Research on spontaneous activity in adult anisometropic amblyopia with regional homogeneity

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Abstract. Amblyopia usually occurs in early childhood and results in monocular visual impairment. The functional magnetic resonance imaging (fMRI) studies have reflected functional anomaly in amblyopia. In resting-state fMRI study, spontaneous activity changes abnormally in anisometropic amblyopia could be revealed by the regional homogeneity (ReHo). Twenty two adult anisometropic amblyopes and Twenty one normal controls participated in this fMRI study. Two sample T test was carried out to analysis ReHo within the whole brain for the inter groups. Compare with normal group, our study found that the amblyopia’s ReHo mainly increased in the left frontal lobe, while decreased in the left cerebellum, the temporal lobe (left and right), and the left parietal lobe. And the ReHo values in middle and inferior temporal lobe, the prefrontal lobe, frontal lobe (positive) and parietal lobe and medial frontal gyrus (negative) could be correlated with the acuity deficit of amblyopia. The results increased in ReHo may indicate compensatory plasticity in higher vision information process, while the decreased in ReHo may reflect decreased ability in eye movement, spatial sense and visuo-motor coordination. The correlation revealed that the vision deficit may correspond to the spontaneous in certain brain area.

1. Introduction
Amblyopia, or “lazy eye”, is a disorder of visual system characterized by vision in one eye is poor despite the other eye being healthy. The disorder may due to monocular deprivation in the early life and is also an important cause of unilateral visual deficit [1, 2].

Recently, neuroimaging studies have been used to analysis the functional abnormalities in amblyopia. Goodear and Hess [3, 4] report that the visual cortex is the origin deficits site of the visual pathway and the primary and extra striate vision region are responsible for the abnormalities in amblyopia. Compare with the task fMRI researches, the resting state studies need no stimulate and could value the spontaneous neuronal activity of human[5]. Regional homogeneity (ReHo) is a statistic way to evaluate the similarity between the time series of certain voxel and its nearby voxels.[6]. The ReHo has been effectively used to study lots of diseases [7-9]. For the vision area, the blind patients have higher ReHo result than the normal group in the visual cortex[10]. Compared with normal vision, Lin[11] first reports that the anisometropic amblyopia shows significant ReHo values change in multiple brain regions. However the subjects have a large range of age and the ReHo results have no relationship with vision acuity deficit. Our study decreases the range of age in order to reduce
the age effect and increase the number of subjects with different rank of acuity deficit, so that we can make a full understanding of the spontaneous brain activity patterns defects in amblyopia.

2. Methods and Materials

2.1 Subjects
This study contained two groups: normal controls (n = 21, mean age: 25.12 ± 1.58 years old) and anisometropic amblyopes (n = 22; mean age: 24.27 ± 2.23 years old). A comprehensive eye examination was carried out by a clinician. All participants had no strabismus and no history of eye pathology before the study (Table 1). All subjects were naive to the purpose of the experiment. This study complied with the Declaration of Helsinki and was approved by the University of Sciences and Technology of China Guidelines on Research Ethics.

| Table 1. Summarized clinical details for the amblyopes |
|---------------------------------------------------------|
| Number | Age (years old) Mean ± SD | 24.27 ± 2.23 |
| | Min: Median: Max | 20:24:28 |
| Gender | Female: Male | 5:17 |
| Best corrected visual acuity (LogMAR) | Mean ± SD | Fellow eye 0.035 ± 0.05 |
| | | Amblyopic eye 0.581 ± 0.33 |
| | Min: Median: Max | Fellow eye 0.0:0.46:1.30 |
| | | Amblyopic eye 0.22:1.30 |

2.2 Magnetic resonance imaging acquisition
Scanning was performed at the Anhui Medical University using a GE Signa HDx 3.0T whole-body with an eight-channel receive-only head coil. Each scanning session began with the acquisition of high-resolution three-dimensional T1 weighted images, which were acquired using an MP-RAGE sequence (TR = 2300 ms; TE = 2.94 ms; flip angle = 9°; 176 slices; voxel size = 1×1×1 mm^3). Functional scans were then conducted immediately thereafter. All functional scans consisted of T2*-weighted gradient-echo planar images depicting blood oxygen level-dependent (TR = 2000 ms; TE = 28 ms; flip angle = 72°; 26 slices; voxel size = 3×3×3 mm^3).

2.3 Data preprocessing
All data processing were carried out using SPM8, DPARSF v2.2(http://restfmri.net) [12]. To avoid start-up magnetization transients, data that were collected in the first 10 seconds (5 × TR) were removed in each functional run. Each subject’s fMRI data were slice-time corrected, motion corrected, and temporally detrended with respect to the head motion and up to order 3 polynomial drift correction. Then the corrected data were registered to the standard Montreal Neurological Institute (MNI) template and further spatially smoothed with a Gaussian kernel with FWHM of 4 mm. Data with a head movement larger than 2 mm was removed from further analysis.

3. ReHo analysis and statistical analysis
ReHo was calculated by Kendall’s coefficient of concordance (KCC) and represented the similarity of the time series of the voxels[13, 14]:

$$W = \sum \frac{(R_i)^2}{n!} - n(\bar{R})^2$$

$$\frac{1}{12} K^2 (n^3 - n)$$
Ri is the sum of the ith time point; K is the number of time series within a measured cluster, R is the mean of the Ri; and n is the number of ranks[6].

An Independent two-sample t-test was carried out to judge if the ReHo value were significantly different between normal and amblyopia groups. The correlation between the ReHo and the amblyopic eye's visual acuity was calculated as the Pearson correlation coefficient (ranging between -1 and 1; 2-tailed).

4. Result
There were no significant differences between the amblyopia group and controls in age (P=0.35, two-sample t-test) and gender (p=0.8, Chi-squared test). Compared with the control groups, the amblyopia showed significantly decreased in the left cerebellum, the temporal lobe (left and right), and the left parietal lobe while increased in the left frontal lobe (figure 1 and table 2).

Fig. 2 shows the correlation between the ReHo and the visual acuity of the amblyopic eye. Pearson correlation analysis showed that there was a significantly positive correlation in the middle and inferior temporal lobe, the prefrontal lobe and frontal lobe while negative correlation in parietal lobe and medial frontal gyrus. Such phenomena existed in the figure 2 and table 3 as we studied here.

Figure1 The group different brain areas in the ReHo for the normal controls and the amblyopia groups. (p<0.05, Alphasim corrected, cluster size 85, 2-tailed independent two-sample t-tests).

Table2 The difference ReHo values of brain areas between normal controls and amblyopia groups (p<0.05, Alphasim corrected, cluster size 85, 2-tailed independent two-sample t-tests).

| Brain region               | Brodmann region | Cluster size | T-values | Coordinates in MNI(x,y,z) |
|----------------------------|-----------------|--------------|----------|--------------------------|
| The left Cerebellum        |                 | 97           | 3.0799   | -30, -69, -21            |
| The right Temporal Lobe    | 22              | 98           | 4.297    | 42, 3, -6                |
| The left Temporal Lobe     | 22              | 112          | 3.3108   | -48, -3, -6              |
| The left Parietal Lobe     | 39              | 85           | 4.6193   | -48, -35, 33             |
| The left Frontal Lobe      | 8               | 128          | -3.867   | -21, 36, 57              |
Figure 2 The significant correlate brain areas (Pearson correlation coefficients) between the ReHo and the visual acuity (logMAR) of the amblyopic eye. (p<0.05, Alphasim corrected, cluster size 85)

Table 3 The significant correlate brain areas between the Reho and the visual acuity (logMAR) of the amblyopic eye. (Pearson correlation coefficients, p<0.05, Alphasim corrected, cluster size 85)

| Brain region                  | Brodmann region | Cluster size | T-values | Coordinates in MNI (x,y,z) |
|-------------------------------|-----------------|--------------|----------|---------------------------|
| The left Temporal Lobe        | 20              | 86           | 0.61813  | -39, -15, -30             |
|                               | 21              | 91           | 0.78747  | -45, 6, -3                |
|                               | 10              | 97           | 0.6753   | -12, 69, 15               |
| The left Frontal Lobe         | 9               | 91           | 0.71099  | -36, 24, 27               |
| The left Parietal Lobe        | 7               | 108          | 0.72901  | -9, -12, 60               |
| The left Medial Frontal Gyrus | 6               | 188          |          |                           |

5. Discussion
The first main findings are the decrease and increase ReHo in several brain areas. The decrease value in cerebellum is believed to affect the control of the eye movement and interact with the frontal lobe[15, 16]. The temporal lobe is involved in processing sensory input into appropriate derived meaning of visual memory[17], so that the amblyopia may have difficulty in this aspect. The parietal lobe integrates sensory information among various modalities, so the decrease may affect the spatial sense and visuo-motor coordination[18] for amblyopia[17]. While the increase in frontal lobe may due to it involves the ability to various cognitive and perceptual tasks, so the amblyopia need more higher cognitive functional to do more work[19].

Further, the ReHo value has positive correlation with the severity of amblyopia in middle and inferior temporal lobe, the prefrontal lobe and frontal lobe. The results are similarity to the above t-test results with normal control group. Its reveal that the anisometropic amblyopia spontaneous activity defects in certain brain areas are related to acuity deficit. And ReHo is a new method to evaluate the level of visual deficit and the correlate is reasonable because the abnormal areas are basically in accordance with the T-test results. The negative correlations reflect the compensatory plasticity in parietal and medial frontal gyrus.

The findings are encouraging, while there still exist several limitations as follows: We need to enlarge the sample number in order to get a more reliable ReHo result. And we should classify the left or right eye impairments amblyopia separately. Further the strabismus amblyopia should be considered to get the more comprehensive understanding about the models of amblyopia.
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