课程编号：1408317005

脑功能成像
Brain Functional Imaging

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University of Electronic Science and Technology of China

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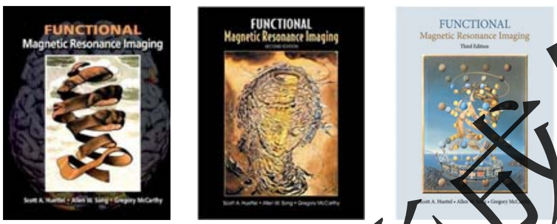
相关课程

- 《医学成像原理》(1408316001) 罗 程
- 《神经网络方法》(1408316003) 陈华富
- 《统计检验方法》(1408317001) 李 凌

2

相关教材

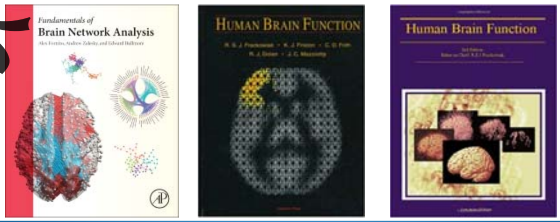
- Functional Magnetic Resonance Imaging
  3rd Ed，Scott A. Huettel, et al.，2014



3

相关参考书

- Fundamentals of Brain Network Analysis
  Alex Fornito, et al. 2016
- Human Brain Function
  2nd Ed，Richard S.J.，et al. 2004



4

教学要求

1、掌握脑成像中fMRI数据分析基本方法

2、了解功能连接的起源和发展，掌握脑网络的构建方法

3、掌握聚类方法分析脑成像数据

4、了解多元模式识别方法及解释

5、探索脑成像数据和临床指标的意义

5

考核方式与成绩评定

- ✓ 学时： 20
- ✓ 成绩评定
  期末考试 （70%） （论文报告）
  平时成绩 （30%） （文献讨论）
- ✓ 教师： 廖伟
- ✓ 联系方式
  E-mail: weiliao@uestc.edu.cn
  地址： 清水河校区4号科研楼529室

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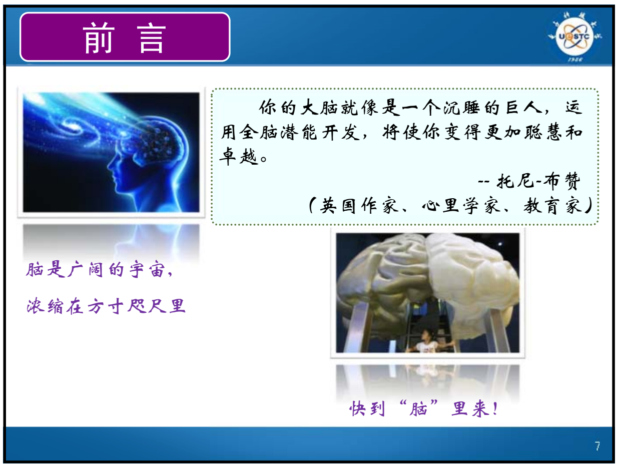
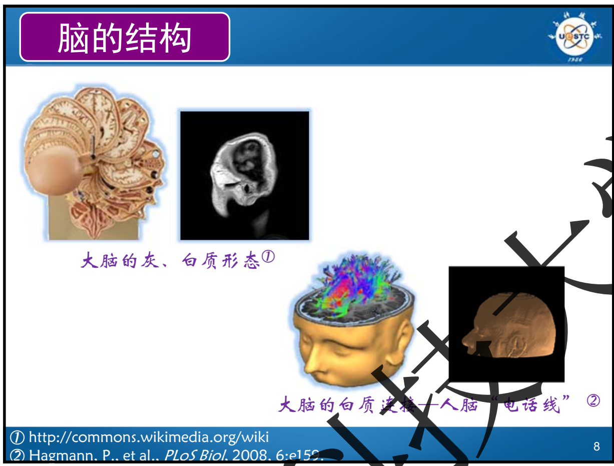
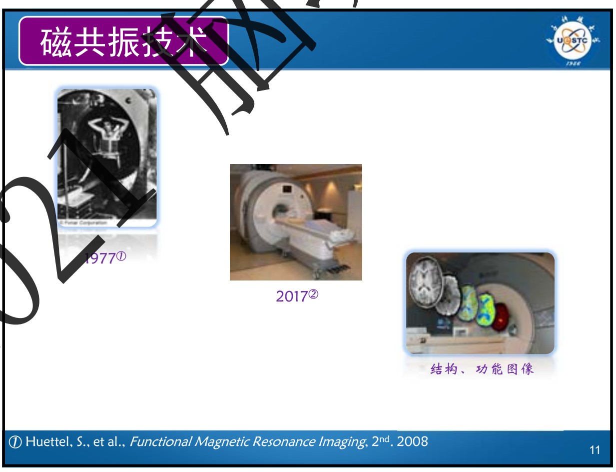
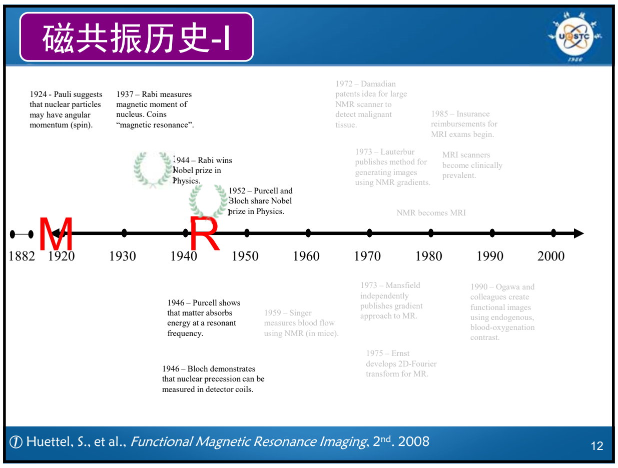

前 言
你的大脑就像是一个沉睡的巨人，运用全脑潜能开发，将使你变得更加聪慧和卓越。
-- 托尼-布赞
（英国作家、心理学家、教育家）
脑是广阔的宇宙，
浓缩在方寸咫尺里
快到“脑”里来！
7


脑的结构
大脑的灰、白质形态①
大脑的白质连接—人脑“电话线”②
① http://commons.wikimedia.org/wiki
② Hagmann, P., et al., PLoS Biol. 2008, 6:e15
8

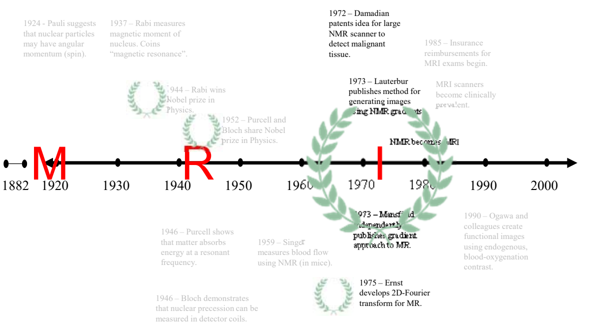

观测测量脑
怎样观测脑？
脑电图
脑磁图
PET
X-线
CT
① Huettel, S., et al., Functional Magnetic Resonance Imaging, 2nd. 2008
9


医学影像博物馆
山东第一医科大学
（泰山医学院）
10


磁共振技术
1977①
2017②
结构、功能图像
① Huettel, S., et al., Functional Magnetic Resonance Imaging, 2nd. 2008
11


磁共振历史-I
1924 - Pauli suggests that nuclear particles may have angular momentum (spin).
1937 – Rabi measures magnetic moment of nucleus. Coins “magnetic resonance”.
1944 – Rabi wins Nobel prize in Physics.
1952 – Purcell and Bloch share Nobel prize in Physics.
1972 – Damadian patents idea for large NMR scanner to detect malignant tissue.
1985 – Insurance reimbursements for MRI exams begin.
1973 – Lauterbur publishes method for generating images using NMR gradients.
MRI scanners become clinically prevalent.
NMR becomes MRI
M
R
1882
1920
1930
1940
1950
1960
1970
1980
1990
2000
1946 – Purcell shows that matter absorbs energy at a resonant frequency.
1959 – Singer measures blood flow using NMR (in mice).
1973 – Mansfield independently publishes gradient approach to MR.
1990 – Ogawa and colleagues create functional images using endogenous, blood-oxygenation contrast.
1975 – Ernst develops 2D-Fourier transform for MR.
1946 – Bloch demonstrates that nuclear precession can be measured in detector coils.
① Huettel, S., et al., Functional Magnetic Resonance Imaging, 2nd. 2008
12

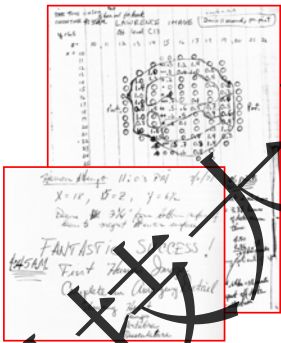
磁共振历史-II



① Huettel, S., et al., *Functional Magnetic Resonance Imaging*, 2nd. 2008

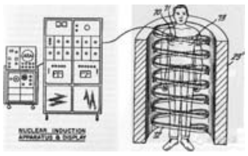
早期磁共振影像

© Fonar Corporation



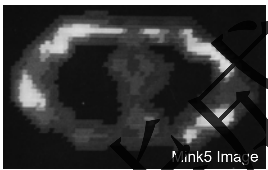
① Raymond Damadian

早期磁共振影像



1972-第一个MRI专利

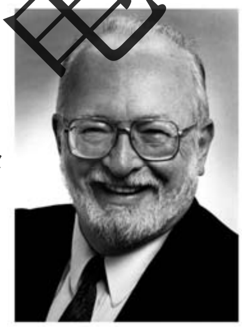
1977/1978
第一台磁共振



Mink5 Image (July 3)

① Raymond Damadian, Larry Minkoff, Michael Goldsmith（左至右）

早期磁共振影像



Paul Lauterbur

Sir Peter Mansfield

① 保罗.劳特布尔（左），彼得.曼斯菲尔德爵士（右）

早期磁共振影像

1973—反投影技术获得第一幅NMR图像（试管）

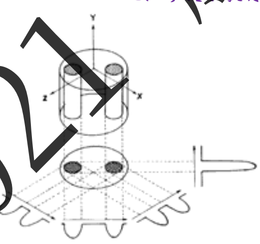


Fig. 1 Relationship between a three-dimensional object, its two-dimensional projection along the Y-axis, and four one-dimensional projections at 45° intervals in the XZ-plane. The arrows indicate the gradient directions.

Fig. 2 Proton nuclear magnetic resonance zeugmatogram of the object described in the text, using four relative orientations of object and gradients as diagrammed in Fig. 1.

① Lauterbur, PC. Image formation by induced local interaction: Examples employing nuclear magnetic resonance. *Nature*. 1973, 242: 190-191.

早期磁共振影像

—磁场梯度
—快速成像（快速梯度变化）(echo-planar imaging, EPI)

① 彼得.曼斯菲尔德爵士（左二）.

2003诺贝尔奖争论

Nobel Press Release
October 6, 2003

Summary

Imaging of human internal organs with exact and non-invasive methods is very important for medical diagnosis, treatment and follow-up. This year's Nobel Laureates in Physiology or Medicine have made seminal discoveries concerning the use of magnetic resonance to visualize different structures. These discoveries have led to the development of modern magnetic resonance imaging, MRI, which represents a breakthrough in medical diagnostics and research. …

This year's Nobel Laureates in Physiology or Medicine are awarded for crucial achievements in the development of applications of medical importance. In the beginning of the 1970s, they made seminal discoveries concerning the development of the technique to visualize different structures. These findings provided the basis for the development of magnetic resonance into a useful imaging method.

Paul Lauterbur discovered that introduction of gradients in the magnetic field made it possible to create two-dimensional images of structures that could not be visualized by other techniques. In 1973, he described how addition of gradient magnets to the main magnet made it possible to visualize a cross section of tubes with ordinary water surrounded by heavy water. No other imaging method can differentiate between ordinary and heavy water.

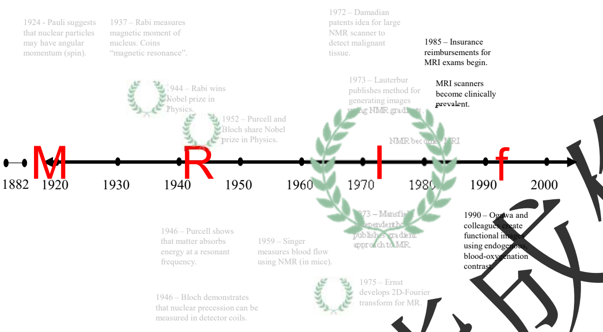
Peter Mansfield utilized gradients in the magnetic field in order to more precisely show differences in the resonance. He showed how the detected signals rapidly and effectively could be analysed and transformed to an image. This was an essential step in order to obtain a practical method. Mansfield also showed how extremely rapid imaging could be achieved by very fast gradient variations (so called echo-planar scanning). This technique became useful in clinical practice a decade later.

2003诺贝尔奖争论

New York Times
October 9, 2003

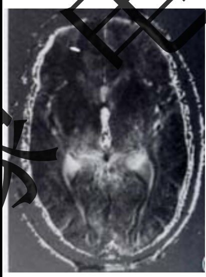
这种无耻行径必须被纠正

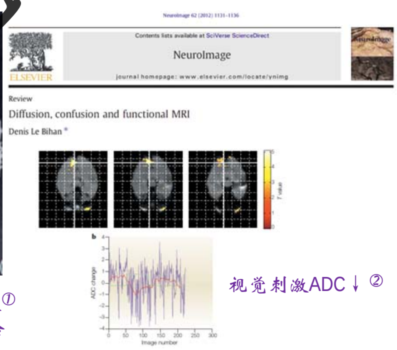
磁共振历史-III



① Huettel, S., et al., *Functional Magnetic Resonance Imaging*, 2nd, 2008

功能磁共振影像



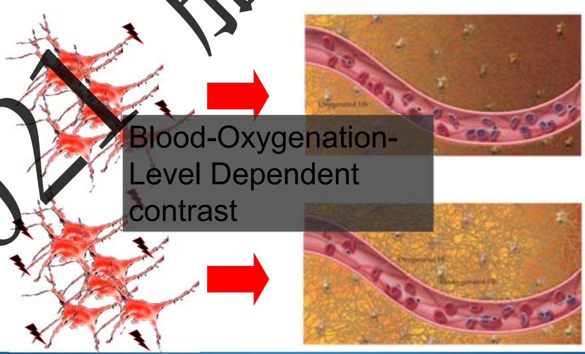


1986—第一篇DWI论文①
提出弥散的概念

视觉刺激ADC↓ ②

① Le Bihan, et al., *Radiology*, 1986, 161:401-407. (Google: 4316)
② Le Bihan, *Nat. Rev. Neurosci.*, 2003, 4(6):469-480.

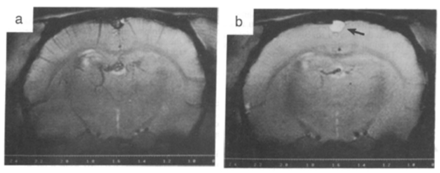
功能磁共振影像



Blood-Oxygenation-Level Dependent contrast

BOLD-I

1990—第一次提出BOLD机制(Rat)



Proc. Natl. Acad. Sci. USA
Vol. 87, pp. 9868–9872, December 1990
Biophysics

Brain magnetic resonance imaging with contrast dependent on blood oxygenation

(cerebral blood flow/brain metabolism/oxygenation)

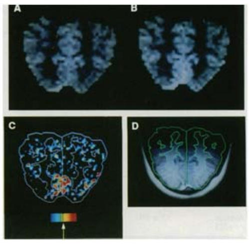
S. Ogawa, T. M. Lee, A. R. Kay, and D. W. Tank

Google: 7760

① Seiji Ogawa (小川诚二)

BOLD-II

1991—第一次人类视觉刺激fMRI图像



视觉刺激CBV↑ ①

① Belliveau JW, et al., *Science*, 1991, 254(5032):716-719. (Google: 2416)

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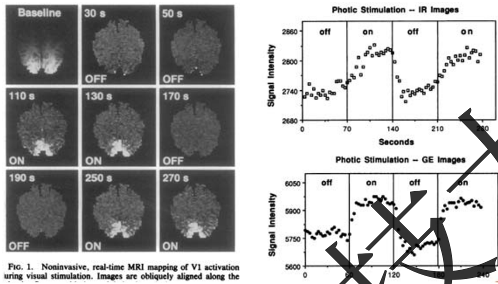
BOLD-III

1992—第一次人类视觉刺激BOLD fMRI图像

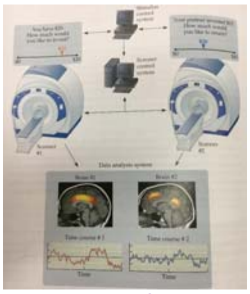


① Kwong, KK., et al., *PNAS*, 1992, 89(12):5675-5679. (Google: 5087)

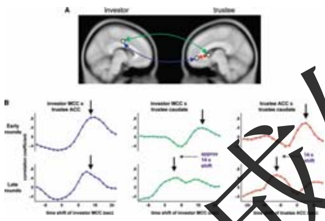
26

Hyperscanning

2005—同时采集2人(以上)fMRI数据



示意图①



activity in investor MCC and trustee ACC②

① Huettel, S., et al., *Functional Magnetic Resonance Imaging*, 3rd, 2014
② King-Casas, et al., *Science*, 2005, 308(5718):78-83.

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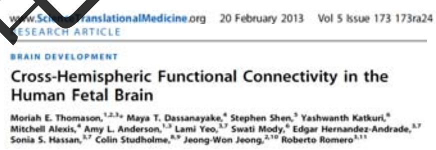
胎儿BOLD

2013—胎儿磁共振成像


www.ScienceTranslationalMedicine.org 20 February 2013 Vol 5 Issue 173 173ra24

RESEARCH ARTICLE

BRAIN DEVELOPMENT

Cross-Hemispheric Functional Connectivity in the Human Fetal Brain

Moriah E. Thomason, Maya T. Dassanayake, Stephen Shen, Yashwanth Katkuri, Mitchell Alexis, Amy L. Anderson, Lami Yeo, Swati Mody, Edgar Hernandez-Andrade, Sonia S. Hassan, Colin Studholme, Jeong-Won Jeong, Roberto Romero

胎儿磁共振成像①②

双胞胎胎儿磁共振成像③

①Thomason, M.E., et al., *Sci Transl Med*, 2013, 5:173ra124. ②http://www.newscientist.com/article/dn23199-first-snaps-made-of-fetal-brains-wiring-themselves-up.html#.Usqdc421snt ③http://www.newscientist.com/article/dn21888#.UsqeJY21snt

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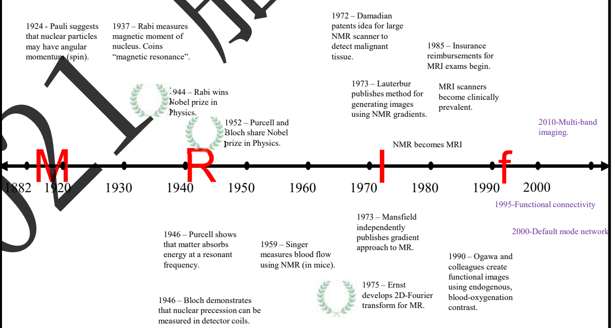
小结-I



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静息态

Eyes closed or open with no task
Quite a few minutes or longer
"Not to fall asleep"
"Not to think of anything in particular"
"let your thoughts go as they come"
Low frequency fluctuation (LFF, 0.01 - 0.08 Hz) (Biswal et al., 1995)

Vincent van Gogh

30

磁共振历史-IV

- 1929 – Hans Berger records first EEG.
- 1984 – Horwitz 'Resting state' on PET.
- 1995 – Biswal Resting state fMRI.
- 1995 – Andreasen Default mode on PET.
- 1995/96 – Buckner Default mode on PET.
- 1997– Shulman Meta-analysis on PET
- 2001 – Raichle DMN.
- 2003 – Greicius Frist discovered DMN using functional connectivity on resting-state fMRI data.

1929 1984 1992 1995 1996/97 2000 2005 2010 2015 2017

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静息态-EEG

1929—首次记录静息态EEG

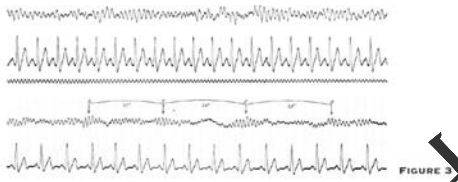

FIGURE 3

Two early high-quality EEG tracings that Berger recorded with the double-coil galvanometer in 1928–1929. The lower curve is recorded from "Dr G[inzberg]" and depicts the most robust EEG finding of the 1930s, 1940s, and 1960s: bursts of alpha waves appearing as the subject lies with his eyes closed in a state of mental and physical rest. In the lower tracing, Berger has attempted to correlate the trains of alpha waves with the "waves of attention" described by experimental psychologists such as Wundt, Lehmann, and others.

NOTE: REPRINTED FROM P. GLOOR, HANS BERGER ON THE ELECTROENCEPHALOGRAM OF MAN (NEW YORK: ELSEVIER, 1969), P. 78.

② Millett D. *Perspect Biol Med.* 2001, 44(4):522-542.

① Berger, H. 1929. Uber das Elektrenkephalogramm des Menschen (On the human electroencephalogram). *Archiv f. Psychiatrie u. Nervenkrankheiten*, 87:527-570.

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静息态-PET

1984—文献使用resting state

Using this approach, we analyzed brain metabolism in healthy adult men under conditions of reduced auditory and visual inputs (henceforth called the "resting state"). In this state, we found strong associations between rCMRglc in many regions of the frontal and parietal lobes, on the one hand, and between regions in the occipital and temporal lobes, on the other, but few associations between the frontoparietal and the temporo-occipital domains. Some of these results have been presented in abstract form (Duara et al., 1983*b*; Rapoport et al., 1983).

① Horwitz. B., et al., J Cereb Blood Flow Metab., 1984, 4(4):484-499.

33

静息态-fMRI

1995—首次使用resting state fMRI

Functional Connectivity in the Motor Cortex of Resting Human Brain Using Echo-Planar MRI

Bharat Biswal, F. Zerrin Yetkin, Victor M. Haughton, James S. Hyde

An MRI time course of 512 echo-planar images (EPI) in resting human brain obtained every 250 ms reveals fluctuations in signal intensity in each pixel that have a physiologic origin. Regions of the sensorimotor cortex that were activated secondary to hand movement were identified using functional MRI methodology (FMRI). Time courses of low frequency (<0.1 Hz) fluctuations in resting brain were observed to have a high degree of temporal correlation ($P < 10^{-3}$) within these regions and also with time courses in several other regions that can be associated with motor function. It is concluded that correlation of low frequency fluctuations, which may arise from fluctuations in blood oxygenation or flow, is a manifestation of functional connectivity of the brain.

Key words: functional connectivity; motor cortex; fMRI; EPI.

INTRODUCTION

Physiological fluctuations in resting brain have been observed by several groups using echo-planar magnetic resonance imaging (EPI, MRI) (1–4). These fluctuations are apparent in a time course of signal intensities from a given pixel as a function of image number (i.e., "time"). A Fourier transform of a typical time course shows peaks at the heart and respiratory frequencies. Peaks are also seen at harmonics of the heart rate and as respiratory sidebands symmetrically disposed about the fundamental heart frequency. In addition, poorly characterized low-frequency fluctuations (<0.1 Hz) are observed. This communication concerns these low-frequency fluctuations.

① Biswal, BB, et al., *Magn. Reson. Med.*, 1995, 34:537-541. (Google: 5415, 6269, 7032, 8885)
② Biswal, BB, *Neuroimage*, 2012, 62(2):938-944.

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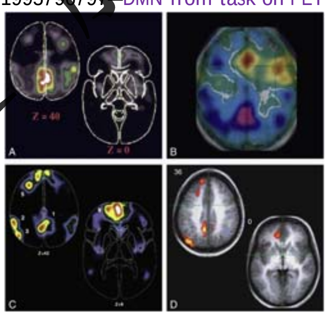
默认网络-I

1995/96/97—DMN from task on PET

Buckner et al. (2005)

Andreasen et al. (1995)



Shulman et al. (1997)

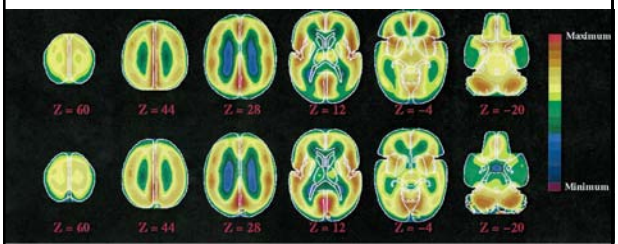
Binder et al. (1999)

① Buckner, RL., *NeuroImage*, 2012, 62:1137-1145.

35

默认网络-II

2001—DMN from resting state on PET



Quantitative maps of blood flow (Upper) and oxygen consumption (Lower) in the subjects from group I while they rested quietly but awake with their eyes closed.

① Raichle, ME., et al., *PNAS*, 2001, 98:676-682. (Google: 8107, 9154, 9886, 12120)

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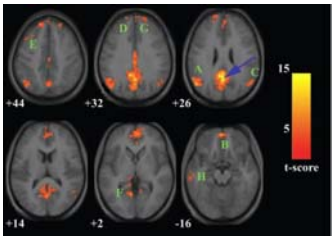
默认网络-III

2003—DMN from resting state on fMRI



Map of the resting-state neural connectivity for the PCC.

① Greicius, MD., et al., *PNAS*, 2003, 100:253-258. (Google: 4261, 5313, 6490)

小结-II

2003 – Greicius
Frist discovered DMN using functional connectivity on resting-state fMRI data.

1929 - Hans Berger records first EEG.

1995 – Biswal
Resting state fMRI.

2001 – Raichle
DMN.

2011 – Eldaief
Manipulating brain functions.

1929 1984 1992 1995 1996/97 2000 2005 2010 2015 2017

1984 – Horwitz
Resting state on PET.

1995 – Andreasen
Default mode on PET.

1995/96 – Buckner
Default mode on PET.

1997– Shulman
Meta-analysis on PET

2005 – Sporns
The human connectome.

2014 – Fox
Using fMRI to guide the TMS for clinical treatment

2001 – Haxby
the first studies using pattern-based analysis to investigate the nature of object representations in the human ventral visual cortex.

总结

REVIEW

doi:10.1038/nature15692

Table 1 | An overview of the levels of analysis and levels of causal inference afforded by different human neuroscience methods

		Level of mechanism			
		Molecules	Cells	Populations	Networks
Strength of causal evidence	Purely observational (associations do not necessarily imply causal relations between mind and brain)	Genetic associations with behaviour, brain function or brain structure Postmortem studies of gene expression Correlations of MRI spectroscopy or PET ligand imaging with psychological traits		Structural morphometry correlated with psychological traits	Resting functional connectivity (fMRI, EEG/MEG) or structural connectivity (sMRI, DTI) correlated with psychological traits
	Manipulate psychological process and observe brain (neural measures may be epiphenomenal)	Task modulation studies using PET with neurotransmitter ligands or MRI spectroscopy	Intracerebral recording in surgical patients	Task activation studies (PET, fMRI, EEG/MEG) Representational analysis (fMRI, EEG/MEG) Computational neuroimaging (fMRI, EEG/MEG)	Task-based functional connectivity (fMRI, EEG/MEG)
	Manipulate brain and observe psychological results (demonstrates causal effect of neural system in behaviour)	Pharmacological manipulation (including hormones)	Direct brain stimulation in surgical patients	Focal cortical lesions Transcranial magnetic stimulation Transcranial electrical stimulation Cortical surface electrode stimulation in surgical patients	Disconnection: white matter lesions

DTI, diffusion tensor imaging; EEG/MEG, electroencephalography/magnetoencephalography; fMRI, functional MRI; MRI, magnetic resonance imaging; PET, positron emission tomography; sMRI, structural MRI.

① Poldrack & Farah, *Nature*, 2015, 526(7573):371-379.

总结

① 20 YEARS OF fMRI 20 YEARS OF fMRI, *NeuroImage*, 2012, 62(2).