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Regional homogeneity of the resting-state brain activity correlates with individual intelligence

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ABSTRACT

Resting-state functional magnetic resonance imaging has confirmed that the strengths of the long distance functional connectivity between different brain areas are correlated with individual differences in intelligence. However, the association between the local connectivity within a specific brain region and intelligence during rest remains largely unknown. The aim of this study is to investigate the relationship between local connectivity and intelligence. Fifty-nine right-handed healthy adults participated in the study. The regional homogeneity (ReHo) was used to assess the strength of local connectivity. The associations between ReHo and full-scale intelligence quotient (FSIQ) scores were studied in a voxel-wise manner using partial correlation analysis controlling for age and sex. We found that the FSIQ scores were positively correlated with the ReHo values of the bilateral inferior parietal lobules, middle frontal, parahippocampal and inferior temporal gyri, the right thalamus, superior frontal and fusiform gyri, and the left superior parietal lobule. The main findings are consistent with the parieto-frontal integration theory (P-FIT) of intelligence, supporting the view that general intelligence involves multiple brain regions throughout the brain.

The relationship between brain and intelligence is a question that attracts many researchers, endeavored to uncover the mysterious veil by using diverse neuroimaging techniques from structure to function. Structural magnetic resonance imaging (MRI) studies have revealed that intelligence was correlated with the total brain volume [1,19,22,24,31], the gray matter volume or density of the prefrontal, parietal and temporal cortical regions [12,20]. Diffusion tensor imaging (DTI) has shown that the integrity of some specific white matter fiber tracts is associated with intelligence [35,29,6,5]. Moreover, DTI investigation on the brain structural network also confirmed that the higher brain network efficiency results in the higher intelligence [16]. Task-based functional MRI (fMRI) has been widely used to study the underlying basis of intelligence, and revealed that activities of some brain regions, especially the parietal and frontal lobes were correlated with intelligence [14]. Recently, resting-state fMRI (rs-fMRI) has been used to study the relationship between the functional connectivity and intelligence. Song et al. [27] have found the positive correlations between individual intelligence scores and the strengths of the functional connectivities between the dorsolateral prefrontal cortex (DLPFC) and a variety of brain areas. Additionally, a positive relationship between intelligence and the efficiency of the resting-state functional network have also been reported [30]. So far, the previous rs-fMRI studies on intelligence have focused either on the efficiency of the whole brain or on the long-distance interregional connectivity. However, there is lack of a study focused on the association between the resting-state local connectivity of the brain and intelligence, which might facilitate the identification of the core brain areas underlying intelligence. In the present study, we used the regional homogeneity (ReHo) as a measure for assessing the local connectivity to investigate the correlation between local connectivity and intelligence.

The ReHo is proposed by Zang et al. [36], which measures the regional homogeneity of the spontaneous blood oxygenation level dependent (BOLD) fluctuations during rest. Unlike the functional connectivity focuses on the long-distance interregional temporal correlations of BOLD signals, the ReHo targets on the local synchronization of voxels within a specific brain area. In this method, Kendall's coefficient of concordance (KCC) [15] was used for measuring the correlation of the time series of a given voxel with its nearest neighbors voxels in a voxel-wise way based on the assumption that significant brain activities would more likely occur in clusters than in a single voxel. The formula to calculate the KCC value has been expounded in the previous study which firstly proposed the ReHo method [36]. In the past several years, the ReHo has been used to study a variety of populations including healthy

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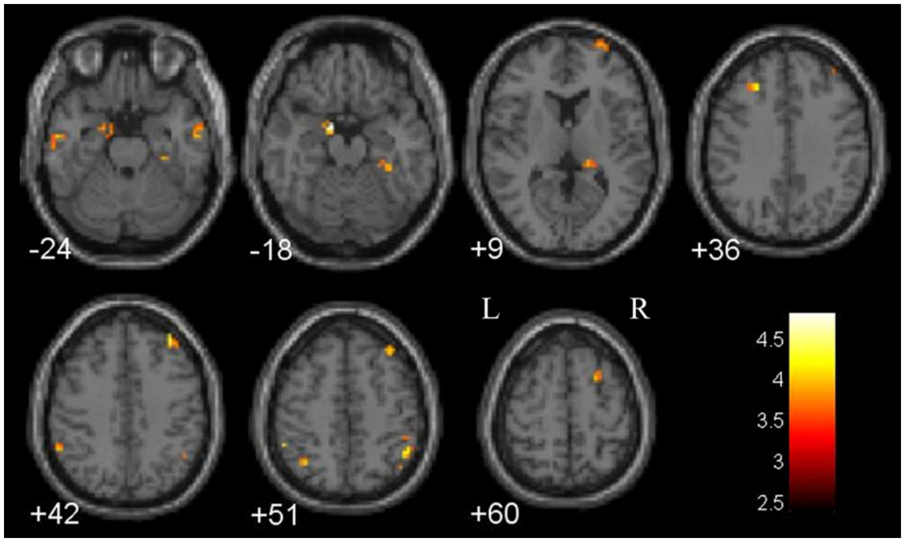

Fig. 1. Brain regions whose ReHo values show correlations ($P < 0.05$, corrected) with the FSIQ scores in 59 healthy adult subjects as revealed by partial correlation analysis controlling for sex and age.

aging [33], schizophrenia [17], depression [34], Parkinson's disease [32], Alzheimer's disease [13], Autism spectrum disorders [21,26] and attention deficit hyperactivity disorder [4,37].

In the present study, 59 healthy right-handed subjects (29 males and 30 females; mean age = 24.6 ± 3.5years, range from 18.5 to 33.3 years) were included. All subjects signed an informed consent form approved by the local Medical Research Ethics Committee. The intelligence of each subject was measured by full-scale intelligence quotient (FSIQ) derived from the Chinese Revised Wechsler Adult Intelligence Scale (WAIS-RC) [10]. The FSIQ score is based on performance of all 11 subtests according to age-based norms. The range of the FSIQ of our subjects was from 90 to 138 with a mean of 119.4 ± 13.9.

MR images were acquired on a 3.0 T MR scanner (Magnetom Trio, Siemens, Erlangen, Germany). Foam pads were used to reduce head movements and scanner noise. Resting-state fMRI scans were performed by an echo planar imaging (EPI) sequence with scan parameters of repetition time = 2000 ms, echo time = 30 ms, flip angle = 90°, matrix = 64 × 64, field of view = 220 mm × 220 mm, slice thickness = 3 mm, and slice gap = 1 mm. Each brain volume comprised 32 axial slices and each functional run contained 270 volumes. During fMRI scans, all subjects were instructed to keep their eyes closed, relax and move as little as possible.

All preprocessing steps were carried out using the statistical parametric mapping (SPM2, http://www.fil.ion.ucl.ac.uk/spm). The first 10 volumes of each functional time series were discarded for the magnetization equilibrium. The remaining 260 images were corrected for time delay between different slices and realigned to the first volume. Head motion parameters were computed by estimating translation in each direction and the angular rotation on each axis for each volume. Each subject had a maximum displacement in any of the cardinal direction (*x*, *y*, *z*) less than 1 mm, and a maximum spin (*x*, *y*, *z*) less than 1°. Following this step, all data were spatially normalized to the standard EPI template and interpolated to 3 mm × 3 mm × 3 mm cubic voxels and smoothed with a 4-mm full width at half maximum (FWHM). Then, several sources of spurious variances including the estimated motion parameters, linear drift and global average BOLD signals were removed from the data through linear regression [8,11]. Finally, a temporal filter (0.01–0.08 Hz) was performed to reduce the effect of low-frequency drifts and high-frequency noise.

At a given voxel, ReHo was defined as the KCC of the time series of this voxel with those of its 26 nearest neighbors. Individual ReHo maps were generated by calculating KCC within a gray matter mask in a voxel-wise way by the REST software (http://restfmri.net/forum/index.php). When the center cube was on the edge of the gray matter mask, we only calculated ReHo for a voxel with all of its 26 nearest voxels within the gray matter mask. The normalization step of dividing KCC of each voxel by the mean whole brain KCC were not performed since this would reduce the variance of the ReHo values of this voxel across subjects.

Considering the possible influence of sex and age on the correlation analysis between the ReHo and FSIQ, we performed partial correlation analysis adjusted for sex and age to assess the correlations between the FSIQ scores and the ReHo of the brain across all subjects in a voxel-wise manner. Then, a combined threshold of contrast maps was set at $P < 0.01$ for each voxel and a cluster size of at least 10 voxels, resulting in a corrected threshold of $P < 0.05$, determined by Monte Carlo simulation (AlphaSim program in AFNI software, http://afni.nimh.nih.gov/. Parameters: single voxel $P = 0.01$, FWHM = 4 mm, cluster connection radius r (mm) = 6.00; with a gray matter mask and a resolution of 3 mm × 3 mm × 3 mm).

The FSIQ scores were positively correlated with the ReHo values of the bilateral inferior parietal lobules, middle frontal, parahippocampal and inferior temporal gyri, the right thalamus, superior frontal and fusiform gyri, and the left superior parietal lobule (Fig. 1 and Table 1). These results were consistent with previous reported parieto-frontal integration theory (P-FIT) of intelligence [14]. There were no brain areas whose ReHo values were negatively correlated with intelligence scores.

To our knowledge, this is the first study focused on the relationship between brain local connectivity and intelligence in healthy subjects at rest. We found that the ReHo values of brain areas of the frontal [Brodmann areas (BAs) 6, 8, 9, 10, 46, 47], parietal (BAs 7, 39, 40) and temporal (BAs 20, 21, 28, 30, 34, 37) lobes were positively correlated with the FSIQ scores. The associations between these brain areas and intelligence have reported in many previous studies. Voxel-based morphometry study found that larger gray matter volumes in the frontal (BAs 9, 10, 46), temporal (BAs 21, 22, 37, 42) and parietal (BAs 3, 43) lobes were associated with higher IQ in healthy adults [12]. Task-based functional neuroimaging study on healthy adults have found that cognitive tasks activated brain areas including the DLPFC (BAs 9, 46), inferior parietal lobule (BAs 39, 40), anterior cingulate, inferolateral temporal (BAs 21, 37) and occipital (BAs 18, 19) cortices [7]. Even during resting-state, the individual intelligence scores were correlated with the strengths of the func-

Table 1
Brain areas whose regional homogeneity showing significant correlation with FSIQ scores across subjects.

Brain areas	Brodmann areas	Peak *t* values	Peak correlation MNI (*x*, *y*, *z*)	Cluster size (voxels)
Right middle frontal gyrus	9/46	3.95	33, 42, 42	31
Right middle frontal gyrus	10	2.96	21, 66, 12	19
Right middle frontal gyrus	47/46	4.07	42, 51, −12	18
Left middle frontal gyrus	9	3.68	−27, 30, 36	14
Right superior frontal gyrus	8/6	3.27	21, 9, 60	13
Right inferior parietal lobule	40/39	3.69	48, −51, 51	32
Left inferior parietal lobule	40	3.98	−54, −45, 54	13
Left superior parietal lobule	7	3.5	−36, −60, 51	11
Left parahippocampal gyrus	28/34	4.82	−15, −3, −18	33
Right parahippocampal gyrus	30/37	4.19	30, −30, −21	21
Right inferior temporal gyrus	20	3.18	45, −9, −36	15
Left inferior temporal gyrus	20/21	3.48	−60, −9, −24	10
Right fusiform gyrus	21/20	3.54	60, −6, −27	22
Right thalamus		3.04	15, −30, 9	10

tional connectivities between the DLPFC (BA 46) and a variety of brain areas including the frontal (BAs 6, 9, 10, 46) and parietal (BA 40) lobes [27]. As shown in a review, Jung and Haier [14] reviewed 37 modern neuroimaging studies and proposed the parieto-frontal integration theory (P-FIT) of intelligence. The intelligence-related brain areas include the DLPFC (BAs 6, 9, 10, 45, 46, 47), the inferior (BAs 39, 40) and superior parietal (BA 7) lobe, the anterior cingulate (BA 32), and regions within the temporal (BAs 21, 37) and occipital lobes (BAs 18, 19). Thus, most of brain areas found in our study were overlapped with the P-FIT model.

The bilateral parahippocampal gyri (PHG) and right thalamus were the only two brain areas that were reported in our study but were not integrated into the P-FIT model. Monkey study has found that the PHG plays an important role in memory function and is a critical component of the medial temporal lobe memory system [28]. Lesion studies of human brain have also confirmed the importance of the PHG in memory processes [2,23]. Since memory is an important component of individual intelligence, it is not surprising that local connectivity of this region correlates with intelligence. The thalamus is an important relay between a lot of subcortical areas and the cerebral cortex. It receives most of the sensory signals and sends them to the corresponding cortical areas. A previous study has reported that gray matter density in the thalamus was positively correlated with FSIQ [9], which supports our finding of the association between the thalamic local connectivity and intelligence.

In the present study, we used the ReHo as a measure of the regional coherence of the spontaneous BOLD fluctuations. As stated by Van Rooy et al. [25], the synchronized oscillatory activity in the cerebral cortex is essential for spatiotemporal coordination and integration of activity of anatomically distributed but functionally related neural elements. Buzsaki and Draguhn [3] suggested that neuronal synchrony may facilitate the coordination and organization of information processing in the brain across several spatial and temporal ranges. Fox et al. [8] also agreed with the notion that neuronal synchronization may efficiently organize the information processing of the brain. Moreover, Long et al. [18] provided convergent evidence that high intra- as well as inter-regional synchronization of spontaneous activity in some brain areas could account for the increased efficiency of transferring information both within nodes and across nodes in the network. From this perspective, we suggest that relative higher ReHo of the brain regions may facilitate information process in them, which may be one of the underlying bases for a relatively higher individual intelligence. An alternative understanding for the associations between the local connectivity and intelligence is that it just reflects that these brain areas are constantly processing cognition-related information.

In the present study, we used the measure of ReHo to study the relationship between local connectivity and intelligence. The brain regions whose ReHo values were positively correlated with FSIQ were largely overlapped with the brain regions of the P-FIT model. Thus we suggest that general intelligence involves multiple brain regions throughout the brain, especially the frontal, parietal and temporal lobes.

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