Overview of Resting-State fMRI

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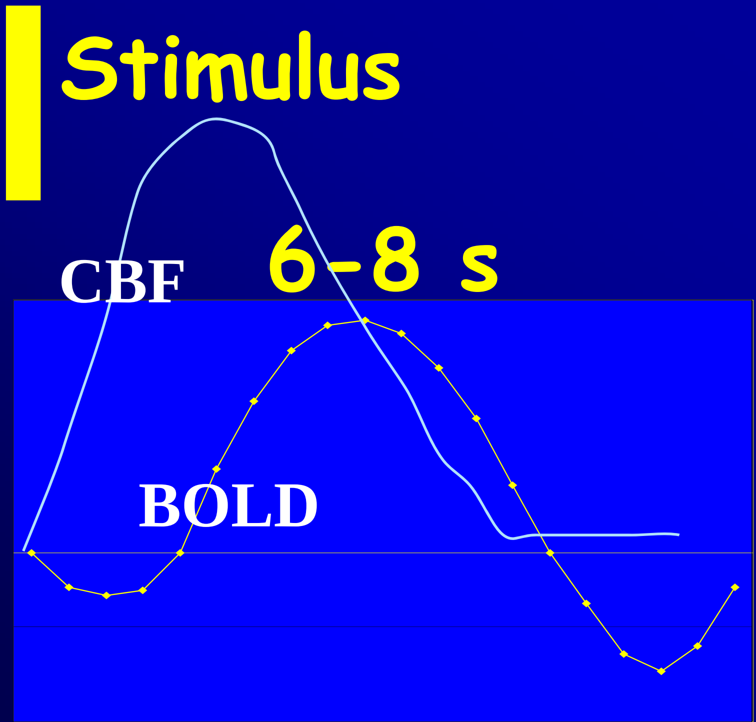
Outline

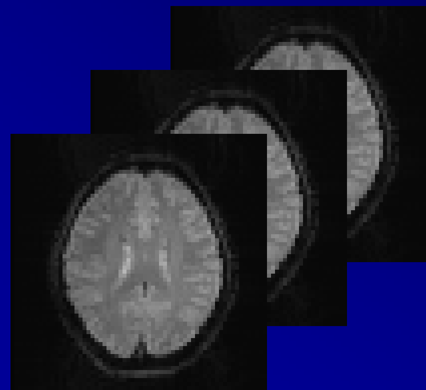
- What is resting-state fMRI?
- Computational methodology
- Applications to brain disorders and cognitive neuroscience

MRI

- **Anatomical: T1, T2……**
- **Diffusion Tensor-MRI**
- **MRS**
- **Perfusion (DSC, ASL…)**
- **fMRI-BOLD** ⇒
- **……**

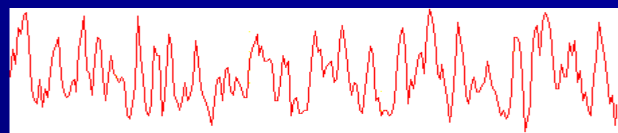
fMRI-BOLD





DeO_2Hb ↓

Signal change: ~1%

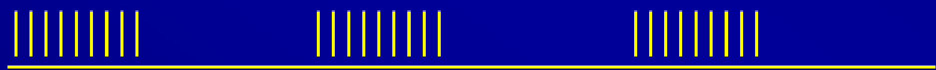


Task-state fMRI?

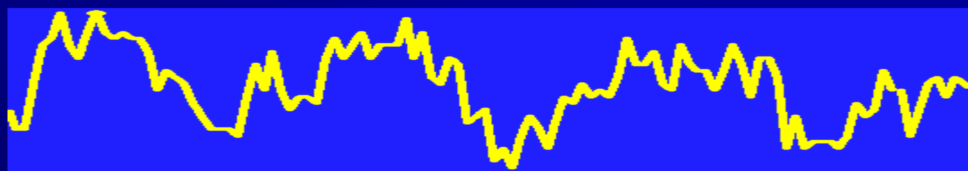
Contrast within a scanning session is necessary!

T C T C T C **Every 30 s alternatively**

Design

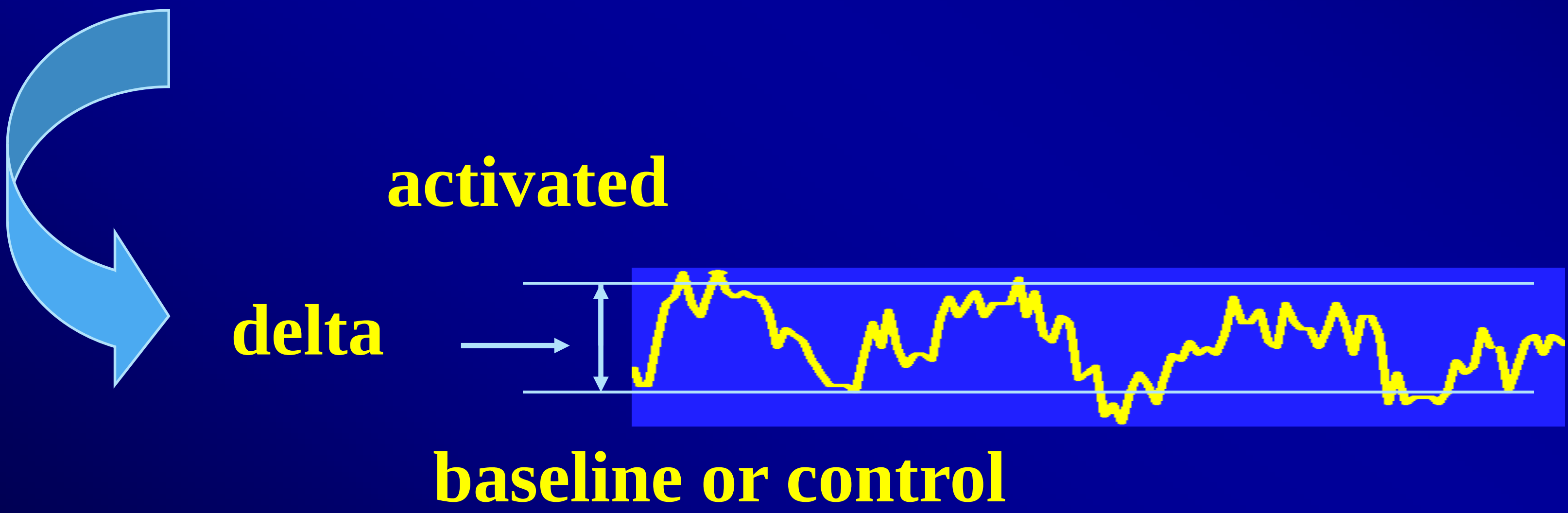


Expected signal



Task-state fMRI

What is activation?

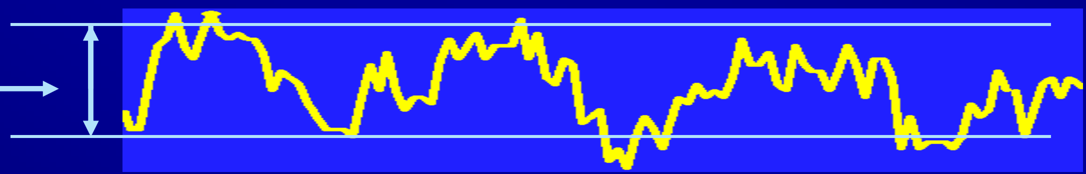


Task-state fMRI

What is abnormal activation for patients?

Abnormal activated level?

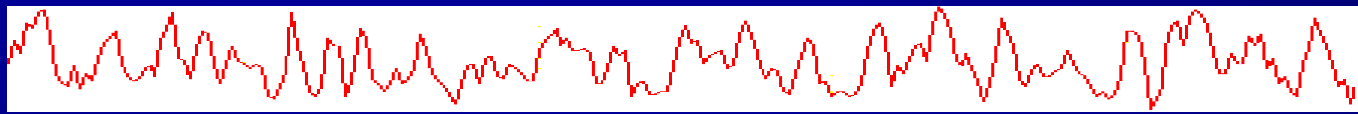
Abnormal delta



Abnormal baseline?

So, baseline state is important!

State-fMRI design vs. time-locked event-related design



- A period of time (quite a few minutes or longer)
- On-going brain activity
- Computation: quite different from task state GLM activation detection
- Resting-state: simple design, baseline

What is resting-state fMRI?

- Eyes closed or open with no task
- Quite a few minutes or longer
- “Not to fall asleep”
- “Not to think of anything in particular”
- Low frequency fluctuation (LFF, 0.01 – 0.08 Hz) (Biswal et al., 1995)

Resting-state BOLD-fMRI signal reflects spontaneous neuronal activity ***(Logothetis et al., 2001, Nature; Rauch et al., 2008, PNAS)***

However, partly due to physiological and physical noises (respiration, cardiovascular pulsation, etc) ***(Cordes et al., 2001; Birn et al., 2006; Goerke et al., 2005)***

Techniques for spontaneous neuronal activity (SNA)

Every functional technique:

- **Single unit recording, MEG and EEG**
- **PET and SPECT**
- **NIRS (Obrig et al., 2000)**
- **perfusion fMRI (Zou et al., 2009)**
- **BOLD fMRI**
- **……**

Outline

- What is resting-state fMRI?
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Computation methods for task-state fMRI

- **Functional segregation**

  (activation detection)

- **Functional integration**

  (inter-regional relationship or connectivity)

Number of papers: former >> latter

Computation methods for resting-state fMRI

- Functional segregation
  (local features)
- Functional integration
  (inter-regional relationship or connectivity)

Number of papers: former << latter

Functional integration or connectivity

- Un-directional: linear correlation, ICA… ➡
- Directional: SEM, DCM, GCA…

Most of resting-state fMRI studies：integration (connectivity)

- **Correlation:** *(Biswal et al., 1995; ……)*
- **ICA:** *(Kiviniemi et al., 2003; van de Ven et al., 2004; Greicius et al., 2004)*
- **Hierarchical Clustering:** *(Cordes et al., 2000; Salvador et al., 2005)*
- **Self Organization Map:** *(Peltier et al., 2003)*
- **....**

The first Resting-state fMRI study

(Biswal et al., 1995, MRM)

Bilateral finger tapping (task vs. rest)

Resting-state correlation of low frequency fluctuation (LFF, 0.01 – 0.08 Hz)

(Courtesy of Dr. WENG Xu-Chu)

Linear Correlation

Spontaneous LFF was highly synchronous among:

- Bilateral motor cortices *(Biswal et al., 1995)*
- Bilateral visual cortices *(Lowe et al., 1998; Kiviniemi et al., 2004)*
- Bilateral auditory cortices *(Cordes et al., 2001)*
- Bilateral amygdala *(Lowe et al., 1998)*
- Bilateral thalamus *(Stein et al., 2000)*
- Language cortices *(Hampson et al., 2002)*
- Default mode network *(Greicius et al., 2003; Fox et al., 2005..)*

Most of resting-state fMRI studies: integration (connectivity)

- **Correlation:** *(Biswal et al., 1995; ……)*
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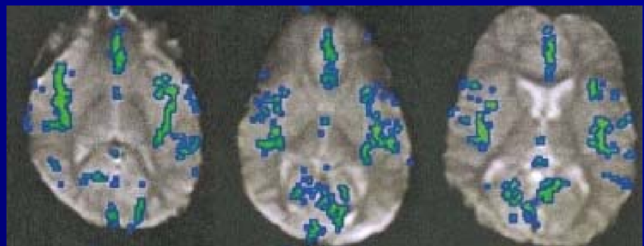
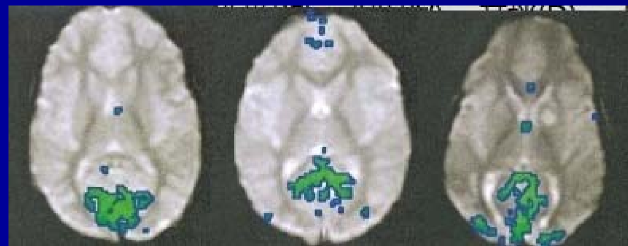
- **....**

Spatial ICA for resting-state fMRI





Vascular component **Visual component**

(Kiviniemi et al., 2000)

Functional integration or connectivity

- Un-directional: linear correlation, ICA…
- Directional: SEM, DCM, GCA… ➡

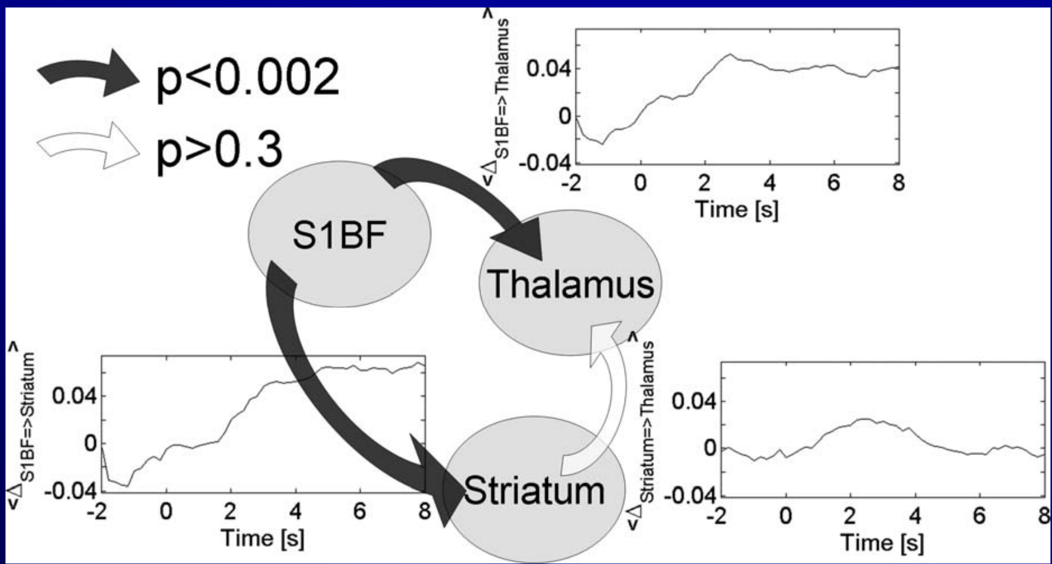
Identifying neural drivers with functional MRI: an electrophysiological validation

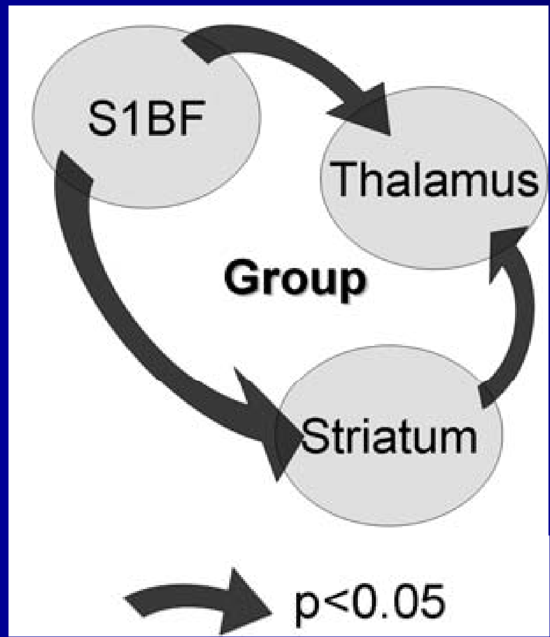
(David et al., 2009, PLoS Biol)

- **Rat model of absence epilepsy showing spontaneous spike-and-wave discharges originating from the first somatosensory cortex (S1BF)**
- **fMRI**
- **Intracerebral EEG: (1) first somatosensory cortex S1BF; (2) ventrobasal thalamus; (3) striatum**

Identifying neural drivers with functional MRI: an electrophysiological validation

(David et al., 2009, PLoS Biol)

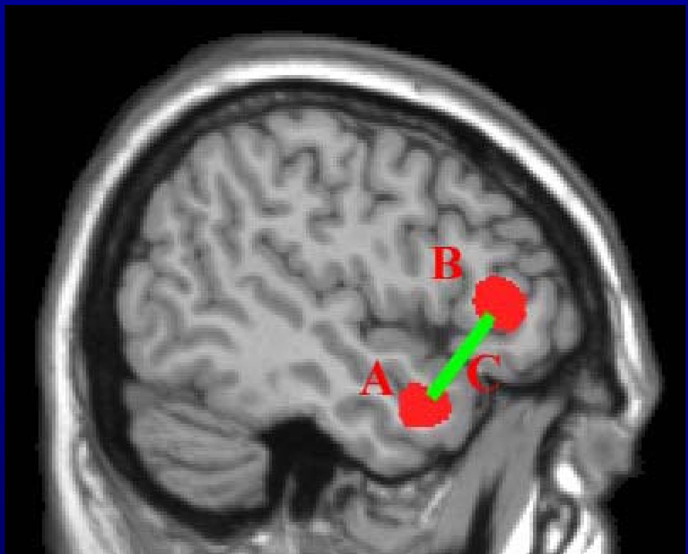




iEEG **fMRI**

Granger Causality

“Integrative” is really good, but:



Decreased

functional connectivity

Question: Is A, B, C, or……abnormal?

Much fewer resting-state fMRI studies: Segregation

- ➡ ❖ **rms, power spectrum, ALFF:** *(Biswal et al., 1995; Li et al., 2000; Kiviniemi et al., 2000; Zang et al., 2007)*
- ➡ ❖ **Regional Homogeneity:** *(Zang et al., 2004)*
- ❖ **TCA:** *(Liu et al., 2000; Morgan et al., 2004)*
- ❖ **Multiple Regressors:** *(Fransson, 2005)*
- ❖ **Autoregressive Noise Model:** *(Cordes et al., 2005)*
- ❖ **Fractional Gaussian Noise:** *(Maxim et al., 2005)*

rms, power, ALFF

For a given frequency:

root mean square (rms)

standard deviation

amplitude

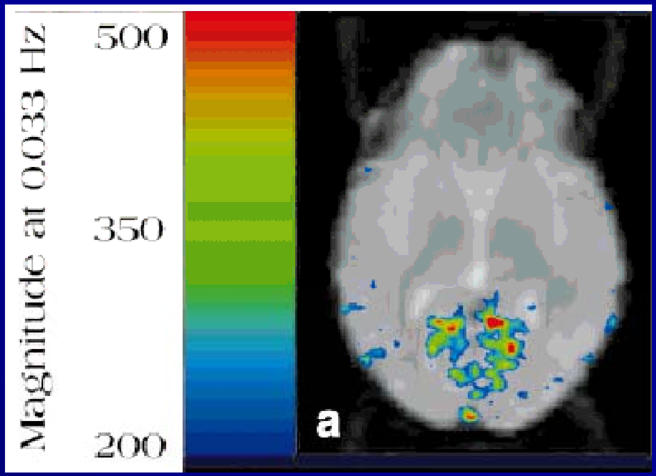
} Square root of the power

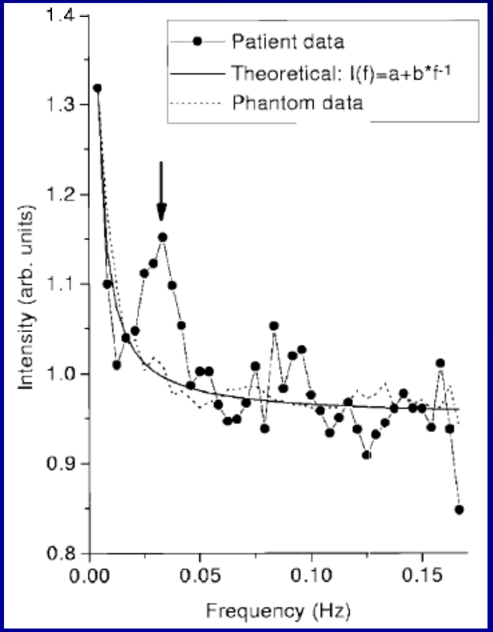
rms: white matter vs. gray matter = 0.6 : 1

(Biswal et al., 1995; Li et al., 2000)

rms, power, ALFF

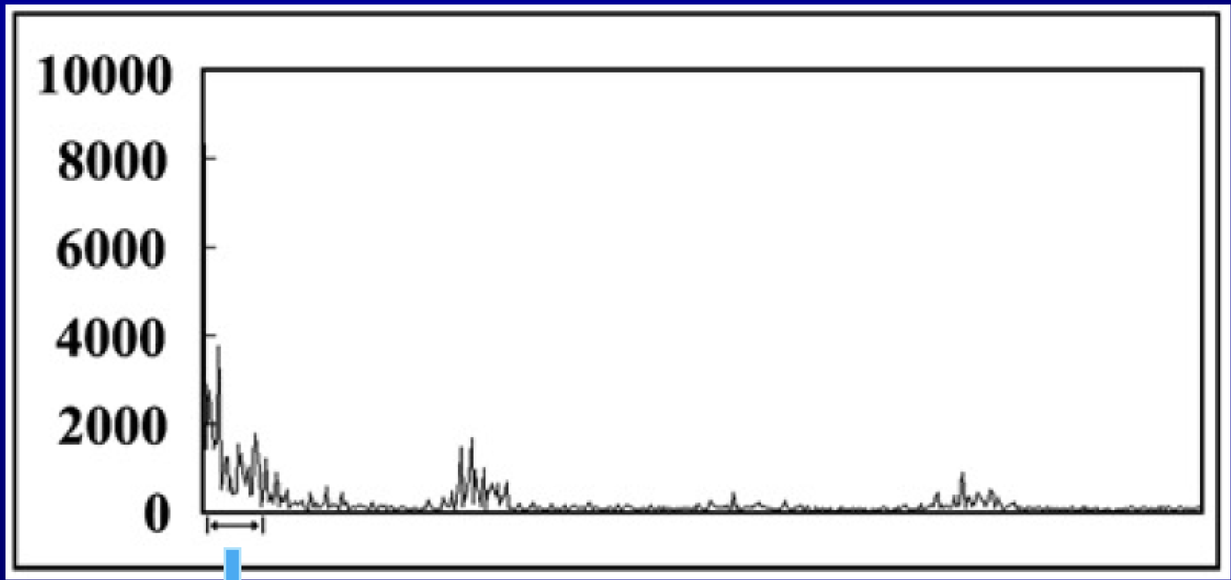
❖ **Power spectrum:**





Higher power at 0.033Hz in visual area ***(Kiviniemi et al., 2000)***

Amplitude of Low Frequency Fluctuation (ALFF) *(Zang et al., 2007, Brain Dev; Yang et al., NeuroImage)*



TR

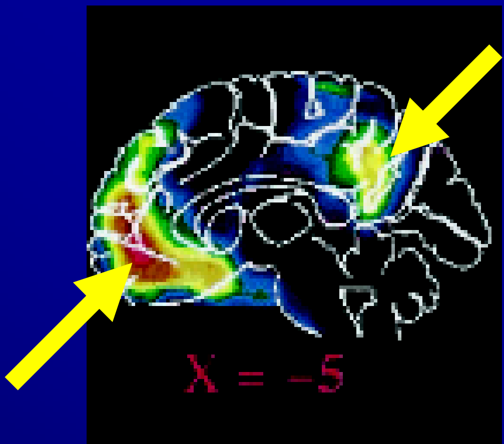
400 ms

1.25 Hz

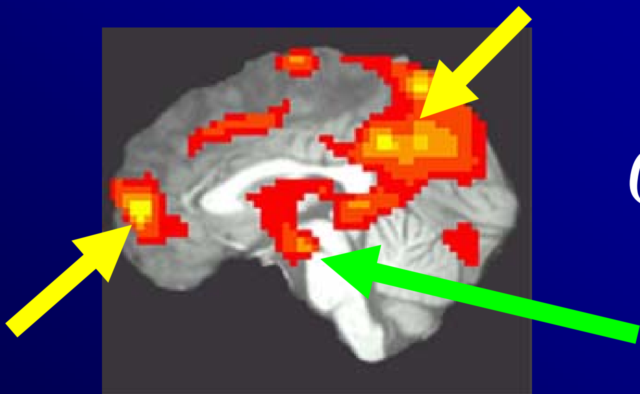
0.01-0.08 Hz

Steps: square root, average of 0.01-0.08 Hz, standardization by global mean

ALFF



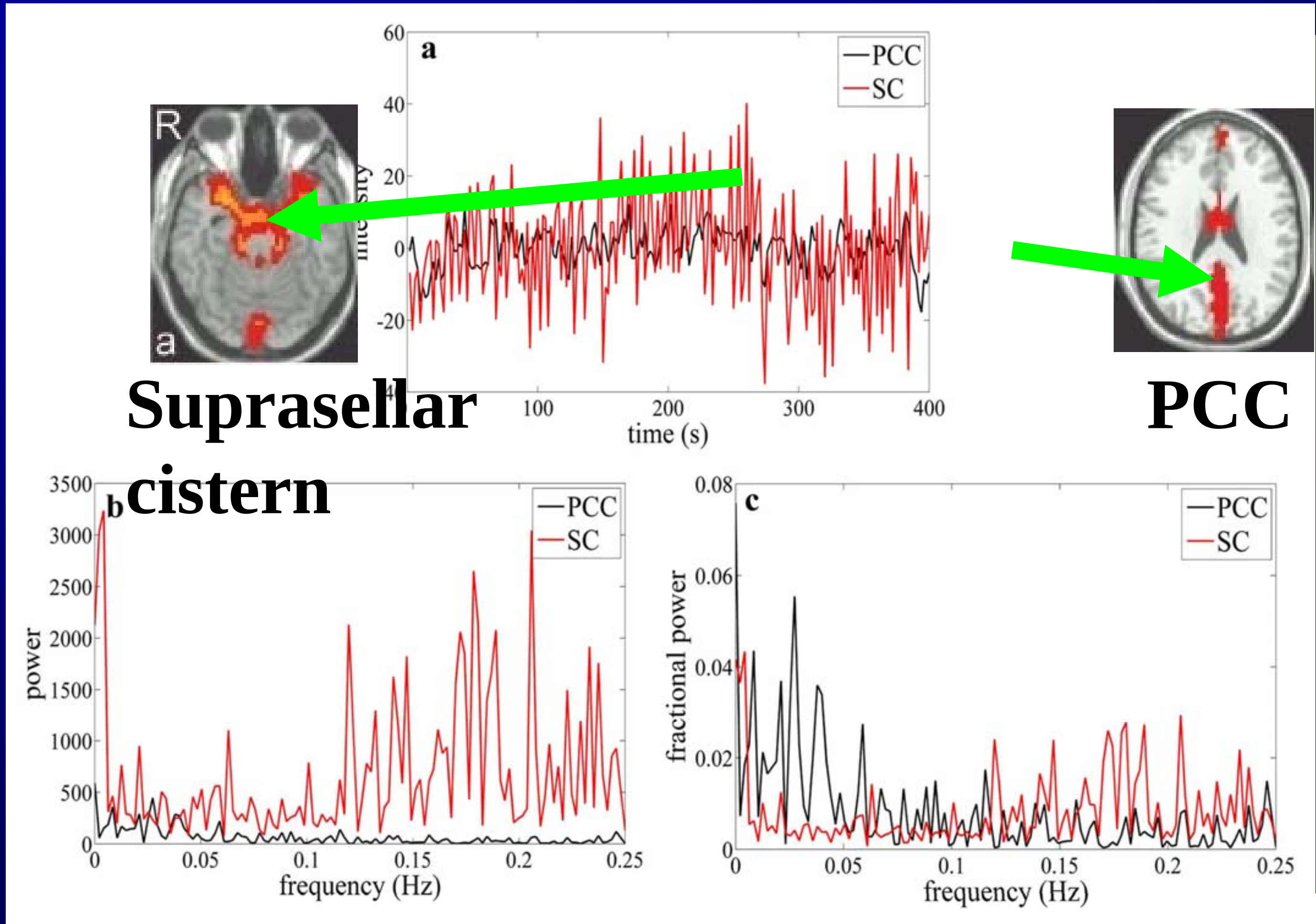
PET
(Raichle et al., 2001)



ALFF
(Zang et al., 2007)

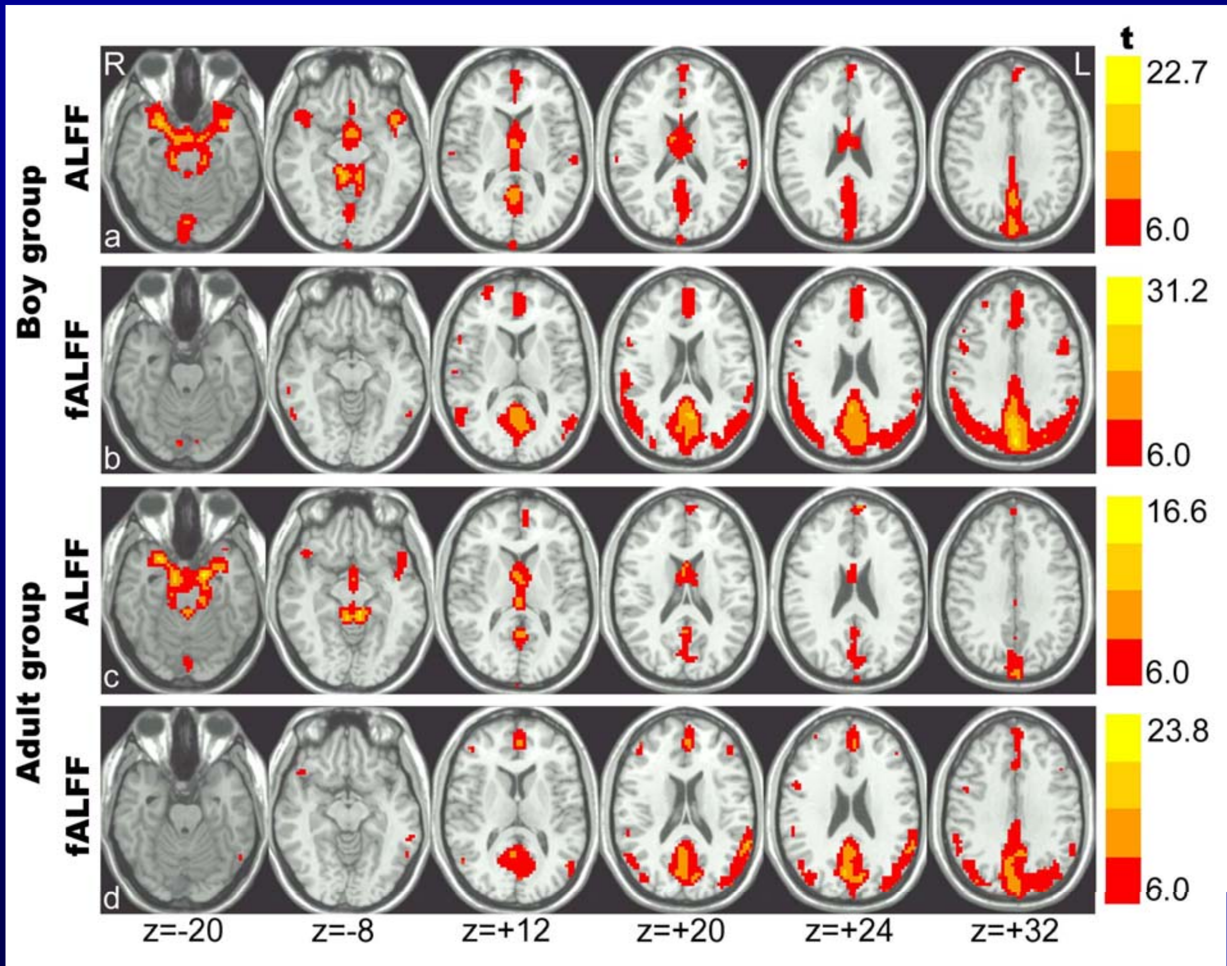
noise

Improvement: fractional ALFF



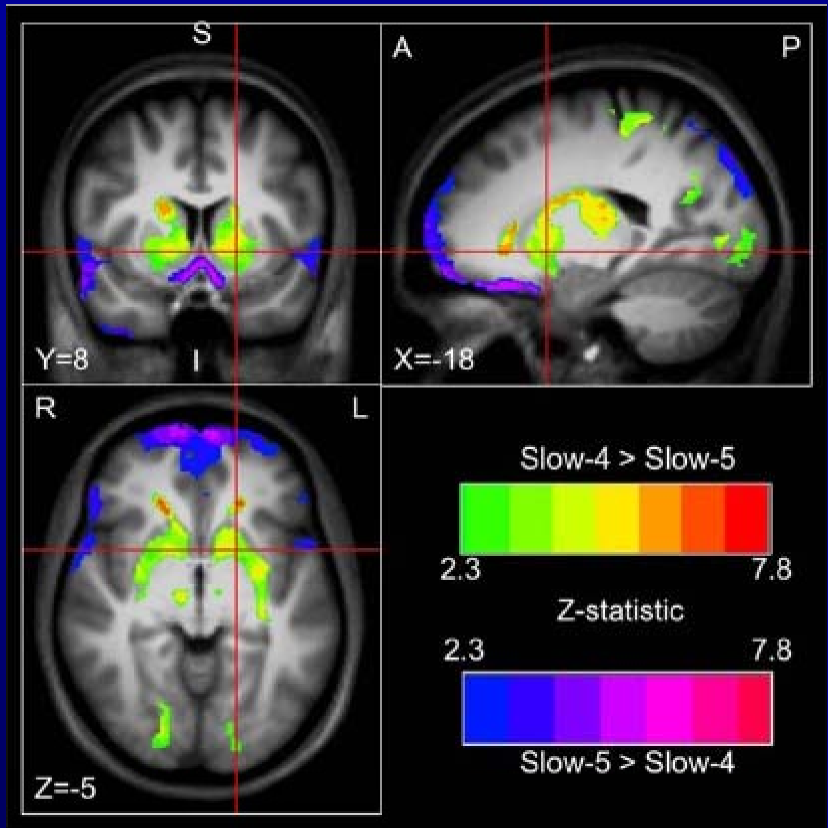
(Zou et al., 2008, J Neurosci Methods)

Improvement: fractional ALFF



(Zou et al., 2008, J Neurosci Methods)

fALFF at different frequency band



Slow 4: 0.027-0.073 Hz
Slow 5: 0.01-0.027 Hz

(Zuo et al., 2009, NeuroImage)

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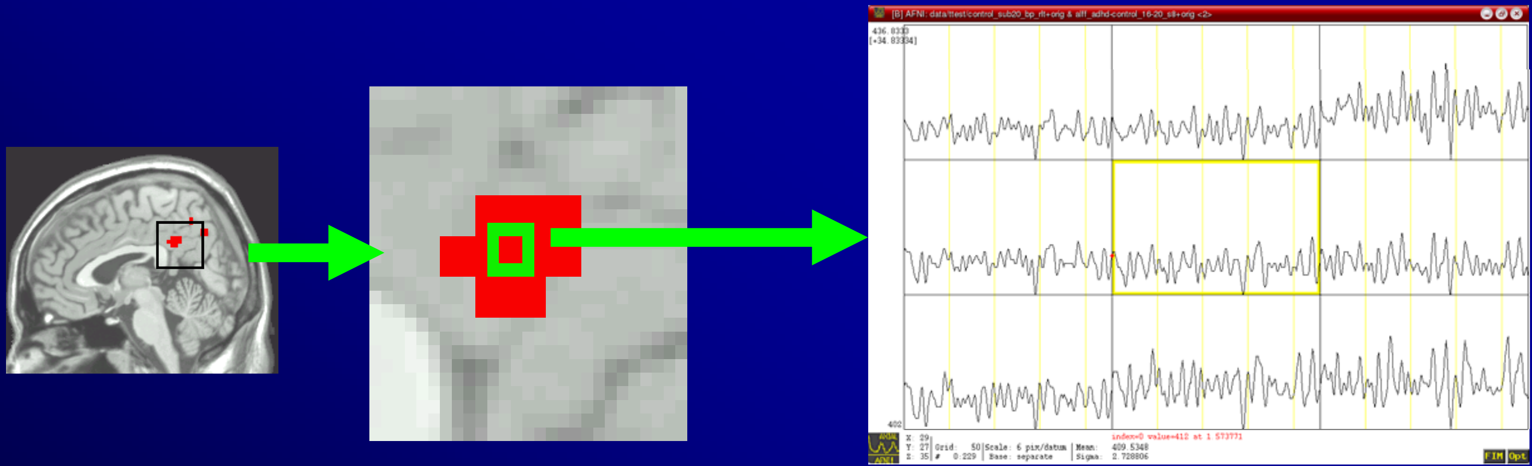
Regional Homogeneity (ReHo)

Similarity or coherence of the time courses within a functional cluster

(Zang et al., 2004, NeuroImage)



ReHo

- **Kendall Coefficient of Concordance (KCC)** ***(Kendall & Gibbons, 1990)***

$$W = \frac{\sum (R_i)^2 - n\left(\overline{R}\right)^2}{\frac{1}{12}K^2\left(n^3 - n\right)}$$

Ri: sum rank of ith time point

$$\overline{R} = \frac{(n+1)\times K}{2}$$

K: number of time series

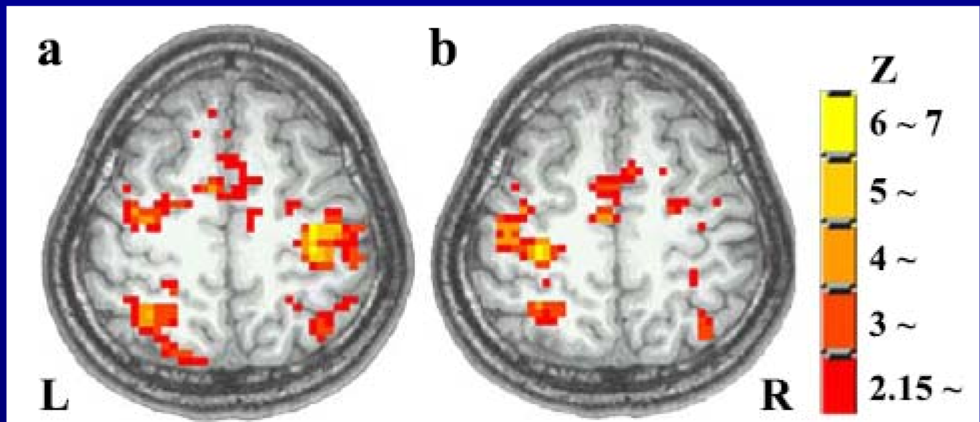
n: number of time points

W= 0 ~ 1

Regional Homogeneity (ReHo)

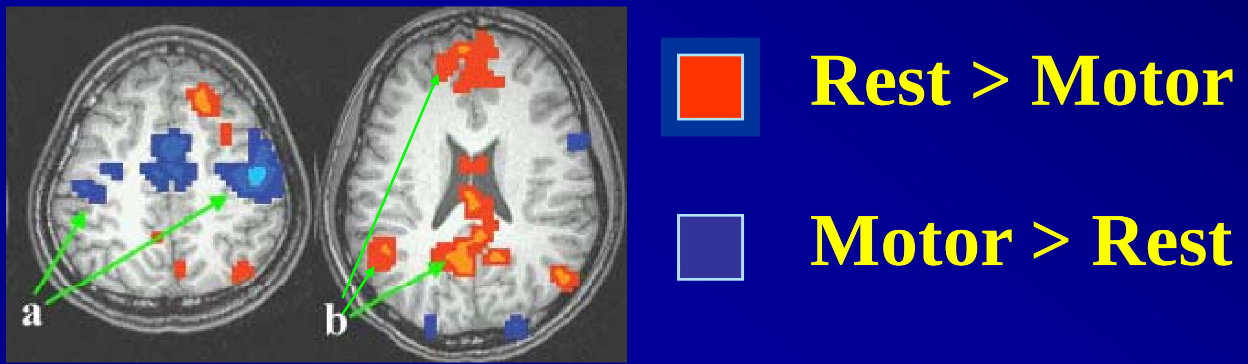
(Zang et al., 2004)

Activation map by general linear model (GLM):



Left finger tapping **Right finger tapping**

ReHo: motor task state vs. continuous resting state *(Zang et al., 2004)*



a) Higher ReHo in bilateral primary motor cortices during right finger tapping than resting-state

b) Higher ReHo in default mode network (PCC, MPFC, IPL) during resting-state *(Raichle et al., 2001; Greicius et al., 2003)*

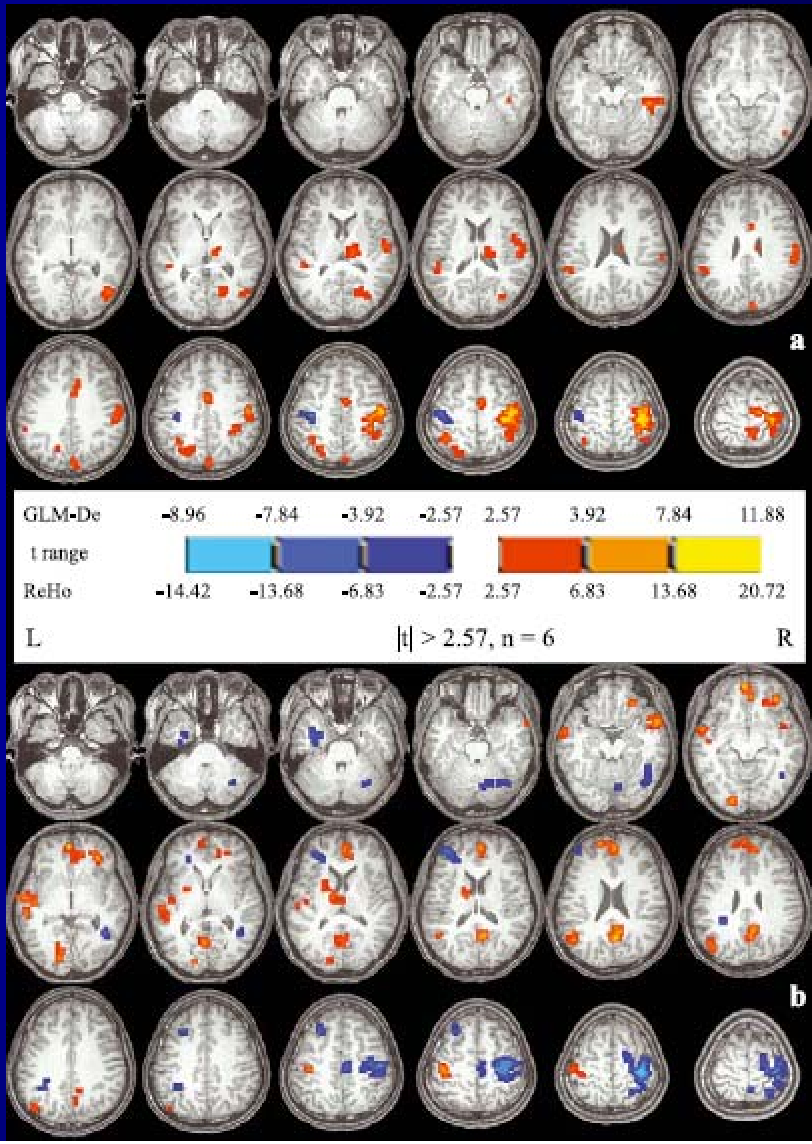
ReHo: Right motor task-state vs. left *(Zang et al., 2004)*

GLM activation

Right > Left

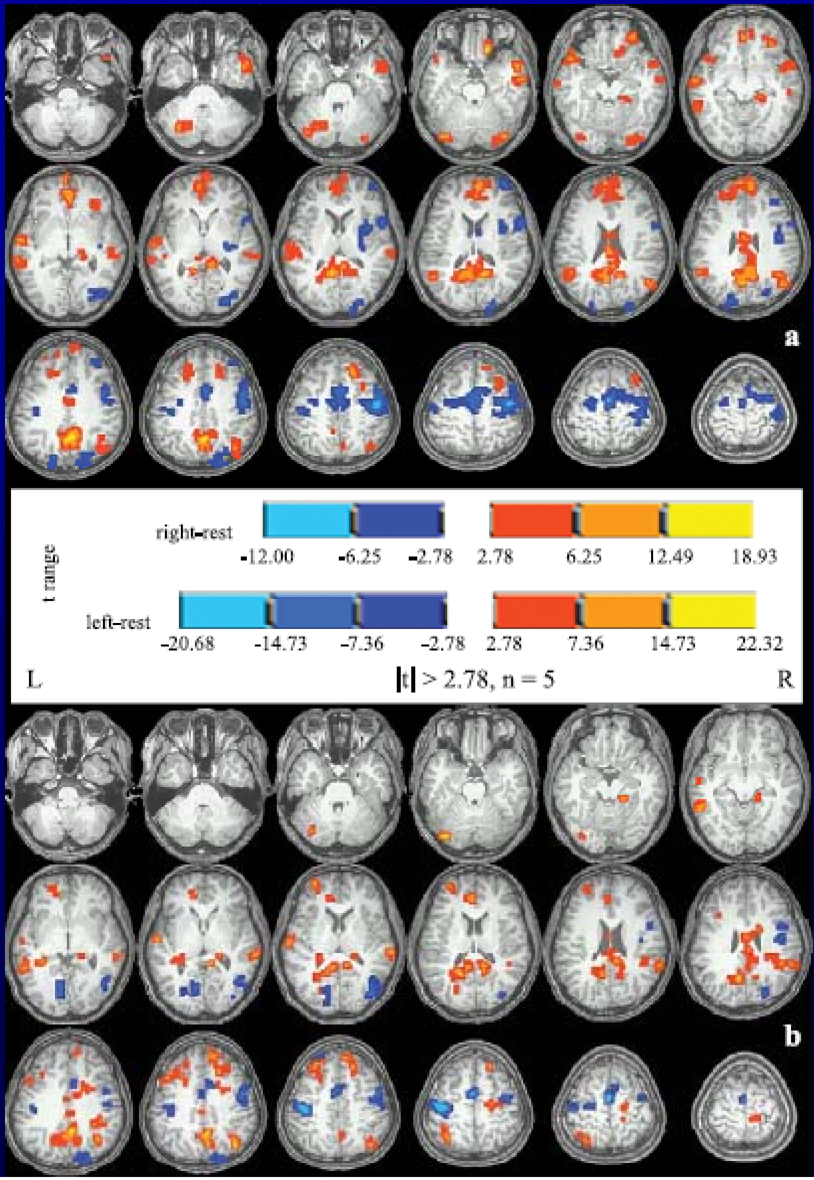
Left > Right

ReHo

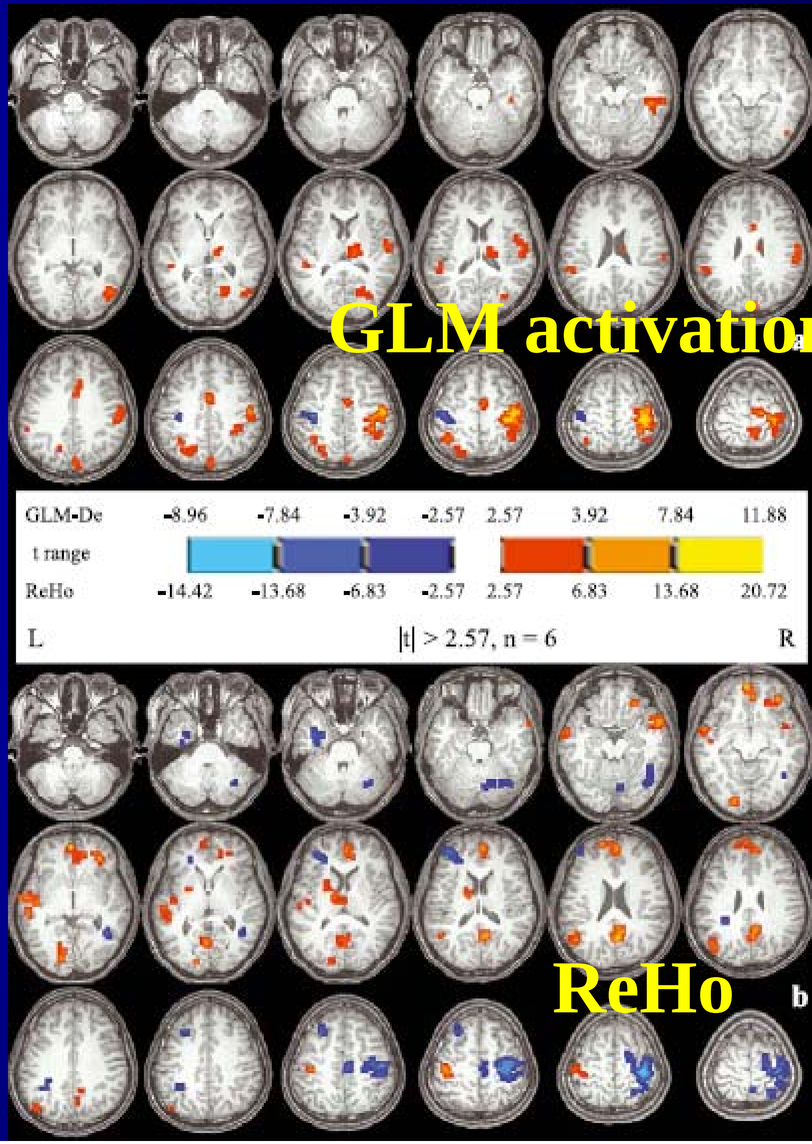


ReHo: *(Zang et al., 2004)*

Task vs. Rest



Task vs. Task



ReHo and ALFF: application to brain disorders

- **ADHD:** ***Zhu et al., 2005, 2007; Cao et al., 2006***
- **AD/MCI:** ***He et al., 2007; Bai et al., 2008***
- **Schizophrenia:** ***Liu et al., 2006; Shi et al., 2007; Hoptman et al., 2009***
- **Aging:** ***Wu et al., 2007***
- **PD:** ***Wu et al., 2008***
- **Depression:** ***Yuan et al., 2008; Yao et al., 2008***
- **Epilepsy:** ***Cheng et al., 2008; Zhang et al., 2008, 2009***
- **PTSD:** ***Lui et al., 2009***
- **Autism:** ***Paakki et al., 2010***

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Acknowledgements

Thanks to all my students and postdoctoral fellows

Thanks to all my collaborators: **Bharat BISWAL, GONG Qiyong, HE Yong, JIANG Tian-Zi, Vesa KIVINIEMI, Michael MILHAM, WANG Yu-Feng, WENG Xu-Chu, Yihong YANG, ZHANG Dai, ZHU Chao-Zhe……**

(In A-Z order)

感谢汤洁女士对我的国际、国内合作提供的帮助

Thanks to Natural Science Foundation of China (NSFC) and Ministry of Science and Technology of China

诚聘博士后（在职、脱产）！

欢迎合作研究！

Thanks for your attention!