

课程编号: 1408317005



脑功能连接及应用

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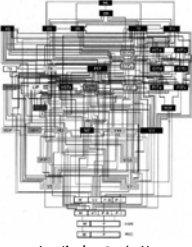
School of Life Science and Technology
University of Electronic Science and Technology of China

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大纲

- 静态脑功能连接的起源及基本原理
- 静态脑功能连接的临床应用
- 动态脑功能连接基本原理

前言



没有人类大脑的连接图谱是不能忍受的事。没有它，我们就没希望精细地了解大脑如何工作

--弗朗西斯·克里克

It is intolerable that we do not have this information for the human brain. Without it there is little hope of understanding how our brains work except in the crudest way. The object of this paper is to make this need more widely known. ①

视觉皮层连接

① Crick F, & Jones E. *Nature*, 1993, 361: 109-110.

推荐阅读

《Connectome》
Sebastian Seung, 2012






基因组让你成为人
连接组让你成为你

--Sebastian Seung ①

① www.ted.com/talks/sebastian_seung.html

THE HUMAN BRAIN



In a place where someone once felt, thought, and loved for centuries, scientists have been battling to understand What this unappealing object is all about

What we know is encoded in cells called neurons

And there are something like a hundred trillion neural connections

This intricate and marvelous network of neurons has been called An enchanted loom

The brain is a very big place in a very small space

No longer at the mercy of the reptile brain, we can change ourselves

It is the most mysterious part of the human body

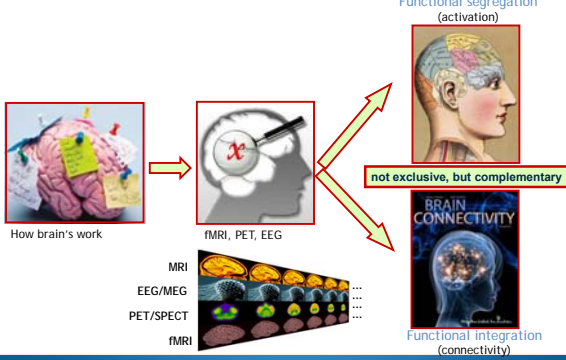
And yet it dominates the way we live our adult lives

It is the brain

Symphony of Science
-An ODE to the BRAIN-

Brain Cell Census			
Number of cortical neurons (profiles)			
Human	~15,000	Mouse	~100,000
Human	~15,000	Mouse	~100,000
Human	~15,000	Mouse	~100,000
Human	~15,000	Mouse	~100,000
Human	~15,000	Mouse	~100,000
Human	~15,000	Mouse	~100,000
Human	~15,000	Mouse	~100,000
Human	~15,000	Mouse	~100,000
Human	~15,000	Mouse	~100,000
Human	~15,000	Mouse	~100,000

BRAIN MAPPING



How brain's work

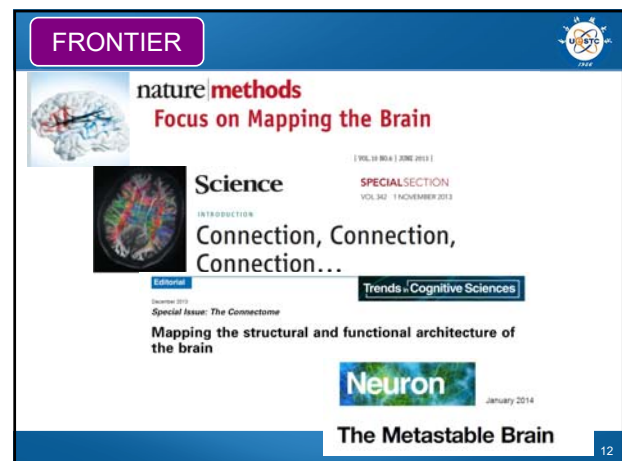
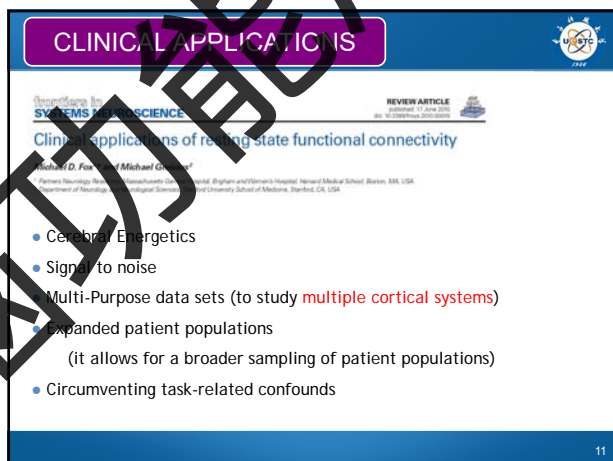
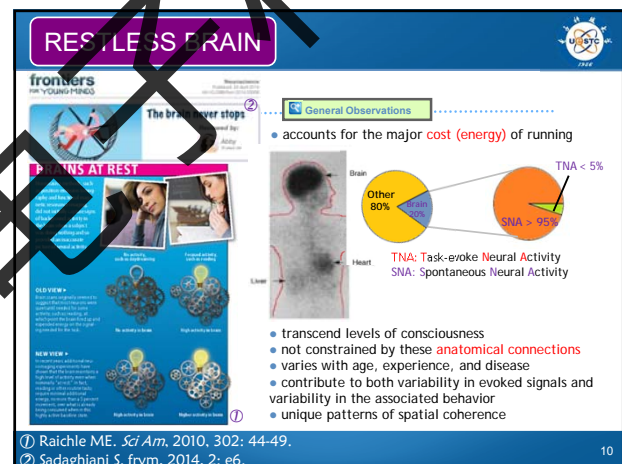
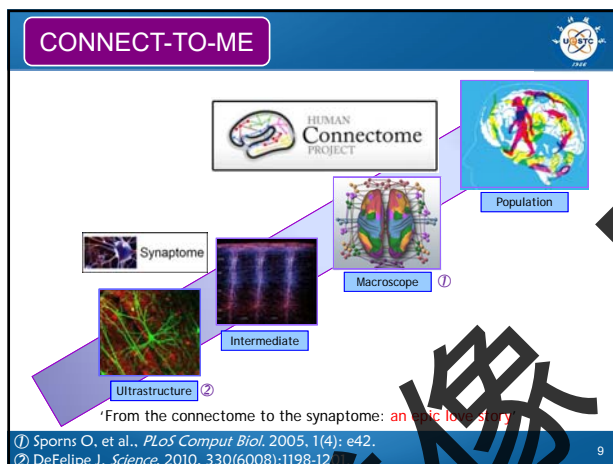
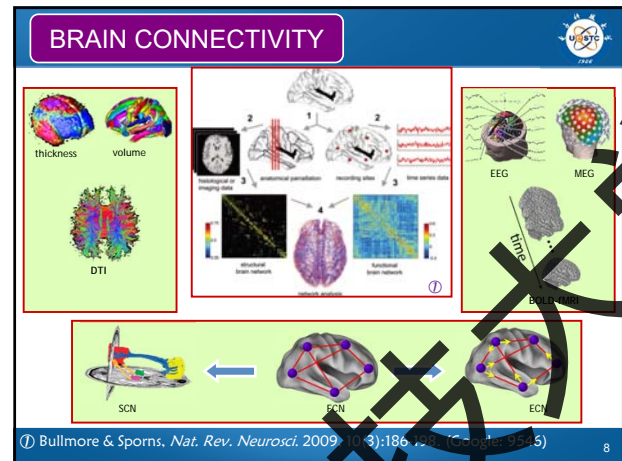
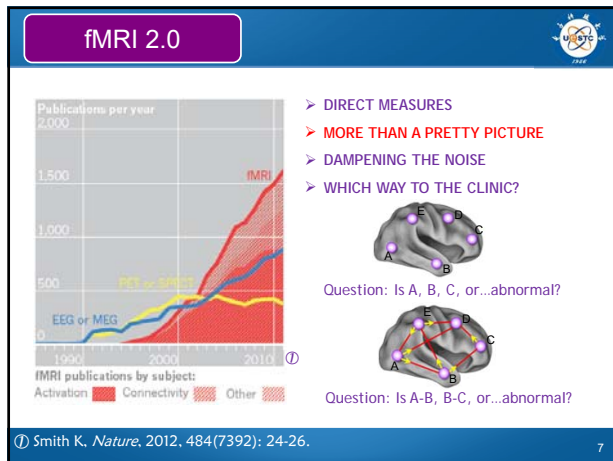
fMRI, PET, EEG

MRI
EEG/MEG
PET/SPECT
fMRI

Functional segregation (activation)

not exclusive, but complementary

Functional integration (connectivity)



What's (intrinsic) Functional Connectivity

- How to compute iFC
- Advanced iFC
- Applications of iFC
- Issues

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BEFORE iFC

Amplitude of Low-Frequency Fluctuations (ALFF)

Zang, et al., *BD*, 2007

Biswal, et al., *PNAS*, 2010

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BEFORE iFC

From coactivation to connectivity

statistical map

① Huettel S., et al., *Functional Magnetic Resonance Imaging*, 3rd, 2010

Network: A description of the relationships among a set of brain regions, including their connectivity and causal relationships.

System: A set of regions that are linked by coactivation, but for which the connectivity and causal relationships remain unknown.

Any complex experimental task will evoke activity (activation) in several brain regions simultaneously.

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temporal iFC

空间上远距离神经生理事件之间的时间相关性
(Temporal correlations between spatially remote neurophysiological events)

--Friston KJ

Varela, et al., *NRN*, 2001

$$r_{xy} = \frac{(1/T) \sum_{t=1}^T [x(t) - \bar{x}] [y(t) - \bar{y}]}{s_x s_y}$$

Fig. 1. Left: fMRI task activation responses to standard left and right finger movements, superimposed on a T1-weighted anatomical image. Right: Functional responses using the methods of this paper. Two sets of independent clusters appear. First is a cluster in posterior, left parietal region.

Active Task

Resting State

Biswal et al., *MRM*, 1995

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ICA

the brain in action is continuously and dynamically "active" even when at "rest"

Smith et al., *PNAS*, 2009

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Same phenomena, many names

R-fMRI/RS-fMRI
capture the imaging method

rs-functional connectivity
analytic approach

- intrinsic activity** Raichle, *TICS*, 2010
ongoing neural and metabolic activity which is not directly associated with subjects' performance of a task.
- intrinsic functional connectivity (iFC) & 'intrinsic connectivity networks' (ICNs)**
to refer to the quantification of coherent intrinsic activity and the functional networks in which it occurs, respectively.

Source: Kelly et al., *TICS*, 2012

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Definition?

Available online at: www.sciencedirect.com/science/article/pii/S1053811905000000

NeuroImage

The elusive concept of brain connectivity

Barry Horowitz*

Brain Imaging and Modeling Center, National Institute on Drug Abuse and Other National Institutes of Health, Bethesda, MD 20892

Available online at: www.sciencedirect.com/science/article/pii/S1053811905000000

NEUROSCIENCE AND BIOBEHAVIORAL REVIEW

Review

Functional connectivity in the brain—is it an elusive concept?

Andrew A. Fingelkurts^{a,b,*}, Alexander A. Fingelkurts^{a,b}, Suppe Kalkkainen^{a,b}

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^bNeuroscience, Engineering Center, Helsinki University Central Hospital, P.O. Box 40, FI-00014 Helsinki, Finland

^cDepartment of Psychology, University of Helsinki, Finland

Summary

functional connectivity not as a single concept or quantity, but rather as forming a class of concepts with multiple members

functional connectivity must be operationally defined by each investigator who evaluates these quantities

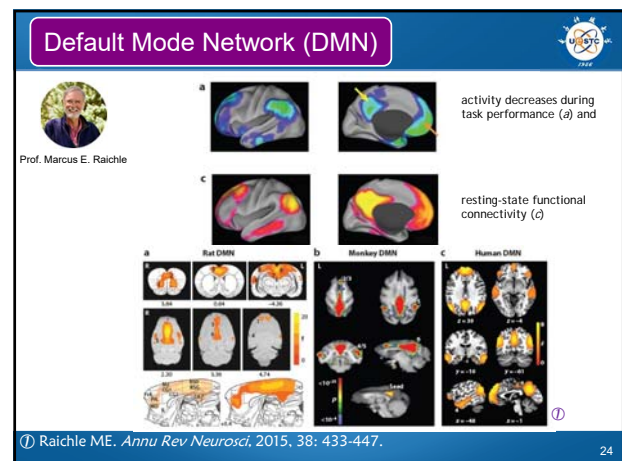
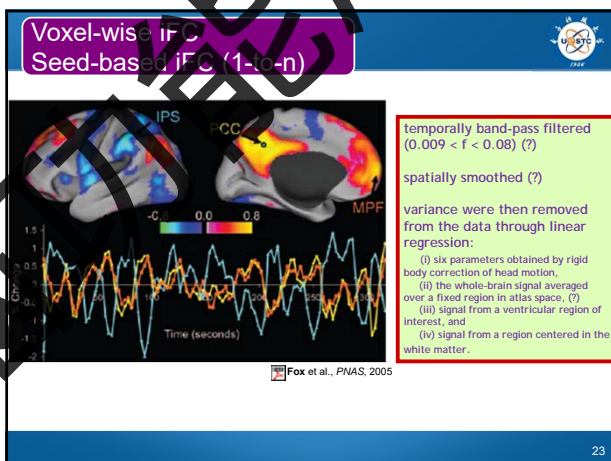
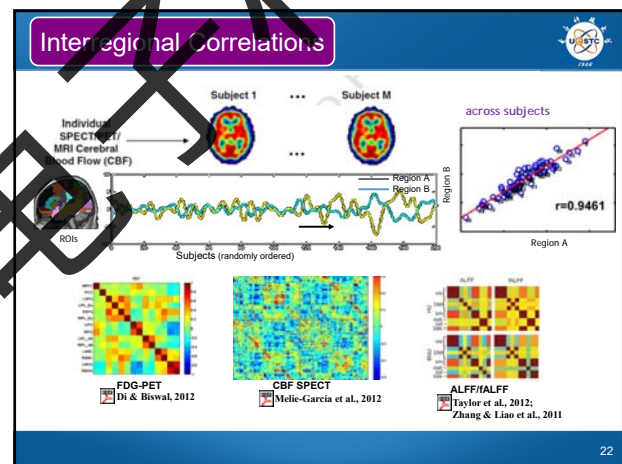
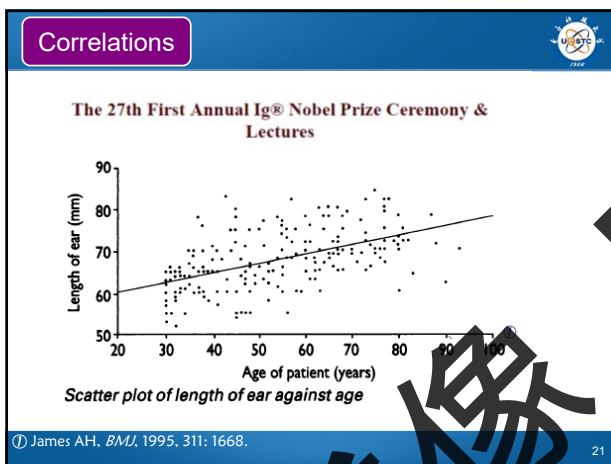
Barry Horowitz

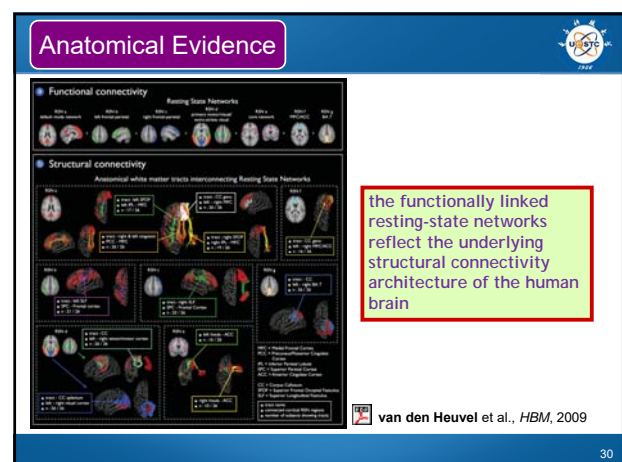
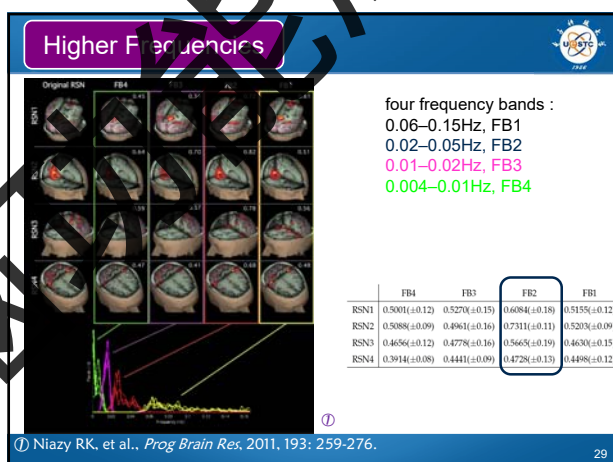
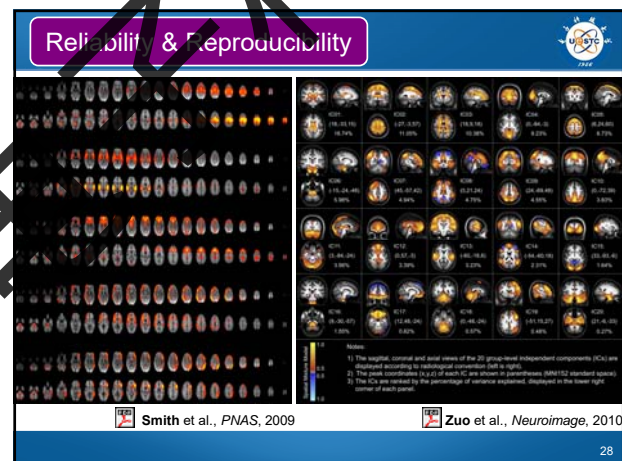
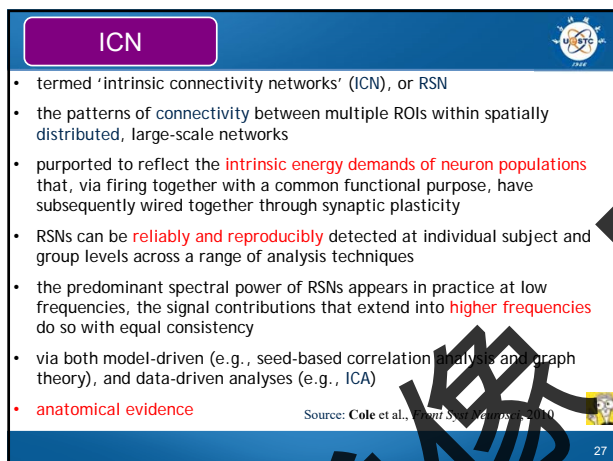
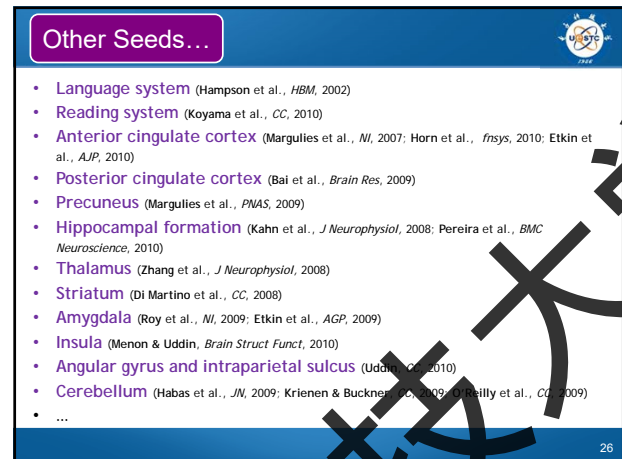
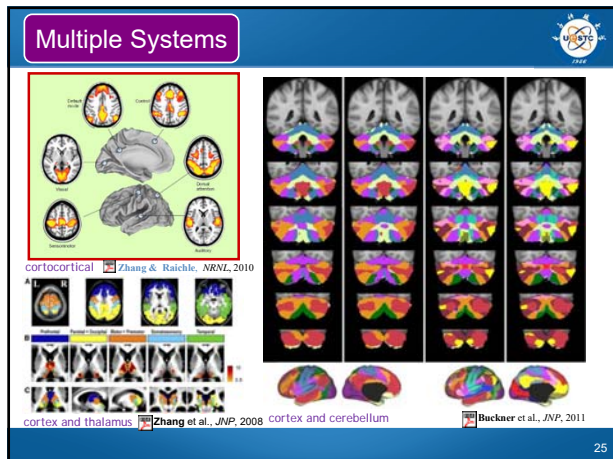
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Definition?

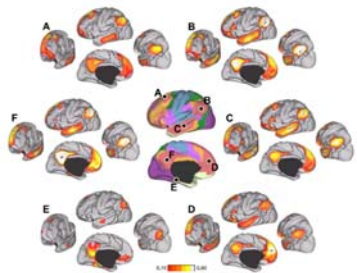
- What's (intrinsic) Functional Connectivity
- How to compute IFC
- Advanced IFC
- Applications of IFC
- Issues

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Fractionation



the seed region in the parahippocampal cortex (E) shows functional connectivity with the retrosplenial cortex, ventral medial prefrontal cortex, and a specific region with the caudal IPL

Summary

a priori
univariate
structured noise

Yeo et al., JNP, 2011

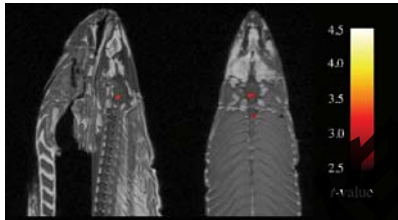
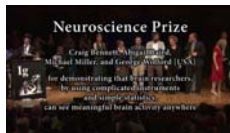
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Case I-Issues

- smoothing (can be)
- regressing (head motion, white matter, CSF, global mean)
- seed(s) location (coordinates; figure showing)
- one-sample t-test (must be, only positive)
- union mask (must be) [group analysis within it]
- multiple comparisons (must be) [$0.05/4 = 0.125$]
- avoiding double dipping/circular analysis
- behavior-brain correlation [voxel-by-voxel correlation]

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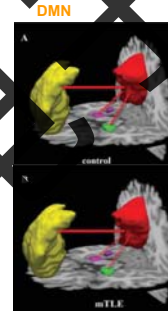
Brain Activity Anywhere?



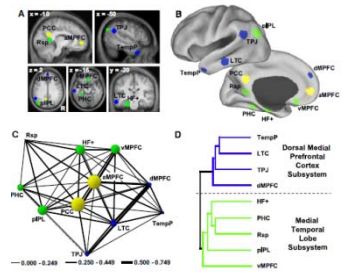
- ① 2012 Ig Nobel Prize
- ② Bennett, CM. et al., J. Serendipitous and Unexpected Results, 2010, 1:1-5

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ROI-wise FC (n-to-n)



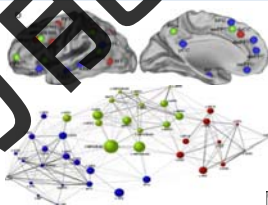
Liao & Zhang et al., HBM, 2011



Andrews-Hanna et al., Neuron, 2010

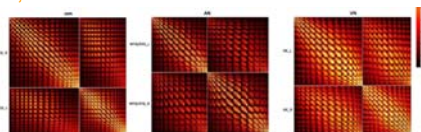
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DMN+CEN+DMN



Speng et al., JoCN, 2013

SMN, VN, AN



Ding & Liao et al., PLoS One, 2011

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Case II-Issues

- smoothing (be careful!)
- regressing (head motion, white matter, CSF, global mean)
- seed(s) location (coordinates; figure showing)
- multiple comparisons (must be) [$0.05/edges$]
- behavior-brain correlation [ROI correlation one by one]

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Thought Question

- Comparing Correlation Coefficients

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推荐阅读

《The 100 most-cited articles in neuroimaging: A bibliometric analysis》①

150

HJ Kim et al. / Neuroimage 139 (2016) 149–156

Table 1

The 100 most-cited neuroimaging articles ranked in order of the number of citations received.

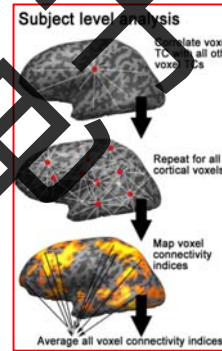
Ranking	Article	No. of citations	No. of citations per year (ranked)
1	Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B, Joliet M. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI SRI single-subject brain. <i>Neuroimage</i> 2002;15(1):273–89.	4184	33.3 (1)
2	Adolphs R, Gauthier GM. Visual-based morphometry—the methods. <i>Neuroimage</i> 2000;11(5 Pt 1):380–21.	3973	24.8 (2)
3	Smith SM. Fast robust automated brain extraction. <i>Hum Brain Mapp</i> 2002;17(1):143–55.	3201	24.1 (3)
4	Blanton R, Yoon H, Hougham VM, Hyde JS. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. <i>Magn Reson Med</i> 1995;34(4):337–41.	2928	14.4 (4)
5	Smith SM, Jenkinson M, Woolrich MW, Beckmann CF, Behrens TE, Johansen-Berg H, Bannister PG, De Luca M, Drobnjak I, Flitney DW, Barker G, Andersson ER, Watkins KE, Zhang Y, De Stefano N, Brady JM, Matthews PM. Advances in functional and structural MR image analysis: implementation as FSL. <i>Neuroimage</i> 2004;23(Suppl 1):S206–20.	2763	13.3 (5)
6	Jenkinson M, Bannister PG, Brady JM, Smith S. Improved optimization for the robust and accurate linear registration and motion correction of brain images. <i>Neuroimage</i> 2002;17(2):825–41.	2683	13.3 (6)
7	Groves CK, Lator NA, Nichols T. Thresholding of statistical maps in functional neuroimaging using the false discovery rate. <i>Neuroimage</i> 2002;15(4):870–8.	2543	13.3 (7)
8	Dale AM, Fischl B, Sereno MI. Cortical surface-based analysis. I. Segmentation and surface reconstruction. <i>Neuroimage</i> 1999;10(2):17–27.	2543	13.3 (8)
9	Good CD, Johnsrude B, Ashburner J, Henson RN, Frisken KJ, Frackowiak RS. A voxel-based morphometric study of ageing in 465 adult human brains. <i>Neuroimage</i> 2001;14(1 Pt 1):21–36.	2483	13.3 (9)
10	Mallat JB, Lantieri P, Kuhl KA, Rudner J. An automated method for neuroanatomic and cytoarchitectonic atlas-based segmentation of fMRI data sets. <i>Neuroimage</i> 2003;19(3):1233–6.	2336	13.3 (10)
11	Jenkinson M, Smith S. Global optimisation method for robust affine registration of brain images. <i>Neuroimage</i> 2001;15(2):143–56.	2192	13.3 (11)
12	Gold BI, Blumenthal J, Jeffries NG, Castellanos FX, Liu H, Zijdenbos A, Paus T, Evans AC, Rapoport SH. Attention-deficit/hyperactivity disorder: a longitudinal MRI study. <i>Nat Neurosci</i> 1999;2:393–397.	2141	13.3 (12)
13	Cohen R, Poline JP. Imaging cognition II: An empirical review of PET and fMRI studies. <i>J Cogn Neurosci</i> 1992;4(1):1–10.	2131	13.3 (13)
14	Fischl B, Sereno MI, Dale AM. Cortical surface-based analysis. II. Inflation, flattening, and a cortical surface-based coordinate system. <i>Neuroimage</i> 2004;23(1):17–31.	2061	13.3 (14)

① Kim HJ. et al., *Neuroimage*, 2016, 139: 149–156

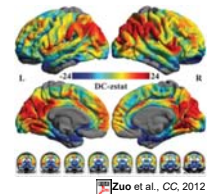
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- What's (intrinsic) Functional Connectivity
- How to compute IFC
- Advanced IFC
- Applications of IFC
- Issues

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Degree Centrality (DC)
Functional Connectivity Density (FCD)

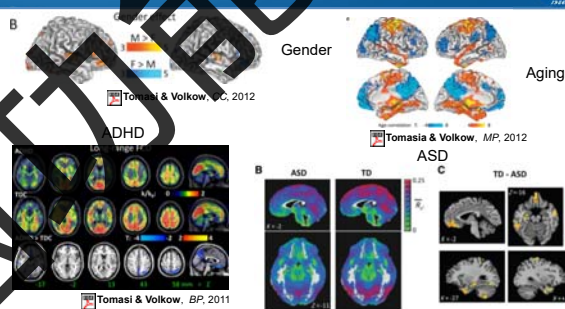
- ✓ Identify hubs in the human brain
- ✓ data-driven
- ✓ voxelwise



Salomon et al., JN, 2011

Tomasi & Volkow, PNAS, 2011

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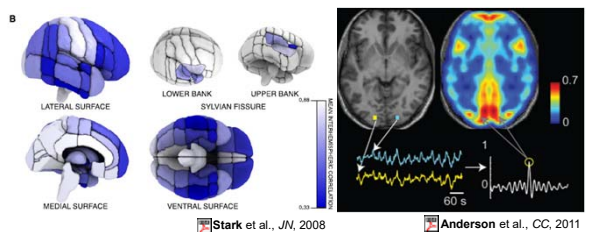


data-driven analysis approach that permits a comprehensive, whole-brain characterization of the altered functional connectivity

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Functional Connectivity Homotopy (FCH)
Voxel-mirrored Homotopic Connectivity (VMHC)

Calculating interhemispheric correlation



- interhemispheric coordination
- Voxelwise
- corpus callosum mediating this coordination

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Clinical Populations

Developmental changes

Control > autism

Control > cocaine addiction

Group Difference

Zuo et al., JN, 2010

Anderson et al., CG, 2011

Kelly et al., BP, 2011

- Robust interhemispheric connectivity comprises one of the dominant modes of functional connectivity
- and might allow for a simple screening technique for regional differences in connectivity in pathophysiological states

What's (Intrinsic) Functional Connectivity

- What's (Intrinsic) Functional Connectivity
- How to compute IFC
- Advanced IFC
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- Issues

癫痫研究的科学问题

THE LANCET Neurology

NEW ENGLAND JOURNAL OF MEDICINE

Adult epilepsy

Epilepsy

科学问题

- 癫痫灶的精确定位
- 癫痫传播网络描绘
- 癫痫脑损伤的评价
- 癫痫活动的起源
- 癫痫活动传播网络
- 癫痫活动对功能影响

癫痫影像研究目标

THE LANCET Neurology

nature REVIEWS NEUROLOGY

Imaging in the surgical treatment of epilepsy

Defining the causes of focal epilepsies

Defining epileptogenic networks

Effect of focal epilepsy on cognitive function

Detecting cause and source of epilepsy

Tractography and epilepsy surgery

Mapping of eloquent functions

- 癫痫源灶的检测
- 癫痫通路网络的确定
- 癫痫重要功能区影响的评价

(一) 癫痫源灶的检测 (EEG-fMRI)

In scanner

Outside scanner

EEG-fMRI配置

EEG signal

(Courtesy of Dr. Zhengge Wang)

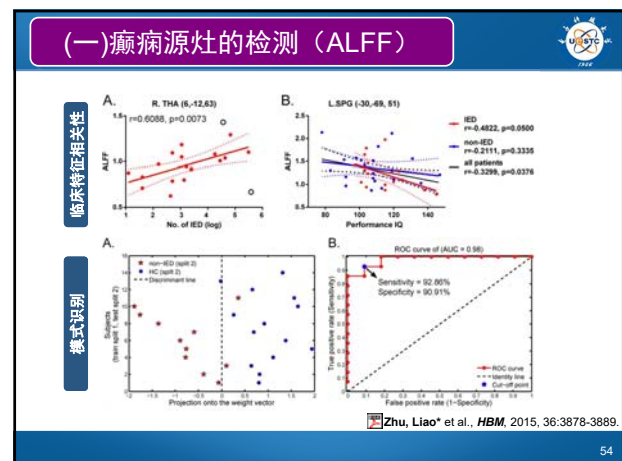
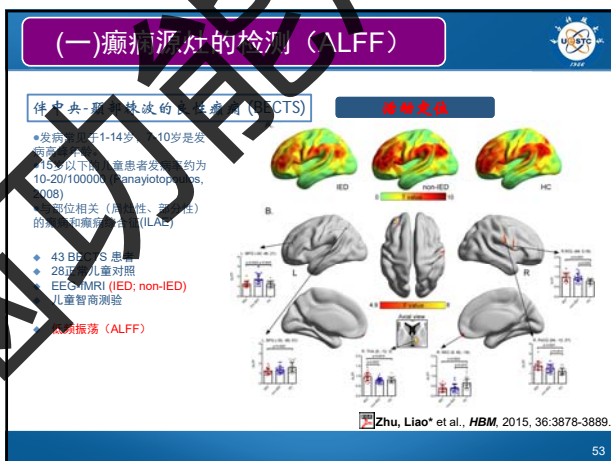
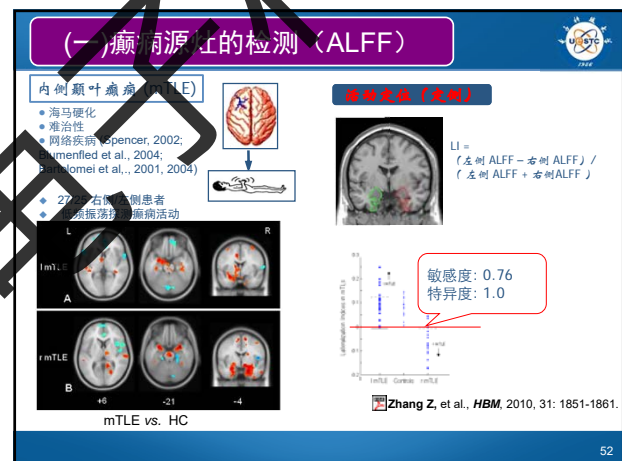
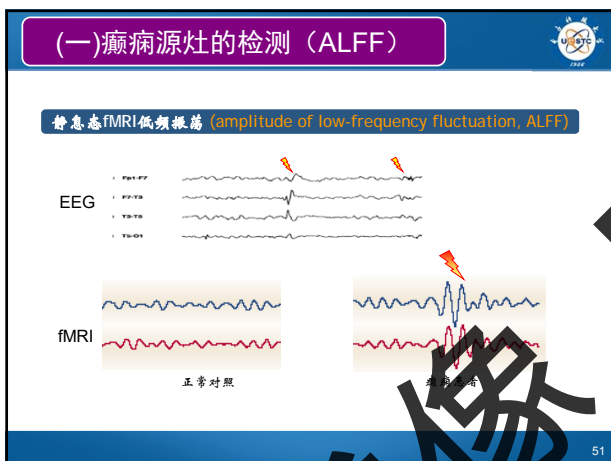
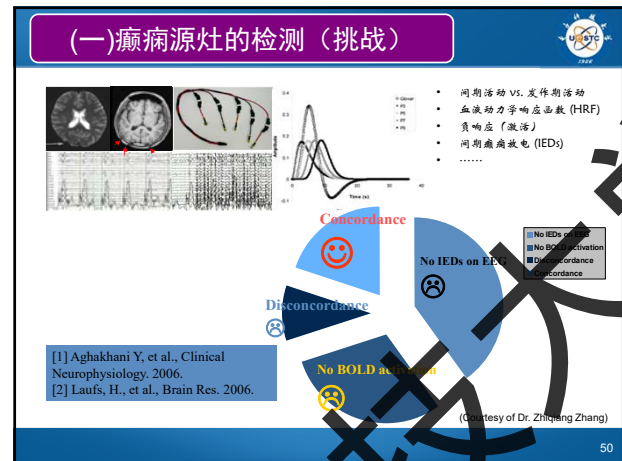
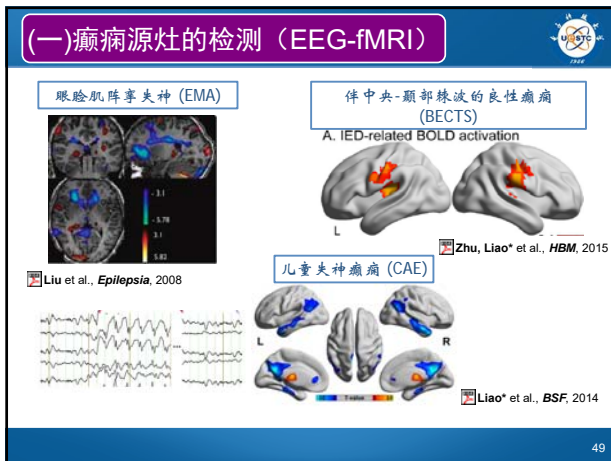
(一) 癫痫源灶的检测 (EEG-fMRI)

同步的脑电记录

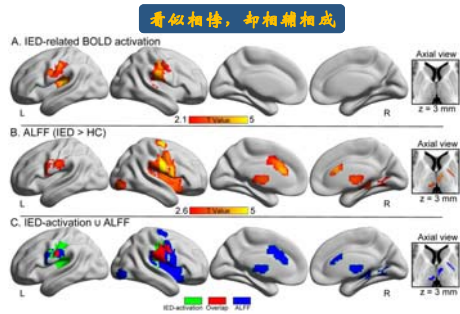
异常：癫痫，噪声

① Chaudhary UJ., et al., HBM, 2013, 34: 447-466.

(Courtesy of Dr. Zhengge Wang)



(一) 癫痫源灶的检测 (小结)

Zhu, Liao* et al., *HBM*, 2015, 36:3878-3889.

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(二) 癫痫网络

Large scale brain models of epilepsy:

dynamics meets connectomics

① Richardson MP. *J Neurol Neurosurg Psychiatry* 2012; 85: 1236-1240.

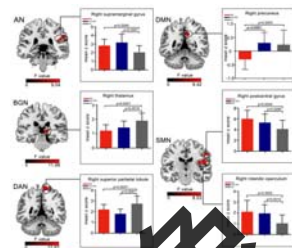
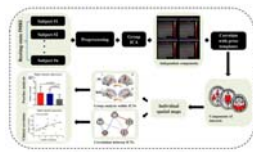
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(二) 癫痫网络 (功能连接网络)

伴中央-颞部棘波的良性癫痫 (BECTS)

- 43 BECTS 患者
- 28 正常儿童对照
- EEG-fMRI (IED; non-IED)
- 儿童智商测验

静态网络

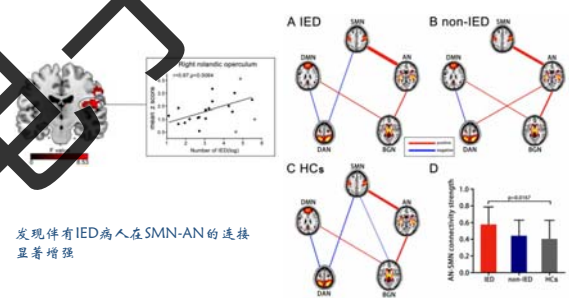


病人在 DMN, DAN, BGN 内部连接等位点出现异常

Li, Liao* et al., *HBM*, 2017, 38:1236-1240.

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(二) 癫痫网络 (功能连接网络)



发现伴有 IED 病人在 SMN-AN 的连接显著增强

Li, Liao* et al., *IJNS*, 2017.

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(二) 癫痫网络 (功能、结构融合)



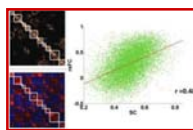
SCN may be the physical substrate of FCN

RSN, functional connectivity

✓ SC are highly predictive of and place constraints on FC

✓ FC reversely exerts effect on SC through mechanisms of plasticity

learning, training...

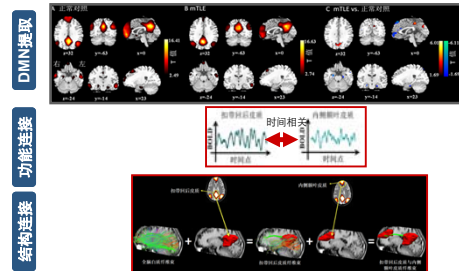
Greicius, et al., *CC*, 2009van den Heuvel, et al., *HBM*, 2009Honey, et al., *PNAS*, 2007; 2009Hagmann, et al., *PNAS*, 2010

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(二) 癫痫网络 (功能、结构融合)

内侧颞叶癫痫 (mTLE)

- 静态fMRI数据
 - 组独立成分，提取默认网络
 - 默认网络内节点之间功能连接分析
- DTI数据
 - 默认网络内节点之间结构连接分析

Liao et al., *HBM*, 2011, 32, 883-895.

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