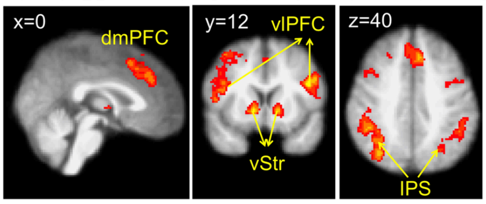
A perceptual decision task

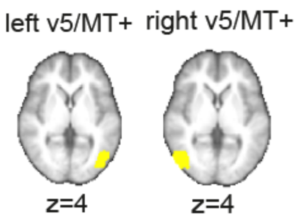


Neural representations of expected reward

<u>Valuation network:</u>
reward, probability, and expected reward

<u>Sensory system:</u>
probability

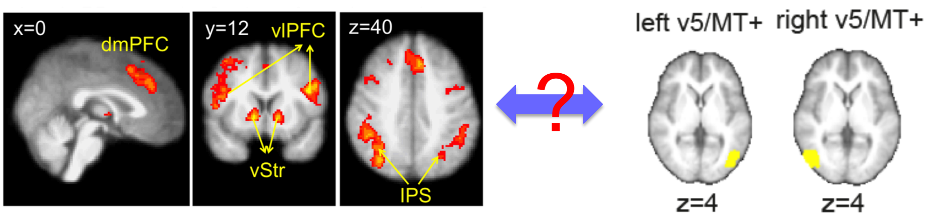




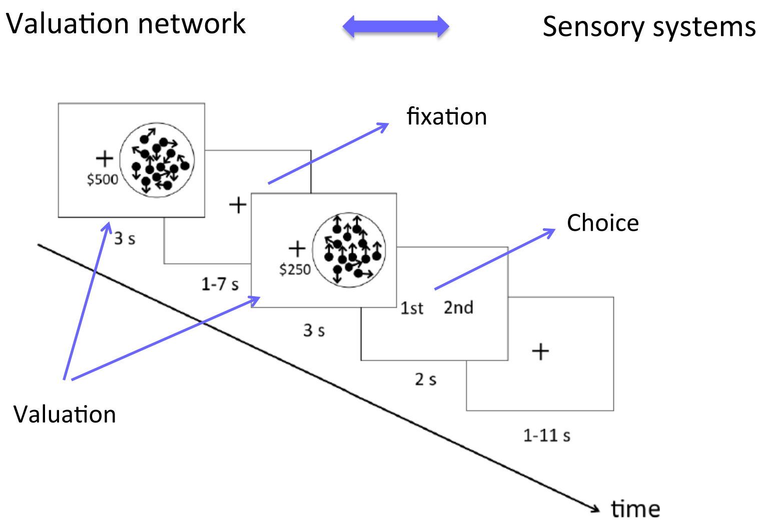
Understanding interactions between networks

<u>Valuation network:</u>
reward, probability, and expected reward

<u>Sensory system:</u>
probability

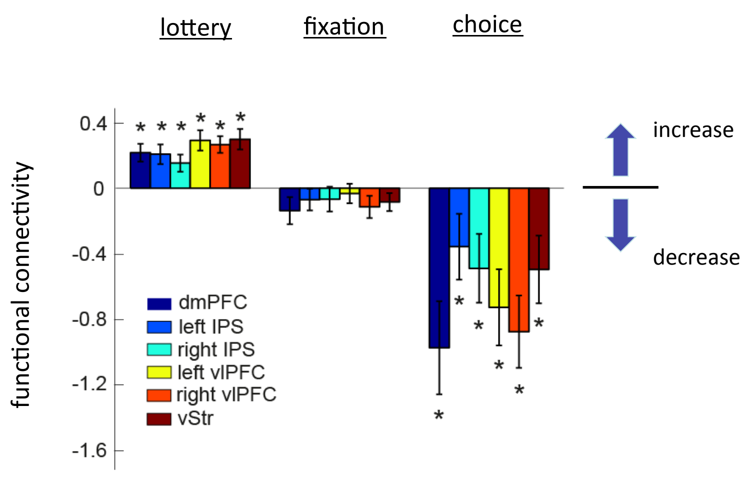


Do the interactions dynamically change during the course of a trial?



Within-trial dynamical interactions

- Using MT as seed

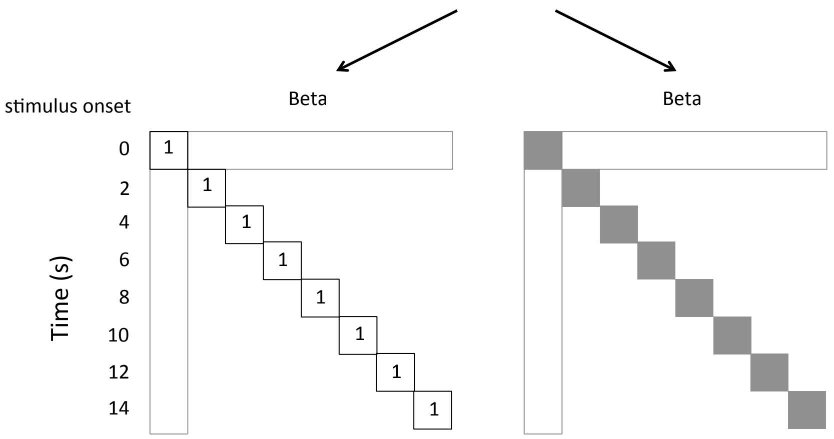


III. Interested in –
characterizing connectivity time-series

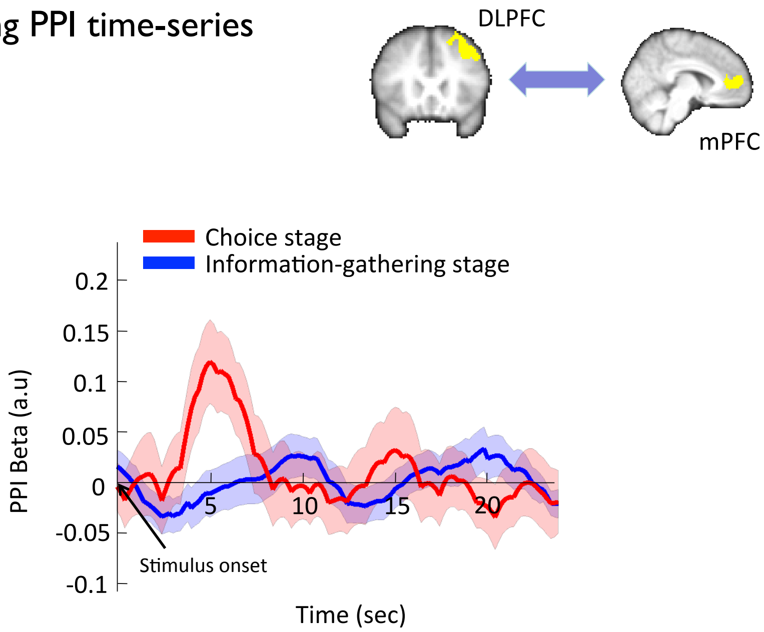
Visualizing the time series of PPI

- FIR-like regression

Model: $\beta_{PPI}(t)=\underline{\beta_A I_A}(t)+\underline{\beta_B I_B}(t), t=[0,24]$



Visualizing PPI time-series



IV. Dynamics of mental representations

- Characterizing the dynamics of mental representations: the temporal generalization method (King & Dehaene, 2014 Trends in Cognitive Sciences)

Objective

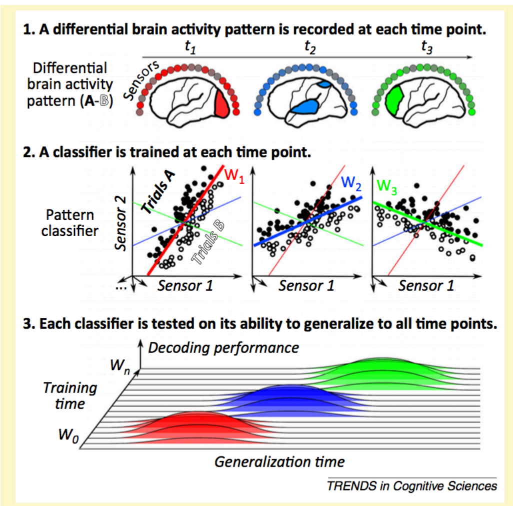
- Understanding how mental representations unfold in time
- Behavioral techniques are limited in revealing the temporal organization of cognitive computations

Data with high temporal resolution: EEG, MEG, and intracranial recordings data

Multivariate pattern analysis (MVPA) analysis using machine learning methods

- Temporal decoding method

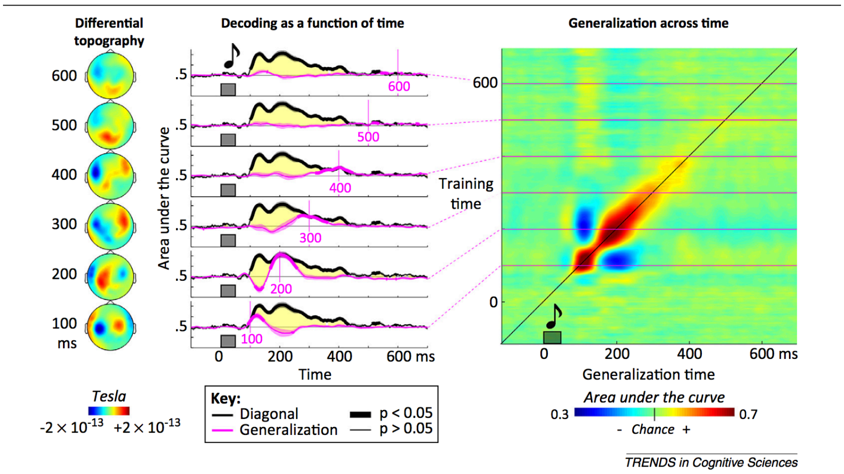
Basic idea



- Look at each time point separately
- Train multivariate classifier (multivariate = spatial) at each time point
- Evaluate if the classifier can successfully predict activity at a different time point

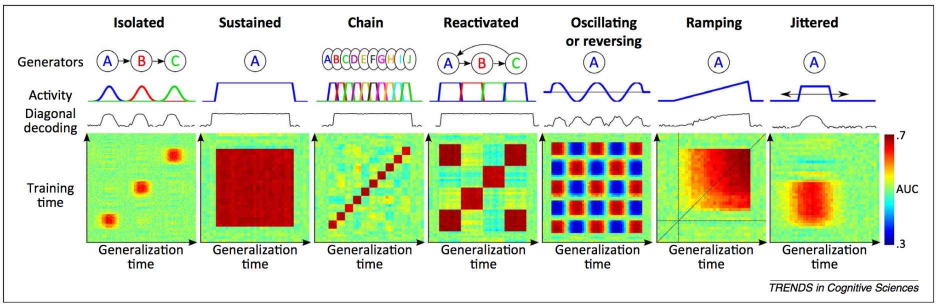
Visualizing classifier performance

- Generalization across time



Principles and possibilities

- Possibility to dissociate different mental operation dynamics
- Key: simply looking at diagonal patterns cannot allow you to distinguish between chained, and reactivated; but they differ in the off-diagonal entries



Summary

- Dynamic pictures of the brain
- Network dynamics and cognition
- Dynamics of network connectivity and cognition