

Brain spontaneous functional connectivity and intelligence

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Many functional imaging studies have been performed to explore the neural basis of intelligence by detecting brain activity changes induced by intelligence-related tasks, such as reasoning or working memory. However, little is known about whether the spontaneous brain activity at rest is relevant to the differences in intelligence. Here, 59 healthy adult subjects (Wechsler Adult Intelligence Scale score, 90–138) were studied with resting state fMRI. We took the bilateral dorsolateral prefrontal cortices (DLPFC) as the seed regions and investigated the correlations across subjects between individual intelligence scores and the strength of the functional connectivity (FC) between the seed regions and other brain regions. We found that the brain regions in which the strength of the FC significantly correlated with intelligence scores were distributed in the frontal, parietal, occipital and limbic lobes. Stepwise linear regression analysis also revealed that the FCs within the frontal lobe and between the frontal and posterior brain regions were both important predictive factors for the differences in intelligence. These findings support a network view of intelligence, as suggested in previous studies. More importantly, our findings suggest that brain activity may be relevant to the differences in intelligence even in the resting state and in the absence of an explicit cognitive demand. This could provide a new perspective for understanding the neural basis of intelligence.

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Introduction

The neural basis of intelligence has been investigated for many years. Researchers have found, using various neuroimaging paradigms that have ranged from the structural (Colom et al., 2006; Gong et al., 2005; Haier et al., 2004; Shaw et al., 2006) to functional imaging (Boivin et al., 1992; Esposito et al., 1999; Fangmeier et al., 2006; Gray et al., 2003; Haier, 2003; Haier et al., 1988; Lee et al., 2006; Prabhakaran et al., 1997), that both frontal and posterior brain regions are associated with intelligence. As a result, it is widely believed that a brain network characterized by interactions between multiple brain regions is likely to be the neural basis of intelligence.

Most of the brain's energy consumption is devoted to ongoing metabolic activity, namely spontaneous neuronal activity not clearly associated with any particular stimulus or task (Raichle, 2006). Although the neurobiological implications of the spontaneous neuronal activity are not very clear, researchers have found that spontaneous fluctuations in the blood oxygenation level-dependent (BOLD) signal are coherent within a variety of brain systems, such as the somatomotor (Biswal et al., 1995); visual (Lowe et al., 1998); language processing (Hampson et al., 2002); auditory (van de Ven et al., 2004); attention (Fox et al., 2006), memory (Vincent et al., 2006) and default mode networks (Greicius et al., 2003). Moreover, a recent study reported that coherent BOLD spontaneous fluctuations were present even in anaesthetized monkey brains, which indicates that the functional architecture of the brain may be intrinsic, rather than limited to any particular stimulus (Vincent et al., 2007). Previous functional studies (for review, see Jung and Haier, (2007)) have strongly shown that the brain activity associated with a specific cognitive task was distinct among subjects with different levels of intelligence. This raises the question whether the spontaneous brain activity at rest, that is, without any particular task, is related to individual differences in intelligence.

Functional connectivity (FC), which studies temporal correlations between BOLD signals in different brain regions, has been widely used in fMRI studies. These temporal correlations suggest direct or indirect interactions between brain regions (Friston et al., 1993). The behavioral significance of BOLD FC has recently been investigated in

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studies not only associated with specific task (Hampson et al., 2006b; He et al., 2007) but also at rest (Hampson et al., 2006a; Liu et al., 2007; Seeley et al., 2007). The connectivity-behavior analysis is a technology for analysis of the correlations between the strength of FC and behavioral performance (Hampson et al., 2006b). The present study investigates the correlations between individual intelligence scores and the strength of the FC at rest.

The lateral prefrontal cortex has been found to be one of the most important brain regions supporting intelligent behavior (Gray and Thompson, 2004). In the present study, we took the bilateral dorsolateral prefrontal cortices (left and right DLPFC) as seed regions and separately measured the interregional FC between these seed regions and each voxel that we identified in all parts of the brain. Then we correlated the Wechsler full-scale intelligence quotient (FSIQ) scores with the strength of FC across subjects to search for the brain regions in which the strength of FC significantly correlated with FSIQ scores separately in the composite functional connectivity map and throughout the entire brain. Finally, stepwise linear regression was performed to predict FSIQ scores with the FC obtained from the searches.

Materials and methods

Subjects

Fifty-nine healthy right-handed subjects were included in this study. All subjects (29 males and 30 females; mean age = 24.6 years, SD = 3.5 years, range = 18.5–33.3 years) were recruited by advertisement. All subjects gave written informed consent, and this study was approved by the ethical committee of Xuanwu Hospital of Capital Medical University.

Intelligence testing

In the present study, the FSIQ score was used to assess individual intelligence using the Chinese Revised Wechsler Adult Intelligence Scale (WAIS-RC), since a factor analytic study showed that the FSIQ score accounted for about 90% of the variance in the general intelligence, or *g* factor (Jensen, 1980). The mean FSIQ of the subjects in this study was 119.4 (SD = 13.9) and the range was 90–138.

Imaging protocol

MR imaging was carried out using a 3.0-Tesla MR scanner (Magnetom Trio, Siemens, Erlangen, Germany). Functional images were collected axially by using an echo-planar imaging (EPI) sequence sensitive to BOLD contrast. The acquisition parameters are as follows: 32 slices, 2000/30 ms (TR/TE), 3.0/1.0 mm (thickness/gap), 220 × 220 mm (FOV), 64 × 64 (resolution within slice), 90° (flip angle). During the resting state scanning, the subjects were instructed to keep still with their eyes closed, as motionless as possible and not to think about anything in particular. For each subject, the fMRI scan during the resting state lasted for 9 min and 270 volumes were obtained.

Preprocessing

Image preprocessing was conducted using SPM2 (<http://www.fil.ion.ucl.ac.uk/spm>). The first 10 volumes of each subject were discarded. The remaining 260 functional scans were first corrected for within-scan acquisition time differences between slices and realigned to the first volume to correct for inter-scan movements. Next, the

functional scans were spatially normalized to a standard EPI template and resampled to the voxel size of 3 × 3 × 3 mm. Subsequently, the functional images were spatially smoothed with a Gaussian kernel of 4 × 4 × 4 mm full-width at half maximum. Then, linear regression was used to remove the influence of head motion, whole brain signals and linear trends (Fox et al., 2006, 2005; He et al., 2007; Tian et al., 2007). Finally, to reduce low-frequency drift and high-frequency noise, the fMRI data were temporally band-pass filtered (0.01–0.08 Hz) with AFNI (<http://afni.nimh.nih.gov/>). The parameters obtained during movement correction showed that the maximum displacement in the cardinal direction (*x*, *y*, *z*) was not greater than 1 mm, and the maximum spin (*x*, *y*, *z*) was not greater than 1° for each participant.

Definition of seed regions

The DLPFC generally refers to BA46 and the ventral part of BA9 and sometimes also includes BA10. This region is relatively unitary in function, but is difficult to anatomically delimit. In order to define the seed regions as precisely as possible, the left and right seed region were separately defined using WFU_PickAtlas (<http://fmri.wfubmc.edu/cms/software>) (Maldjian et al., 2003), which has been used in the previous studies (Schon et al., 2005; Williams et al., 2004; Zhou et al., 2007). We defined the left DLPFC seed region by intersecting BA46, the left middle frontal gyrus and gray matter in WFU_PickAtlas, and then resliced the generated regions into the same spatial resolution as the preprocessed fMRI images (3 × 3 × 3 mm) with the toolbox “Coregister” in SPM2. Thus, the resulting left seed region consisted of 31 voxels. Using the same procedure, the right DLPFC seed region was obtained with 57 voxels.

Individual functional connectivity maps

The functional connectivity analysis was performed separately for the left and right seed regions. Connectivity maps were produced by averaging the BOLD time series in a seed region, and then computing the Pearson's correlation coefficient between the seed average time series and those from each voxel in the brain. The resulting correlations were transformed to approximate Gaussian distribution using Fisher's *z* transformation (Press, 1992). This yielded a map representing the strength of the FC to the seed region in terms of the *z* values for each subject.

Composite functional connectivity maps

For each of the two seed regions, the respective individual *z*-valued functional connectivity maps were entered into a random effect one-sample *t*-test in a voxel-wise manner to determine the brain regions that showed significantly positive or negative correlation to the seed region. This yielded two composite functional connectivity maps, one for the left seed region and another for the right seed region. The two composite functional connectivity maps were both obtained with a threshold of $P < 0.05$ (FWE (family-wise error) corrected; $T = 5.41$, $df = 58$) and cluster size ≥ 270 mm³ (10 adjacent voxels).

Connectivity-behavior analysis

Connectivity-behavior analyses were separately performed for the left and right seed regions. For the left seed region, we firstly computed correlations between FSIQ scores and the *z*-valued strength of the FC across subjects in a voxel-wise manner. Then, to

evaluate the significance of the connectivity-behavior correlation in each voxel, the statistic $t(t = \frac{\sqrt{df}r}{\sqrt{1-r^2}})$ was computed, where r denotes to the Pearson's correlation coefficient between the FSIQ scores and the strength of the FC, and df is the degrees of freedom. Here, df was equal to 57. Thus, we obtained t map for the left seed region. Next, in the t map, we performed the searching procedure within two searching ranges, that is, the left composite functional connectivity map and the whole brain, to identify the brain regions in which the strength of the FC to the left seed region significantly correlated with FSIQ scores. Using the same procedure, we performed the connectivity-behavior analysis for the right seed region. For simplicity, we referred to the search in the composite func-

tional connectivity map as a *a priori* search and the search throughout the entire brain as the entire brain search.

In the *a priori* search, we restricted the searching range within the composite functional connectivity map. The composite functional connectivity map was comprised of brain regions that had significant FC to the seed region. So, using the *a priori* search, we could find the brain regions in which the strength of the FC to seed region was significantly correlated with FSIQ score. At the same time, the brain regions that were found in the *a priori* search may also show significant FC to the seed region. Thus, the *a priori* search may lose some information, for example, the condition whether more intelligent individuals recruit different/additional FC

Table 1
Functional connectivity showing significant correlation with FSIQ scores across subjects

Seed region		Connected region	BA	Size	Peak correlation MNI (x, y, z)	r	P	Previously reported ^a
<i>In the a priori search</i>								
L. DLPFC								
	Frontal	R.DLPFC	46/10	41	(39,39,12)	0.47	0.0002	Duncan et al., 2000
		R.IFGoper	wm	18	(33,24,-6)	0.45	0.0004	Lee et al., 2006
		R.IFG/MFG	9	15	(42,6,36)	0.43	0.0006	Lee et al., 2006
		L.DLPFC	46	18	(-48,33,21)	0.43	0.0006	Duncan et al., 2000
		R.SFG/MPFG	10	18	(15,60,15)	-0.38	0.0028	Haier et al., 2004
		L.MPFG	10	14	(-6,57,18)	-0.38	0.0033	Haier et al., 2004
		R.SFG/MPFG	10	20	(6,66,30)	-0.36	0.0046	Haier et al., 2004
	Parietal	R.IPL	40	34	(51,-42,54)	0.44	0.0006	Gray et al., 2003
R. DLPFC								
	Frontal	R.DLPFC	46	24	(42,39,9)	0.40	0.0015	Duncan et al., 2000
		L.DLPFC	46	16	(-45,30,27)	0.37	0.0043	Duncan et al., 2000
	Parietal	R.IPL	40	25	(51,-42,54)	0.41	0.0012	Gray et al., 2003
		L.IPL	40	12	(-54,-48,51)	0.40	0.0017	Gray et al., 2003
<i>In the entire brain search</i>								
L. DLPFC								
	Frontal	R.DLPFC	46/10	45	(39,39,12)	0.47	0.0002	Duncan et al., 2000
		R.IFGoper	wm	20	(33,24,-6)	0.45	0.0004	Lee et al., 2006
		R.IFG/MFG	9/6	36	(39,6,36)	0.44	0.0005	Gray et al., 2003
		L.MFG/PreG	wm	25	(-21,-21,57)	0.42	0.0010	-
		L.PreG	wm	22	(-36,0,24)	0.40	0.0017	-
		L.Frontoparietal region	wm	22	(-24,-24,45)	0.39	0.0025	-
		L.SFG/MPFG	10	38	(-18,69,15)	-0.48	0.0001	Haier et al., 2004
		R.SFG/MPFG	10	20	(6,66,30)	-0.36	0.0046	Haier et al., 2004
		L.Premotor cortex	wm	26	(-24,6,72)	-0.36	0.0048	-
	Parietal	R.IPL	40	38	(51,-42,54)	0.44	0.0006	Gray et al., 2003
	Occipital	B.LG	17/18	121	(3,-84,-3)	-0.42	0.0009	Duncan et al., 2000
		B.Cu	18	24	(-12,-81,18)	-0.38	0.0027	Duncan et al., 2000
	Limbic	R. HP	-	29	(27,-12,-18)	0.49	0.0001	Haier et al., 2004
R. DLPFC								
	Frontal	R.DLPFC	46	24	(42,39,9)	0.40	0.0015	Duncan et al., 2000
		L.Premotor cortex	wm	39	(-27,-3,57)	-0.40	0.0019	-
	Parietal	R.IPL	40	25	(51,-42,54)	0.41	0.0012	Gray et al., 2003
	Occipital	B.LG	18	71	(3,-87,-12)	-0.45	0.0003	Duncan et al., 2000
		L.Cu	18	20	(-6,-75,12)	-0.42	0.0011	Duncan et al., 2000
	Subcortex	R.Brainstem	-	30	(3,-15,-42)	0.51	0.0000	Haier et al., 2004
		L.Brainstem	-	23	(-3,-24,-42)	0.48	0.0001	Haier et al., 2004
		R.Caudate	-	28	(9,18,3)	0.42	0.0011	Haier et al., 2004

Size, number of $3 \times 3 \times 3$ mm voxels; r , Pearson's correlation coefficient between the strength of FCs and FSIQ scores; P , the significance for the corresponding r . Abbreviations: BA, Brodmann's area; L, left; R, right; B, bilateral; DLPFC, dorsolateral prefrontal cortex; MFG, middle frontal gyrus; IFG, inferior frontal gyrus; MPFG, medial frontal gyrus; SFG, superior frontal gyrus; PreG, precentral gyrus; IPL, inferior parietal lobules; Cu, cuneus; LG, lingual gyrus; HP, Hippocampus; IFGoper, inferior frontal gyrus opercular portions; wm, white matter; ^a, these regions have been reported in previous studies on the neural basis of intelligence, please see the text for details.

to support intelligent behavior than less intelligent ones. Accordingly, we extended the search range to the whole brain and performed the search in the entire brain.

In the *a priori* search, the single voxel threshold was set at $P < 0.01$ ($|t(57)| \geq 2.39$) and a minimum cluster size of 270 mm^3 (10 adjacent voxels) was used to correct for multiple comparisons. This yielded a corrected threshold of $P < 0.0035$ for the *a priori* search of the left seed region and $P < 0.004$ for the *a priori* search of the right seed region, as determined by Monte Carlo simulation (See program AlphaSim by D. Ward in AFNI software. Parameters were as follows: single P value = 0.01; FWHM = 4 mm; Cluster connection radius: $\text{rmm} = 6.00$; with a mask of the respective composite functional connectivity map). Similarly, in the entire brain search, a Monte Carlo simulation was used to correct for multiple comparisons. In this case, a larger cluster size threshold was adopted. The single voxel threshold was set at $P < 0.01$ ($|t(57)| \geq 2.39$) and a minimum cluster size was 540 mm^3 (20 adjacent voxels). This yielded a corrected threshold of $P < 0.0001$ (In AlphaSim, the parameters were as follows: the single P value = 0.01; FWHM = 4 mm; Cluster connection radius: $\text{rmm} = 6.00$; with the mask consisting of the within-brain regions in the EPI template with a resolution of $3 \times 3 \times 3 \text{ mm}$).

Thus, through these searches, we identified the brain regions in which the strength of the FC to the seed region was significantly correlated with the FSIQ score.

Stepwise linear regression analysis

After finding the FCs that correlated with intelligence differences, we further investigated which set of FCs, among the searched FCs, were the most predictive for intelligence differences and how much the set of FCs accounted for intelligence differences. Since the *a priori* search found differences in the magnitude of the FC and the entire brain search could additionally find differences in the pattern of the FC, we constructed a regression model for each of the two searches separately. In the two models, the dependent variable was the FSIQ score, and the independent variables were the average strength of the FC in each cluster obtained from the corresponding search. The searched FCs to the left seed region and the searched FCs to the right seed region were all involved in the resulting model.

Stepwise linear regression was carried out using SPSS 13.0 (SPSS Inc., Chicago, IL, USA). The FSIQ score and the average strengths of all the FCs included in the model were normally

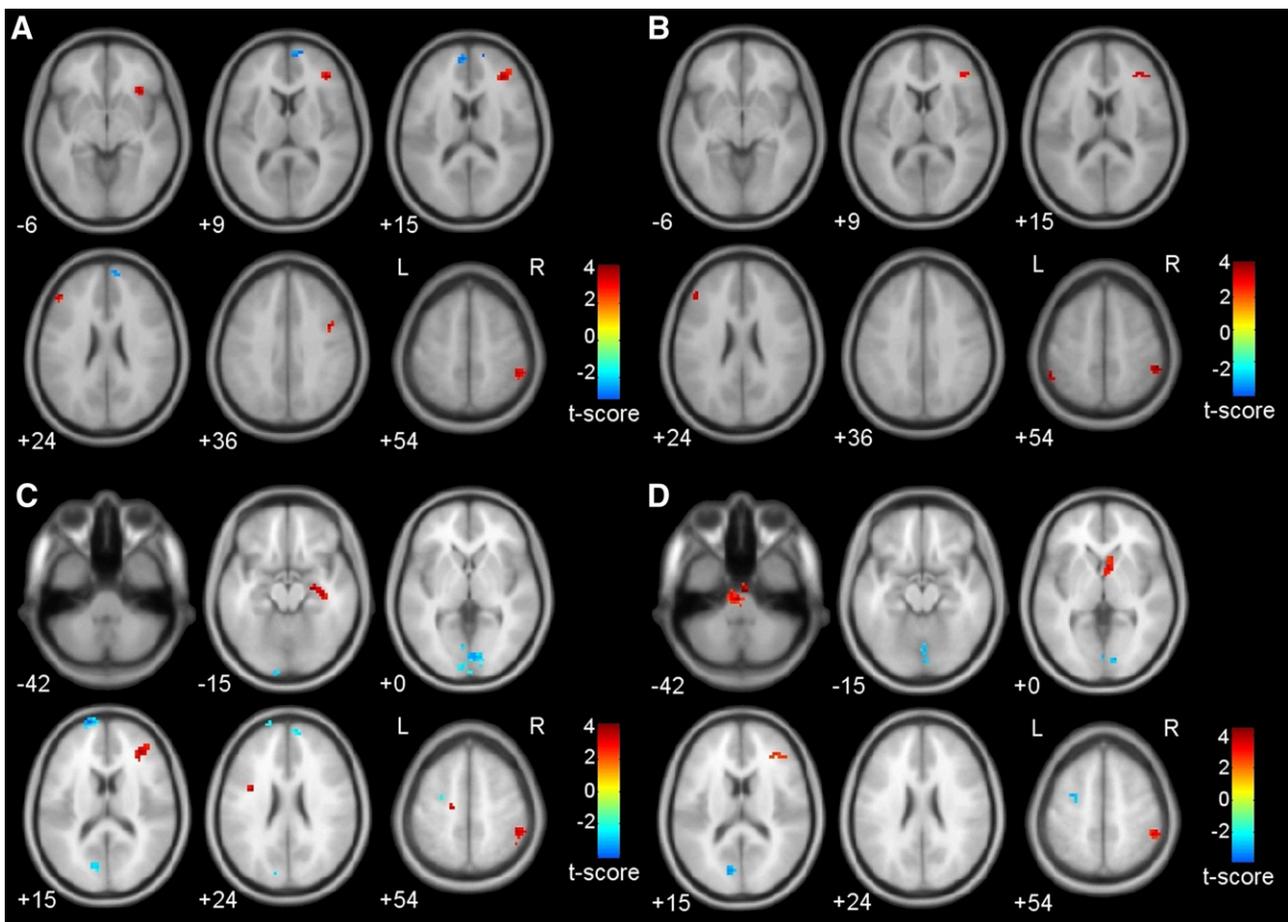


Fig. 1. Brain regions in which the strength of functional connectivity to the seed region is significantly correlated with the FSIQ score. The seed region is the left DLPFC in A and C, and the right DLPFC in B and D. A and B are obtained from the *a priori* search, and C and D are from the entire brain search (A, B: in the *a priori* search, single voxel threshold $P < 0.01$, adjacent size ≥ 10 voxels, corrected threshold $P < 0.0035$ for left *a priori* search and $P < 0.004$ for right *a priori* search; C, D: in the entire brain search, single voxel threshold $P < 0.01$, adjacent size ≥ 20 voxels, corrected threshold $P < 0.0001$). Positive correlations are shown in warm colors, while negative correlations are shown in cold colors.

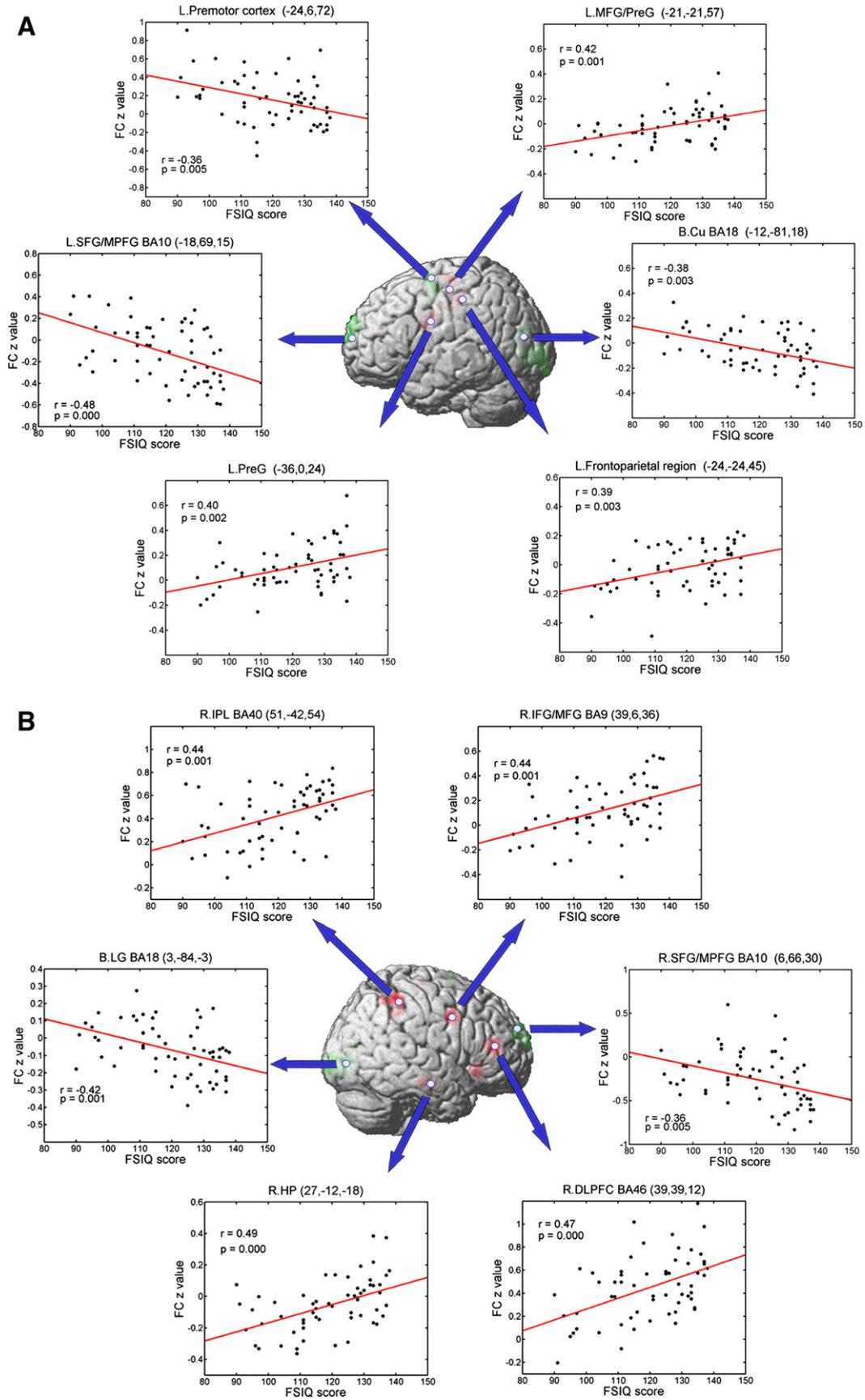


Table 2
Stepwise linear regression

Stepwise multiple regression					Predictor variable		
Model					Variable	Beta	P
Adjusted R^2	F	df	P	Durbin–Watson			
<i>In the a priori search</i>							
0.473	16.452	3,55	0.000	1.763	L.DLPFC_R.DLPFC	0.379	0.001
					L.DLPFC_R.IPL40	0.339	0.001
					L.DLPFC_L.DLPFC	0.27	0.013
<i>In the entire brain search</i>							
0.73	27.176	6,52	0.000	2.116	R.DLPFC_R.Brainstem	0.211	0.018
					R.DLPFC_B.LG18	−0.368	0.000
					L.DLPFC_R.HP	0.244	0.003
					L.DLPFC_L.Frontoparietal region	0.218	0.016
					L.DLPFC_R.IPL40	0.19	0.015
					R.DLPFC_R.Caudate	0.172	0.027

Variable represents the average strength of the FC between the seed region and the connected regions.

distributed according to Komologrov–Simirov test of normality ($P > 0.05$). The P to enter in the stepwise selection process was set to 0.05, while the P to remove was set to 0.1.

Results

The composite functional connectivity maps for the left and right seed regions are shown in Fig. S1 in the Supplementary materials. As shown in Fig. S1, positive correlations were apparent in the bilateral frontal lobe and the superior parietal lobe, while negative correlations were apparent in the anterior and posterior cingulate cortices and the angular gyrus. These results were consistent with those reported in previous studies (Fox et al., 2005; Greicius et al., 2003).

Results from the connectivity-behavior analysis are summarized in Table 1 and shown in Fig. 1. In the *a priori* search, we found that some brain regions in which the strength of the FC to the seed regions were significantly correlated with the FSIQ score were located in the frontal and parietal lobes, including the inferior frontal gyrus (IFG) (BA9), medial frontal gyrus (MPFG) (BA10), middle frontal gyrus (MFG) (BA9, 46), superior frontal gyrus (SFG) (BA10) and the inferior parietal lobules (IPL) (BA40). Similarly in the entire brain search, we observed that some FCs, such as IPL (BA40), MPFG and IFG (BA10), found in the *a priori* search still showed significant correlations with FSIQ scores at a more stringent threshold. Additionally, we found that many brain regions, including the brainstem, hippocampus, caudate, cuneus (Cu) (BA18) and lingual gyrus (LG) (BA17, 18), showed significant correlations between the strength of their connectivity to the seed regions and the FSIQ scores. To illustrate the correlations between the FSIQ scores and the strength of the FC across subjects, the scatter plots of the FCs obtained in the entire brain search of the left seed region are shown in Fig. 2.

The results in the stepwise linear regression analysis are summarized in Table 2 and shown in Fig. 3. Three FCs were

retained in the regression model of the *a priori* search (adjusted $R^2=0.473$; $F=16.452$; $df=3,55$; $P<0.000$), while 6 FCs were retained in the regression model of entire brain search (adjusted $R^2=0.73$; $F=27.176$; $df=6,52$; $P<0.000$).

Discussion

To our knowledge, this is the first study to investigate the relationship between spontaneous BOLD signal fluctuations and intelligence differences. A prominent difference between the present study and previous functional studies on the neural basis of intelligence was that the present study was conducted at rest and in the absence of any explicit memory, reasoning or problem solving demand. Using connectivity-behavior analysis, we found that the strength of some specific FCs was significantly correlated with intelligence differences across subjects. These FCs were distributed both within the frontal lobe, and between the frontal and the parietal, occipital and limbic lobes. These finding suggest that the interactions within the frontal lobe and between the frontal and posterior brain regions were both closely associated with intelligence differences, even when no explicit reasoning or working memory demand was required.

Although the neural basis of intelligence is not clearly understood, individual differences in intelligence may have a structural basis. Using VBM analysis in two independent samples, Haier and colleagues (Colom et al., 2006; Haier et al., 2004) found that greater amounts of gray matter were associated with higher IQ in discrete brain regions, including the frontal (BA10, 46, 9), temporal (BA21, 37, 22, 42), parietal (BA40, 43, 3), occipital (BA19) lobes and the subcortex structure, such as the brainstem and caudate. These findings suggest that the volume of regional gray matter showing significant correlations with individual levels of intelligence appear to be extensively distributed in the brain. These regions overlapped with our results, which appears to provide neuroanatomical evidence for the findings of the present functional study.

Fig. 2. Correlations between FSIQ scores and the strength of the FC to the left seed regions across subjects. The brain regions were obtained in the entire brain search of the left seed regions. In the left (A) and right (B) hemispheres, positive correlations are shown in red, while negative correlations are shown in green.

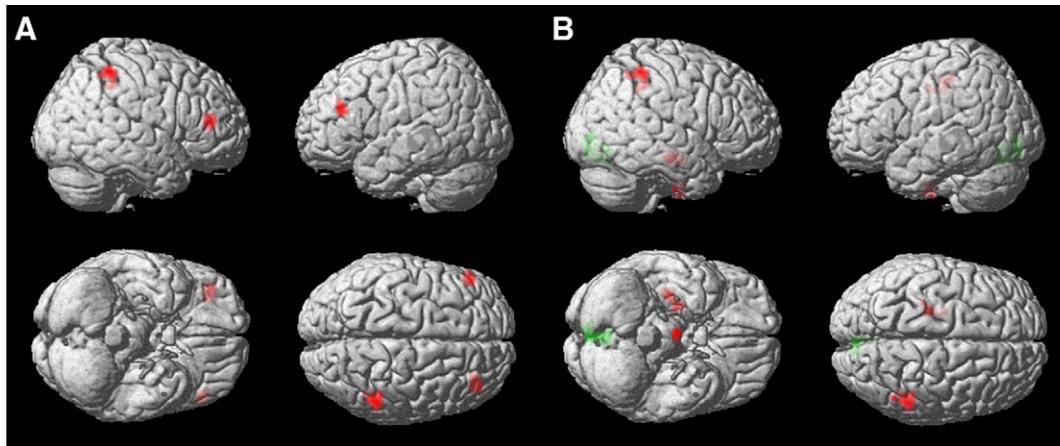


Fig. 3. Brain regions in which the strength of the FC to the bilateral seed regions is the most predictive for the variation in FSIQ scores. These data were obtained from stepwise multivariable linear regression analysis based on the average strength of the FC obtained from the prior search (shown in A, adjusted $R^2=0.473$; $F=16.452$; $df=3,55$; $P<0.000$) and the entire brain search (shown in B, adjusted $R^2=0.73$; $F=27.176$; $df=6,52$; $P<0.000$). The red means that the strength of the FC here has a positive correlation with the FSIQ score; while green means that the correlation is negative.

Many functional neuroimaging studies associated with intellectually demanding tasks have been conducted to investigate the neural basis of intelligence. The tasks ranged from working memory (Gray et al., 2003) to a variety of reasoning tasks, including verbal and non-verbal reasoning (Duncan et al., 2000; Esposito et al., 1999; Fangmeier et al., 2006; Haier et al., 1988; Lee et al., 2006; Prabhakaran et al., 1997). Although completely consistent activated brain regions were not derived from these studies due to differences in the tasks and the cohort of subjects, taken together they suggest that specific brain regions may be related to the neural basis of intelligence. For example, Gray et al. (2003) found that more intelligent subjects had greater event-related neural activity in discrete brain regions, such as lateral prefrontal cortex (BA46, 44, 10, 9), dorsal anterior cingulate (BA24), parietal lobe (BA40, 31) and temporal lobe (BA22, 39) during a challenging 3-back working memory task. Additionally, that study found that the DLPFC and the parietal cortex (BA40) might mediate the relationship between individual differences in intelligence and behavioral performance. Esposito et al. (1999) found converging activation across tasks within the DLPFC (BA9, 46), IPL (BA39, 40), anterior cingulate (BA32), inferior/lateral temporal lobe (BA21, 37) and occipital cortices (BA18, 19) in a PET study with two non-verbal reasoning tasks. Using a reasoning task, Lee et al. (2006) found that the frontal lobe, including the DLPFC, and the posterior brain regions were significantly activated in both gifted and average subjects; more importantly, the study found the posterior brain regions (BA7, 40, 19) showed stronger activation in the gifted subjects in comparison to the average participants. These findings suggest that the interactions between the frontal and posterior brain regions play an important role in the neural basis of intelligence. This is consistent with our findings derived from resting state fMRI analysis.

Intriguingly, Jung and Haier (2007) recently reviewed 37 neuroimaging studies associated with the neural basis of intelligence ranging from structural imaging (DTI and MRI) to functional imaging (PET, fMRI and Magnetic Resonance Spectroscopy) paradigms, and found that the variations in a distributed network were closely related with individual differences in intelligence. They proposed the Parieto-Frontal Integration Theory (P-FIT) to describe this brain network, which included dorsolateral prefrontal

cortex (BA6, 9, 10, 45, 46, 47), the inferior (BA39, 40) and superior parietal (BA7) lobes, the anterior cingulate (BA32), and regions within the temporal (BA21, 37) and occipital lobes (BA18, 19). We noted that the brain regions that were found to be associated with the differences in intelligence in the present study were similar to the P-FIT.

In the present study, we found a resting state brain network associated with the differences in intelligence. The brain regions involved in this network have been commonly reported in previous structural and functional studies on the neural basis of intelligence. This indicates that the brain activity in the network appears to be related to differences in intelligence even at rest, and that individuals with higher intellectual ability may process information differently from the ones with lower intellectual ability, even when no explicit reasoning or working memory demand was required. We suggest that consistent or reciprocal activity in the network, both under specific task conditions and in the resting state, would be a likely intrinsic mechanism for supporting intelligent behavior.

Some pioneering studies that investigated the relationship between resting state FC and human behavioral have been done. For example, Hampson et al. (2006a) investigated the relationship between the default mode network and working memory performance. Seeley et al. (2007) investigated the relationship between the salience network and a prescan anxiety rating, and the relationship between the executive control network and a subject's executive ability. These studies suggested that spontaneous brain activity appears to be related to individual cognitive ability. This was further investigated in the present study. However, there were some significant differences between the present study and previous studies. First, previous studies mainly focused on a specific cognitive ability and a relevant neural network. The present study investigated intelligence, a very general mental capability. Second, the present study was mainly based on a method of exploration and searching. Thus far, researchers have known about some of the brain regions associated with intelligence, for example, the lateral frontal cortex and parts of the parietal, temporal and occipital lobes. But, how the neural network is associated with intelligence is not very clear yet. The present study took the DLPFC, a brain area clarified by others as

being important for intelligence, as the seed region. We searched the FCs that correlated with intelligence differences and then investigated the most predictive FCs for intelligence differences. These might be suggestive of the interactions between brain regions that are associated with intelligence and the influence of the interactions to intelligence differences. On the other hand, the search, especially the entire brain search, found a few brain areas, which had not been reported in previous studies (see Table 1). These brain areas were mainly located in white matter and in the intersection between lobes. We were unable to rule out the possibility that these areas could have resulted from the effects of noise, the error of registration, the limitations of having a small sample size or other reasons. Further validation is required. Additionally, future work will investigate other regions of interest. These future studies should provide additional information that will be needed in order to make a wider investigation of the neural basis of intelligence.

Intelligence is a general cognitive mental ability and WAIS-RC includes a variety of cognitive tests (Wechsler et al., 1981). In the Supplementary materials, we separately investigated the correlation between the strength of FC and two subscores of WAIS-RC (verbal and non-verbal). We found that most of the results with the two subscores overlapped with those with FSIQ score, except the results of non-verbal subscore in the entire brain search (for detail, see Tables S1, S2, S3 and Figs. S2, S3, S4). These differences should result from the different neural network mediating different cognitive abilities. However, we found that there were plenty of brain areas which were both associated with the two subscores. So, we think that the connectivity-behavior analysis with FSIQ score could suggest the general brain areas associated with intelligence.

In particular, as shown in Fig. 2, some FCs showing a significant correlation between their strength and FSIQ scores were between DLPFC and IPL, IFG/MFG, MPFG and premotor cortex. These brain regions are associated with the executive functions (Miller and Cohen, 2001; Seeley et al., 2007). This suggests that the coordination between the brain regions within executive control network might be an important neural basis of general intelligence. Our resting state fMRI study further indicates that the strength of functional connectivity within executive control network could be associated with intelligence differences even in the resting state.

In conclusion, using connectivity-behavior correlation analysis, we found that the FCs significantly correlated with intelligence differences were distributed not only within the frontal lobe, but also between the frontal lobe and posterior brain regions. This supports the hypothesis that the brain network associated with intelligence is likely to be characterized by the interaction between multiple brain regions. More importantly, we found that brain activity in the network appears to be relevant to intelligence differences even in the resting state and in the absence of explicit reasoning or working memory demand, which could reflect an underappreciated aspect of the intrinsic brain functional organization that is associated with intelligence. This would provide a new perspective for understanding the neural basis of intelligence.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.neuroimage.2008.02.036](https://doi.org/10.1016/j.neuroimage.2008.02.036).

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