Overview of Resting-State fMRI

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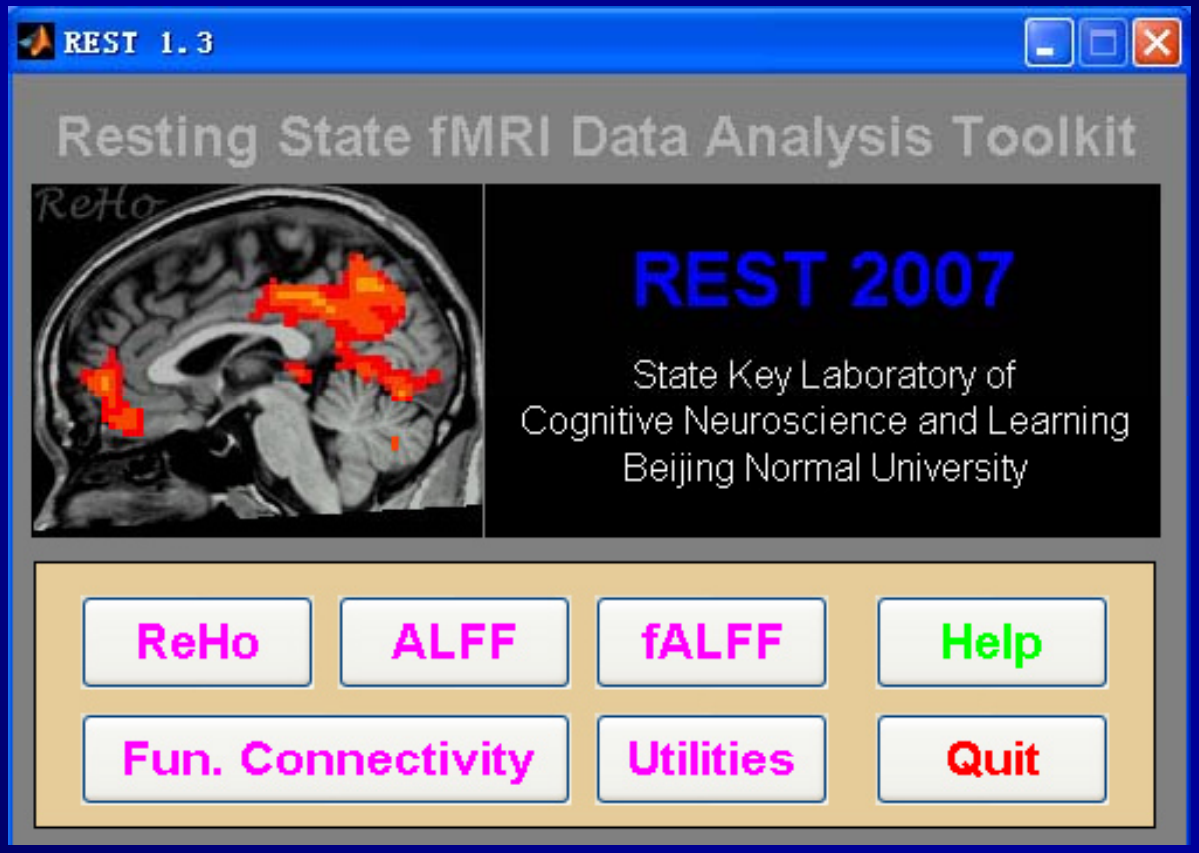
Outline

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

RESTing-state fMRI data analysis toolkit (REST)



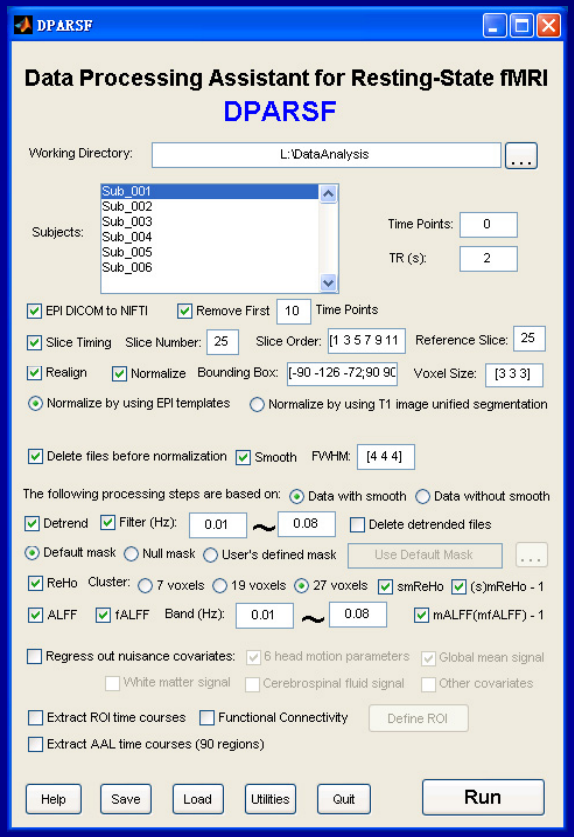
By 宋晓伟等, http://www.restfmri.net

维护、更新：严超赣、董章晔等

Data Processing Assistant for Resting-State fMRI (DPARSF)

Based on

- **REST**
- **SPM**
- **MATLAB**

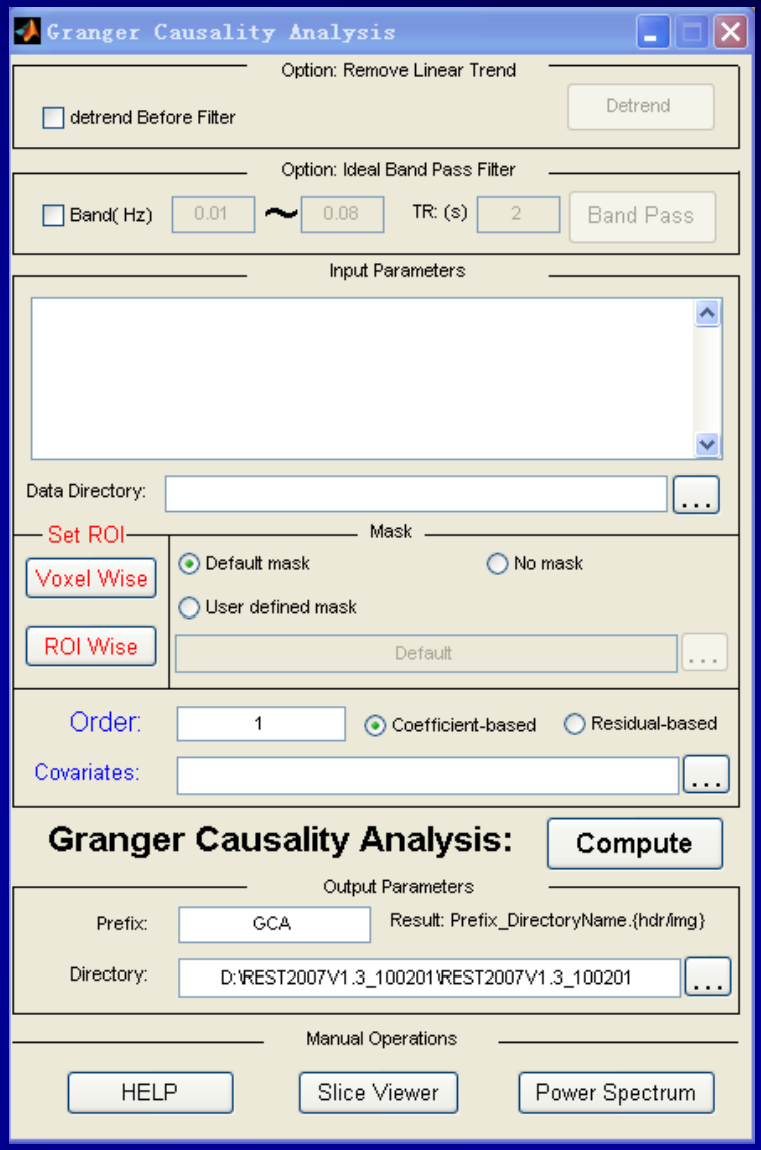


By 严超赣, http://www.restfmri.net

REST-GCA

Based on

- **REST**
- **MATLAB**



By 臧振享等, http://www.restfmri.net

Some issues about resting-state fMRI

- **Definition and instruction?**
- **Sampling rates (TR)**
- **Length**

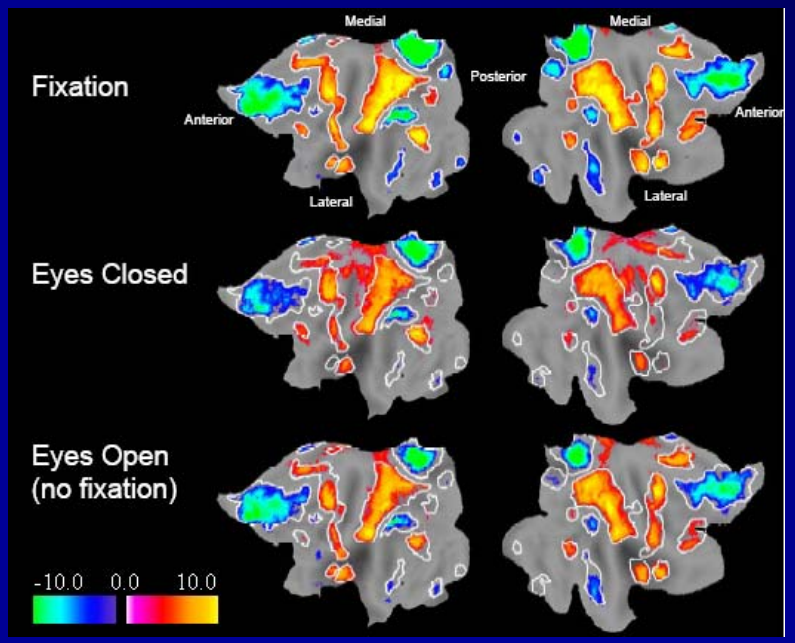
Definition and Instruction?

- **Eyes closed or open with no cognitive task**
- **“Not to fall asleep”**
- **“Not to think of anything in particular”**

ill defined!

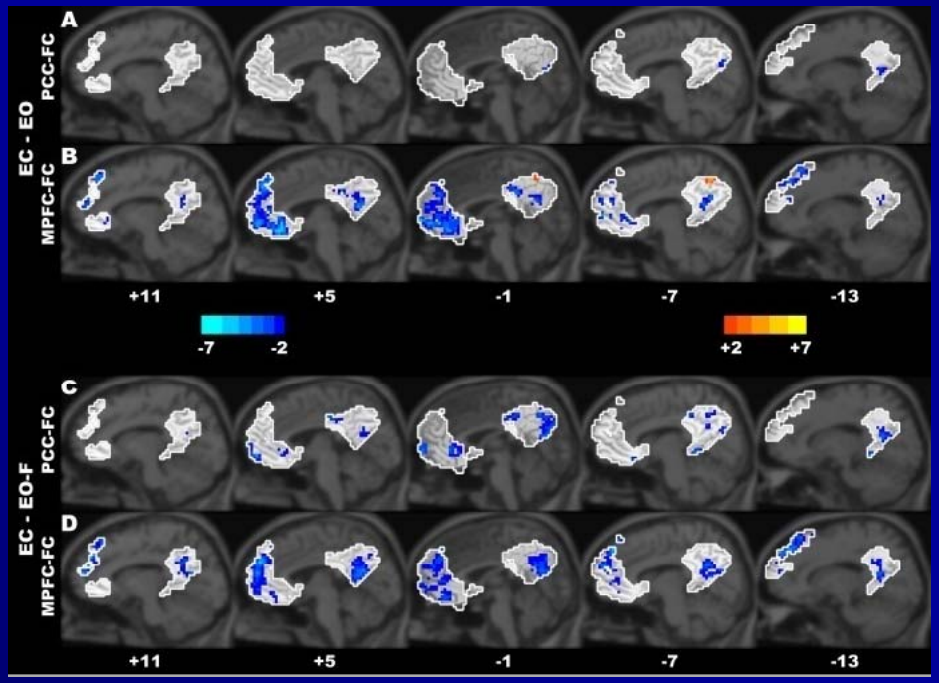
Different resting conditions?

The functional connectivity patterns of the default mode network was minimally disturbed during different resting conditions with limited cognitive demand ***(Greicius et al., 2003; Fransson, 2005; Fox et al., 2005)***



(Fox et al., 2005, PNAS)

Different resting conditions?

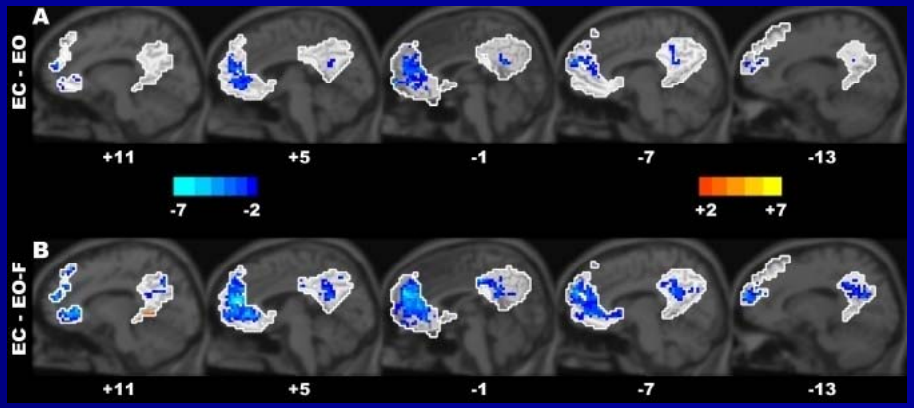


Functional connectivity maps

Significantly different between different resting conditions with limited cognitive demand

(Yan et al., 2009, PLoS ONE)

Different resting conditions?

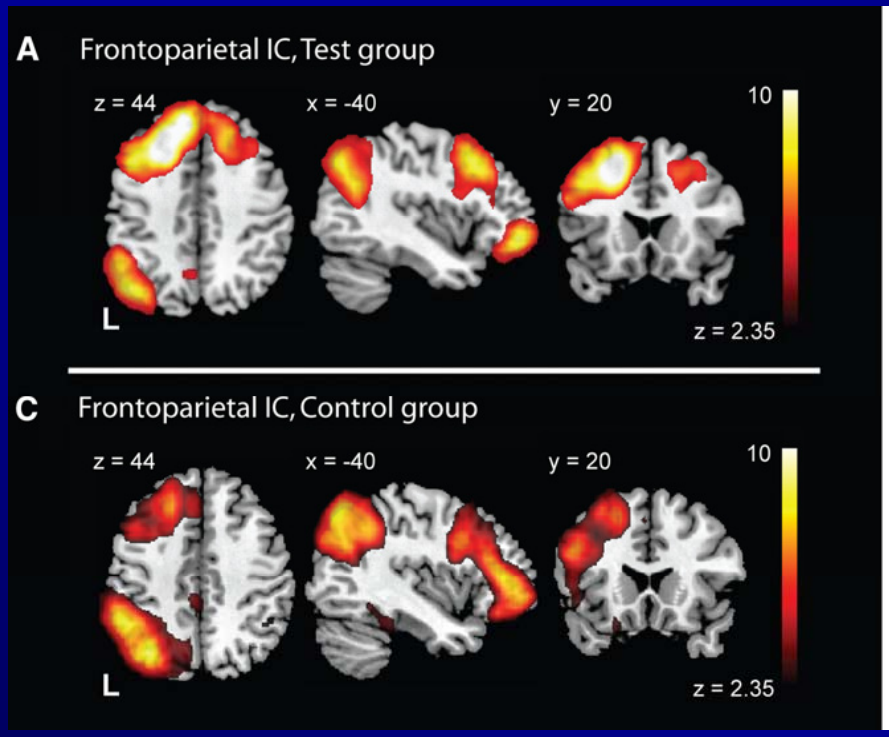


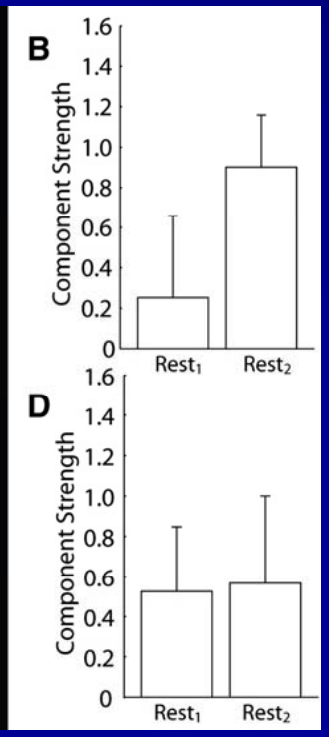
Regional activity (ALFF)

Significantly different between different resting conditions with limited cognitive demand

(Yan et al., 2009, PLoS ONE)

Different resting conditions?





Motor learning group

Control group

Motor learning but not motor performance modulated subsequent frontal-parietal resting-state network

(Albert et al., 2009, Curr Biol)

Some issues about resting-state fMRI

- Definition and instruction?
- Sampling rates (TR)
- Length

Some issues about resting-state fMRI

Sampling rates (TR)

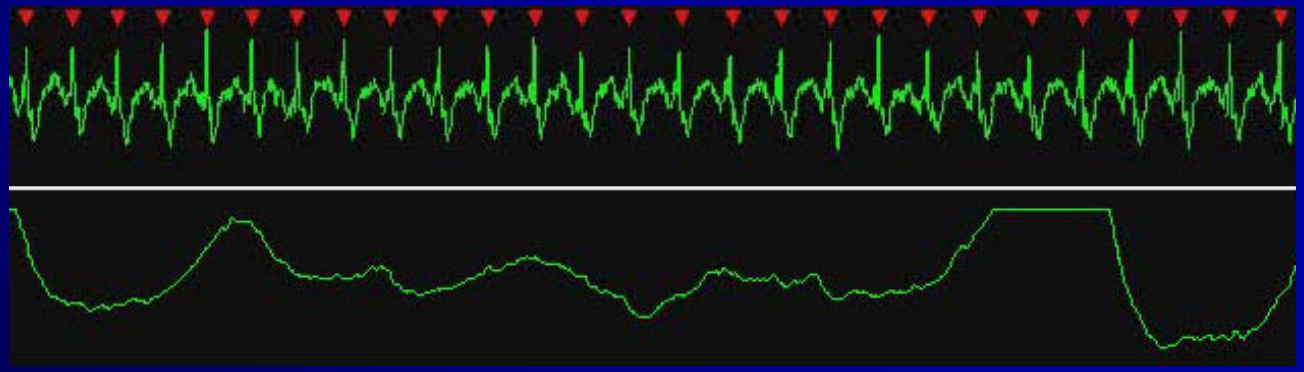
Nyquist sampling theorem:

- **Shorter TR (<400 ms, >2.5 Hz)**
- **for heart beating (around 1.3 Hz)**

Sampling rate and physiological noise

But for respiration (around 0.3 Hz)?

Is TR <1.5 s fast enough?



Courtesy of SONG Xiao-Wei

Simultaneous recording of respiration and heart beat to remove physiological noise ***(Hu et al., 1995, MRM)***

Some issues about resting-state fMRI

- Definition and instruction?
- Sampling rates (TR)
- Length

Some issues about resting-state fMRI

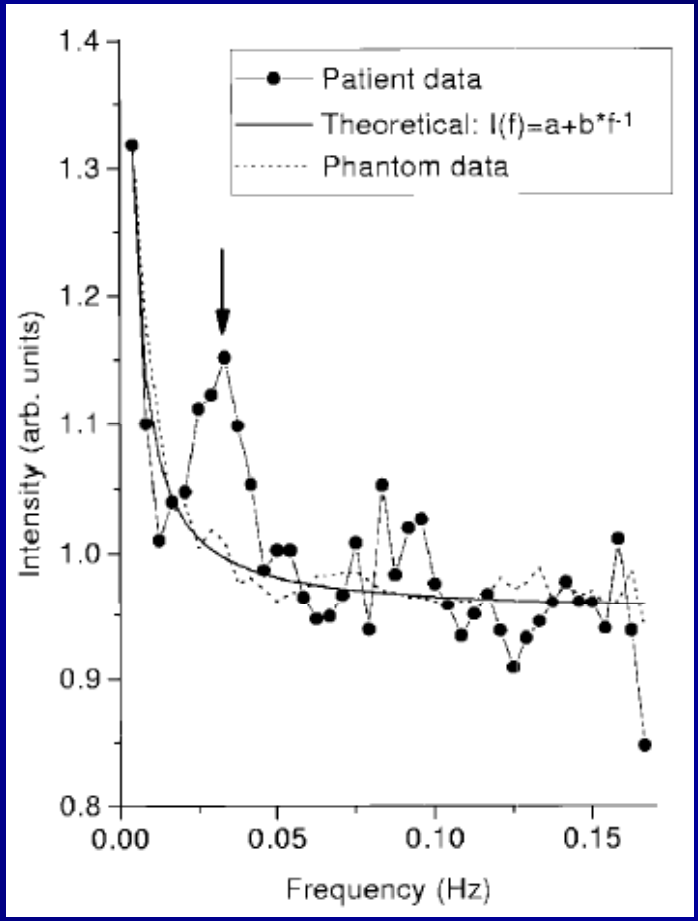
Length?

LFF: 0.01-0.08 Hz

Peak around 0.033 Hz

(Kiviniemi et al., 2000, MRM)

≈2/min



Examples in brain disorders

- **Attention Deficit Hyperactivity Disorder** 
- **AD/MCI, APOE genotype and episodic memory consolidation**
- **Presurgical planning**

Background of Attention Deficit Hyperactivity Disorder (ADHD)

- **Rates in school-aged boys and girls:**
  10% and 4%, respectively
- **The most common neurobehavioral disorder of childhood**
- **Core symptoms:**
  inattention, impulsivity and hyperactivity

(Furman, 2005, J Child Neurol)

fMRI in ADHD

- Totally about 50 research papers, > 80% are task state
- Tasks:

  conflict & inhibition (Go/No-Go, Stop signal, Stroop, flanker, Simon)

  working memory (verbal, spatial)

  alertness

  reward and feedback

  temporal perception (timing)

  mental rotation

  odd ball

  ……

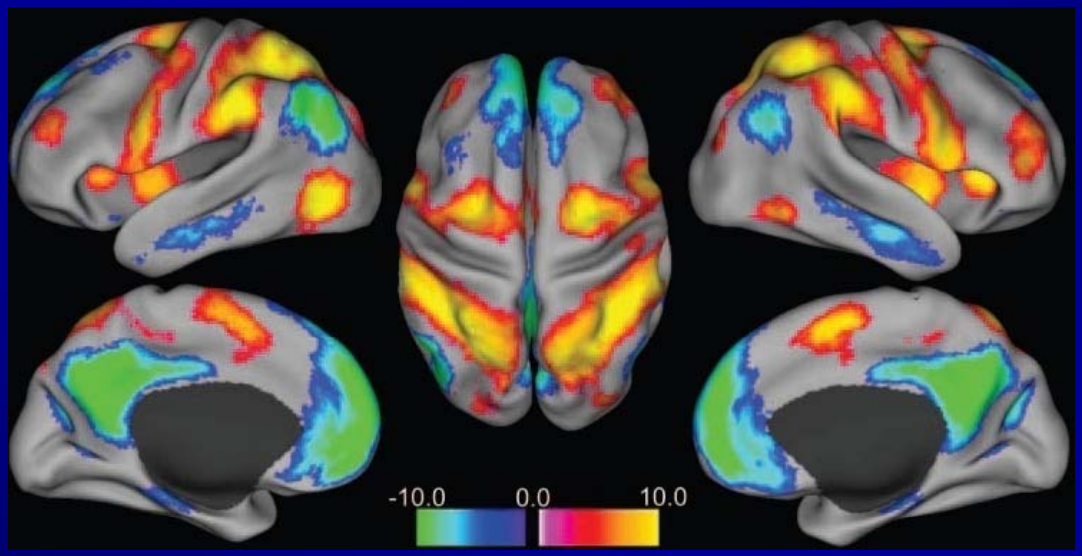
Interesting topics from studies using resting-state fMRI in ADHD

- **Interaction of the dorsal anterior cingulate cortex (dACC) and default mode network**

- **Interaction of the right inferior frontal gyrus (IFG) or frontal-insular cortex (FIC) and dACC**

“The human brain is intrinsically organized into dynamic, anticorrelated functional networks”

(Fox et al., 2005, PNAS)



Anti-correlation between default mode network and attentional network

Functional connectivity of dACC

- **Spherical ROI**

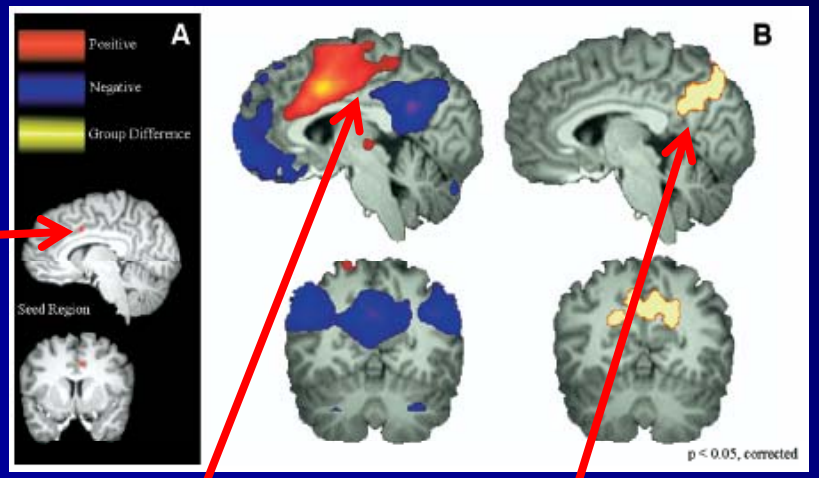
  (Weissman et al., 2006, Nat Neurosci)

- **Linear correlation**

  with removing global trend

- **dACC: negative connectivity with DMN**

- **ADHD, decreased negative connectivity of PCC/Pcu with dACC, indicating abnormal balance between attentional network and DMN**

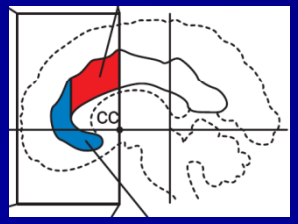


(Castellanos et al., 2008, Biol Psychiatry)

Functional connectivity of dACC

- **Cognitive diviонsion of ACC**

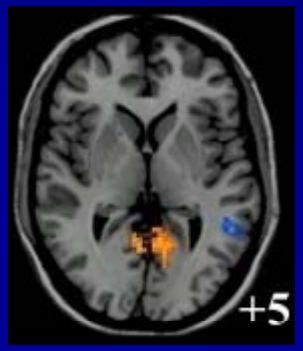
  (Bush et al., 2000, Trends Cogn Sci)



- **Linear correlation**

  with removing global trend

- **dACC: negative connectivity with DMN**



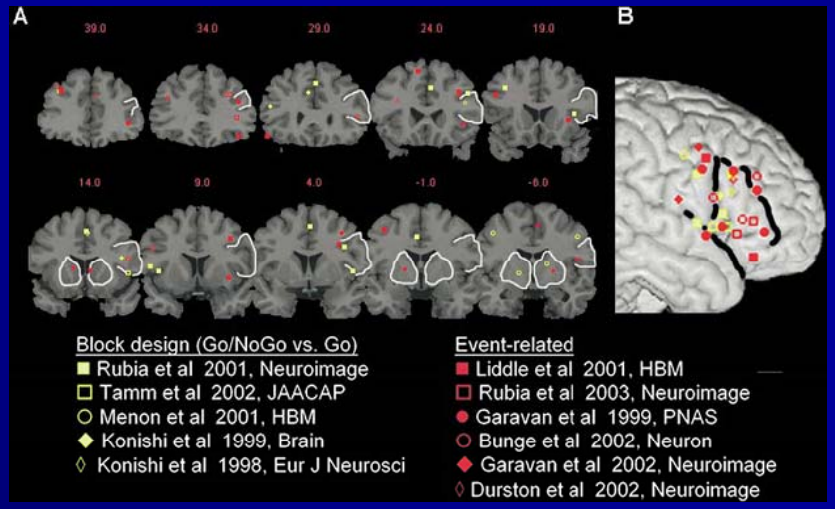
- **ADHD, decreased negative connectivity of retrosplenial cortex, indicating abnormal balance between attentional network and DMN**

(Sun et al., under review)

Interesting topics from studies using resting-state fMRI in ADHD

- **Interaction of the dorsal anterior cingulate cortex (dACC) and default mode network**
- **Interaction of the right inferior frontal gyrus (IFG) or frontal-insular cortex (FIC) and dACC**

Right IFG, fMRI & ADHD



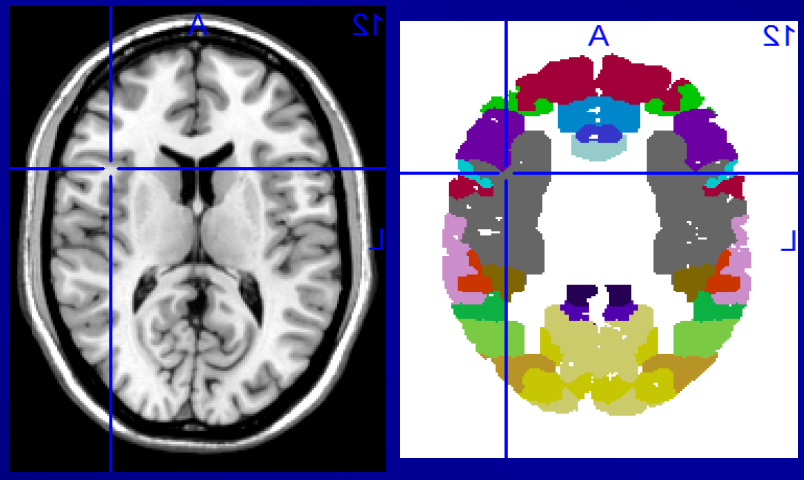
Right IFG: inhibition in normal adults

(Aron & Poldrack, 2005, Biol Psychiatry)

The mean coordinates of the 11 studies in that review

(42, 16, 12)

Fronto-insula



(Made by ZHANG Li-Jie)

Right IFG, fMRI & ADHD

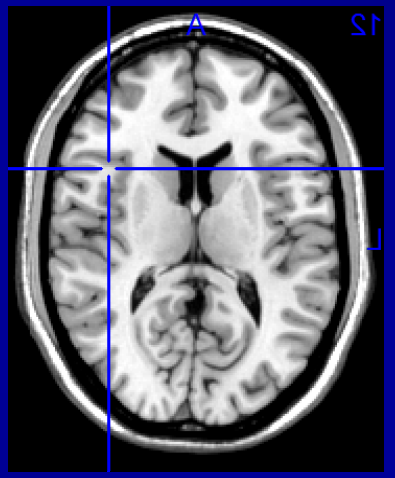
7 papers on response inhibition: found group difference in the right IFG between ADHD and controls

- 5: ADHD < control
- 2: ADHD > control

The mean coordinates of the 7 studies:

41, 19, 3

right fronto-insula



(Made by ZHANG Li-Jie)

Right IFG and ADHD: location

41, 19, 3 mean coordinates of 7 studies of inhibition

(Made by ZHANG Li-Jie)

42, 16, 12 mean coordinates of 11 normal adult studies ***(Aron & Poldrack, 2005, Biol Psychiatry)***

(Made by ZHANG Li-Jie)

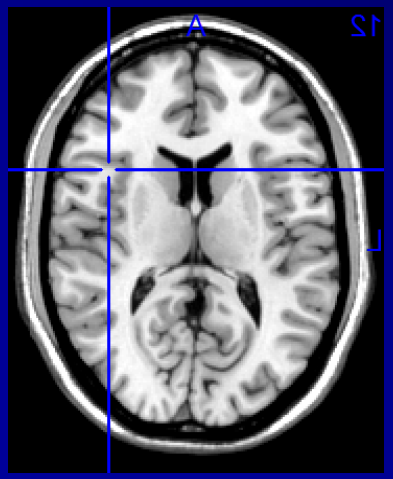
46, 19, 5 peak coordinates, decreased ALFF in ADHD in a resting-state fMRI study

(Zang et al., 2007, Brain Dev)

Functional connectivity of the right FIC with dACC

- **Spherical ROI (41, 19, 3)**
- **Linear correlation**

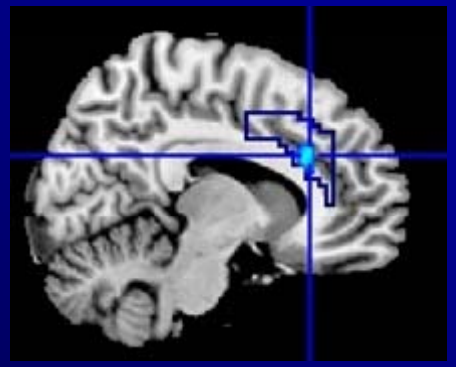
  with removing global trend



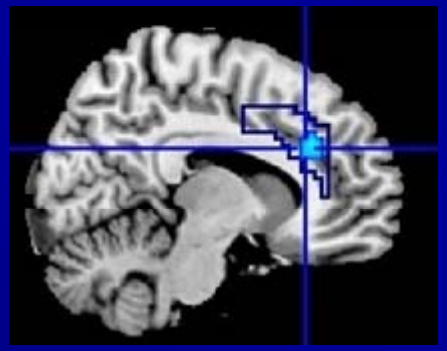
(Zhang et al., in preparation)

Functional connectivity of the right FIC with dACC

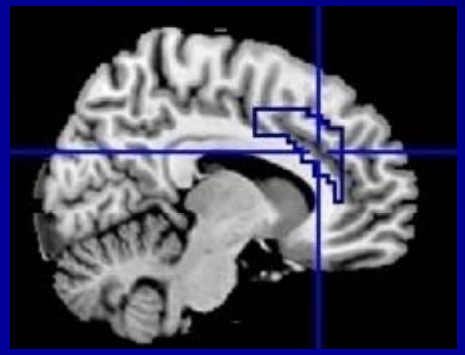
Stimulant-naïve boys with ADHD
Subtypes: inattention type; combined type



All ADHD vs. controls



ADHD-C vs. controls



ADHD-I vs. controls

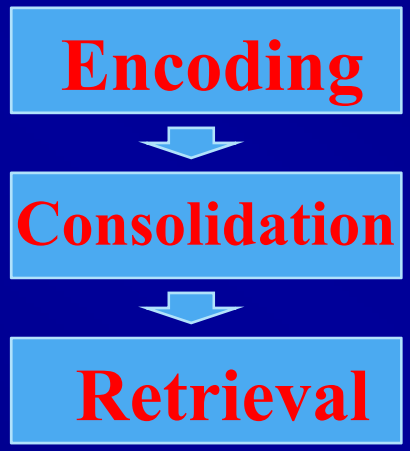
(Zhang et al., in preparation)

Examples in brain disorders

- **Attention Deficit Hyperactivity Disorder**
- **AD/MCI, APOE genotype and episodic memory consolidation** 
- **Epilepsy**
- **Parkinson disease**

Episodic memory and Alzheimer disease:

- **Subtle change of episodic memory is the earliest cognitive deficit in AD (Schwindt & Black, 1999)**
- **Consistently decreased activation in AD patients during both encoding and retrieval stages of episodic memory (Schwindt & Black, 2009)**
- **Mechanism of episodic memory consolidation after encoding?**



Schwindt GC, Black SE.Neuroimage. 2009 Mar 1;45(1):181-90.

Spontaneous brain activity & memory consolidation

- Awake rat: **Hippocampal place cells in awake after learning in rat (Foster & Wilson, 2006)**
- Awake human: **resting-state fMRI, motor learning can modulate subsequent resting-state networks, memory consolidation (Albert et al., 2009)**

Foster DJ, Wilson MA. Nature. 2006 Mar 30;440(7084):680-3.
Albert NB, Robertson EM, Miall RC. Curr Biol. 2009 in press.

AD/MCI, APOE genotype & spontaneous brain activity (resting-state PET)

- **Lower glucose metabolism in PCC in AD/MCI (Minoshima et al., 1994)**
- **Lower glucose metabolism in PCC in ApoE ε4 healthy carriers (Reiman et al., 1996; 2004; 2005)**

Minoshima S, Foster NL, Kuhl DE. Lancet. 1994 Sep 24;344(8926):895.
Reiman EM, Caselli RJ, Yun LS, Chen K, Bandy D, Minoshima S, Thibodeau SN, Osborne D. N Engl J Med. 1996; 334:752-8.
Reiman EM, Chen K, Alexander GE, Caselli RJ, Bandy D, Osborne D, Saunders AM, Hardy J. PNAS 2004; 101(1):284-9.
Reiman EM, Chen K, Alexander GE, Caselli RJ, Bandy D, Osborne D, Saunders AM, Hardy J. PNAS 2005;102:8299-302.

AD/MCI & spontaneous brain activity (Resting-state fMRI)

- **Lower functional connectivity of default mode network including PCC in AD/MCI (Greicius et al., 2004; Wang et al., 2006)**

- **Lower regional homogeneity in PCC in AD/MCI (He et al., 2007; Bai et al., 2008)**

Greicius MD, Srivastava G, Reiss AL, Menon V. Proc Natl Acad Sci U S A. 2004 Mar 30;101(13):4637-42.
He Y, Wang L, Zang Y, Tian L, Zhang X, Li K, Jiang T. Neuroimage. 2007 Apr 1;35(2):488-500.
Bai F, Zhang Z, Yu H, Shi Y, Yuan Y, Zhu W, Zhang X, Qian Y. Neurosci Lett. 2008 Jun 13;438(1):111-5.

APOE genotype & spontaneous brain activity (resting-state fMRI)

- **Increased "default mode network" coactivation (not including PCC) in ApoE ε4 healthy carriers (Filippini et al., 2009)**
- **However, the resting condition was after a memory task (Filippini et al., 2009)**
- **Significant difference between two resting-conditions separated by tasks, suggesting memory consolidation (Albert et al., 2009; Yan et al., 2009)**

Filippini N, MacIntosh BJ, Hough MG, Goodwin GM, Frisoni GB, Smith SM, Matthews PM, Beckmann CF, Mackay CE. Proc Natl Acad Sci U S A. 2009 Apr 28;106(17):7209-14.
Albert NB, Robertson EM, Miall RC. Curr Biol. 2009 in press.
Yan CG, Liu DQ, He Y, Zou QH, Zhu CZ, Zuo XN, Long XY, Zang YF. PLoS One 2009, In press.

Aims of our current study:

- By using resting-state fMRI in the first scanning session, to replicate the lower spontaneous activity in PCC in ApoE ε4 healthy carriers in previous PET studies (first scanning session)
- Between genotypes: the modulation of spontaneous brain activity by an episodic memory task may be different in PCC and other brain areas

Suggesting different mechanism of episodic memory consolidation?

Design

- Two groups of healthy APOE carriers: ε4/3 vs. ε2/3, n = 20 vs 20, (half males), 18 – 23 yrs from BNU, match for IQ and education
- All participants gave their written informed consent. The study was approved by the local IRB.

Design

- **Scanning sessions (3T Siemens):**

S1	**Resting-state (Rest1)**	**8 min**
S2	**Pictures (indoor or outdoor) (encoding)**	**5 min**
S3	**3D structure**	**8 min**
S4	**Resting-state (Rest2)**	**8 min**
S5	**Retrieval: old or new (2 runs)**	**10 min**

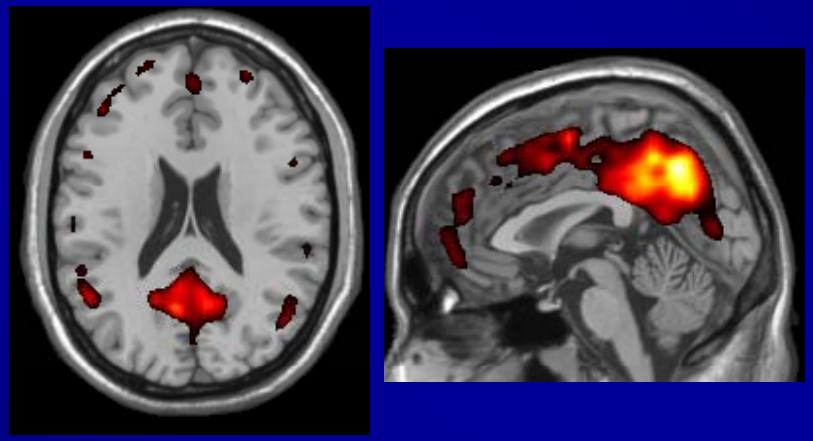
- **Rest2 – Rest1: episodic memory consolidation?**

Result 1: retrieval performance

	d' mean	SD	t	p
2/3	2.46	0.68	-0.387	0.7
3/4	2.54	0.63		

No significant difference between the two groups

Result 2: One-sample t-test of ReHo in Rest 1

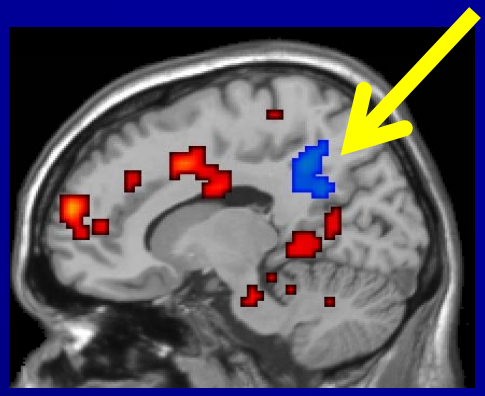


T > 13, n = 40

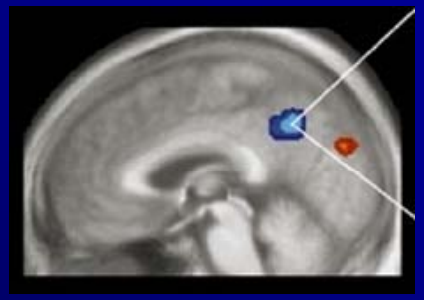
Significant greater ReHo in the default mode network than the global mean ReHo, well consistent with previous results (Long et al., 2008)

Long XY, Zuo XN, Kiviniemi V, Yang Y, Zou QH, Zhu CZ, Jiang TZ, Yang H, Gong QY, Wang L, Li KC, Xie S, Zang YF. J Neurosci Methods. 2008 Jun 30;171(2):349-55.

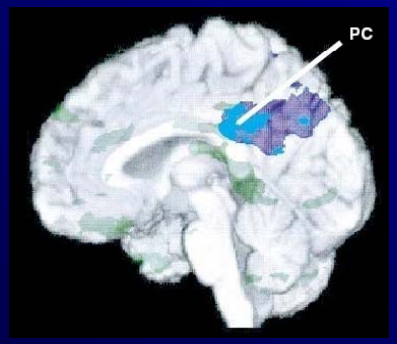
Result 3: Two-sample t-test of ReHo in Rest 1



Lower ReHo in ε4/3 in left PCC
(P < 0.05, uncorrected)



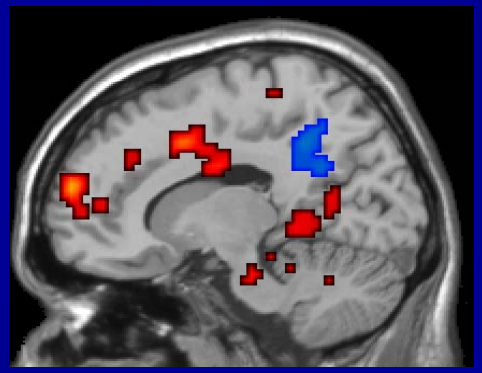
Lower ReHo in AD/MCI
(He Y et al., 2007)



Lower glucose metabolism in ε4 healthy carrier (Reiman et al., 1996)

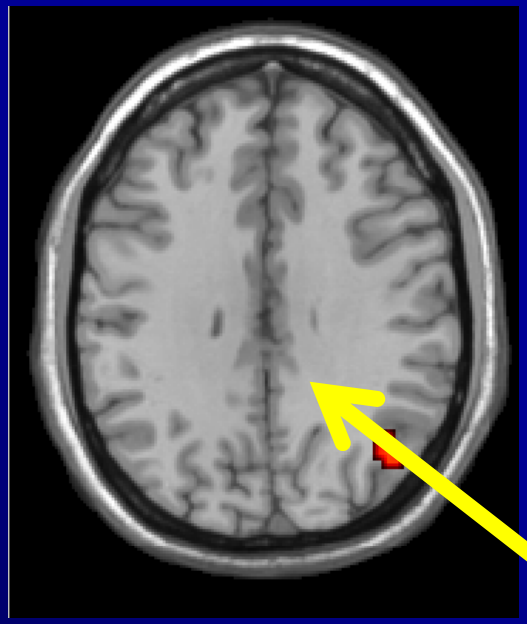
He Y, Wang L, Zang Y, Tian L, Zhang X, Li K, Jiang T. Neuroimage. 2007 Apr 1;35(2):488-500.
Reiman EM, Caselli RJ, Yun LS, Chen K, Bandy D, Minoshima S, Thibodeau SN, Osborne D. N Engl J Med. 1996 Mar 21;334(12):752-8.

Result 3: Two-sample t-test of ReHo in Rest 1



An inclusive template was generated for further comparisons

Result 4: Two-sample t-test of ReHo in Rest2



Higher ReHo in ε4/3 in left angular gyrus
(P < 0.05, corrected)

No significant difference in PCC between the two groups event at P<0.05, uncorrected

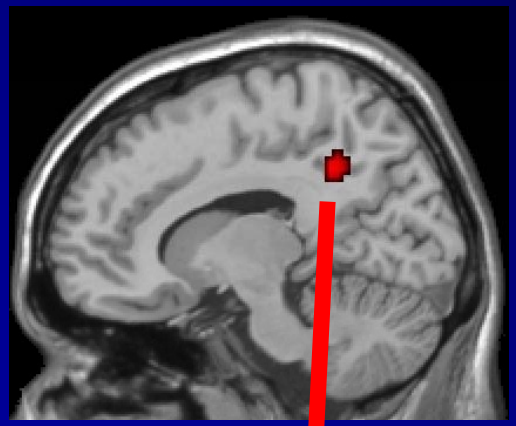
Result 5: Two-sample t-test of ReHo in Rest2-Rest1

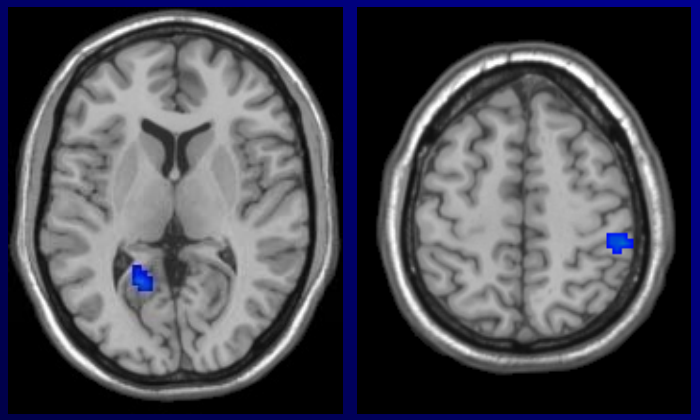
ReHo change:

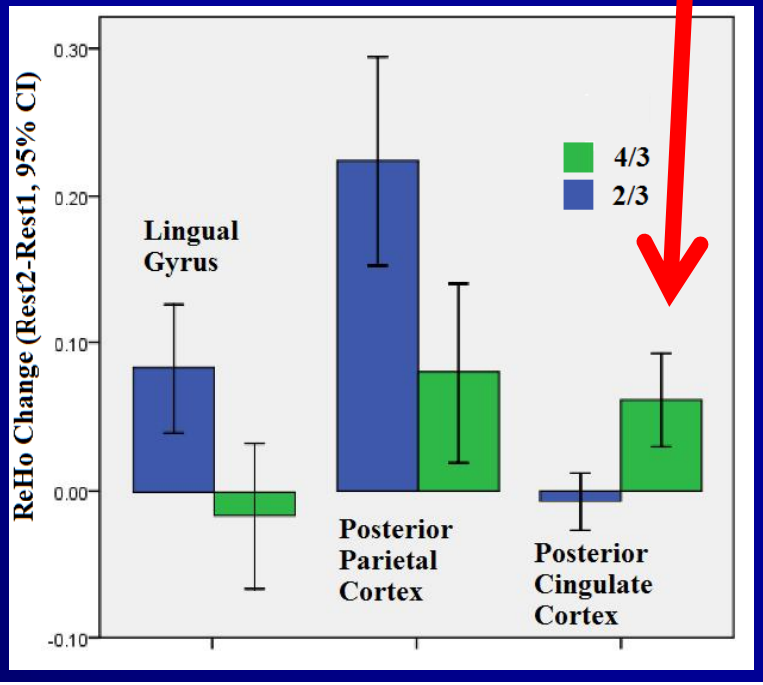
ε4/3 > ε2/3 in PCC

ε4/3 < ε2/3 in lingual gyrus and posterior parietal cortex

(P < 0.05, corrected)







Conclusions

Resting-state fMRI can replicate the lower spontaneous activity in PCC in ε4/3 healthy carriers than ε2/3

ApoE ε4/3 and ε2/3 healthy carriers showed different pattern of modulation of the spontaneous activity by the episodic memory encoding, suggestting different mechanisms of episodic memory consolidation

E.g., compensatory mechanism in PCC for memory consolidation?

Presurgical functional localization by resting-state fMRI

Totally 4 papers

Kokkonen SM, Nikkinen J, Remes J, Kantola J, Starck T, Haapea M, Tuominen J, Tervonen O, Kiviniemi V. Preoperative localization of the sensorimotor area using independent component analysis of resting-state fMRI. Magn Reson Imaging. 2008 Dec 24.

Zhang D, Johnston JM, Fox MD, Leuthardt EC, Grubb RL, Chicoine MR, Smyth MD, Snyder AZ, Raichle ME, Shimony JS. Preoperative sensorimotor mapping in brain tumor patients using spontaneous fluctuations in neuronal activity imaged with functional magnetic resonance imaging: initial experience. Neurosurgery. 2009 Dec;65(6 Suppl):226-36.

Shimony JS, Zhang D, Johnston JM, Fox MD, Roy A, Leuthardt EC. Resting-state spontaneous fluctuations in brain activity: a new paradigm for presurgical planning using fMRI. Acad Radiol. 2009 May;16(5):578-83.

Liu H, Buckner RL, Talukdar T, Tanaka N, Madsen JR, Stufflebeam SM. Task-free presurgical mapping using functional magnetic resonance imaging intrinsic activity. J Neurosurg. 2009 Oct;111(4):746-54.

Preoperative sensorimotor mapping in brain tumor patients using spontaneous fluctuations in neuronal activity imaged with fMRI: initial experience

(Zhang et al., Neurosurgery, 2009)

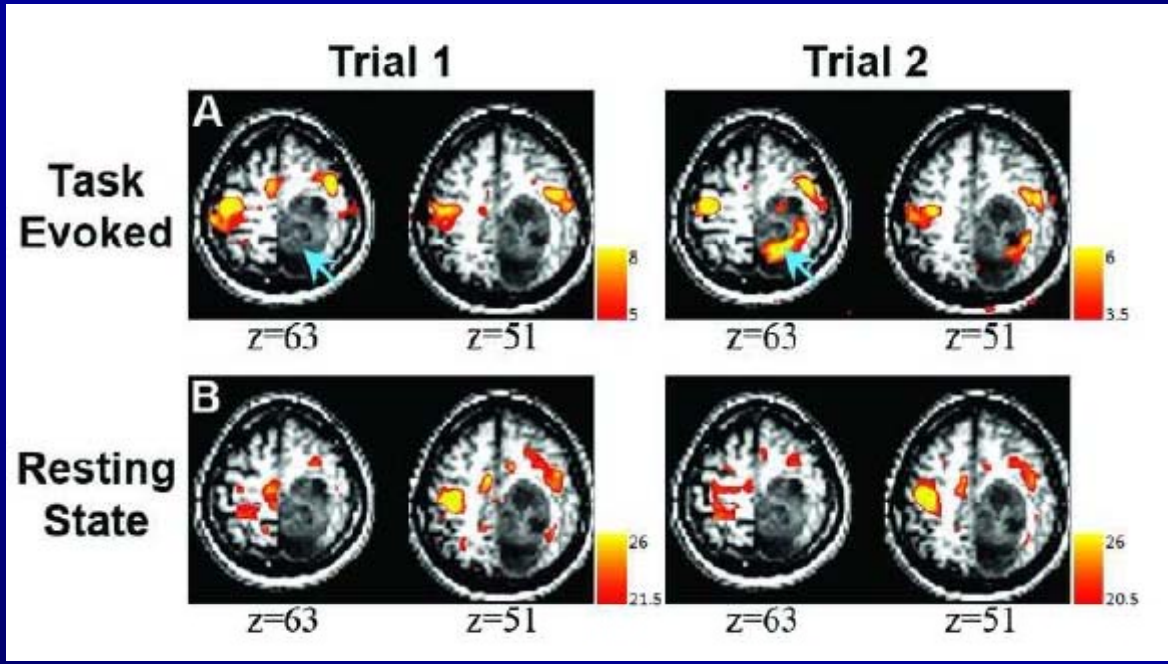
Preoperative, sensorimotor, tumor, RS-fMRI

(Zhang et al., Neurosurgery, 2009)

- 4 patients with brain tumor near sensorimotor cortex, and 17 healthy controls
- Linear correlation: The left sensorimotor cortex Talairach coordinate (-39, -26, 51) from previous finger tapping study
- Linear correlation: The intra-parietal sulcus 25, -58, 52) from previous RS-fMRI study
- ICA:
- Cortical stimulation:

Preoperative, sensorimotor, tumor, RS-fMRI

(Zhang et al., Neurosurgery, 2009)

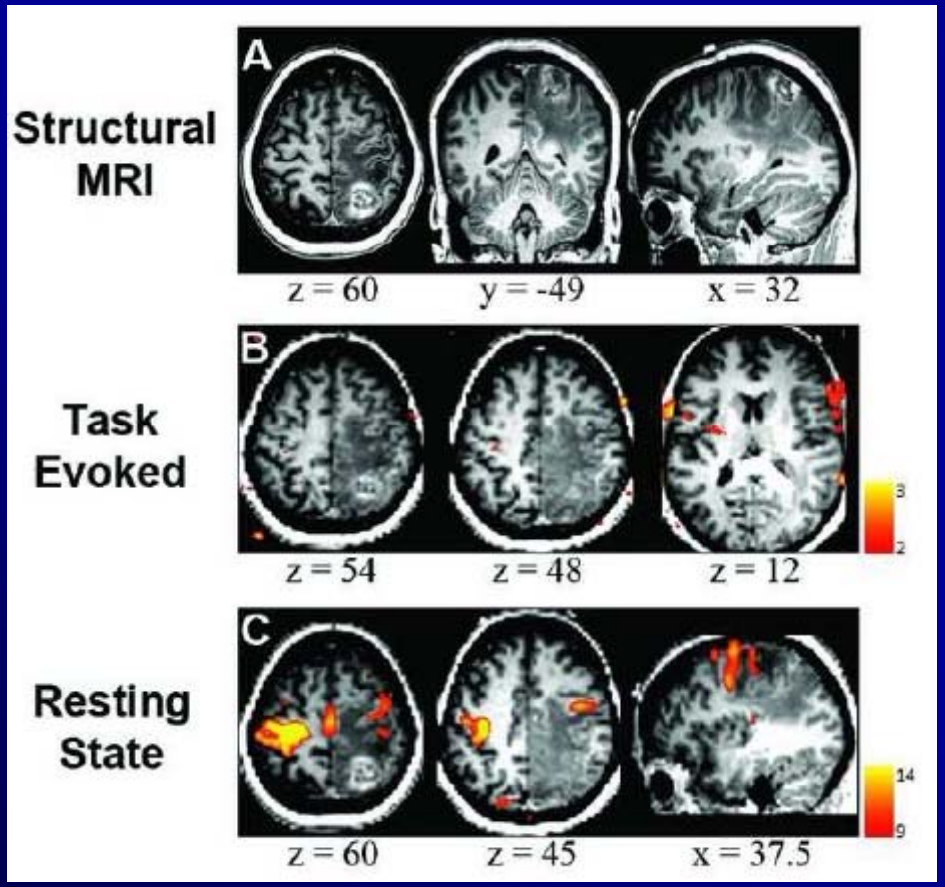


Task vs. Resting: Case 1

Activation in tumor in trial 2

Preoperative, sensorimotor, tumor, RS-fMRI

(Zhang et al., Neurosurgery, 2009)

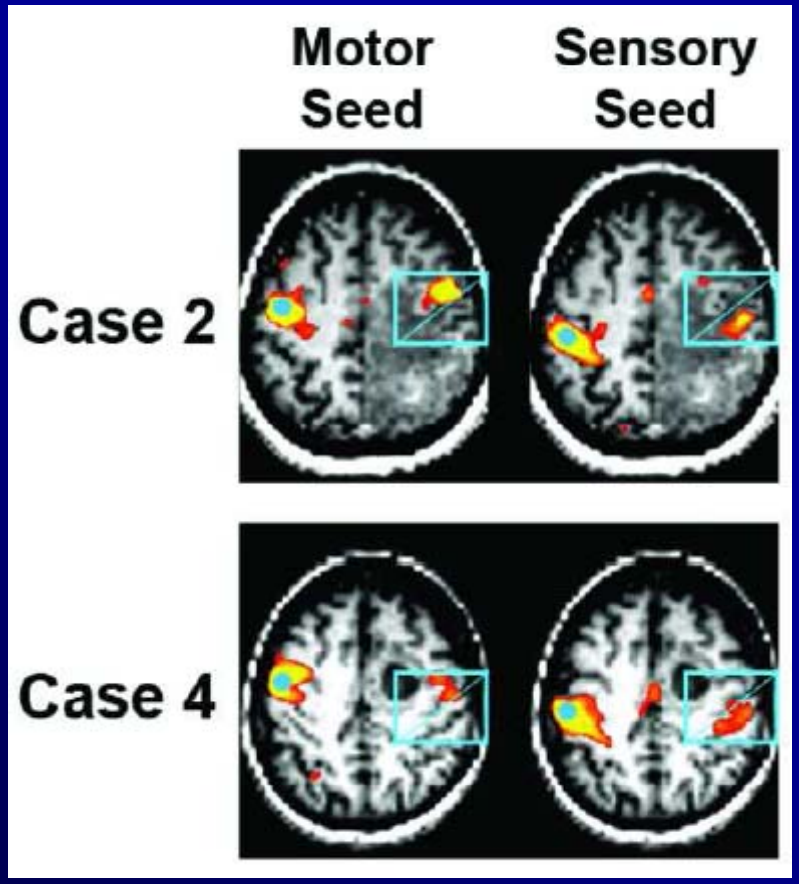


Task vs. Resting: Case 2

No activation in task state

Preoperative, sensorimotor, tumor, RS-fMRI

(Zhang et al., Neurosurgery, 2009)



Partial correlation:

Motor specific

Sensory specific

Thanks for your attention!