



## Resting-State fMRI: Current Research, Methodological Issues and Its Applications

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## Outline

- ▶ • Principles & Computational Algorithms
  - Methodological Issues & Computational Platform
  - Applications to Brain Disorders
- 

### Resting-State fMRI: Principles



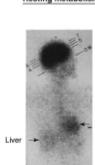
All of the human high mental functions such as thinking, emotion and consciousness rely on brain, an extremely complex system (Singer, 1999)

<http://psychcentral.com/news/2010/11/03/new-insights-on-brains-internal-wiring/20500.html>



### Resting-State fMRI: Principles

Resting metabolism





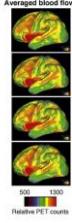
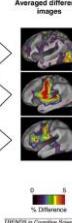
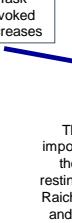
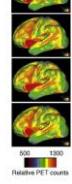
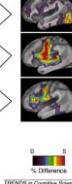
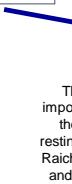
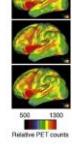
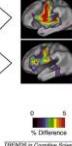
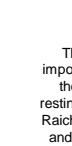
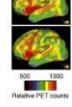
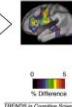
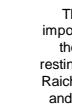
Caloric intake  
Weight gain  
Gross energy consumption  
**20%**

Raichle et al., 2010. Trends Cogn Sci



### Resting-State fMRI: Principles

Task performance

	Averaged blood flow	Conditions	Averaged difference images
Visual fixation			
Viewing words			
Reading words			
Generating verbs			

**Task evoked increases**

**<5%**

**Resting-state energy consumption**

There are very important activities in the brain during resting-state (Fox and Raichle, 2007; Zhang and Raichle, 2010)

TRENDS in Cognitive Sciences

500 1300 Resin PET counts

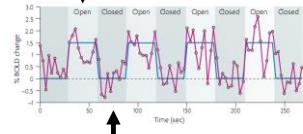
% Difference

Raichle et al., 2010. Trends Cogn Sci



### Resting-State fMRI: Principles

Task



Baseline

Open - Closed +

• Traditional fMRI analysis

→ Noise?

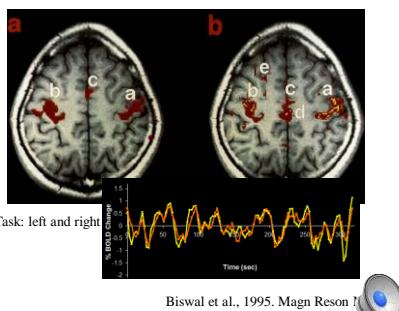
Activities in the baseline state (usually resting-state)

Fox and Raichle, 2007. Nat Rev Neurosci



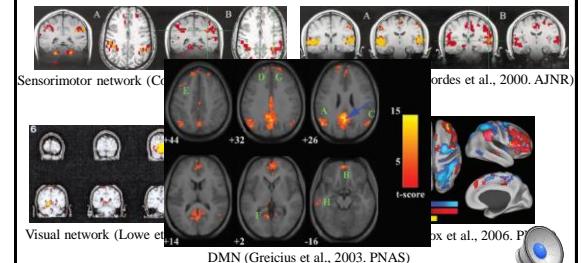
## Resting-State fMRI: Principles

- Temporal synchrony of spontaneous fluctuations

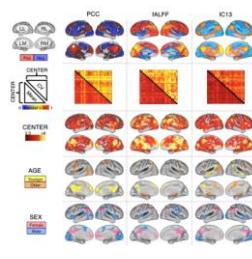
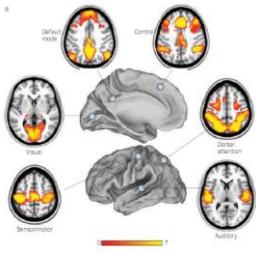


## Resting-State fMRI: Principles

- Functional networks identified by functional connectivity with resting-state fMRI (RS-fMRI)



## Resting-State fMRI: Principles



## Resting-State fMRI: Principles

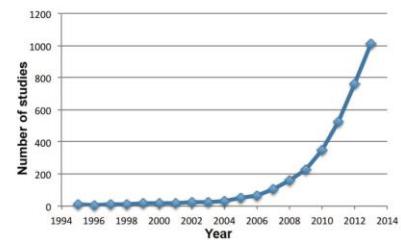


Figure 1. Number of R-fMRI related studies in PubMed (key words: "resting+state+fMRI").

Yan et al., 2015. F1000Res

## Outline

- Resting-State fMRI: Principles
- • Data Analysis: Computational Algorithms
- Data Analysis: Methodological Issues
- Data Analysis: Computational Platform
- Applications to Brain Disorders



## Computational Methodology

- Integration approach
- Regional approach
- Graphical approach



## Computational Methodology

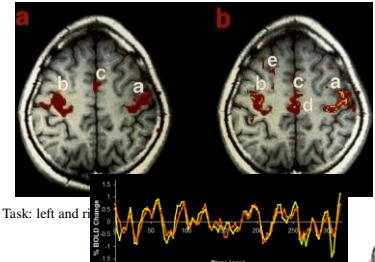
### Integration approach

- Functional Connectivity
- 
- a
- Effective Connectivity: (Friston et al., 2002)
- Hierarchical Clustering: (Cordes et al., 2000; Salvador et al., 2005)
- Self Organization Map: (Peltier et al., 2003)
- ....



## Computational Methodology

- Correlation: Temporal synchrony of spontaneous fluctuations



## Computational Methodology

### The “Resting” Brain



Courtesy of Dr. Daniel Margulies

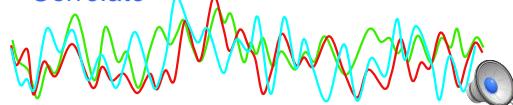


## Computational Methodology

- How do we detect organized patterns of intrinsic activity?



Correlate

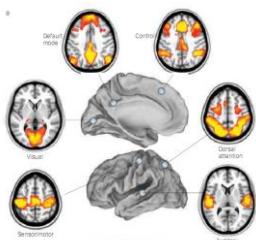


Resting State Functional Connectivity



## Computational Methodology

### • Correlation

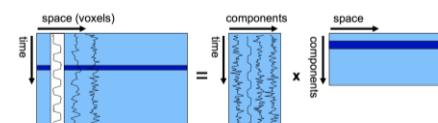


Zhang and Raichle, 2010. Nat Rev Neurol

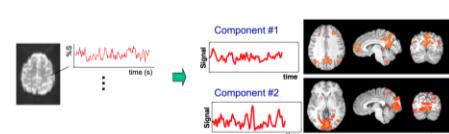


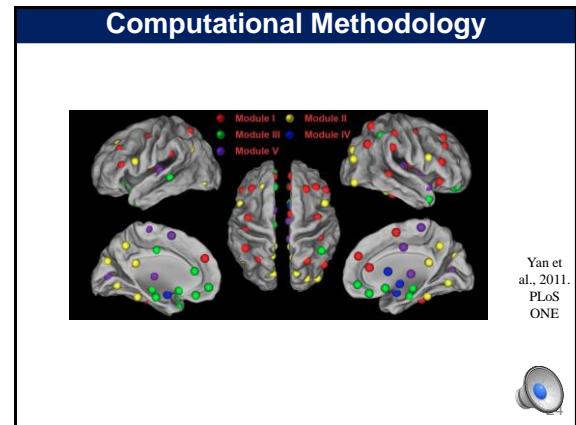
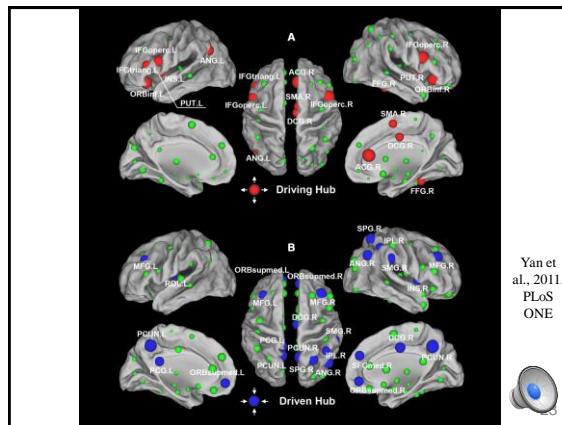
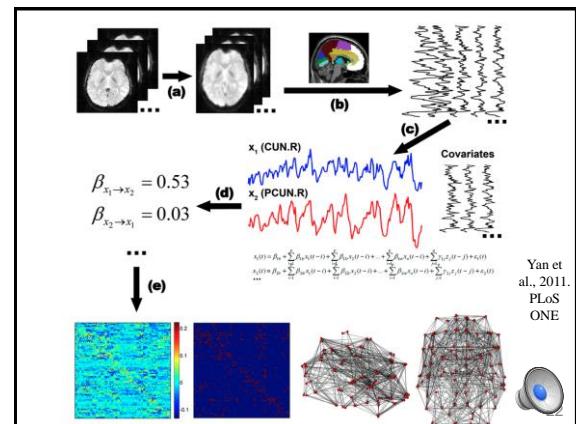
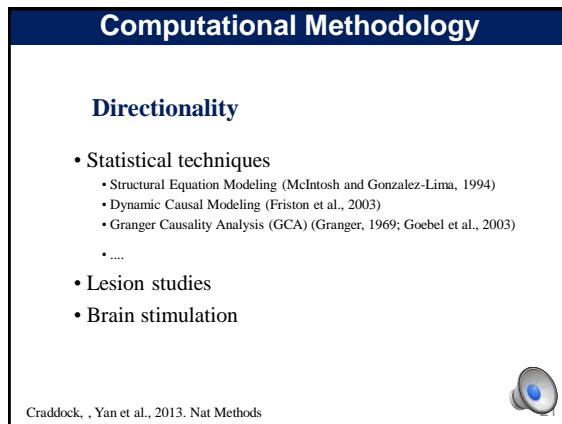
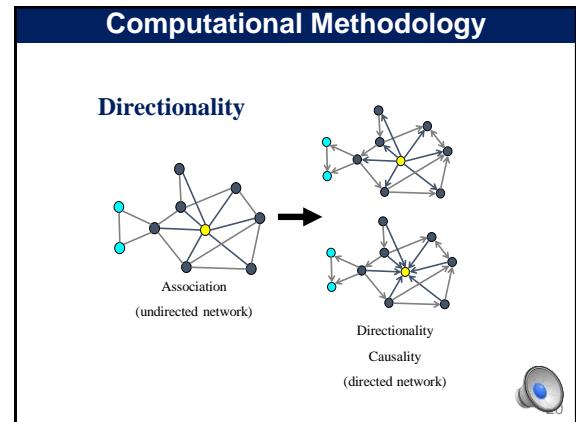
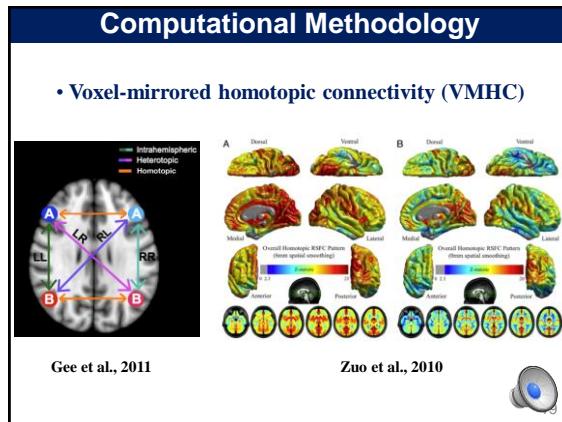
## Computational Methodology

### • Independent Component Analysis



Birn  
2015

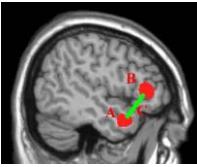




### Computational Methodology

Regional approach

“Integrative” is really good, but:



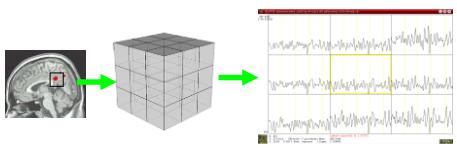
Decreased functional connectivity

Question: Is A, B, C, or.....abnormal?

### Computational Methodology

#### Regional Homogeneity (ReHo)

Similarity or coherence of the time courses within a functional cluster

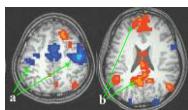


$$W = \frac{\sum(R_i)^2 - n(\bar{R})^2}{\frac{1}{12}K^2(n^3 - n)}$$

(Zang et al., 2004)

### Computational Methodology

#### ReHo: motor task state vs. pure resting state



- Rest > Motor
- Motor > Rest

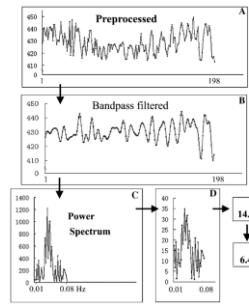
a) Higher ReHo in bilateral primary motor cortices during motor task

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

(Zang et al., 2004)

### Computational Methodology

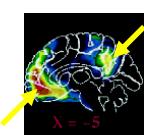
#### Amplitude of low frequency fluctuations



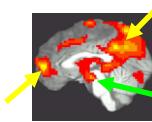
Zang et al., 2007

### Computational Methodology

#### ALFF



PET  
(Raichle et al., 2001)

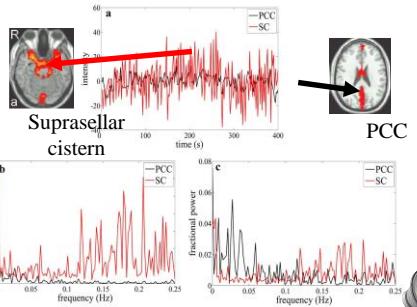


ALFF  
(Zang et al., 2007)

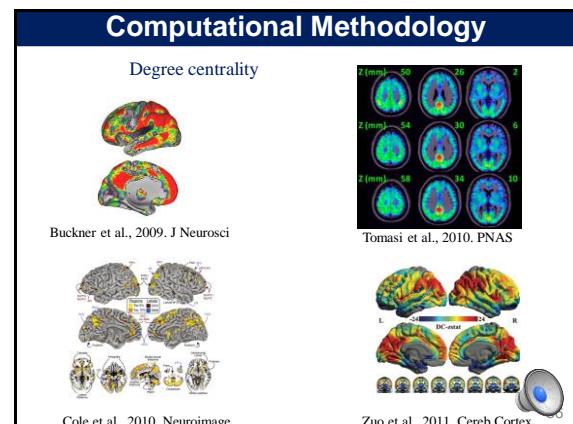
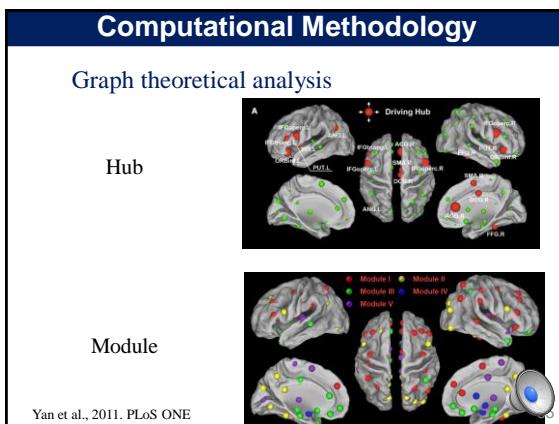
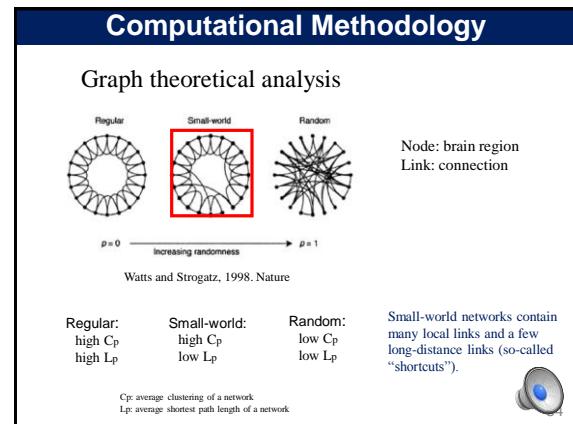
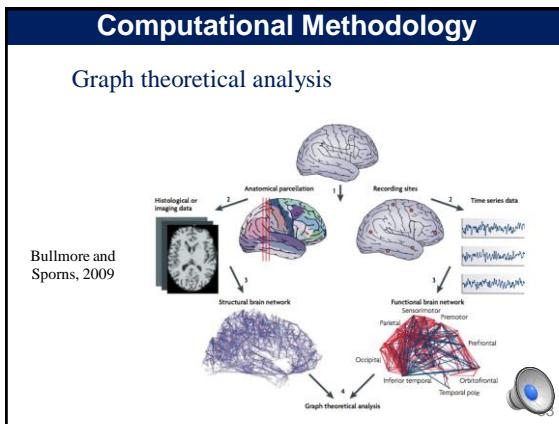
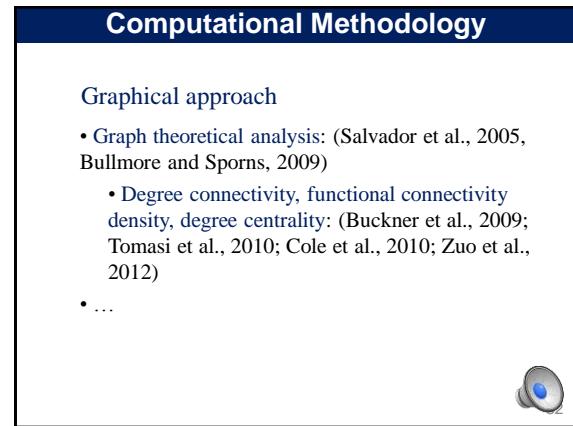
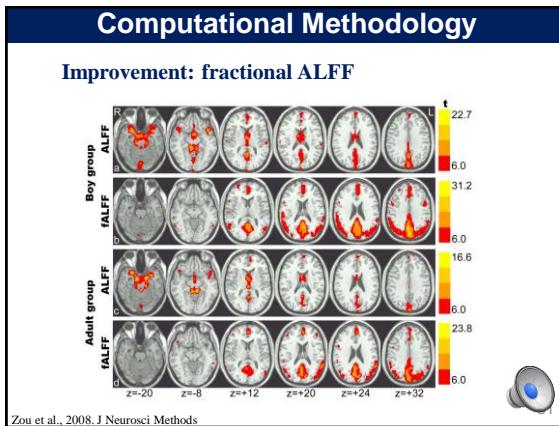
noise

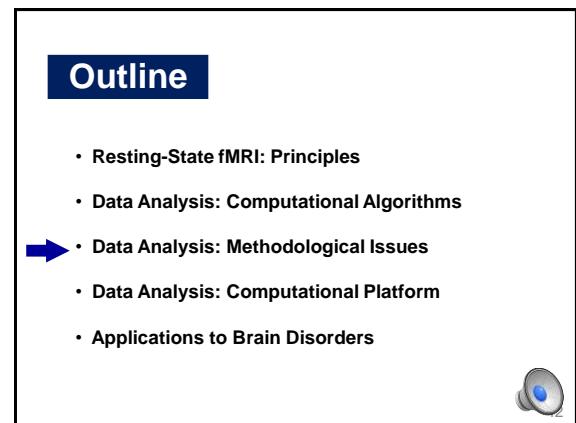
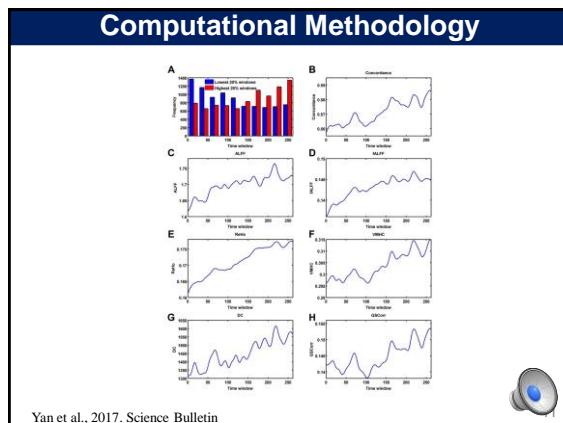
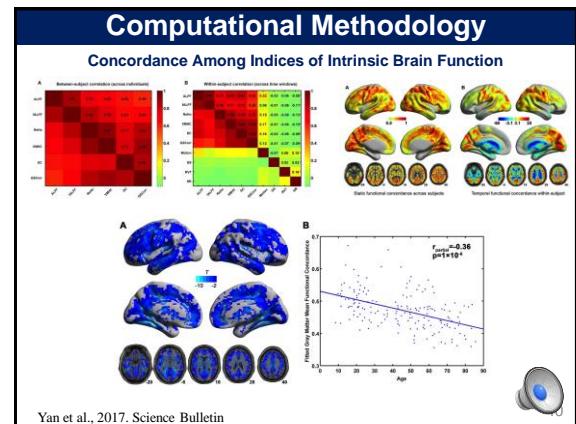
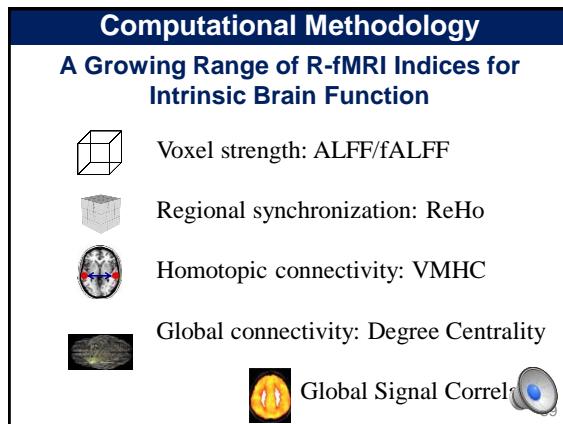
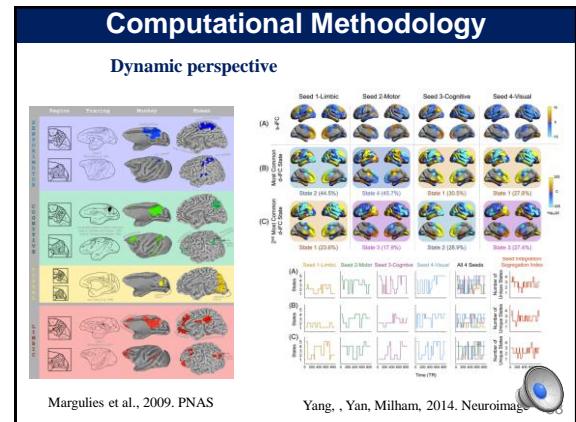
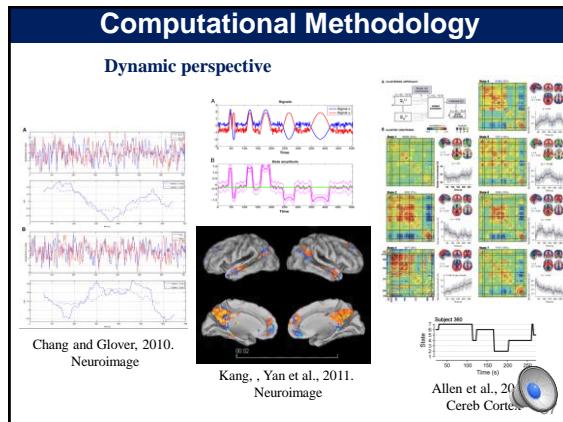
### Computational Methodology

#### Improvement: fractional ALFF



Zou et al., 2008, J Neurosci Methods





## Methodological Issues

- Head motion
- Standardization
- Multiple-comparison correction
- And many many more...

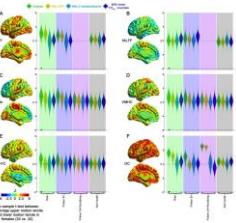
*Yan et al., 2013a. Neuroimage*  
*Yan et al., 2013. Front Hum Neurosci*

*Yan et al., 2013b. Neuroimage*

*Chen, Lu, Yan\*. 2017. Human Brain Mapping*



## Methodological Issues: Head Motion



**Proposed an effective head motion correction strategy**

- Individual-level correction with the Friston-24 model
- Group-level correction with head motion covariate

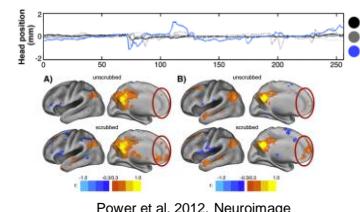
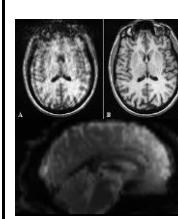
- Cited: 573 times
- ESI Top 1% highly cited paper

*Yan et al., 2013a. Neuroimage*



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## Methodological Issues: Head Motion



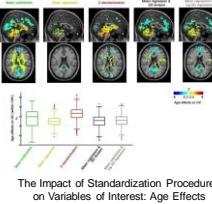
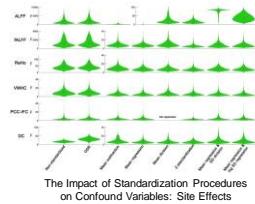
Head motion is a critical factor in R-fMRI data processing.

Need an effective motion correction strategy!



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## Methodological Issues: Standardization



**Proposed an effective standardization strategy**

Mean regression + SD division

*Yan et al., 2013b. Neuro*



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## Methodological Issues: Standardization

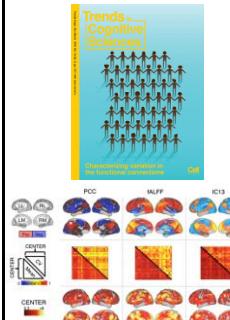


Table 1. Factors can introduce unintended variations in fMRI measurement.

Category	Factor
1. Acquisition-related variations	Scanner make and model (Friedman and Glover, 2006b), sequence type (Buckner et al., 2004; Hwang et al., 2006; Winkler et al., 2002), parallel vs. conventional acquisition (Pfefferbaum et al., 2010; Lin et al., 2005), coil type (surface vs. volume, number of channels, orientation), slice timing (inter-slice time, slice order, slice gap), echo time, and acquisition volume (field of view, voxel size, slice thickness, matrix size, number of slices, number of averages) (Winkler et al., 2006).
2. Experimental-related variations	Participant instructions (Harlais et al., 2011), eyes-open/eyes-closed (Yan et al., 2009; Yang et al., 2007), visual stimulus, experiment duration (Yan et al., 2009; Yang et al., 2007; Giedd et al., 2004), video (Culver et al., 2009), head-motion restraint techniques (e.g., vacuum bag, foam pad, bite-bar, plaster cast head holder) (Edward et al., 2000; Giedd et al., 2004; Harlais et al., 2011; Hwang et al., 2006; Veltman et al., 2006).
3. Environment-related variations	Sound alteration measures (Cho et al., 1998; Elliott et al., 1998); temperature (Kang et al., 2009; Kim et al., 2009; Kim et al., 2010), video (Culver et al., 2009), head-motion restraint techniques (e.g., vacuum bag, foam pad, bite-bar, plaster cast head holder) (Edward et al., 2000; Giedd et al., 2004; Harlais et al., 2011; Hwang et al., 2006; Veltman et al., 2006).
4. Participant-related variations	Age (Yan et al., 2009; Harlais et al., 2011; Hwang et al., 2006; Veltman et al., 2006), gender (Yan et al., 2009; Harlais et al., 2011; Hwang et al., 2006; Veltman et al., 2006), prandial (Hwang et al., 2006), caffeine (Nack-Gasser et al., 2009), and nicotine status (Tanabe et al., 2011), sleepiness (annual Horowitz et al., 2006), sleep deprivation (Suzuki et al., 2009), alcohol (Veltman et al., 2006), and menstrual cycle status (for women) (Popogrebscu et al., 2005).

*Yan et al., 2013b. Neuroimage*



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## Methodological Issues

### Standardization

Collaborate with Dr. Xi-Nian Zuo @ IPCAS

Dr. Jia-Hong Gao @ PKU



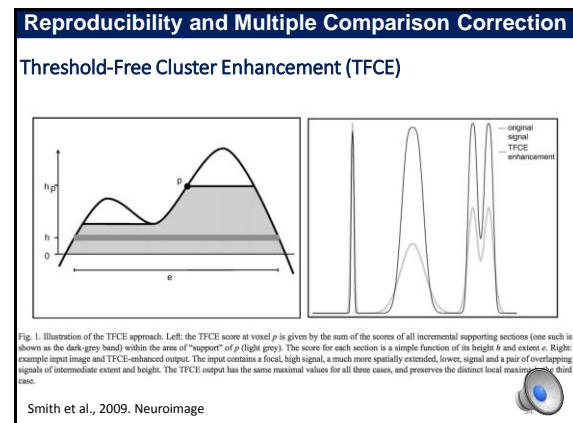
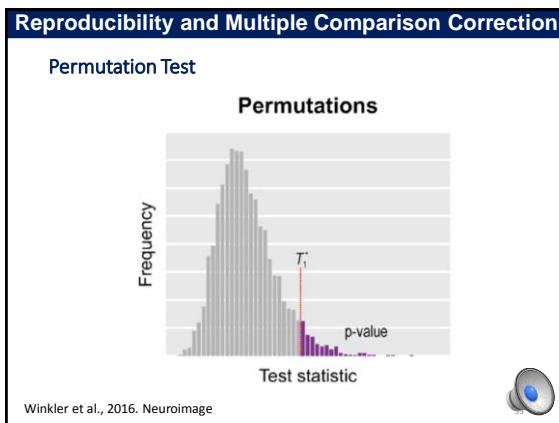
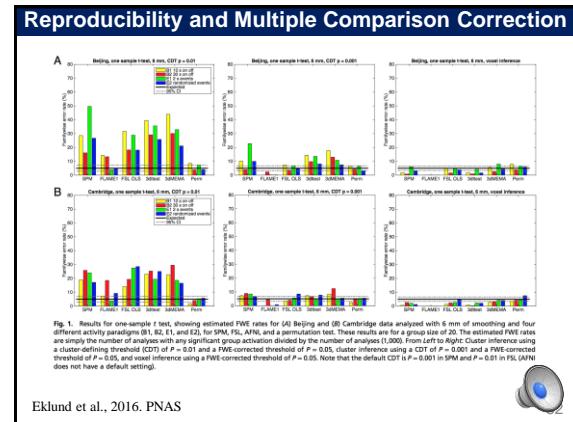
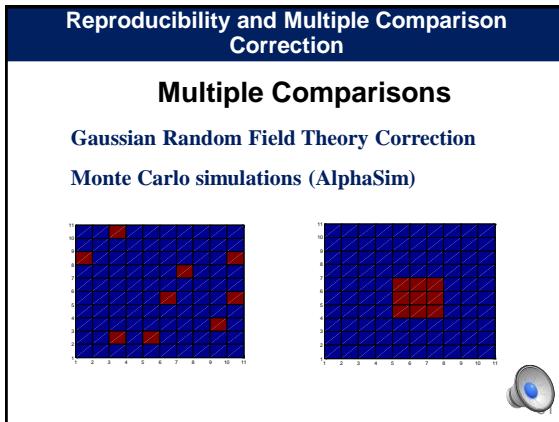
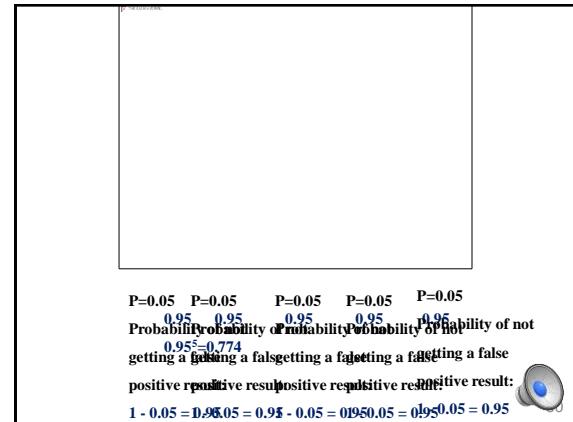
National Natural Science Foundation of China (81671774) (PI: Yan)

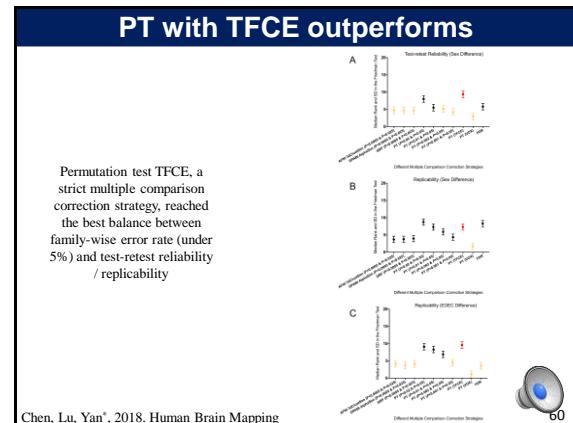
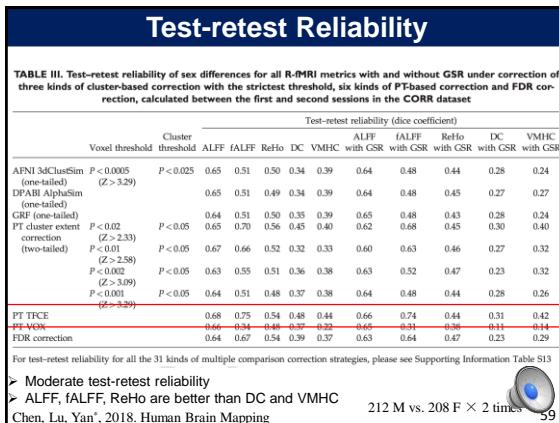
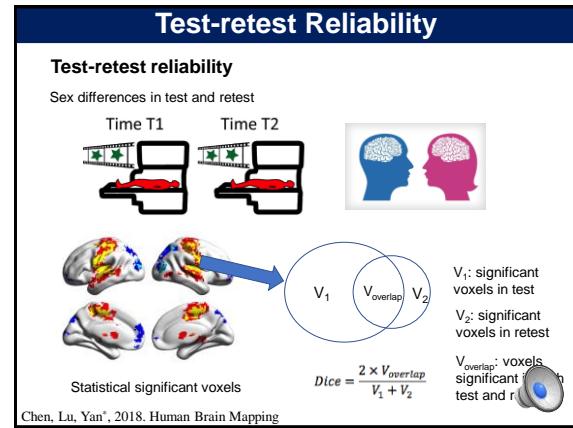
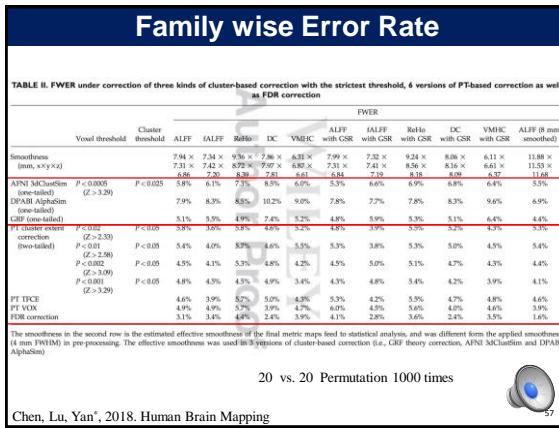
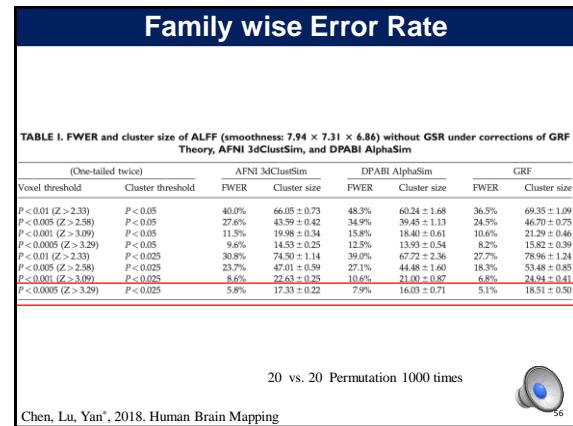
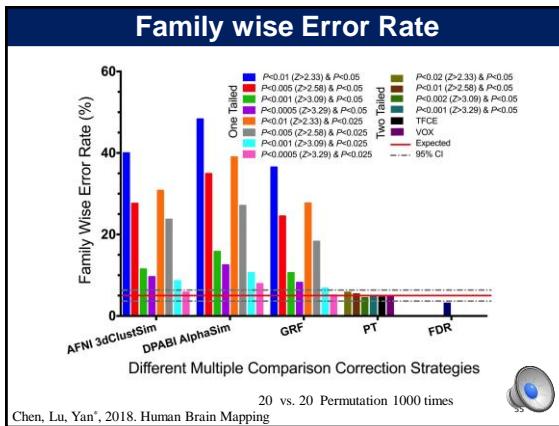
Beijing Municipal Science & Technology Commission (Z161100000216152) (PI: Gao)

National Basic Research (973) Program (2015CB351702) (Co-I: Zuo)



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**静息态功能磁共振数据处理平台**

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DPARSF: A MATLAB toolbox for "pipeline" data analysis of resting-state fMRI

Yan Chen<sup>1</sup> and Zeng-Yi Wang<sup>2</sup>

<sup>1</sup> Beijing University of Chinese Medicine, Beijing, China; <sup>2</sup> Tsinghua University, Beijing, China

Yan and Zeng, 2010. Front Syst Neurosci.

共同通讯作者：持续更新至今

Cited: 1500 times

DPARSF: 流水线式fMRI数据处理软件

传统fMRI处理软件：参数多，设置繁，易出错

时间校正 头动校正 生理噪声回归 配准 平滑 滤波

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**同行评价及影响**

BRAIN CONNECTIVITY, Volume 8, Number 1, 2010, DOI: 10.1007/s10548-010-9248-2

COMMUNICATION

Reporting of Resting-State Functional Magnetic Resonance Imaging Preprocessing Methodologies

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Twelve different software packages were used in the 100 studies. Many articles utilized the use of multiple software for analysis. The most commonly used software was SPM (56%) followed by DPARSF (29%) and FSL (25%). Other less commonly used software included AFNI and various MATLAB toolboxes, such as the GIFT toolbox and the Conn toolbox.

12种不同的软件...使用得最多的软件是SPM (56%)，然后是DPARSF (29%) 和FSL (25%) ...

Haris I. Sair  
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**数据处理与共享平台**

➤ 整合方法学改进  
➤ 处理流程规范化  
➤ 统计分析  
➤ 大数据共享平台

Yan et al., 2016. Neuroinformatics

Cited: 181 times. ESI top 1% highly cited

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**DPARSF**

## Data Organization

ProcessingDemoData.zip

**FunRaw**

- Sub\_001
- Sub\_002
- Sub\_003

Functional DICOM data

**T1Raw**

- Sub\_001
- Sub\_002
- Sub\_003

Structural DICOM data

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**Resting State fMRI Data Processing**

Template Parameters

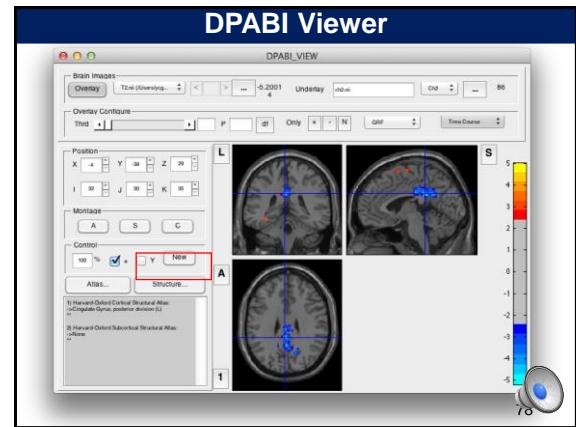
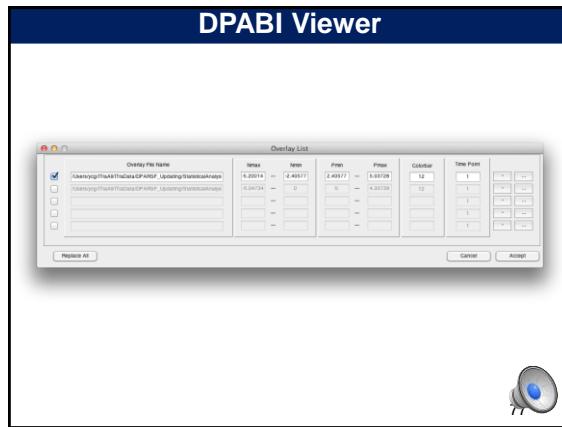
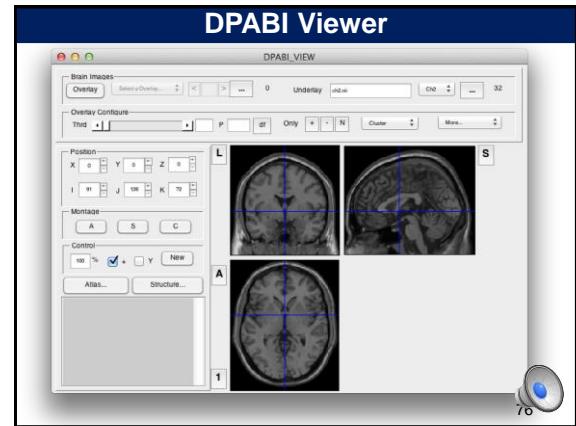
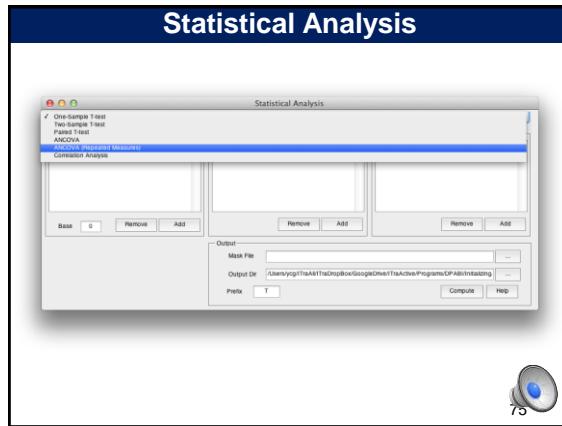
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**DPABI**

Yan et al., 2016. Neuroinformatics

ESI Top 1% Highly Cited Paper

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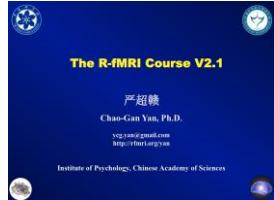


## Future Directions

- R-fMRI methodology
- Mechanism of R-fMRI: electrophysiology/fMRI recording
- Modulation and intervention: medication and brain stimulation
- Application to brain disorders

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## Further Help



<http://rfmri.org/Course>



<http://rfmri.org/wiki>



The R-fMRI Journal Club



Official Account: RFMRLab

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### Preprints of the R-fMRI Network



Preprints of the R-fMRI Network (PRN) is a preprint, open-access, free-submission, open-discussion, community funded Preprints of R-fMRI related research. The goal of PRN is to supplement the peer reviewed journal publication system – by more rapidly communicating the latest research achievements across the globe.

[F1000Research](#) | [CrossMark](#)

**SOFTWARE TOOL ARTICLE**  
PRN: a preprint service for catalyzing R-fMRI and neuroscience related studies [v2; ref status: indexed, <http://f1000r.es/5qyj>]

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## 数据分析与深度培训



静息态功能磁共振成像深度数据分析

功能磁共振成像越来越成为一种主流的科研手段,然而功能磁共振的数据分析却是一项具有高挑战性的工作。海量的数据,繁多的分析步数,复杂的分析方法都让研究者们无所适从,恰当的分析方法可以从普通的数据中挖掘出富有创新性的结果,而不适当的分析则可能让精心收集的数据黯然失色。深度大脑公司联合中国科学院 The R-fMRI Lab 的专业脑功能成像研究团队推出一站式功能磁共振数据分析解决方案,助您从容应对功能磁共振数据带来的挑战。

<http://deepbrain.com>



静息态功能磁共振成像数据处理深度特训

从您见到这条消息开始,您便将有机会与中国科学院 The R-fMRI Lab 的静息态功能磁共振专家团队共同探索大脑的奥秘!深度跟班特训期间,您将会亲身体验:

- 数据处理 专家指导下高效学习静息态功能磁共振成像数据处理
- 路路设计 与国际知名专家讨论形成研究思路
- 文论撰写 系统的 SCI 论文写作训练

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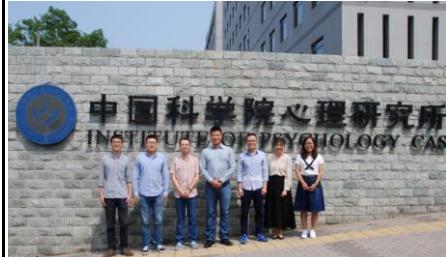
## The R-fMRI Lab



WeChat Official Account: RFMRLab

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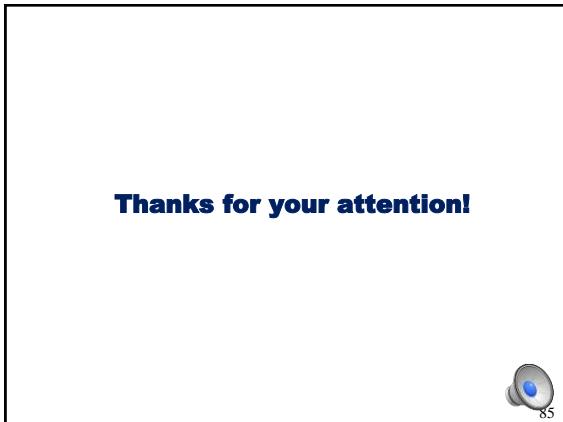
## Acknowledgments



Chinese Academy of Sciences  
Xi-Nian Zuo  
Hangzhou Normal University  
Yu-Feng Zang  
NYU Child Study Center  
F. Xavier Castellanos  
Child Mind Institute  
Michael P. Mitham

- National Natural Science Foundation of China
- National Key R&D Program of China
- Chinese Academy of Sciences

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