Applications of Granger Causality to Neuroscience

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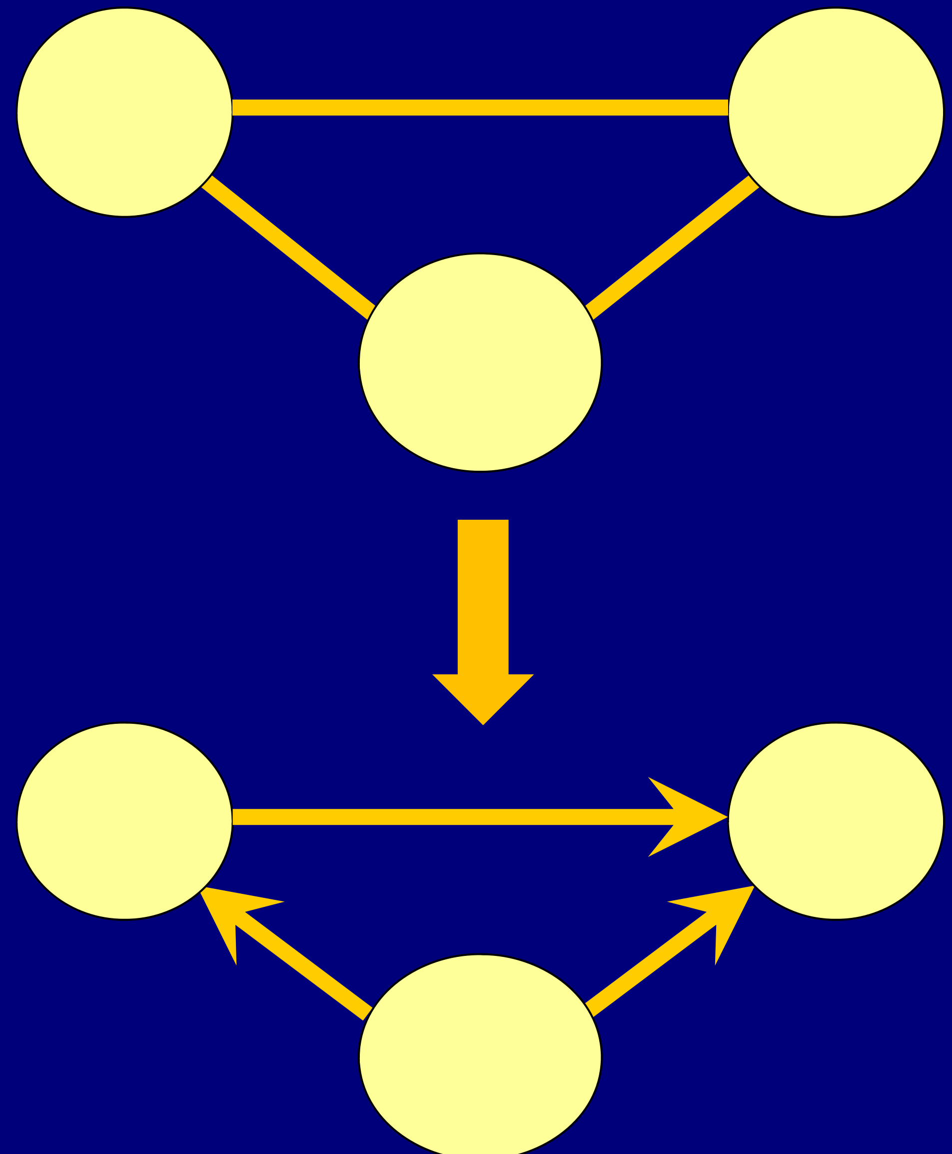
From Undirected to Directed via Granger Causality

Functional Connectivity



Effective Connectivity

Outline

Validation:

- Laminar organization of alpha oscillations in visual cortex (LFP and MUA)
- Interaction of theta generators in hippocampus (LFP)

Application to scalp EEG:

- Top-down control of sensory biasing in visual spatial attention and verbal working memory

Application to fMRI:

- Top-down regulation of default mode activity (task fMRI)
- Granger causality and fMRI data (simulation)
- Linking functional and structural connectivity quantitatively (DWI and rest fMRI)

Validation

Study One

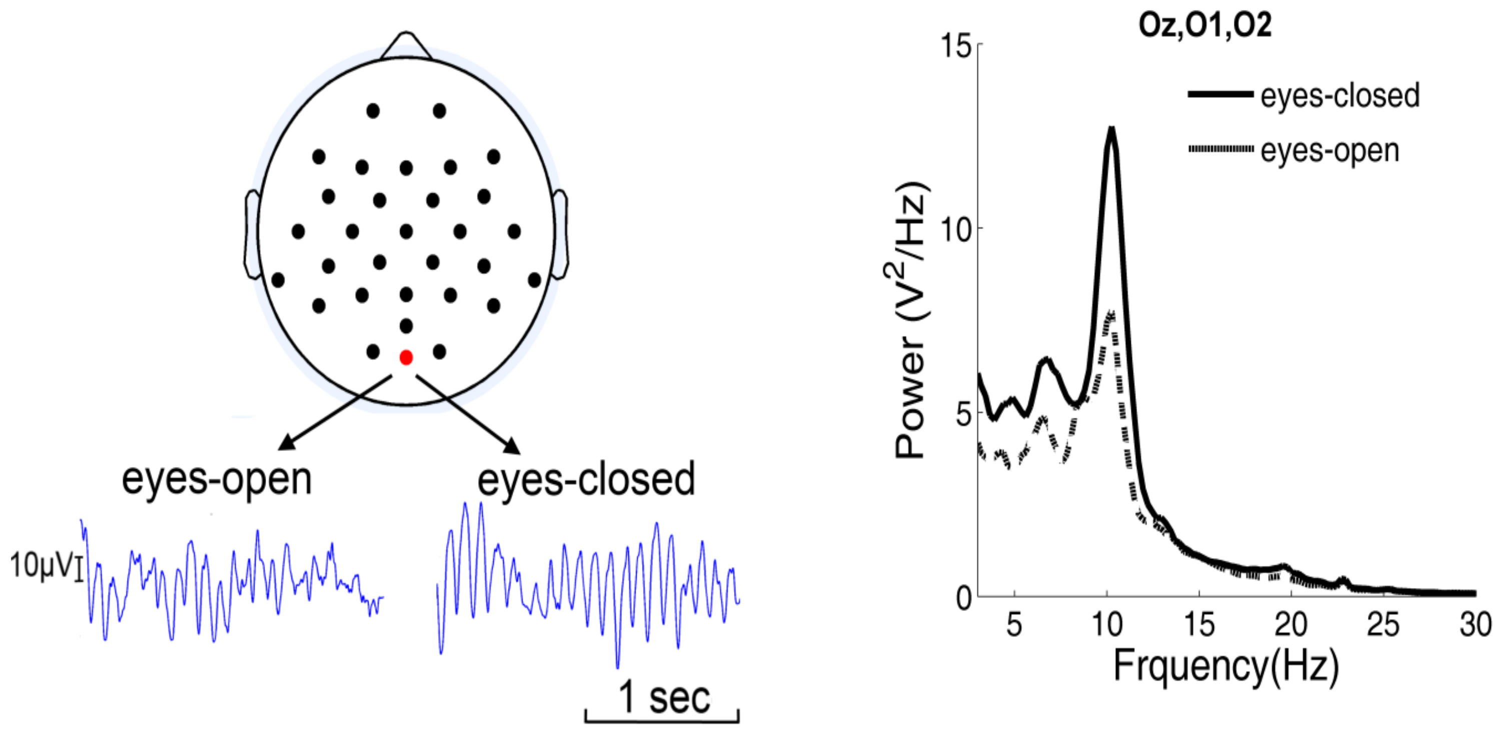
9976 • The Journal of Neuroscience, October 1, 2008 • 28(40):9976–9988

Behavioral/Systems/Cognitive

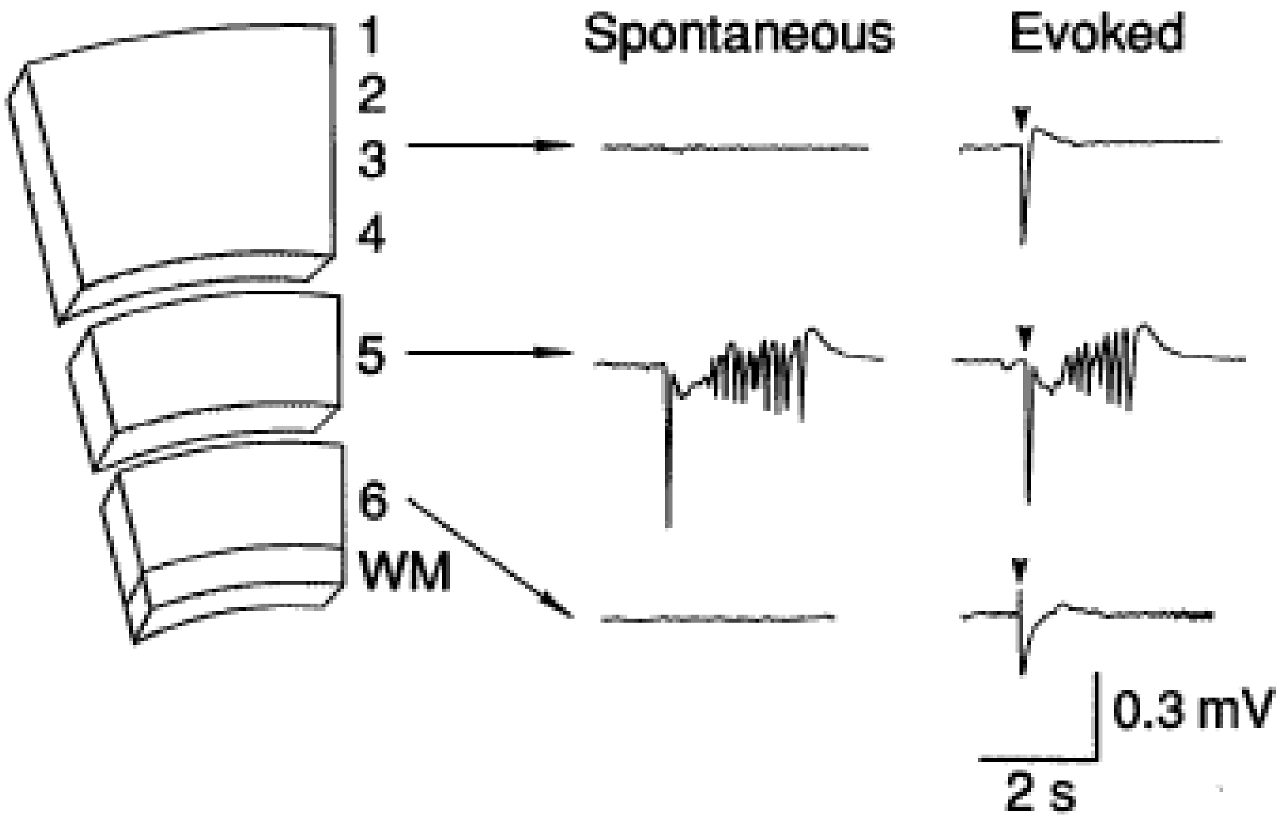
Neuronal Mechanisms of Cortical Alpha Oscillations in Awake-Behaving Macaques

Anil Bollimunta,[1] Yonghong Chen,[1] Charles E. Schroeder,[2,3] and Mingzhou Ding[1]
[1]J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, Florida 32611, [2]Nathan Kline Institute for Psychiatric Research, Orangeburg, New York 10962, and [3]Columbia University College of Physicians and Surgeons, New York, New York 10027

Human Alpha Rhythm



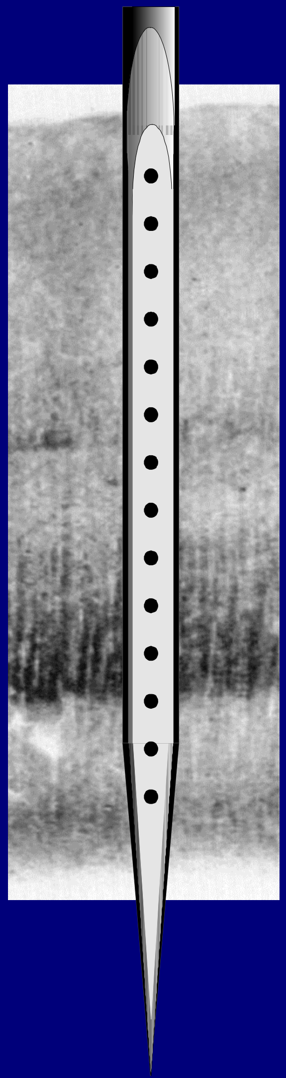
Laminar Alpha Pacemakers



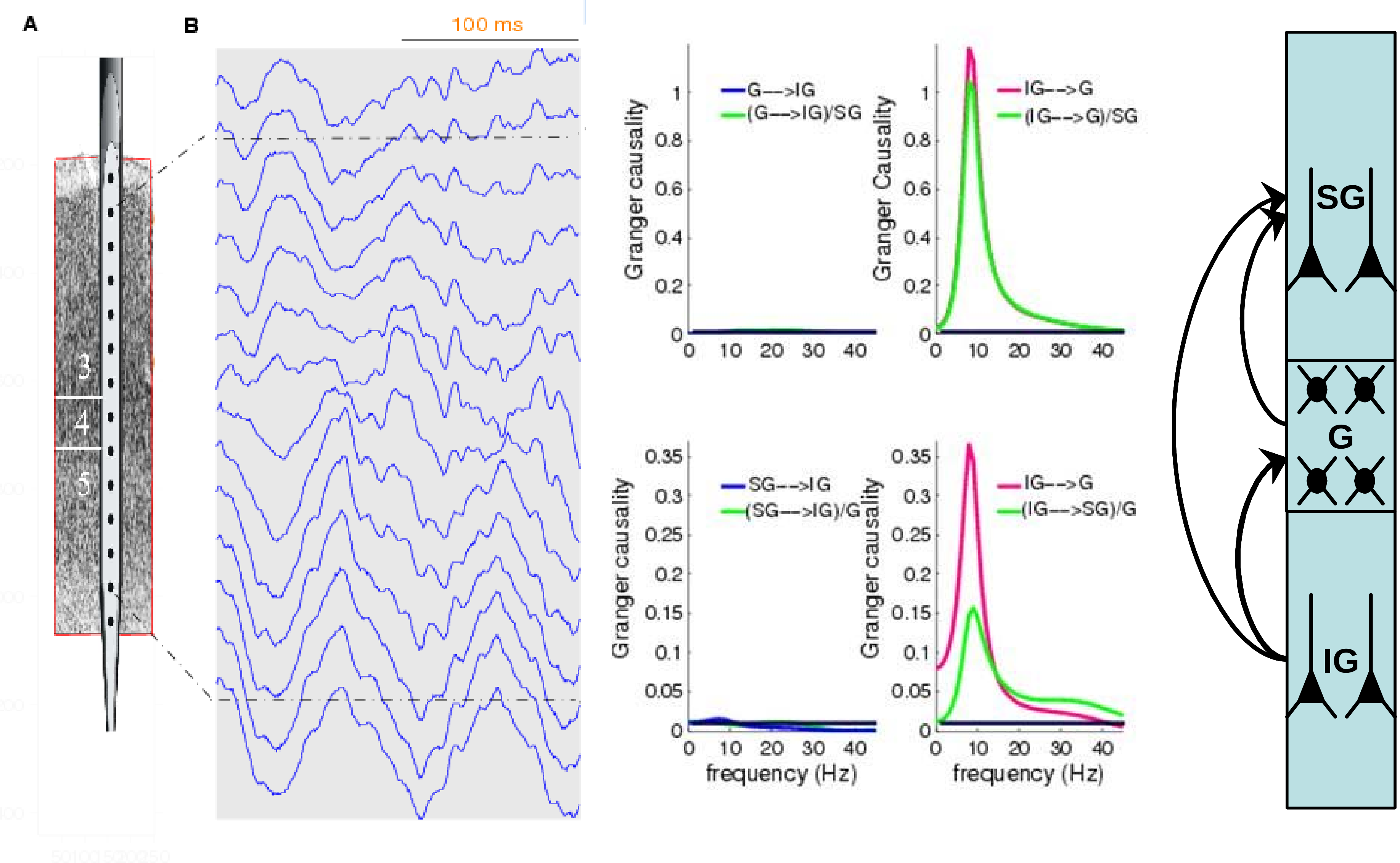
Silva et al. (1991)

Description of Dataset

Spontaneous local field potential (LFP) and multiunit activity (MUA) were recorded with linear depth electrodes in V1, V2, V4 and inferotemporal cortex of macaques



Results from V4



Summary One

Direction of Granger causal influence agrees with known direction of synaptic transmission in columnar alpha generation

Study Two

frontiers
in Systems Neuroscience

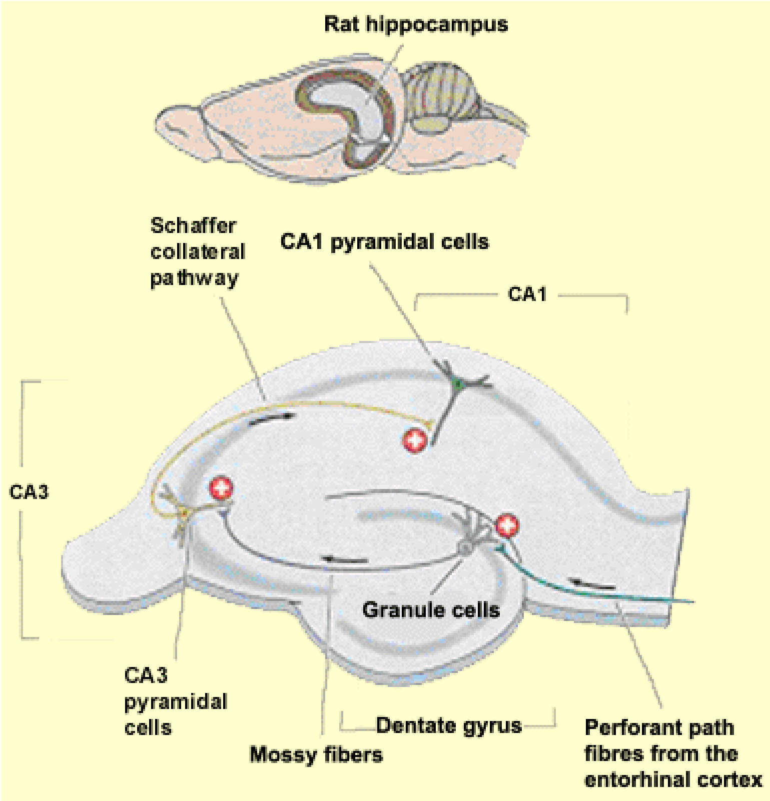
METHODS
published: 20 January 2016
doi: 10.3389/fnsys.2015.00189

Assessing Granger Causality in Electrophysiological Data: Removing the Adverse Effects of Common Signals via Bipolar Derivations

*Amy Trongnetrpunya[1], Bijurika Nandi[1], Daesung Kang[1], Bernat Kocsis[2], Charles E. Schroeder[3,4] and Mingzhou Ding[1]**

[1] J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL, USA, [2] Department of Psychiatry at Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA, [3] Nathan S. Kline Institute for Psychiatric Research, Orangeburg, NY, USA, [4] Department of Neurosurgery, Columbia University, New York, NY, USA

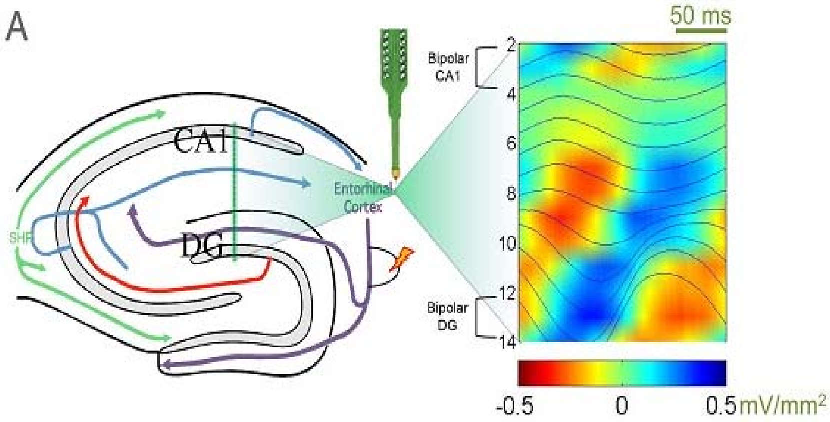
The Trisynaptic Circuit in Hippocampus

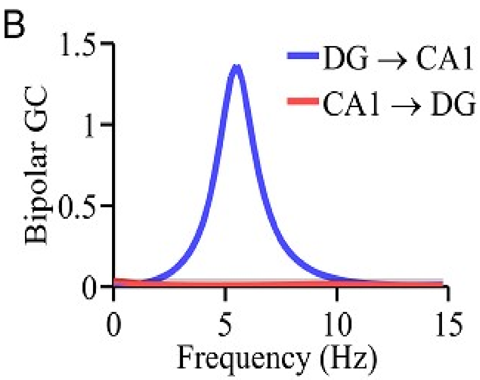


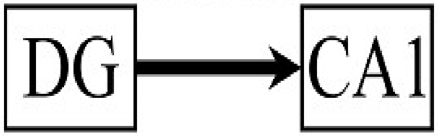
Synaptic transmission: DG→CA3→CA1

Granger Causality During Theta Rhythm

Rat anesthetized; theta rhythm elicited by brainstem stimulation







Summary Two

Direction of Granger causal influence agrees with anatomically predicted synaptic transmission in hippocampus

Application to Scalp EEG

Study Three

frontiers in Human Neuroscience

ORIGINAL RESEARCH
published: 20 January 2016
doi: 10.3389/fnhum.2016.00015

Top-Down Control of Visual Alpha Oscillations: Sources of Control Signals and Their Mechanisms of Action

*Chao Wang, Rajasimhan Rajagovindan, Sahng-Min Han and Mingzhou Ding**

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Alpha: Indexing the State of Visual Cortex

Alpha power decreases during visual spatial attention

Alpha power increases during verbal working memory retention

Visual spatial attention
Decreased alpha power reflects increased excitability over visual cortices to enhance stimulus processing.

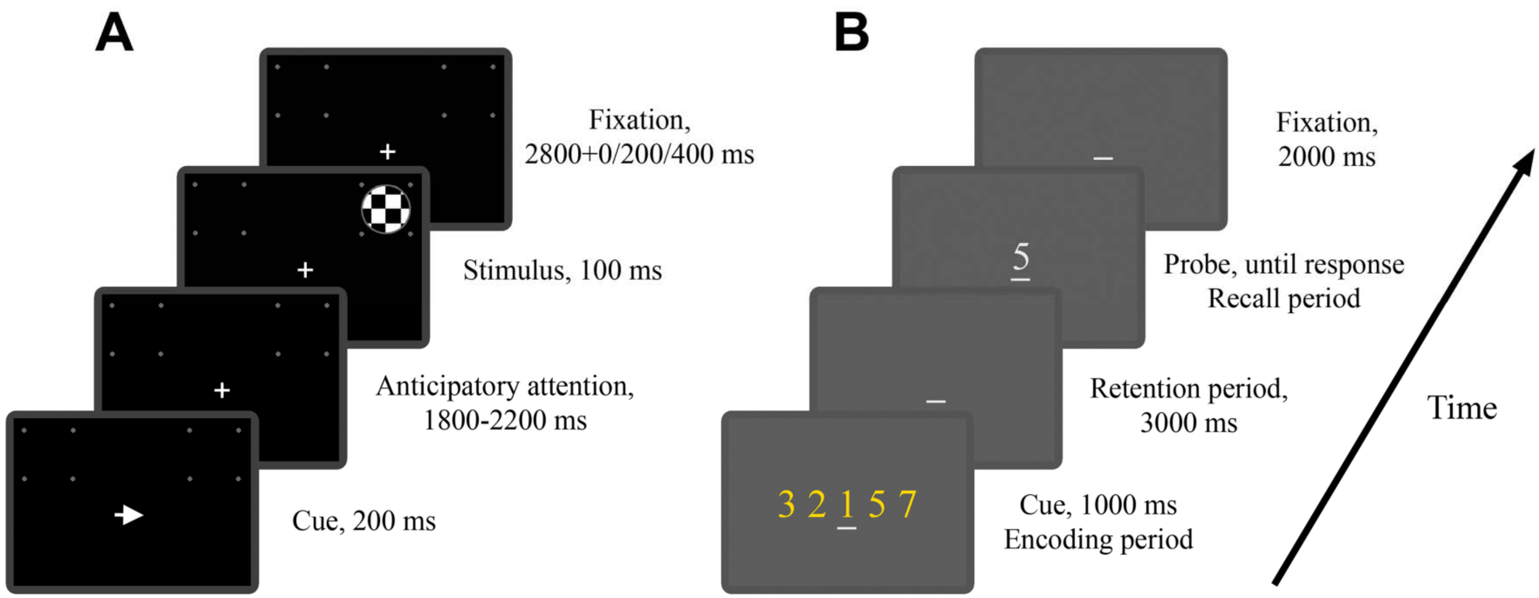
Verbal working memory
Increased alpha power reflects decreased excitability over visual cortices to protect the information held online from external interference.

Top-Down Control of Sensory Biasing

The goal-directed alpha modulation, reflecting sensory biasing, is likely to be effected by top-down influences from higher-order control areas (e.g., fronto-parietal network).

- What are the signals that mediate the top-down control?
- Are these top-down signals issued in a task-specific manner or by a common set of brain areas?
- What is the likely mechanism underlying top-down control?

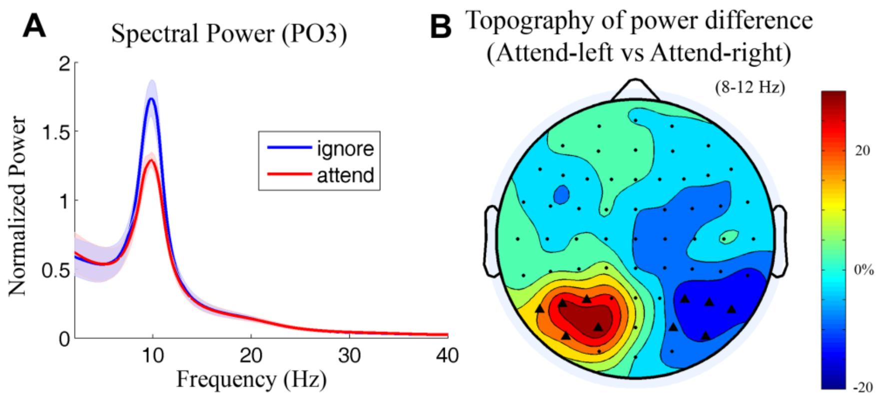
Experiments



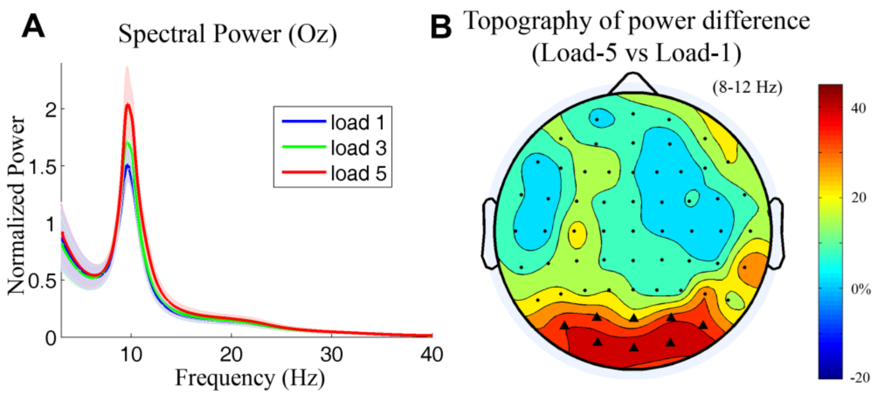
- 21 healthy subjects for each experiment
- 128-channel EEG

Alpha Modulation

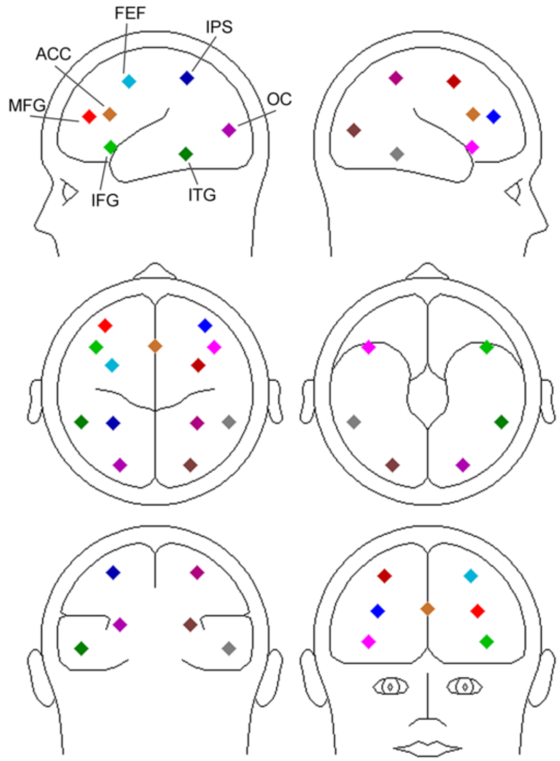
Spatial Attention



Working Memory

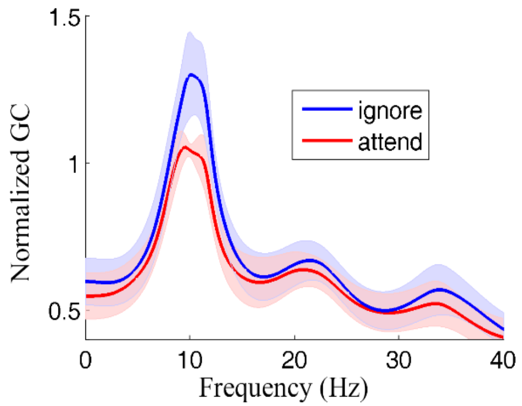


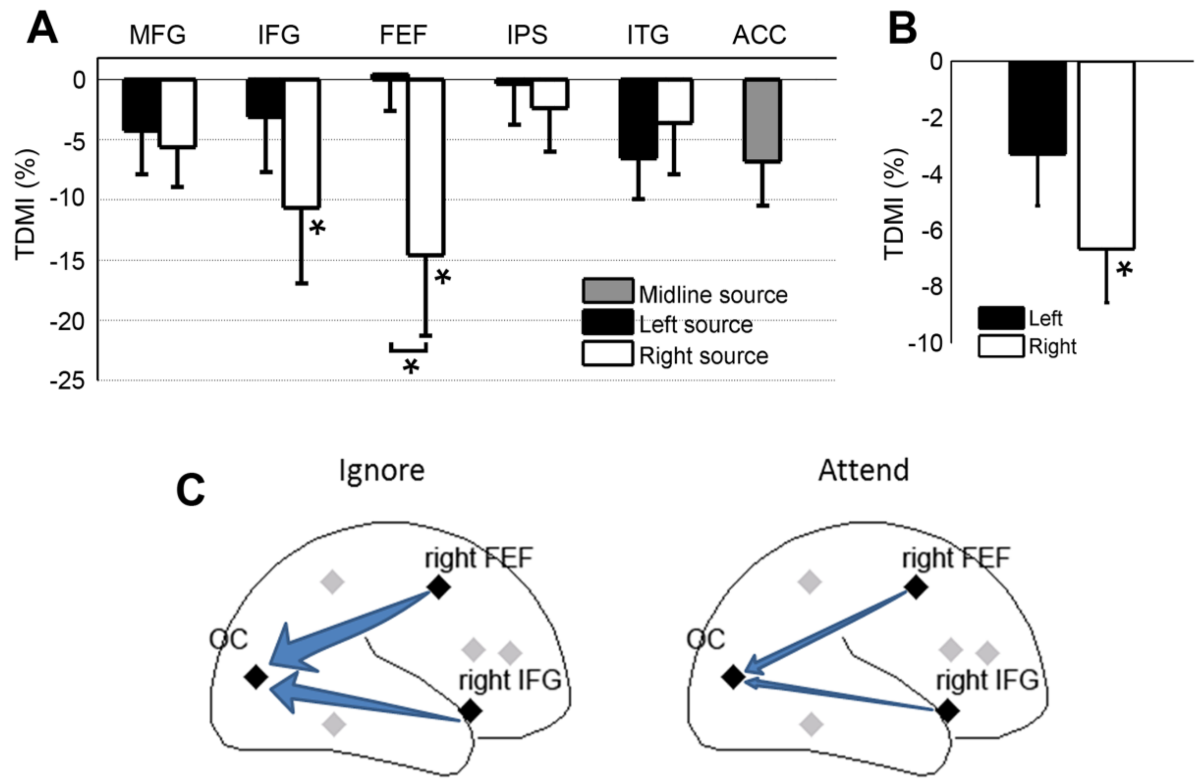
Dipole Sources



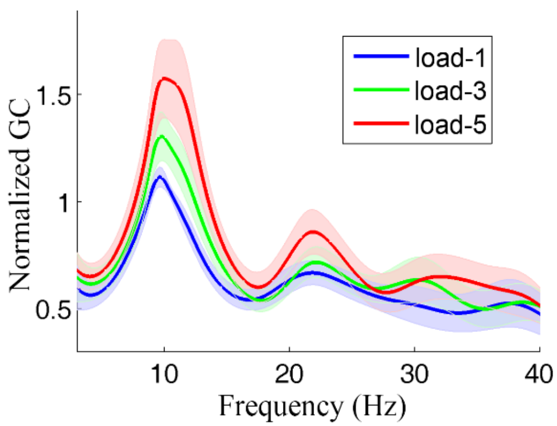
Source ID	Brodmann Area (Approx)	Proximate cortical region	X	Y	Z
MFG	46	Middle Frontal Gyrus	±35	39	27
IFG	45,44	Inferior Frontal Gyrus	±42	23	2
ACC	33	Anterior Cingulate Cortex	0	21	27
FEF	6,8	Frontal Eye Field	±30	1	51
IPS	7,40	Intraparietal Sulcus	±30	-51	48
ITG	20	Inferior Temporal Gyrus	±52	-42	-10
OC	18,19	Occipital Cortex	±25	-83	5

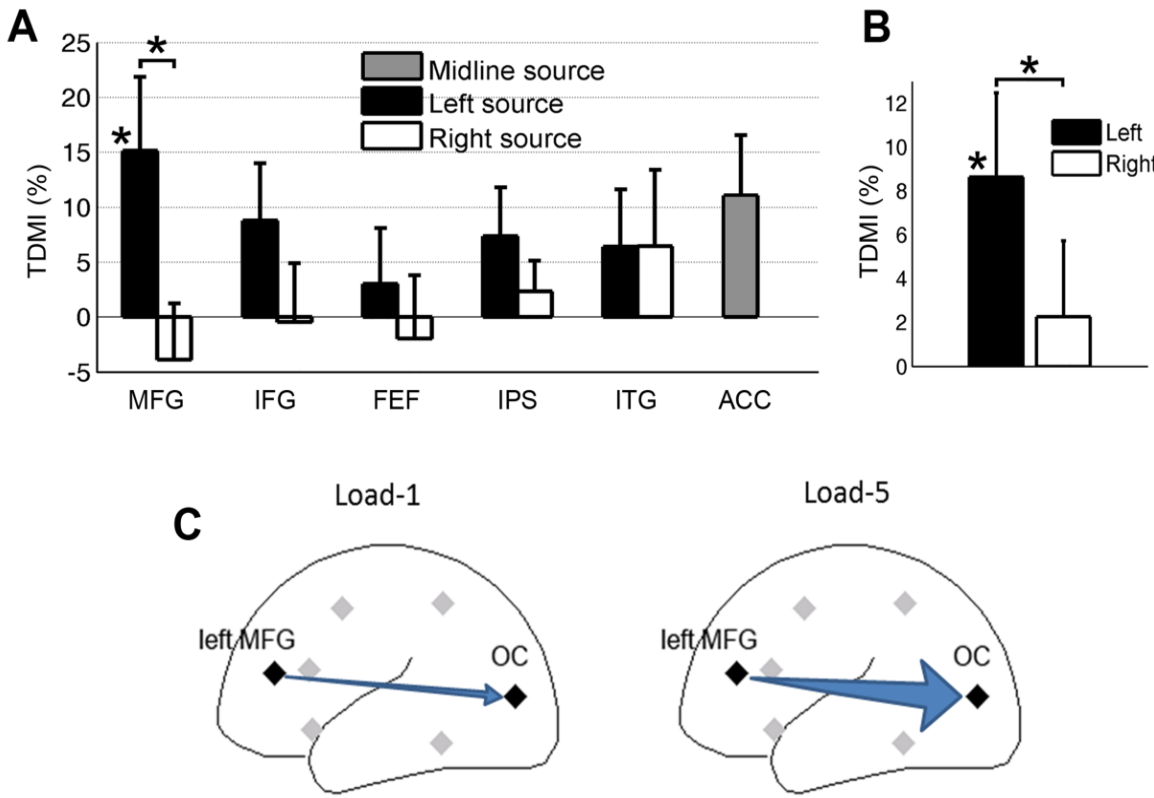
GC Analysis: Spatial Attention





GC Analysis: Working Memory





Summary Three

- The top-down control is likely mediated by alpha synchrony
- The “top” brain regions are task-specific
- The top-down signals achieve sensory biasing via an inhibition-disinhibition mechanism

Application to fMRI

Study Four

6444 • The Journal of Neuroscience, April 10, 2013 • 33(15):6444–6453

Behavioral/Cognitive

Top-Down Regulation of Default Mode Activity in Spatial Visual Attention

Xiaotong Wen,[1] Yijun Liu,[2,3] Li Yao,[4,5] and Mingzhou Ding[1]

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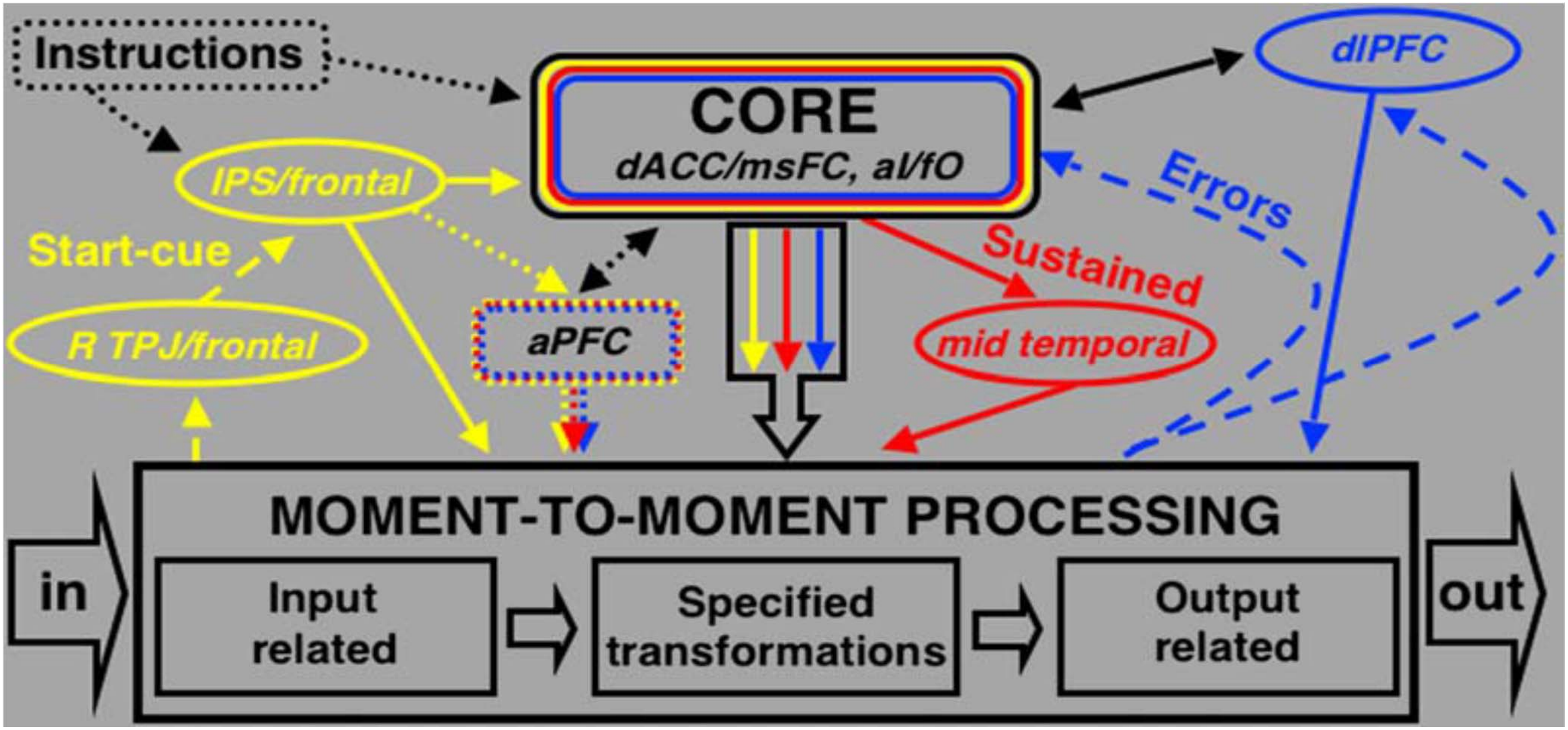
Questions

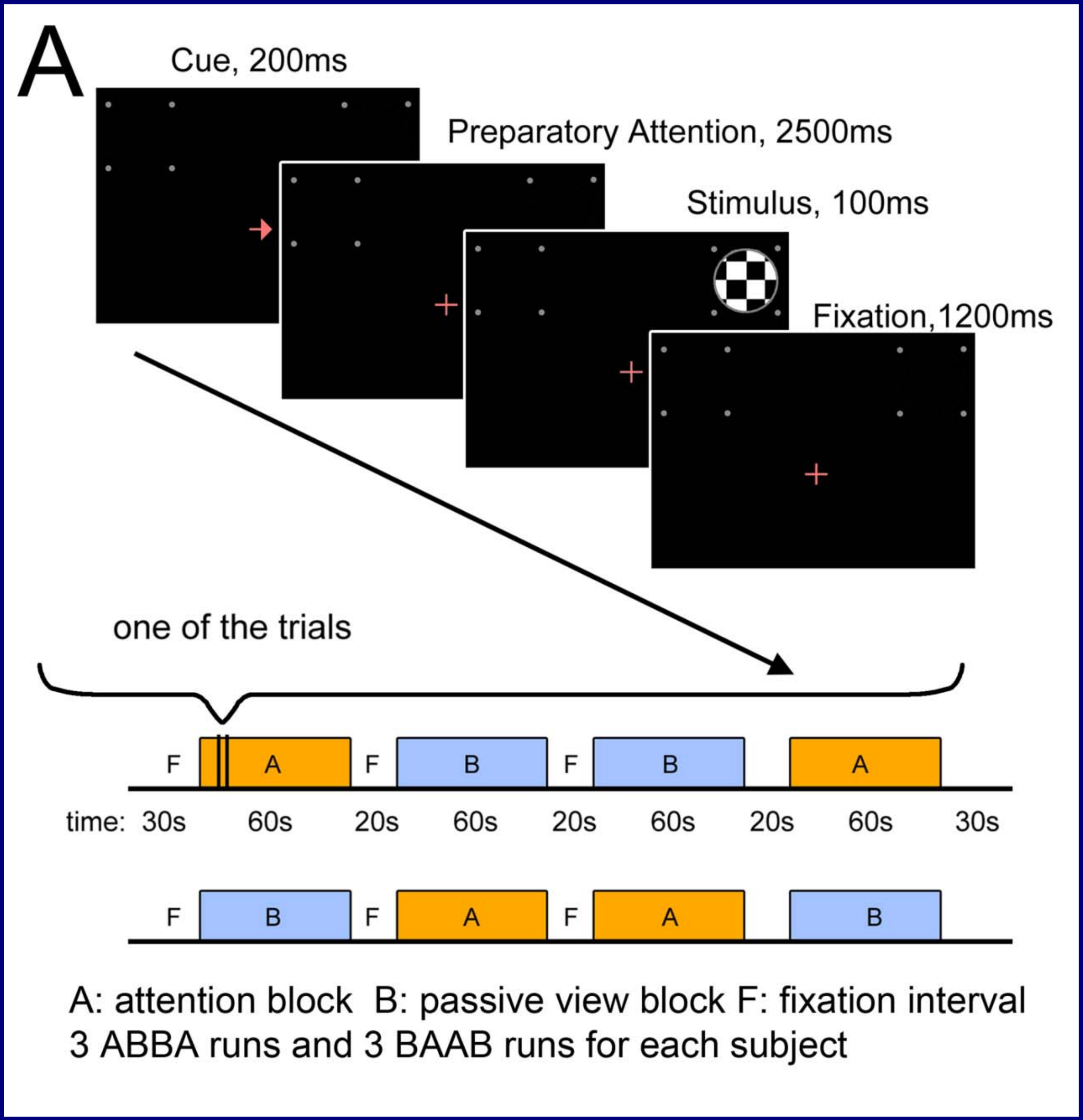
- During externally oriented attention, DMN is deactivated. If this is the consequence of top-down control, where does the control signal come from?
- Insufficient DMN deactivation is negatively correlated with behavioral performance. What is the consequence of DMN's influence on other brain areas (DMN intrusion)?

Task Control (Salience) Network

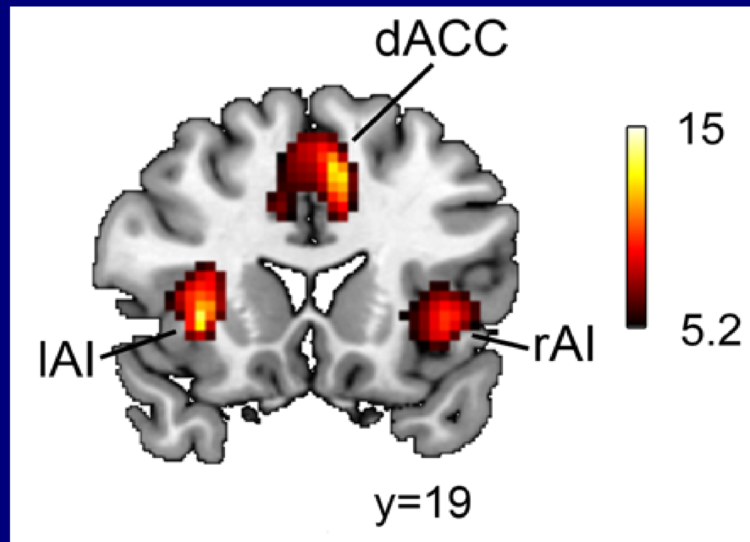


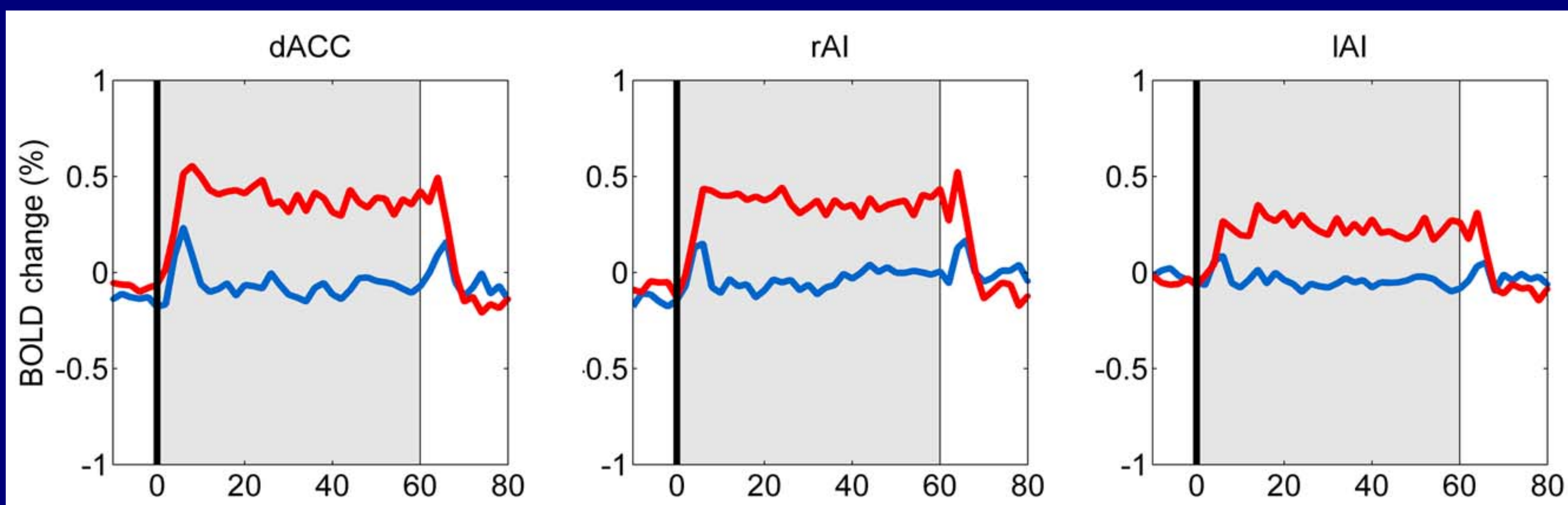
Dosenbach et al. 2006, 2007

Paradigm

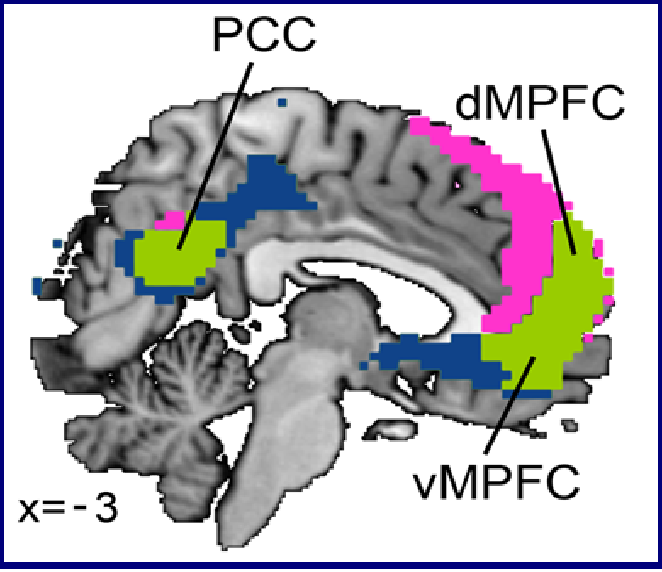

A
Cue, 200ms
Preparatory Attention, 2500ms
Stimulus, 100ms
Fixation,1200ms
one of the trials
F
A
F
B
F
B
A
time: 30s
60s
20s
60s
20s
60s
20s
60s
30s
F
B
F
A
F
A
B
A: attention block B: passive view block F: fixation interval
3 ABBA runs and 3 BAAB runs for each subject

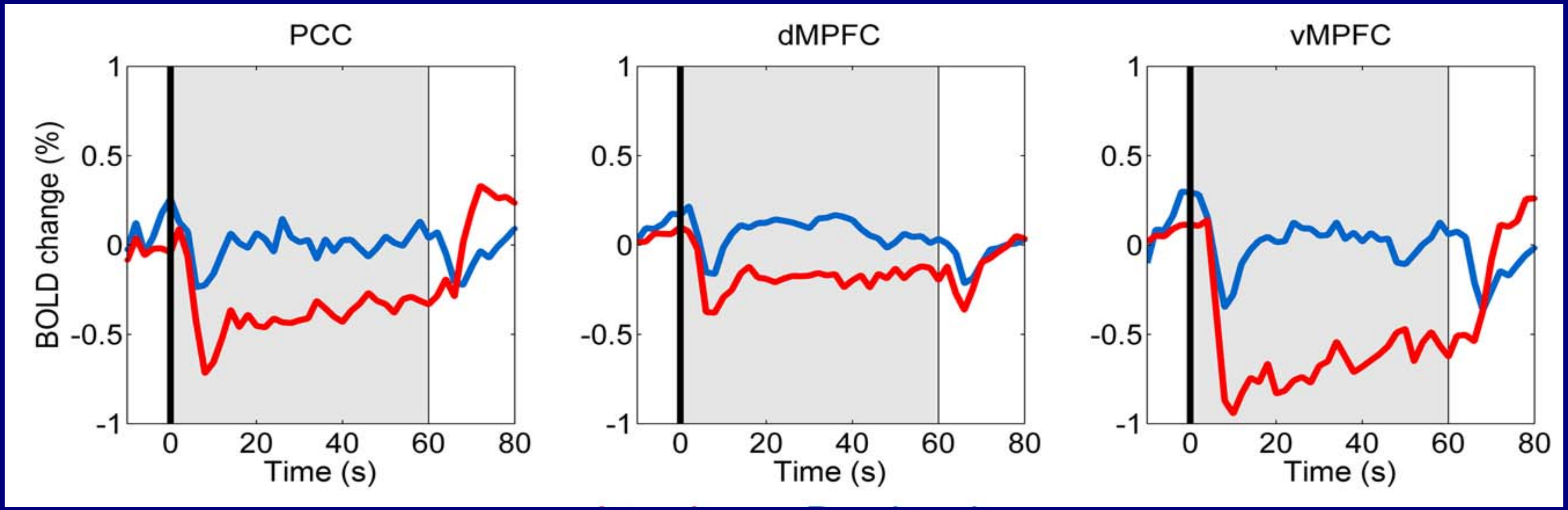
Activation


dACC
15
5.2
lAI
rAI
y=19


dACC
rAI
lAI
BOLD change (%)
1
0.5
0
-0.5
-1
0
20
40
60
80

Deactivation

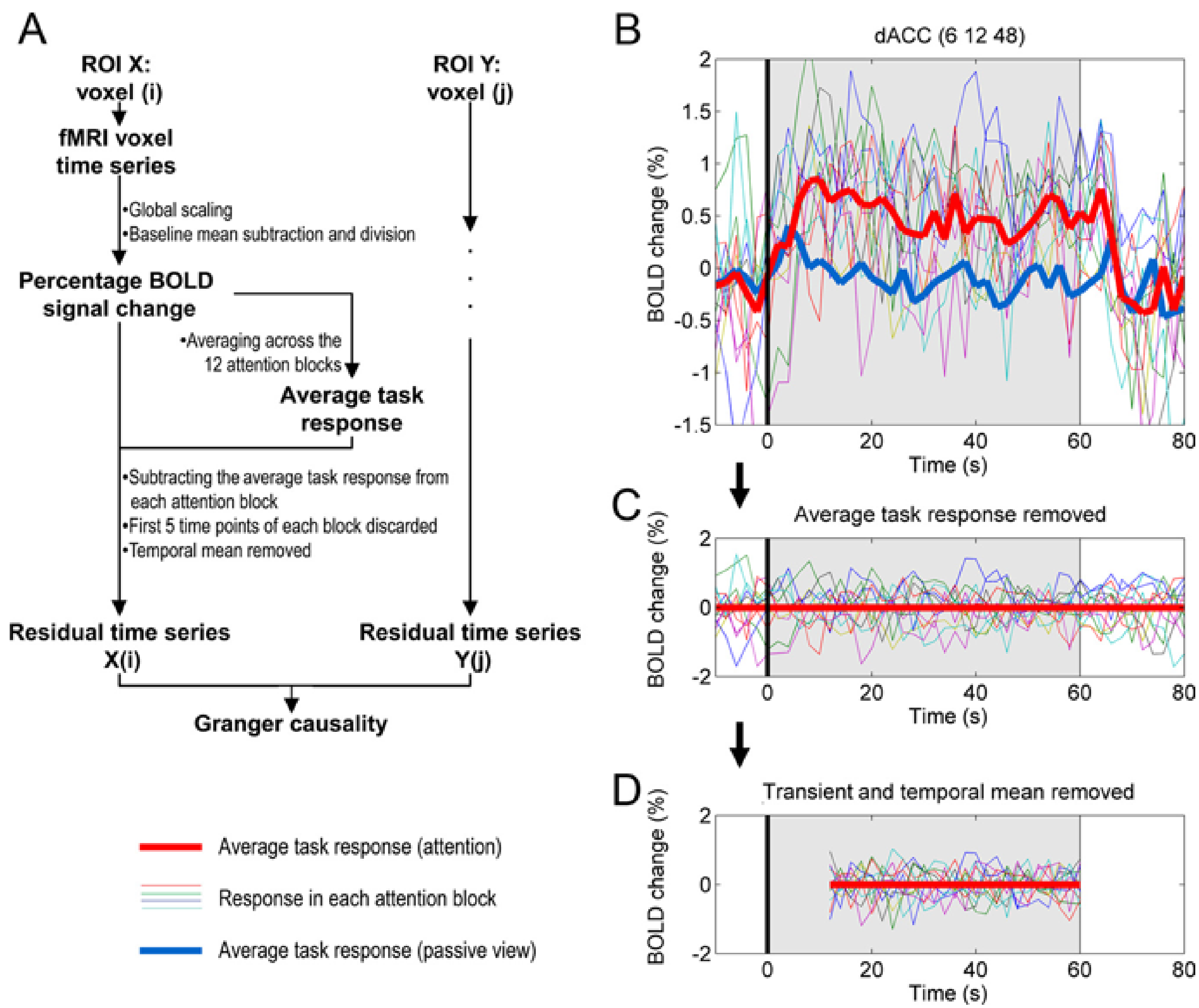




Hypotheses

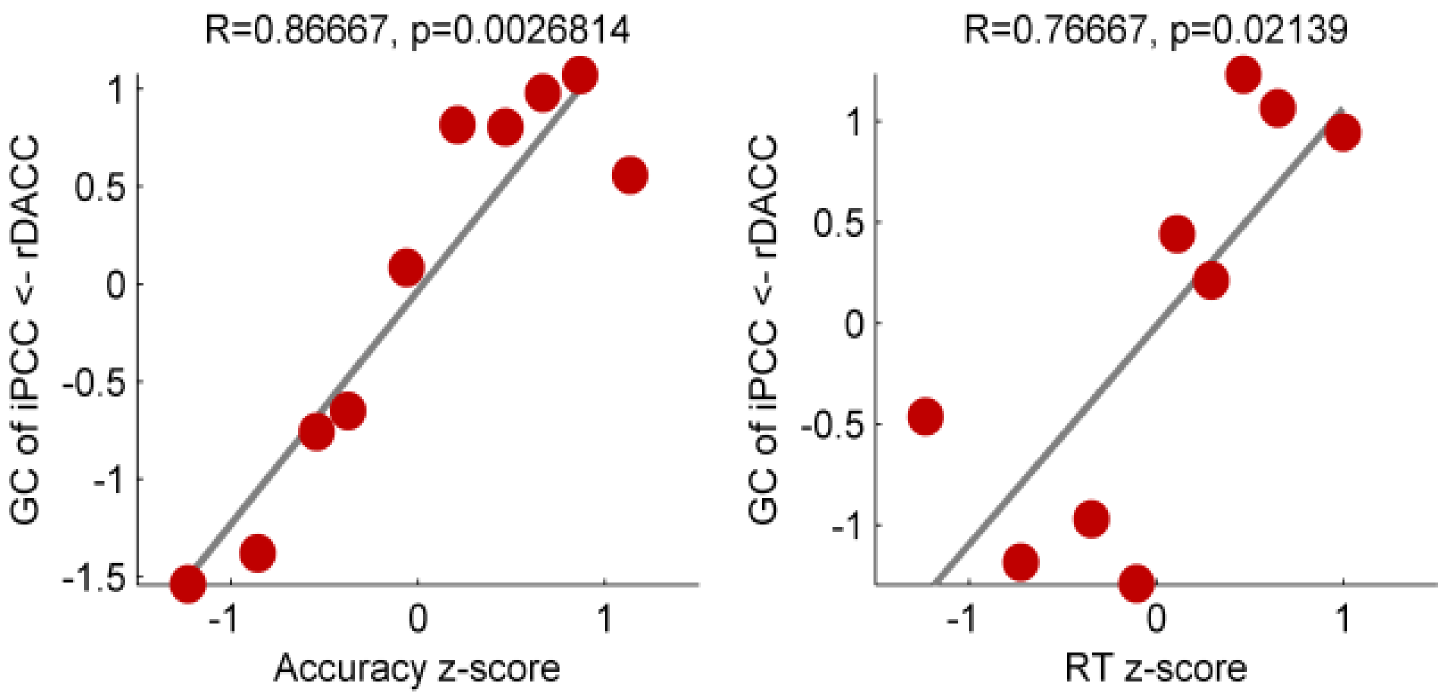
- TCN→DMN enhances behavioral performance
- DMN→TCN degrades behavioral performance

Analysis Flow



dACC→PCC and Performance

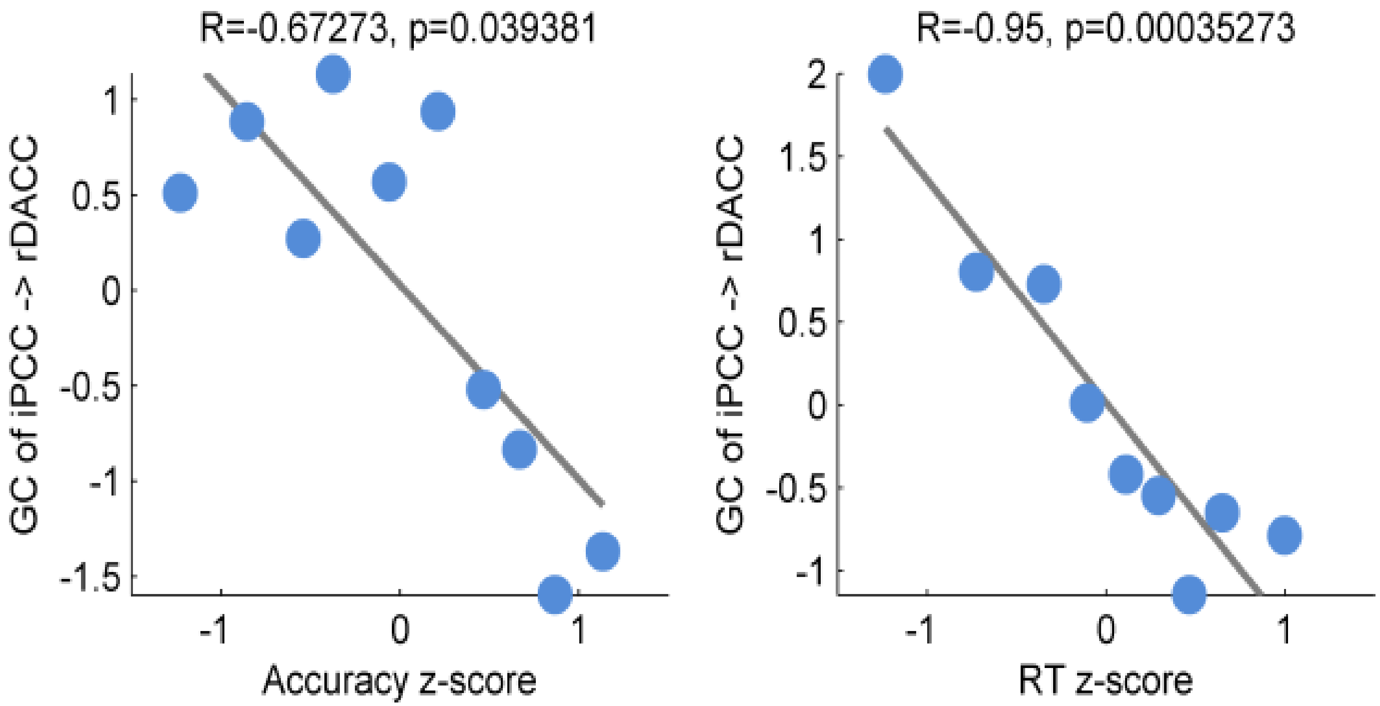
dACC→PCC



Better performance →

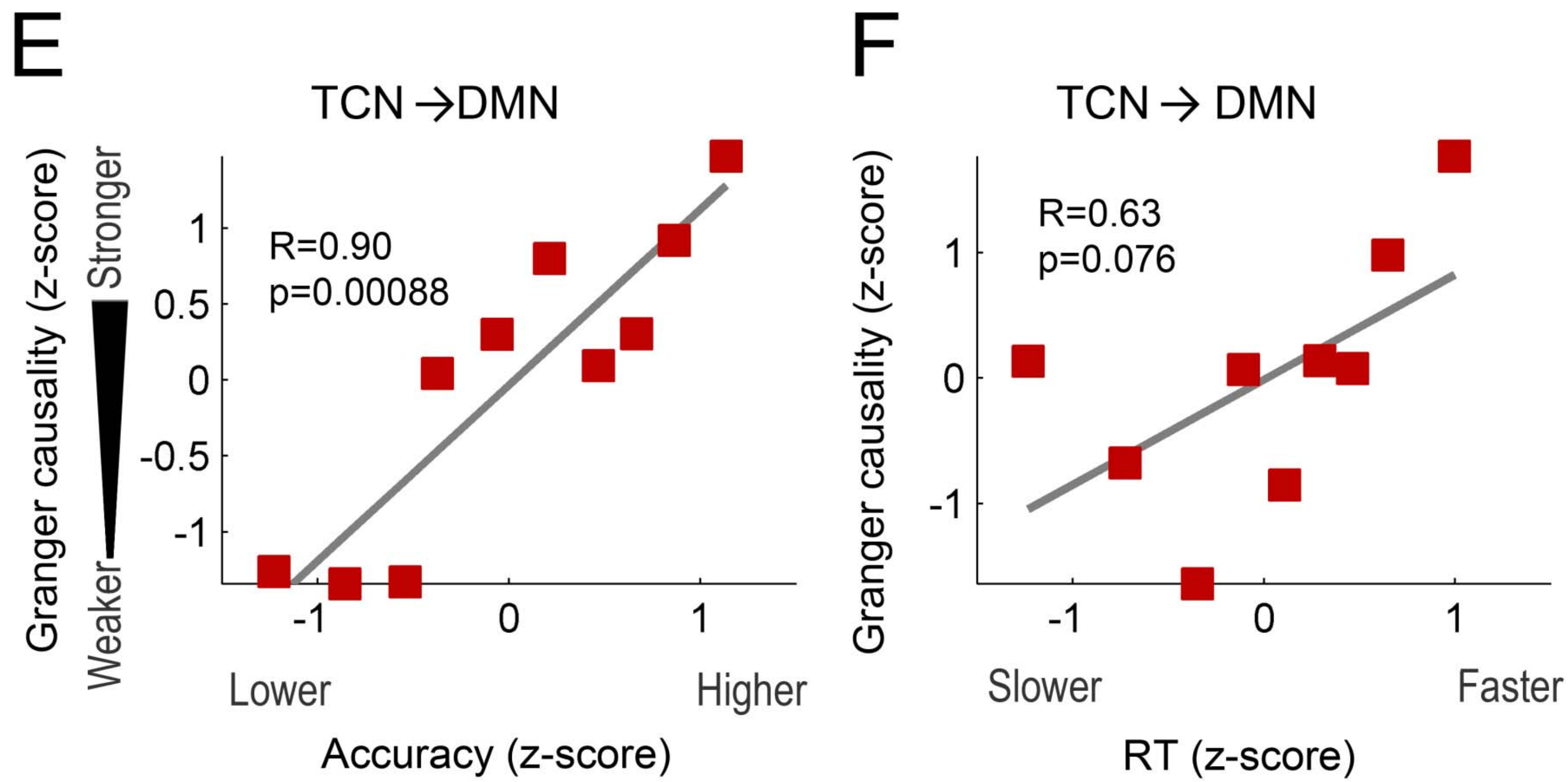
PCC→dACC and Performance

PCC→dACC



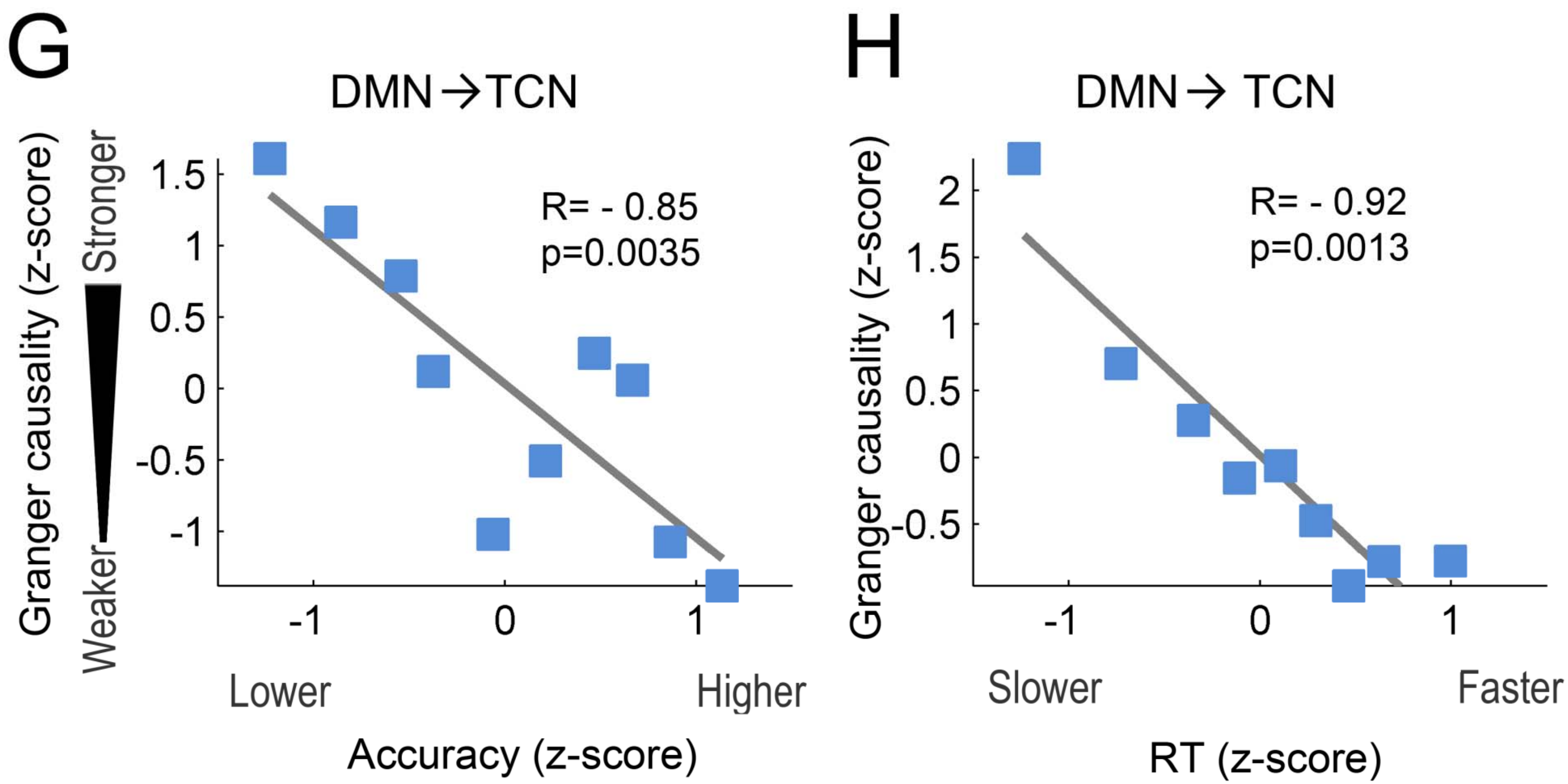
Better performance →

TCN→DMN and Performance



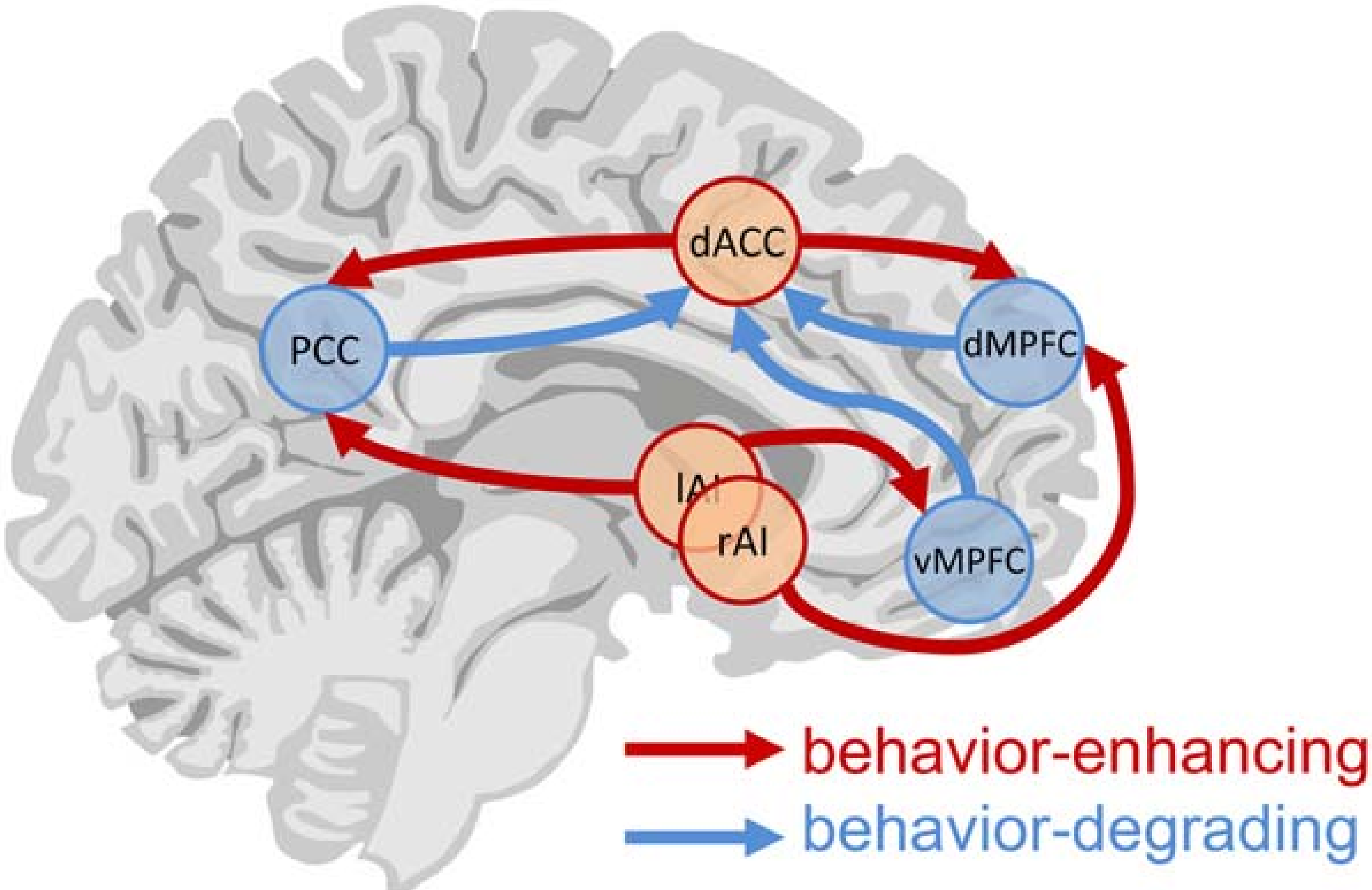
Better performance →

DMN→TCN and Performance



Better performance →

Network Interactions



Summary Four

- TCN issues signals to regulate DMN activity to optimize behavioral performance.
- DMN, acting as a source of “internal noise,” disrupts behavioral performance during external attention by issuing signals to interfere with TCN activity.

Study Five

OPEN ACCESS Freely available online PLOS | ONE

Is Granger Causality a Viable Technique for Analyzing fMRI Data?

Xiaotong Wen[1], Govindan Rangarajan[2], Mingzhou Ding[1]*

1 The J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, Florida, United State of America, **2** Department of Mathematics and Centre for Neuroscience, Indian Institute of Science, Bangalore, India

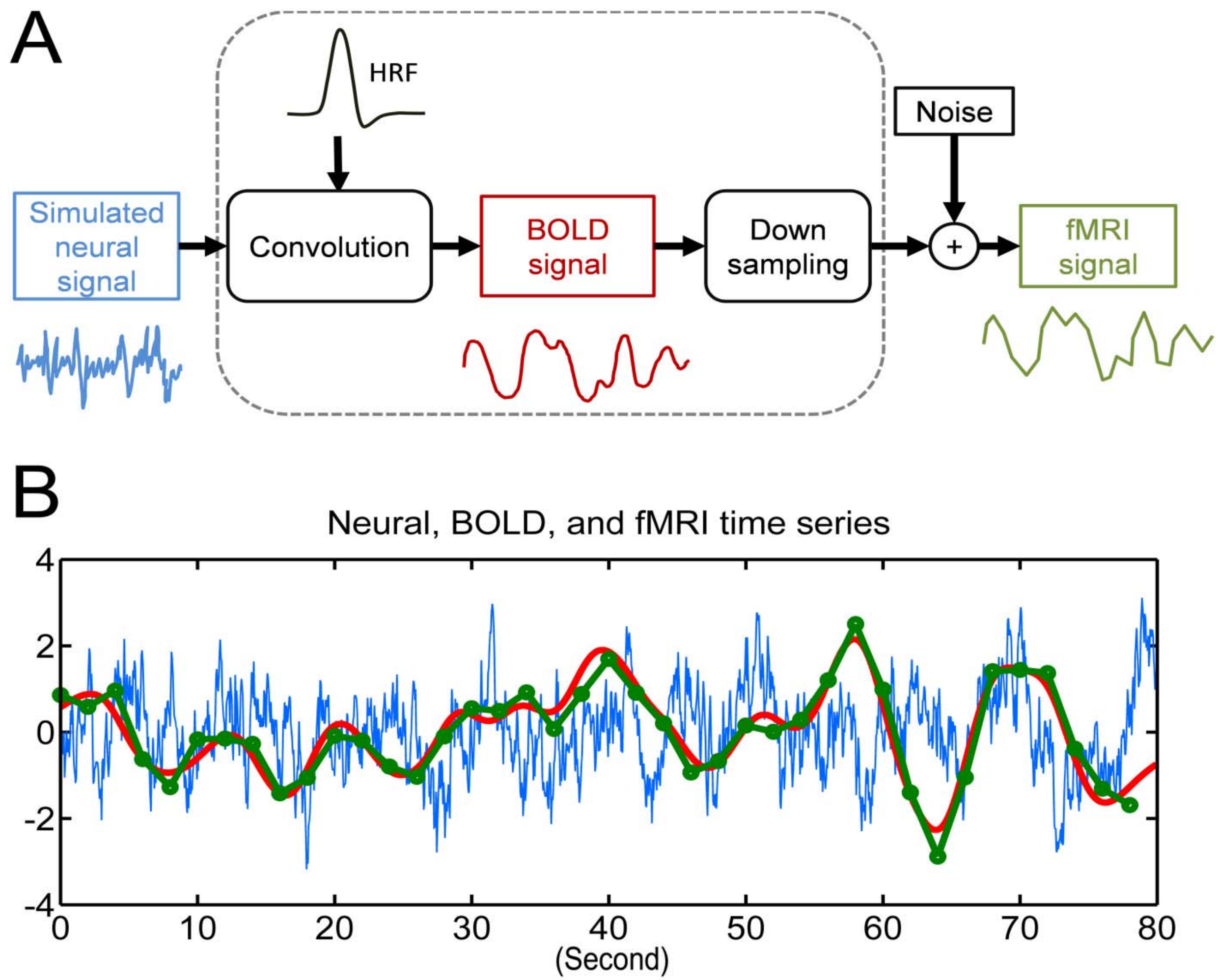
Issues

- fMRI has low sampling rate (~s) relative to the time scale of typical neural activity (~ms).
- Hemodynamic response (e.g., latency) may have significant region-to-region variability across the brain.
- Past work has shown that GC gives spurious results in simulations where the correct answer is known (e.g., Smith et al., 2011).

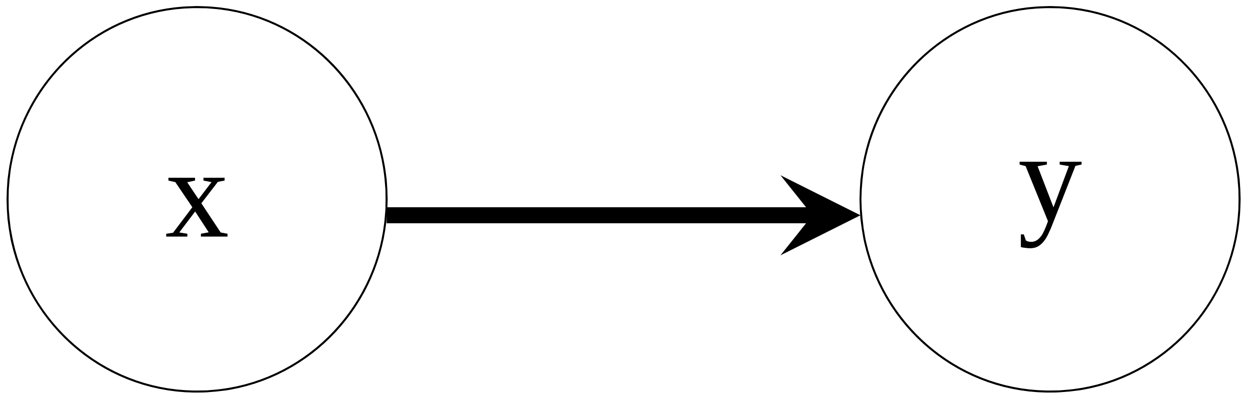
Strategy

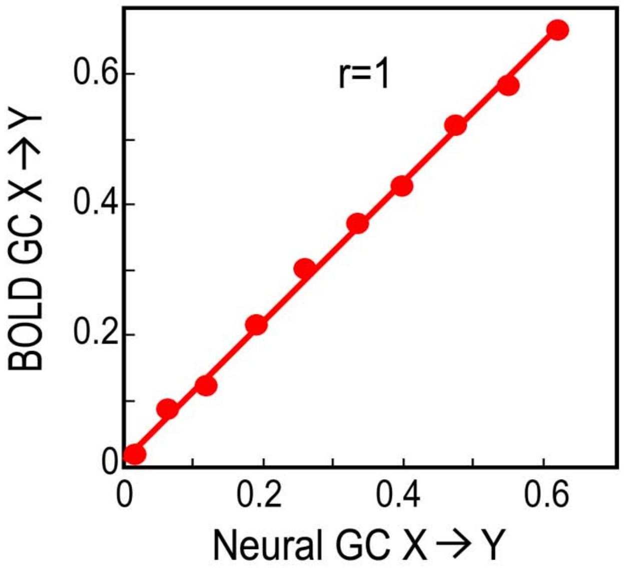
Recognizing that in cognitive neuroscience, it is often the change of a dependent variable (e.g., GC) between experimental conditions that is of interest, we address the question of whether there exist systematic relationships between GC at the fMRI level and that at the neural level.

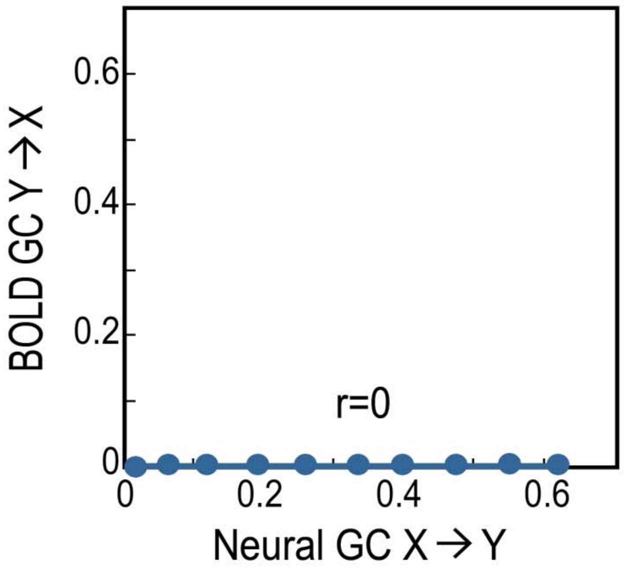
Neural→BOLD→fMRI



Neural GC-BOLD GC Monotonicity

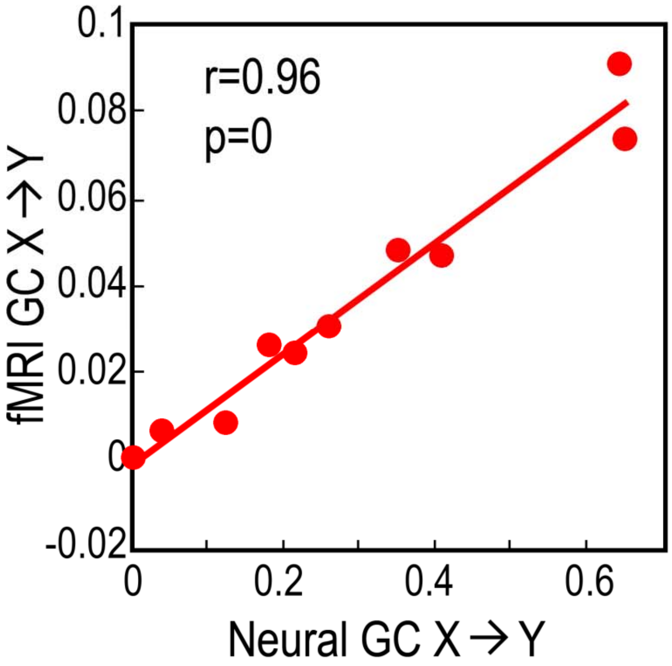


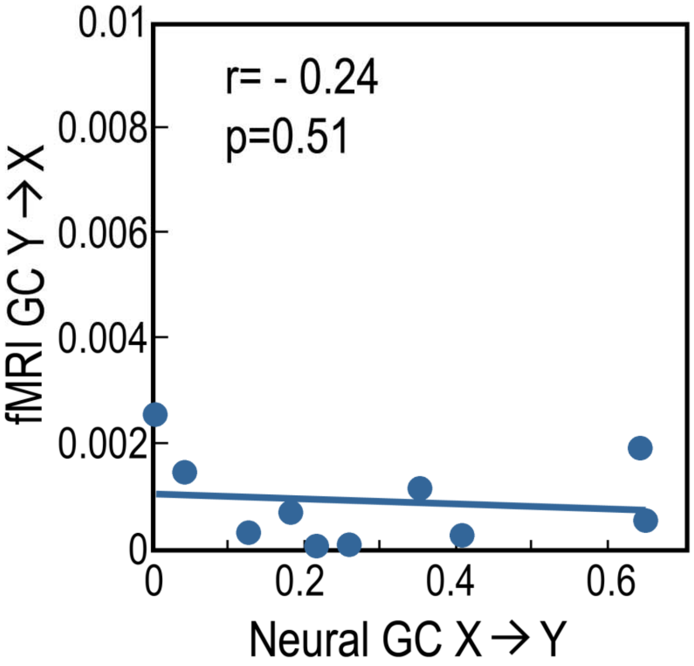




Neural GC-fMRI GC Monotonicity

TR=2s, noise=20%





Summary Five

- GC, as an empirical measure, can always be applied to characterize fMRI time series.
- A monotonic relationship between fMRI GC and neural GC implies that increase or decrease of fMRI GC as experimental condition is varied can be interpreted in terms of increase or decrease of underlying neural GC.

Misce

Software Packages

- The Ding lab maintains up-to-date software
- BSMART: A Matlab/C Toolbox for Analyzing Brain Circuits
- Anil Seth: Causal Connectivity Toolbox
- AFNI has basic routines for estimating GC
- Fieldtrip: Matlab Toolbox for LFP/EEG/MEG analysis
- BrainVoyager
- …

Spike Trains or Spike-Field Mixed Recordings

Question: What about spike trains or spike-field mixed recordings?

Answer: Nonparametric Granger causality (Dhamala, Rangarajan, Ding, *NeuroImage*, 2008; Kang et al., *Journal of Neurophysiology*, 2015)

Unipolar vs Bipolar

Unipolar recordings:

Area X: $X_1(t) - R(t)$; $X_2(t) - R(t)$

Area Y: $Y_1(t) - R(t)$; $Y_2(t) - R(t)$

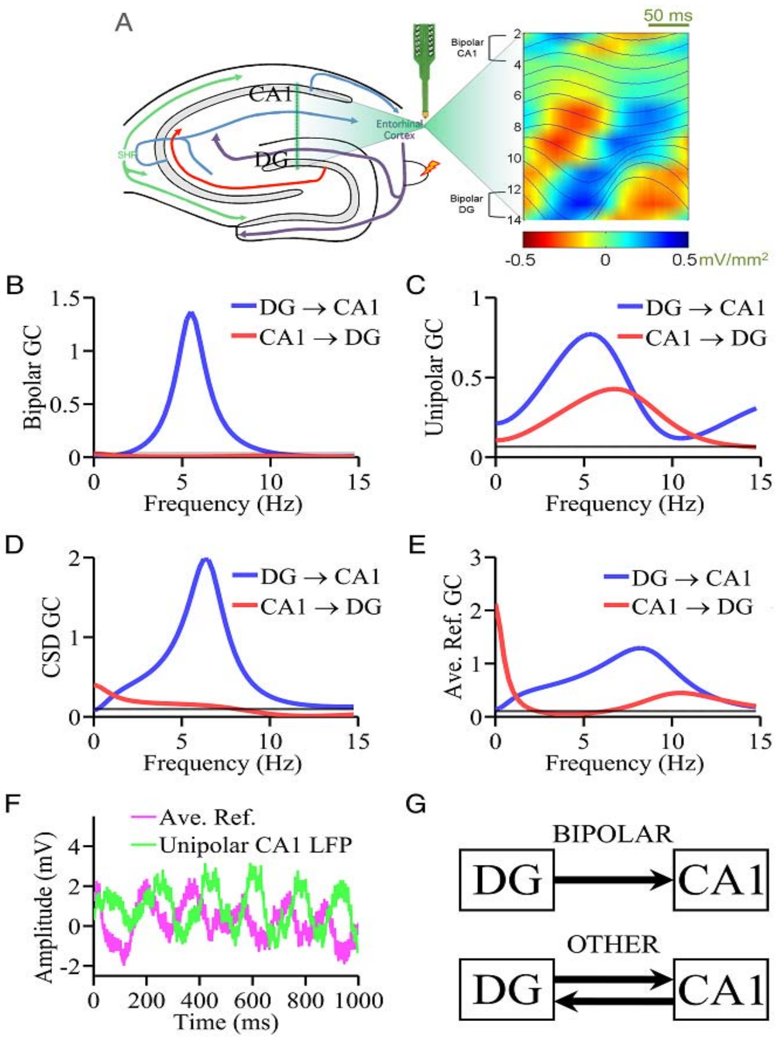
Here $R(t)$ is the common reference.

Bipolar derivations:

Area X: $(X_1(t) - R(t)) - (X_2(t) - R(t))$
$= X_1(t) - X_2(t)$

Area Y: $(Y_1(t) - R(t)) - (Y_2(t) - R(t))$
$= Y_1(t) - Y_2(t)$

Theta in Hippocampus



Only bipolar derivations yield results that agree with the ground truth.

Collaborators

- Anil Bollimunta (UF/BME)
- Yonghong Chen (UF/BME)
- Haiqing Huang (UF/BME)
- Chao Wang (UF/BME)
- Xiaotong Wen (UF/BME)
- Charlie Schroeder (Nathan Kline/Columbia)
- Yijun Liu (UF/Psychiatry)
- Li Yao (Beijing Normal University)
- Govindan Rangarajan (IISc)
- Bernat Kocsis (Harvard/Beth Israel)