Brain Structural and Functional Image Analysis of Amblyopia

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Outline

- Overview and Background
- Structural and Functional Deficit in Amblyopia
- Functional Connectivity Analysis in Amblyopia
- Conclusion
Background

- Medical Treatment:
  - *qualitative analysis* → *quantitative analysis*
  (experience based)  (knowledge based)
Background - 19~20 Century

To see the pathological changes

- **Structure imaging**
  - X-ray
  - CT
  - Image processing and analyzing system
Background - 1990s, 20 Century

- To see the functions
  - *Functional imaging*
    - fMRI
    - PET
    - SPECT
Background - 21 Century

To see the cell, molecular

- **Molecular Imaging**
  - Optical Imaging
  - Nuclear Imaging

Realtime, Live
Background - 21 Century

Human-Computer Interaction
– *Brain Computer Interface*
(Brain Machine Interface)
Overview---Research Framework

- Pattern Recognition
- Image Processing
- Medical Imaging
- Clinical Information
- Research & Analysis
- Bio-markers
- Therapist
- Early Diagnosis
- Diagnosis Assistance
- Prognosis

Theory | Method | Application
Research Fields

- Algorithm & Theory
- Algorithm platform
- Software system
- Visual System
- Network Analysis
- Spike Data Analysis
Background---Visual Pathway

Where are the lesions

The relationship between lesions

Struc. VS Func.
外侧膝状体与视觉通路

外侧膝状体（LGN）

结构细小，突触连接复杂，缺乏有效的活体内定位、观察手段。

Courtesy of http://anatome.ncl.ac.uk/tutorials/clinical/eye/page6.html#title
结合概率模板和区域增长的LGN半自动分割方法

Li, He*, et.al, AJNR 2012 (JCR 1区, IF=3.4)
Li, Li, He*, et. al, British Journal of Radiology, JCR 2区, IF=2.4, 2011
弱视结构损伤和功能损伤的定位

Lv, He*, et al, NeuroScience Letters 2008  IF=2.2
Based on cortical thickness measurements, the study by Lv, Li, He*, et al., published in NeuroImage 2010, (JCR 1区, 5 year IF=6.8) presents a network of structural correlations. The cortical parcellation involves 54 subjects, and the cross-correlation matrix is visualized, followed by a binarized matrix. FDR (False Discovery Rate) is applied to the data.
Voxel-based time courses
Threshold and rearrange FC edge weight

CC400 Template
Time courses of 351 ROIs

Functional Parcellation
RS-fMRI data preprocessing
Voxel-based time courses

FC edge features
Threshold and rearrange FC edge weight

Pearson Correlation

FC Matrix

Bayes 网络对神经元交互模式的分析

Sang, Lv, He*, et al. IEEE Intelligent Systems, 2011, JCR 1区，IF=2.6
冠状动脉手术导航系统
Background- fMRI BOLD Signal

Blood Oxygen Level Dependent signal

↑ neural activity ➔ ↑ blood flow ➔ ↑ oxyhemoglobin ➔ ↑ T2* ➔ ↑ fMRI signal

Basal state

- normal flow
- basal level [Hbr]
- basal CBV
- normal MRI signal

Activated state

- increased flow
- decreased [Hbr] (lower field gradients around vessels)
- increased CBV
- increased MRI signal (from lower field gradients)

Source: fMRIB Brief Introduction to fMRI
Background - fMRI Activation Detection

Function of MRI

Open - Closed

% BOLD change

Fox and Raichle 2007
Background --- Retinotopic Organization

From visual field to primary visual cortex

- Left to right
- Upper to lower
From Engel et al, Cerebral Cortex, 1997
Retinotopy Mapping
Amblyopia

- Amblyopia is poor vision in an eye that did not develop normal sight during early childhood.

- Different with myopia, can't be rectified by glasses.

- Most caused by Strabismus, Refractive Error, and so on.
Amblyopia

- Esotropia
- Exotropia
- Hypertropia
Amblyopia

How common is amblyopia?

approximately 3% of the world population
Background of amblyopia study

- How is amblyopia treated?
Background of amblyopia study

- What causes amblyopia?

Motivation

- Perform the retinotopic mapping to identify the visual areas;

- Investigate whether there is the functional deficit in visual area;

- Investigate whether there is the structural deficit (cortical thickness, lobe volume) and its relationship with functional deficit.
Subjects

- 11 amblyopes (7M/4F, 22.57 ± 3.45)
- 11 normal control (7M/4F, 25.34 ± 1.53)
- 7 anisometropic and 4 strabismic

The best-corrected visual acuities of their sound eye were all 1.0, while that of their amblyopia eye were less than 0.6 (mean 0.31 ± 0.26).
Experiment Design

- Two kinds of visual stimuli: polar-angle and eccentricity

- Wedge rotating clockwise or counterclockwise
- Ring dilating or contracting
Image Acquisition

- Anatomic MRI 3D 256*256*124 FOV 256mm*256mm
- Functional MRI (64*64*30  EPI TR=3s TE=51ms, slice thickness 4mm, 128 Volumes)
- 1.5T GE Scanner, JinLing Hospital, Medical School of Nanjing University
Structural MRI process pipeline

Segmentation

3D Recon

Inflation

Sphere Mapping

Flatten

Structural Imaging
fMRI preprocess pipeline

Conventional preprocess steps--SPM
fMRI process pipeline

- Fourier transform (FFT)

\[
F_{u_o}(i) = \sum_{i=1}^{N} f(x_i, t_i) \exp(\pm i 2\pi u_o (t_i - t_H))
\]

\[
A(i) = |F_{u_o}(i)|, \quad \phi(i) = \text{arg}(F_{u_o}(i))
\]
fMRI process pipeline

- Conventional preprocess steps
- Fourier transform (FFT)
- Visual field sign identification (VFS)

\[
\nabla E_{cc} = \left( \frac{\partial \phi_{ecc}}{\partial x}, \frac{\partial \phi_{ecc}}{\partial y}, \frac{\partial \phi_{ecc}}{\partial z} \right)
\]

\[
\nabla Pol = \left( \frac{\partial \phi_{pol}}{\partial x}, \frac{\partial \phi_{pol}}{\partial y}, \frac{\partial \phi_{pol}}{\partial z} \right)
\]

\[
\nabla Ana = \left( \frac{\partial A}{\partial x}, \frac{\partial A}{\partial y}, \frac{\partial A}{\partial z} \right)
\]

\[
VFS = \text{sign}(\nabla E_{cc} \times \nabla Pol) \cdot \nabla Ana
\]

\[
VFS_{\text{weighted}} = A(i) \cdot VFS
\]

\[
= |F_v(i)| \cdot \text{sign}(\nabla E_{cc} \times \nabla Pol) \cdot \nabla Ana
\]
Retinotopic visual areas

Individual Analysis

--- BOLD Response Curve

Fixing

amblyopic
Activation Magnitude Analysis

Normal                         amblyopic
Phase Analysis

Normal                          amblyopic

[Bar charts showing variance of phase for different regions (V1 to V4) for normal and amblyopic conditions.]
Parcellate the brain to compute the volume
**Functional Difference**

\[
FD = \left( \frac{F_{\text{fix}} - F_{\text{amb}}}{F_{\text{fix}} + F_{\text{amb}}} \right)
\]

- \(F_{\text{fix}}\): means the activation of the fix eye
- \(F_{\text{amb}}\): means the activation of the amblyopic eye
Structural-Functional Correlation

\[ \text{Corr}(\text{FD}, \text{VOL}_i) = \frac{\sum (\text{FD} - \overline{\text{FD}})(\text{VOL}_i - \overline{\text{VOL}_i})}{\sqrt{\sum (\text{FD} - \overline{\text{FD}})^2 \sum (\text{VOL}_i - \overline{\text{VOL}_i})^2}} \]
Structural-Functional Correlation Results

![Bar chart showing correlation coefficients for different brain regions.

- Frontal: 0.04
- Parietal: -0.06
- Occipital: -0.15
- Temporal: -0.2
- Calcarine: -0.3
- Thalamus: -0.35]
Cortical thickness
Results and Summary

- No significant difference on global mean cortical thickness and V1/v2 mean cortical thickness
- There were significant main effect of hemisphere ($F(1, 22) = 6.37, P < 0.05$) and main effect of group ($F(10, 22) = 2.95, P < 0.05$)
The fMRI bold response of amblyopic eye has the reduced \( t \) statistic, in comparison with the fixing eye.

Structural morphology changes with functional dysfunction in the visual cortex.

Functional deficit could be consistent with volume in some anatomical areas, especially the occipital lobe.

The hemisphere difference exist in the unilateral amblyopia subjects.

Lv, et al, NSL, 2008
Outline

- Overview
- Structural and Functional Deficit in Amblyopia
- Functional Connectivity Analysis in Amblyopia
- Conclusion
Motivation

- Investigate whether there is functional connectivity abnormality in amblyopia subjects with resting state fMRI
Subjects and Image Acquisition

- 17 amblyopes (10M/7F, 22.57 ± 3.45)
- 17 normal control (10M/7F, 25.34 ± 1.53) sMRI:
  - T1 TR/TE = 8.9/3.5ms, slice thickness = 1 mm, flip angle = 13°, matrix = 256 × 256, FOV = 24 × 24 cm²
- rsfMRI:
  - (64*64*28 TR/TE = 2s/35ms, slice thickness 5mm, flip angle = 90° FOV = 24 × 24 cm²), scanning time=6min40s 200 Volumes
- 3T GE Scanner, Beijing Tongren Hospital
Analysis of functional connectivity

- Seeded-based FC with the primary visual cortex
- Whole brain network
Preprocessing of resting state fMRI

- Slice & Motion correction
- Smoothing
- Spatial normalisation
- Standard template

fMRI time-series → kernel

0.01 → 0.08
Analysis of functional connectivity

- Seeded-based FC with the primary visual cortex

Primary visual cortex: Brodann 17 (BA17)

Bilateral circular ROIs with radius 6mm in BA17 centered at \((-8, -76, 10)\) and \((6, -76, 10)\) in MNI space.
Analysis of functional connectivity

- fMRI time-series
- kernel
- Slice & Motion correction
- Smoothing
- Spatial normalisation
- Standard template
- Connectivity with the other voxels
- temporal BPF

0.01 - 0.08
Analysis of functional connectivity

Whole brain network

fMRI time-series → kernel

Slice & Motion correction → Smoothing

Spatial normalisation → Standard template

Connectivity between ROIs
Seeded-based FC with the **left** primary visual cortex: FDR corrected, p<0.05

Figure 1. The significant regions in the FC with the left primary visual cortex. (a) the brain regions showing significantly higher FC than 0 in normal controls. (b) the brain regions showing significantly higher FC than 0 in amblyopia patients. (c): the brain regions with decreased FC in amblyopia patients.
Seeded-based FC with the **left** primary visual cortex:

Dorsal stream

Ventral stream

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<th>Anatomical Loc</th>
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<th>x</th>
<th>y</th>
<th>z</th>
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FDR corrected, p<0.05, threshold=20 voxels, x, y, z : MNI coordinates, k: the number of voxels in the cluster.
Experiments and Results

Seeded-based FC with the right primary visual cortex:

FDR corrected, p<0.05

Figure 2. The significant regions in the FC with the right primary visual cortex. (a) the brain regions showing significantly higher FC than 0 in normal controls. (b) the brain regions showing significantly higher FC than 0 in amblyopia patients. (c): the brain regions with decreased FC in amblyopia patients.
Experiments and Results

Seeded-based FC with the **right** primary visual cortex:

Table:

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FDR corrected, p<0.05, threshold=20 voxels, x, y, z: MNI coordinates, k: the number of voxels in the cluster.
Experiments and Results

Whole brain network:

Figure 3. The correlation matrices for 116 AAL regions of two groups. (a) normal controls, (b) amblyopia patients.
Experiments and Results

Whole brain network:

Figure 4. The abnormality of the whole brain network in amblyopes. Yellow nodes represent regions. Red represents increases in FC and blue represents decreases in FC.
### Experiments and Results

Whole brain network: (uncorrected $P<0.001$)

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**Temporal cortex**

**Cerebellum**
Summary

**Seed-based FC:** decreased FC with the primary visual cortex was found in the superior occipital gyrus and the lingual gyrus. The results suggested that functional deficits exist in both dorsal stream and ventral stream.

**Whole brain network:** decreased functional connectivities most concentrate in the temporal cortex, then in the cerebellum. These results suggest that amblyopia may be caused by the deficits in the visual information transmission.

Conclusion and future work

- Introduce two kinds of amblyopia study, task fMRI and resting state fMRI
- Will try to reconstruct the whole visual pathway and make connectivity analysis
- Will try to combine multi-modality imaging, such as DTI, fMRI, OCT, and VEP, etc.
Human Brain Connectome

MRI Acquisition

1. Diffusion Spectrum Imaging
2. T1w high res.
3. Segmentation
3a. Partition into 66 anatomical subregions
3b. Partition into 1000 ROIs
4. Tractography
5. Whole brain structural connection network

fcMRI
DSI
CBF
EEG
fMRI
MEG

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