



## Sex differences in the intrinsic reading neural networks of Chinese children

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### ABSTRACT

Sex differences in reading performance have been considered a relatively stable phenomenon. However, there is no general agreement about their neural basis, which might be due to that sex differences are largely influenced by age. This paper focuses on the sex differences in the reading-related neural network of Chinese children and its interaction with age. We also attempt to predict reading abilities based on neural network. Fifty-three boys and 56 girls (8.2–14.6 years of age) were recruited. We collected their resting-state fMRI and behavioural data. Restricted sex differences were found in the resting-state reading neural network compared to extensive age by sex interaction effect. Specifically, the interactions between sex and age indicated that with increasing age, girls showed greater connectivity strength between visual orthographic areas and other brain areas within the reading network, while boys showed an opposite trend. After controlling age, the prediction models of reading performance for the girls mainly included interhemispheric connections, while the intrahemispheric connections (particularly the phonological route) mainly contributed to predicting the reading ability for boys. Taken together, these findings suggest that sex differences in reading neural networks are modulated by age. Partialling out age, boys and girls also show the stable sex differences in relationship between reading neural circuit and reading behaviour.

### 1. Introduction

The study of sex differences in language ability can be traced back to the twentieth century (Etchell et al., 2018). Numerous studies have attempted to explore sex differences in language skills. Recently, the PISA (Programme for International Student Assessment) and other large-scale studies have consistently shown that sex differences in reading performance might be a relatively stable predictor cross cultures and time (Wilsenach and Makaure, 2018). Specifically, the sex differences feature as the reading advantages of females compared to males, which cannot be explained by the socio-economic factors including the level of economic development, gender equality, education or the teaching method, but more likely by the biologically cognitive difference between the two sexes (Stoet and Geary, 2013, 2015; Chiu and McBride-Chang, 2006). Furthermore, research on dyslexia also showed sex differences in incidence rates and behaviour patterns (Logan and Johnston, 2010; Krafnick and Evans, 2019). Thus, the sex differences in reading might be a relatively stable phenomenon.

Sex differences in reading performance may be age-related. A study found that girls perform better in reading comprehension, phonological

development and phonological awareness than boys, and the gap is larger in grade 2 than in kindergarten (Chipere, 2014). A literature review (Etchell et al., 2018) also suggests that reading-related sex differences in the brain are not independent of age. For example, whether there are sex differences in the development of IFG, a reading related region, depends on age. Therefore, when we study sex differences, it is necessary to consider age factor at the same time (Etchell et al., 2018). Similarly, a more recent study in women showed that activation in the left medial orbitofrontal cortex did not significantly change with increasing age during a single-word reading task (18–78), but activation decreased for nonwords task with age. However, in men, the activation significantly decreased with increasing age but increased for nonwords during a reading task. The results indicate that the sex difference in orthography-phonology conversion is related to age (Graves et al., 2019). Consequently, it is important for us to study the interaction between sex differences and age in reading to identify the sex differences that interact with age and independent of age, which will deepen our understanding of sex differences in the development of reading.

Reading is a complex cognitive skill that needs to be acquired through continuous learning. The dual routes theory of reading holds

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that the development of reading is a process of integrating orthography, phonetics and semantics (Coltheart et al., 2001). In both children and adults, with more reading experience, the reading process becomes increasingly automatic. As becoming more proficient readers like adults, children gradually shift their reading-related pathway from orthographic-phonetic-semantic pathways to orthographic-semantic pathways in both alphabetic (e.g., English) and logographic (e.g., Chinese) reading (Booth et al., 2004; Church et al., 2008; Cao et al., 2009). Their reading-related brain regions are also developing, which is reflected not only by the different activation patterns of those regions, but also by the changes in connectivity patterns among reading-related brain regions (Dehaene et al., 2015; Kristanto et al., 2020). For example, a meta-analysis showed that children activated the bilateral supplementary motor area (SMA) and left inferior frontal gyrus (IFG) more than adults, while adults activated the bilateral cerebellum, left middle frontal gyrus (MFG) and middle occipital gyrus (MOG) regions more than children (Martin et al., 2015). In addition, a longitudinal study found that with age, the improvement of reading ability is related to the connection between the inferior occipital and fusiform cortex (Wise Younger et al., 2017). To thoroughly investigate the neural mechanism of reading, age is a very important factor to consider.

Resting-state fMRI is a task-independent experimental method. Studies have shown that human brain activity at rest is not a meaningless noise. On the contrary, the spontaneous activity of the brain is an important part of maintaining normal human activities (Fox and Greicius, 2010; Mitra and Raichle, 2016). Resting-state activity patterns of the brain can also reveal some group characteristics and individual differences (Fox and Raichle, 2007). In addition, the study of resting-state spontaneous brain activity has deepened our understanding of brain structure and functional organisation (Buckner et al., 2008; Biswal et al., 2010). Specifically for reading, many studies have also investigated its resting-state functional connectivity network. For example, Koyama and others found that children and adults have different network connectivity patterns related to reading performance (Koyama et al., 2011). Researchers have also used this method to explore the differences in resting-state functional connectivity between normal controls and people with dyslexia (Zhou et al., 2015; Schurz et al., 2015). One study reported that RSFC was related to the response time of the single Chinese character reading task. Furthermore, this study also reported that although most functional connections were similar in both sexes, only in female adults did the functional connection between the left inferior frontal gyrus and right thalamus/bilateral precuneus lobes show significant negative correlations with reading performance (Wang et al., 2012). However, sex differences and the development of sex differences in the intrinsic neural circuits of reading remain unclear, especially for children and adolescents.

Therefore, this study aimed to explore the interaction between sex and age to help deepen our understanding of sex differences in reading development. Individual development is accelerated in children and adolescents, with the role of sex hormones in promoting many physiological and psychological changes in boys and girls. Therefore, we intended to explore the sex differences in the resting-state reading neural network of Chinese children and adolescents from 8 to 15 years old, and we attempted to link the different neural bases to different aspects of the reading abilities in boys and girls in this particular age group.

## 2. Method

### 2.1. Participants

There were 109 normal developing participants (53 boys and 56 girls) enrolled from primary and secondary schools in Beijing. The mean age of the participants was 11.4 years (from 8.2 to 14.6,  $SD = 1.74$ ). All participants were right-handed except one boy. All participants had above average intelligence; that is, the nonverbal intelligence quotients

by Raven's Standard Progressive Matrices (Raven, 1938) of all the participants were above the 50th percentile (from 50% to 95%,  $SD = 13.9\%$ ). The participants were all Chinese native speakers with normal hearing, vision or corrected-to-normal vision. The subjects did not have psychiatric disorders and did not take drugs that affected the nervous system. This study was approved by the Beijing Normal University Research Ethics Committee. The participants and their guardians gave informed consent before the experiment.

### 2.2. Reading performance test

We used a character recognition test (Bi et al., 2007) and the silent sentence reading test (You et al., 2011) to evaluate the reading accuracy and reading comprehension of the participants, respectively.

The character recognition test consisted of 195 characters selected from the Chinese textbooks of primary and secondary schools. Among the 195 characters, 150 were from primary school books (Bi et al., 2007), and the other 45 were from secondary school books. The 195 characters were arranged in sequence from easy to hard, according to their order of appearance in the textbooks, frequency and visual complexity. In this test, the subjects were asked to read the consecutive sequence of Chinese characters aloud until they read 15 wrong characters in a row. The number of correct words was counted as the reading accuracy score. All participants had a character recognition test and character recognition scores.

The silent sentence reading test had 95 multiple-choice questions, with each consisting of a simple sentence and five pictures. The sentence lengths were roughly sorted from short to long, ranging from 4 to 41 characters. The participants were required to choose the matched pictures according to the sentence content. The more correct questions they answered in 7 min, the higher the reading comprehension score they would get. Ninety-nine participants (48 boys and 51 girls) had reading comprehension scores. The participant information is shown in Table 1.

### 2.3. Image acquisition

Brain imaging data were collected from the participants using a Siemens 3T MRI scanner in the MRI centre of State Key Laboratory of Cognitive Neuroscience and Learning at Beijing Normal University, with T2 weighted gradient echo planar imaging (EPI). The scanning parameters of resting-state functional images were as follows: pulse repetition interval (repetition time, TR) was 2400 ms; echo time (TE) was 30 ms; flip angle was  $81^\circ$ ; slice thickness was 3 mm; gap was 0.48 mm; number of slices was 40; FOV was  $256 * 256 \text{ mm}^2$ , and scanning matrix was  $64 * 64 * 40$ .

High-resolution structure (T1) images of each participant were also collected. The scanning parameters were as follows: axial slices = 176, slice thickness = 1 mm, FOV =  $256 * 256 \text{ mm}^2$ , matrix =  $256 * 256 * 176$ , voxel size =  $1 * 1 * 1 \text{ mm}^3$ , TR = 2300 ms, and TE = 4.18 ms.

During the scanning, participants were asked to open their eyes and stare at a white cross on the screen with a black background. The scanning time of resting-state functional imaging was 7.2 min and that of structural imaging was 6.75 min. Before entering the scanner, participants were adapted to the MRI simulation room to familiarise them with the experimental equipment.

### 2.4. Data analysis

#### 2.4.1. Image preprocessing

We used DPARSF software (<http://rfmri.org/DPARSF>) to preprocess participant resting-state fMRI data (Chao-Gan and Yu-Feng, 2010). The steps and operation settings were as follows: 1) The first 10 scanning time points were removed to ensure the stability of the signal; 2) Time layer correction, which corrected the acquisition time of each layer of all functional images to the acquisition time of the middle layer; 3) Head motion correction, which screened out the data with dynamic

**Table 1**  
The age, IQ, and reading performance of the participants.

Groups	Number	Age				IQ				Character recognition			Silent sentence reading			
		Range	Mean (SD)	t	p	Range	Mean (SD)	t	p	Mean (SD)	t	p	Number	Mean (SD)	t	p
Boys	53	8.22–14.50	11.04 (1.89)	1.897	0.061	50–95	80.1 (13.1)	1.010	0.315	94.8 (35.5)	1.916	0.058	48	45.5 (11.3)	1.200	0.233
Girls	56	8.72–14.60	11.66 (1.52)			50–95	77.4 (14.5)			110 (47.1)			51	48.1 (10.2)		

displacement exceeding 3 mm or rotation exceeding 3 degrees; 4) The structural image of each participant was applied to the average functional image of all participants; 5) The structural image was segmented into grey matter, white matter and cerebrospinal fluid signals; 6) The structural image was standardised, and the functional image was registered into MNI (Montreal Neurological Institute) standard space and resampled to a voxel size of  $3 \times 3 \times 3 \text{ mm}^3$ ; 7) Linear drift was removed; 8) The high pass filter was applied (0.01–0.1 Hz); 9) Gaussian smoothing, FWHM = 6 mm was used for Gaussian smoothing; 10) Regressing interference variables, including 6 head movement parameters, white matter signal and cerebrospinal fluid signal.

#### 2.4.2. ROI selection and functional connectivity calculation

After preprocessing, we calculated the functional connectivities between the brain regions of Chinese reading neural circuits. The neural circuits of Chinese reading defined in this study were composed of nine brain regions critical for Chinese reading that were selected based on a meta-analysis of Chinese reading studies (Bolger et al., 2005). These regions included the bilateral posterior fusiform gyrus (pFFG. L, pFFG. R), bilateral inferior occipital gyrus (IOG. L, IOG. R), left superior temporal gyrus (STG. L), left inferior temporal gyrus (ITG. L), left dorsal inferior frontal gyrus (dIFG. L), and left ventral inferior frontal gyrus (vIFG1. L, vIFG2. L). The location coordinates and Brodmann partition of these brain regions are shown in Table 2. The same nine ROIs have also been used in several previous studies of Chinese reading (Wang et al., 2012; Bolger et al., 2005). The MNI coordinates of Chinese reading-related brain regions provided in meta-analysis research were taken as the ball centre, and spheres with a radius of 6 mm were taken as the regions of interest (ROIs). The mean blood oxygen level-dependent (BOLD) signals of all voxels in 9 ROIs were extracted from each participant. Thirty-six Pearson correlation values between the time series of BOLD signals in 9 ROIs were calculated. These correlation coefficients reflect the strength of functional connections between brain regions. The higher the correlation coefficient is, the higher the time synchronisation of functional activities in two brain regions is. The 36 correlation

**Table 2**  
Brodmann's area and MNI coordinates of the regions of interest (ROIs).

Regions	Brodmann's area	MNI coordinates	
ROI1	pFFG.L <sup>a</sup>	18	-39, -80, -12
ROI2	IOG.L <sup>b</sup>	19	-24, -98, -6
ROI3	ITG.L <sup>c</sup>	37	-52, -56, -9
ROI4	STG.L <sup>d</sup>	40	-67, -21, 1
ROI5	vIFG1.L <sup>e</sup>	9	-44, 24, 2
ROI6	vIFG2.L <sup>e</sup>	45	-48, 36, 1
ROI7	dIFG.L <sup>f</sup>	9	-50, 14, 29
ROI8	IOG.R <sup>g</sup>	18	33, -94, -6
ROI9	pFFG.R <sup>h</sup>	19	37, -71, -14

<sup>a</sup> The left posterior fusiform gyrus.

<sup>b</sup> The left inferior occipital gyrus.

<sup>c</sup> The left inferior temporal gyrus.

<sup>d</sup> The left superior temporal gyrus.

<sup>e</sup> The left ventral inferior frontal gyrus.

<sup>f</sup> The left dorsal inferior frontal gyrus.

<sup>g</sup> The right inferior occipital gyrus.

<sup>h</sup> The right posterior fusiform gyrus.

coefficients were transformed by Fisher's Z transformation, that is, the R value was transformed into the Z value to make it conform to the normal distribution.

#### 2.4.3. Regression analysis

To analyse the effect of sex, age and their interaction, regression analysis was performed. The strength of every resting-state functional connection was defined as a dependent variable, and the independent variables were age and sex. IQ was also included in the regression equation as a control variable. The regression equation was as follows:

$$y = \beta_0 + \beta_1 \text{Sex} + \beta_2 \text{Age} + \beta_3 \text{IQ} + \beta_4 (\text{Age} \times \text{Sex})$$

In this case, we tested whether the regression coefficients significantly differed from zero. To eliminate the accumulated Type-I error, FDR correction was used for multiple comparisons correction, making the corrected  $P < 0.05$ .

#### 2.4.4. Prediction model

To explore whether resting-state fMRI connections (RSFCs) could predict reading performance and whether there were sex differences in the prediction models that were independent of age, we conducted prediction model analysis using the connection strengths as predictors and reading accuracy and reading comprehension as dependent variables for males and females separately. To exclude the influence of age and IQ, we calculated the residuals of the regression equation as the reading comprehension and accuracy scores. After standardising and centralising the data, we obtained a new dataset for the next analysis step. The prediction model used ensemble learning based random forest and bagged trees models as implemented in the SuperLearner packages (R version 4.0.3; van der Laan et al., 2007; <https://www.rdocumentation.org/packages/SuperLearner/versions/2.0-22/topics/SuperLearner>). Random forest is a representative ensemble learning algorithm. All its base evaluators are decision trees. The decision tree is used as the weak classifier. Each classifier is independent of each other, and the final results are voted by all models (for classification problems) or averaged (for regression problems) (Breiman, 2001; Strobl et al., 2009). When the number of features is large, the random forest model performs better (Andreas and Inke, 2014; Couronné et al., 2018). To eliminate the influence of the data set partition method, we randomly divided the data set 200 times. Seventy-five percent of the data set was used as the training set to generate the model, and the rest was used as the test set to test the model. A 10-fold cross-validation method was used to prevent overfitting. After obtaining the best model, we used it to predict the test set reading scores and calculated the mean absolute errors (MAE) of prediction ( $MAE = |true\ value - predict\ value| \div n$ ). The lower MAE, the better the model. And for each model, we used 1000 permutation analysis to test its performance. We also used boys' best model to predict girls' behaviour scores, and compared the performance of model to girls'. And vice versa.

Because we wanted to find the most important RSFCs for predicting reading performance, we used the random forest method for feature selection and searched the smallest RSFC set as the most important connections. The feature selection procedure used caret packages (R version 4.0.3; Kuhn, 2008; <https://github.com/topepo/caret/>). The most effective set of RSFC values was used to construct the reading

models, and we selected the most important RSFCs that could predict reading accuracy and reading comprehension for boys and girls separately.

For determining the differences between different subsets of the selected features, we encoded the selected feature subsets. Next we calculated the Mahalanobis distances within and between all feature subsets of boys and girls, and used t-test to test the difference of distances. In order to further control age, we also tried another approach by dividing the subjects into youngers (age from 8.2 to 11, including 25 girls and 36 boys) and elders (age from 11 to 14.6, including 26 girls and 15 boys), and tested the difference of Mahalanobis distances in the same way.

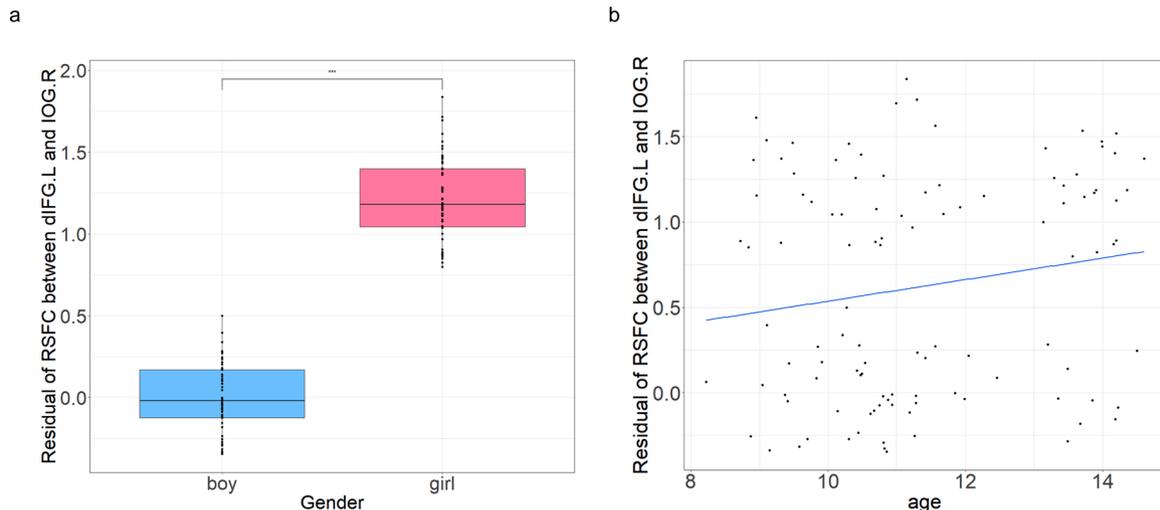
### 3. Results

#### 3.1. Behavioural results

As seen from Table 1, there was a marginally significant difference between the boys and girls in reading accuracy, as reflected by character recognition ( $t = 1.916$ ,  $df = 101.9$ ,  $p = 0.058$ ), but the sex difference in reading comprehension, as reflected by silent sentence reading, was not significant ( $t = 1.200$ ,  $df = 94.713$ ,  $p = 0.233$ ). The sex difference in IQ was also not significant ( $t = 1.010$ ,  $df = 107$ ,  $p = 0.315$ ).

#### 3.2. Regression analysis

Only one RSFC that connected the left dIFG with the right IOG showed a significant sex difference ( $\beta = 1.211$ ,  $SE = 0.322$ ,  $t = 3.766$ ,  $p = 0.010$ ), with the girl strength of connection being significantly higher than that of the boys (Fig. 1). This connection also showed a significant age effect ( $\beta = 0.074$ ,  $SE = 0.022$ ,  $t = 3.421$ ,  $p = 0.001$ ). Specifically, with increasing age, the strength of the connection increased significantly. Regarding the interaction between age and sex, there were many connections showing significant effects (Table 3). Apart from the connection between the left dIFG and right IOG, all other connections showed greater strength with age increasing for girls, but the boys showed an opposite trend. However, a contradictory trend was found in the connection between the left dIFG and right IOG; that is, as age increased, the strength of this connection increased for boys but decreased for girls. The locations and the pattern of interactions of these connections are depicted in Fig. 2.



**Fig. 1.** a) Illustration of the residual of the RSFC between dIFG.L and IOG.R for boys and girls. Using pink to represent girls, and blue to represent boys. The dot represents each participant's residual of activation of the connection. The girls' activations of connection are significantly higher than boys. b) The relationship between age and the residual of RSFC between dIFG.L and IOG.R. The X axis represents the age of participants, and Y axis represents the residual of the RSFC. The dot represents each participant's data. The line represents the linear fitting curve. dIFG.L = the left dorsal inferior frontal gyrus, IOG.R = the right inferior occipital gyrus.

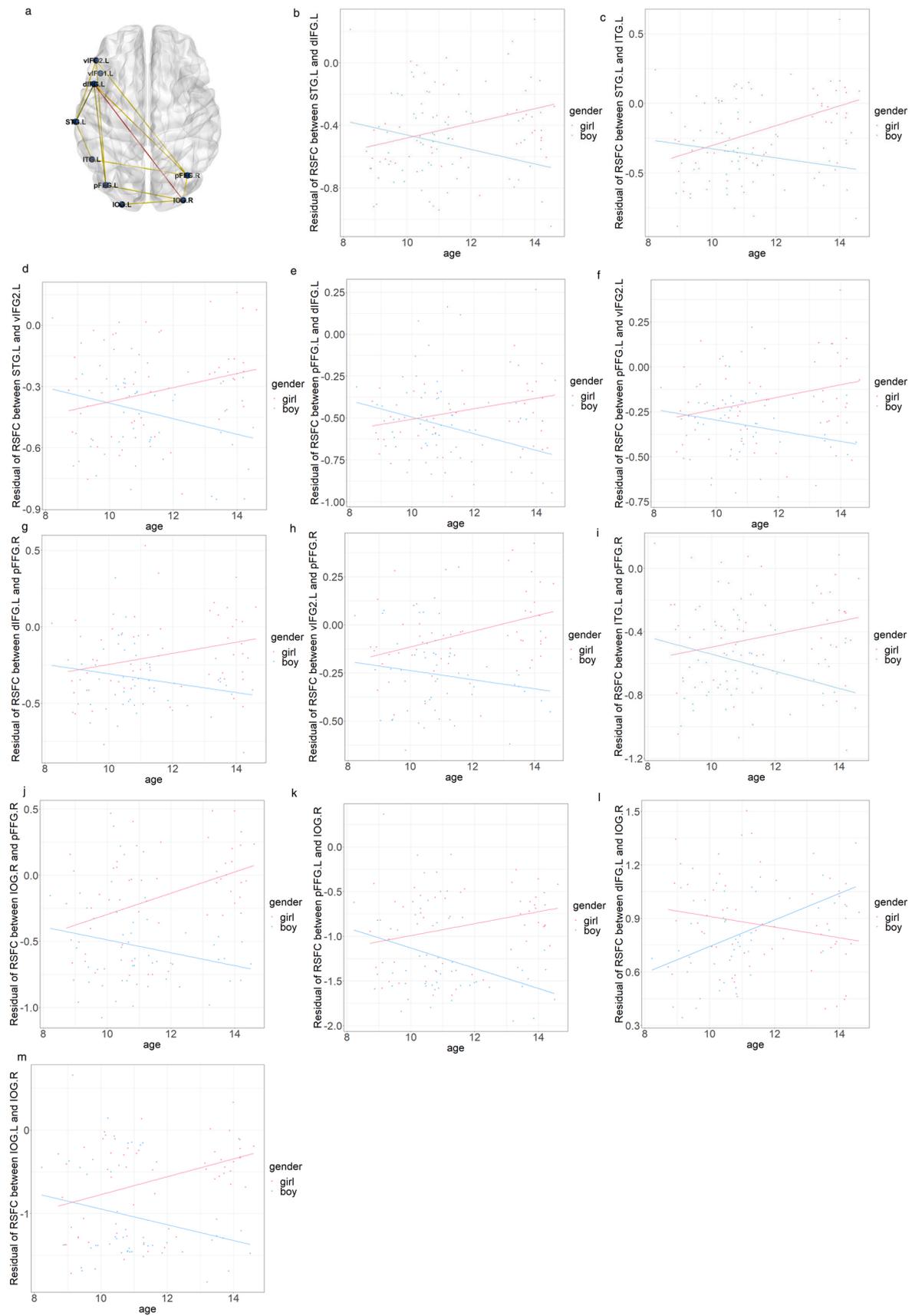
**Table 3**

The connections which showed age by gender interaction effects.

ROI1	ROI 2	$\beta$	SE	t	$P$ (FDR corrected)
STG.L	dIFG.L	0.093	0.030	3.065	0.017
STG.L	vIFG2.L	0.073	0.026	2.780	0.021
STG.L	ITG.L	0.104	0.030	3.502	0.008
pPFG.L	vIFG2.L	0.067	0.024	2.71	0.022
pPFG.L	dIFG.L	0.081	0.026	3.096	0.013
pPFG.R	ITG.L	0.095	0.031	3.021	0.013
pPFG.R	vIFG2.L	0.064	0.023	2.722	0.022
pPFG.R	dIFG.L	0.067	0.027	2.465	0.039
IOG.R	IOG.L	0.202	0.062	3.259	0.011
IOG.R	dIFG.L	-0.104	0.028	-3.704	0.008
IOG.R	pPFG.L	0.181	0.051	3.524	0.008
IOG.R	pPFG.R	0.129	0.040	3.257	0.011

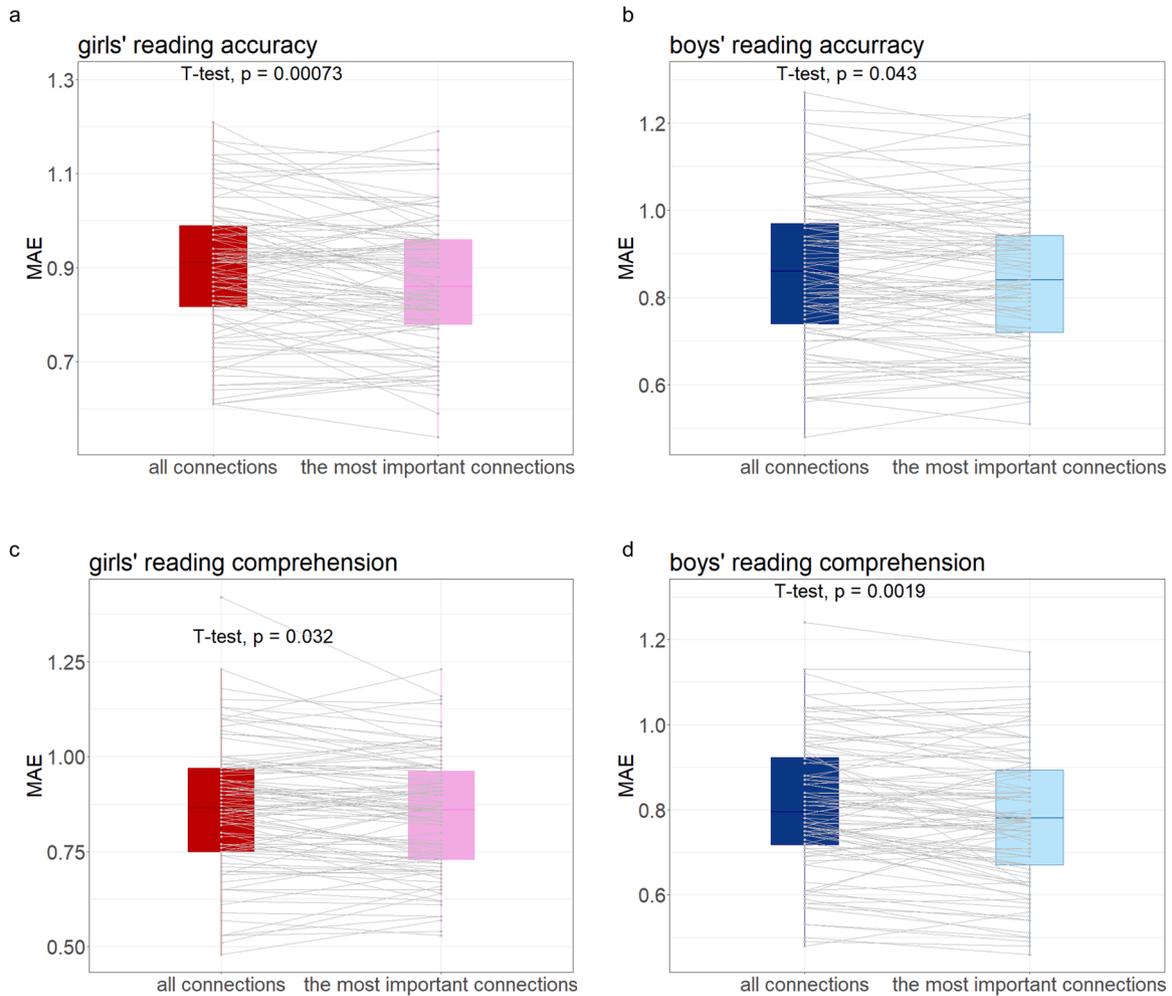
#### 3.3. Prediction model

We compared the model with all the resting-state fMRI connections (model 1) and the smallest, best feature subset model (model 2) to predict reading performances separately for reading accuracy and reading comprehension for boys and girls. The mean absolute errors (MAE) of reading accuracy were significantly decreased after feature selection for both girls (MAE-model1 = 0.90, MAE-model2 = 0.87,  $t = 3.52$ ,  $df = 99$ ,  $p$ -value < 0.01) and boys (MAE-model1 = 0.86, MAE-model2 = 0.84, paired  $t = 2.13$ ,  $df = 99$ ,  $p$ -value = 0.04). The mean absolute errors of the prediction of reading comprehension also significantly decreased after feature selection for both girls (MAE-model1 = 0.86, MAE-model2 = 0.85, paired  $t = 2.16$ ,  $df = 99$ ,  $p = 0.03$ ) and boys (MAE-model1 = 0.81, MAE-model2 = 0.78, paired  $t = 3.19$ ,  $df = 99$ ,  $p < 0.01$ ). These results are shown in Fig. 3. In addition, the results of permutation analysis showed that prediction performance of the best fitting models was significantly higher than random level (Table 4). Further, boys' best model was used to predict girls' behaviour scores, and the results showed that the performance of the model was significantly lower than that of girls (Table 5). And vice versa (Table 5). These results further confirmed that there were significant group differences between boys' and girls' best fitting models. Therefore, we found the most important resting-state fMRI connections for predicting reading performance for boys and girls separately (Table 6). The locations of these important connections are shown in Fig. 4.



(caption on next page)

**Fig. 2.** **a)** The locations of RSFCs which showed significant interaction effect of age and gender. The blue nodes represent the locations of ROIs. The yellow edges represent connections whose strength increasing with age for girls and decreasing with age for boys. We used red edge to display the connection between dIFG.L and IOG.R, which showed an opposite pattern of interaction. **b–m)** display the pattern of interaction of age and gender. The Y axis represents residual of RSFC's activation, and X axis represents age. Using pink dots to represent girls' data, and blue dots to represent boys'. The pink lines show the linear fitting curves for girls, and blue lines belong to boys. **b)** display the pattern belongs to the RSFC between STG.L and dIFG.L. **c)** display the pattern belongs to the RSFC between STG.L and ITG.L. **d)** display the pattern belongs to the RSFC between pFFG.L and dIFG.L. **e)** display the pattern belongs to the RSFC between pFFG.L and vIFG2.L. **f)** display the pattern belongs to the RSFC between dIFG.L and pFFG.R. **g)** display the pattern belongs to the RSFC between vIFG2.L and pFFG.R. **h)** display the pattern belongs to the RSFC between ITG.L and pFFG.R. **i)** display the pattern belongs to the RSFC between IOG.R and pFFG.R. **j)** display the pattern belongs to the RSFC between IOG.R and dIFG.L. **k)** display the pattern belongs to the RSFC between IOG.R and IOG.L. **l)** display the pattern belongs to the RSFC between IOG.R and dIFG.L. **m)** display the pattern belongs to the RSFC between IOG.R and IOG.L. STG.L = the left superior temporal gyrus; dIFG.L = the left dorsal inferior frontal gyrus; ITG.L = the left inferior temporal gyrus; vIFG2.L = the left ventral inferior frontal gyrus; pFFG.L = the left posterior fusiform gyrus; pFFG.R = the right posterior fusiform gyrus; IOG.R = the right inferior occipital gyrus; IOG.L = the left inferior occipital gyrus.



**Fig. 3.** The MAEs of predicting reading performances which using all the connections and selected most important connections for boys and girls separately. The red boxes represent all connections for girls, and pink boxes represent selected connections for girls. The dark blue boxes represent all connections for boys, and light blue boxes represent selected connections for boys. Each dot represents the MAE of predicting reading performances dividing the data set each time (200 times in total). Using grey lines to connect the different MAEs with the same segmentation of Data Set. **a)** represent the results of predicting girls' reading accuracy. **b)** represent the results of predicting boys' reading accuracy. **c)** represent the results of predicting girls' reading comprehension. **d)** represent the results of predicting boys' reading comprehension.

**Table 4**  
The mean absolute error (MAE) and its standard deviation (SD) for each prediction model. P value represents the result of permutation analysis.

Model	MAE (SD)	P-value
Girls' reading accuracy	0.87 (0.16)	< 0.001
Boys' reading accuracy	0.84 (0.14)	0.001
Girls' reading comprehension	0.85 (0.16)	< 0.001
Boys' reading comprehension	0.78 (0.15)	< 0.001

As shown in Fig. 4, there was only one common connection between boys and girls for predicting reading accuracy, which was located between the left superior temporal gyrus and the left dorsal inferior frontal gyrus. This connection also predicts reading comprehension in boys. Although both reading accuracy networks for boys and girls have exactly two interhemispheric connections, for girls, a majority of the most important connections belong to interhemispheric connections (two-thirds of the connections are interhemispheric for predicting reading accuracy, and four out of five connections are interhemispheric for

**Table 5**

The mean absolute error (MAE) and its standard deviation (SD) for each model. P value represents the result of t-test between two models.

Behaviour	MAE (SD)		P-value
Reading accuracy	Predict girls' behaviour using boys' model	Predict girls' behaviour using girls' model	0.022
	0.94 (0.15)	0.87 (0.16)	
Reading comprehension	Predict boys' behaviour using girls' model	Predict boys' behaviour using boys' model	< 0.001
	0.90 (0.07)	0.84 (0.14)	
Reading comprehension	Predict girls' behaviour using boys' model	Predict girls' behaviour using girls' model	0.030
	0.90 (0.18)	0.85 (0.16)	
Reading comprehension	Predict boys' behaviour using girls' model	Predict boys' behaviour using boys' model	0.001
	0.85 (0.14)	0.78 (0.15)	

**Table 6**

The most important connections for predicting reading accuracy and reading comprehension separately for girls and boys.

Behaviour	Group	ROI 1	ROI 2
Reading accuracy	Girls	STG.L	dIFG.L
		vIFG2.L	pFFG.R
		pFFG.L	IOG.R
		STG.L	dIFG.L
		vIFG2.L	vIFG1.L
	Boys	vIFG2.L	ITG.L
		IOG.L	pFFG.L
		IOG.L	IOG.R
		pFFG.R	STG.L
		pFFG.R	IOG.R
Reading comprehension	Girls	IOG.L	STG.L
		IOG.R	ITG.L
		IOG.R	vIFG1.L
		IOG.R	vIFG2.L
		pFFG.R	vIFG2.L
	Boys	IOG.L	pFFG.L
		IOG.L	vIFG2.L
		dIFG.L	STG.L
		dIFG.L	ITG.L

predicting reading comprehension). However, for boys, a majority of the most important connections belong to intrahemispheric connections (five-sevenths connections are intrahemispheric for predicting reading accuracy, and all connections are intrahemispheric for predicting reading comprehension). In addition, there were more connections between the left ventral inferior frontal gyrus and visual areas (such as the inferior occipital gyrus) for girls but more connections between the left dorsal inferior frontal gyrus and other areas for boys, especially for predicting reading comprehension. In addition, short-range connections within the visual areas also seem to be important for boys, such as the connection between the left inferior occipital gyrus and the left posterior fusiform gyrus.

Taking into account of variability among models, we further examined the whole set of feature subsets, whose performances were better than the model using all features. We found that there was no subset of exactly the same features between boys and girls. And the Mahalanobis distances between boys and girls were significantly greater than the distances within boys' or girls' whole feature subsets (Table S1). The results were similar among younger subjects (Table S2) and older subjects (Table S3). Besides, the most important features also play important role in the youngsters and the elders. (Performance of the best-fitting model for all-age group was better than 84% of other feature subsets for younger girls, and the best-fitting model for all-age group was also the best-fitting model for younger boys. Considering the relatively small

sample size of the elder group, the performances of the models may be unstable. Therefore, the data analysis is just exploratory. This exploratory data analysis showed that performance of the best-fitting model for all-age group was better than 50% of other feature subsets for older boys, and the best-fitting model for all-age group was also the best-fitting model for older girls.).

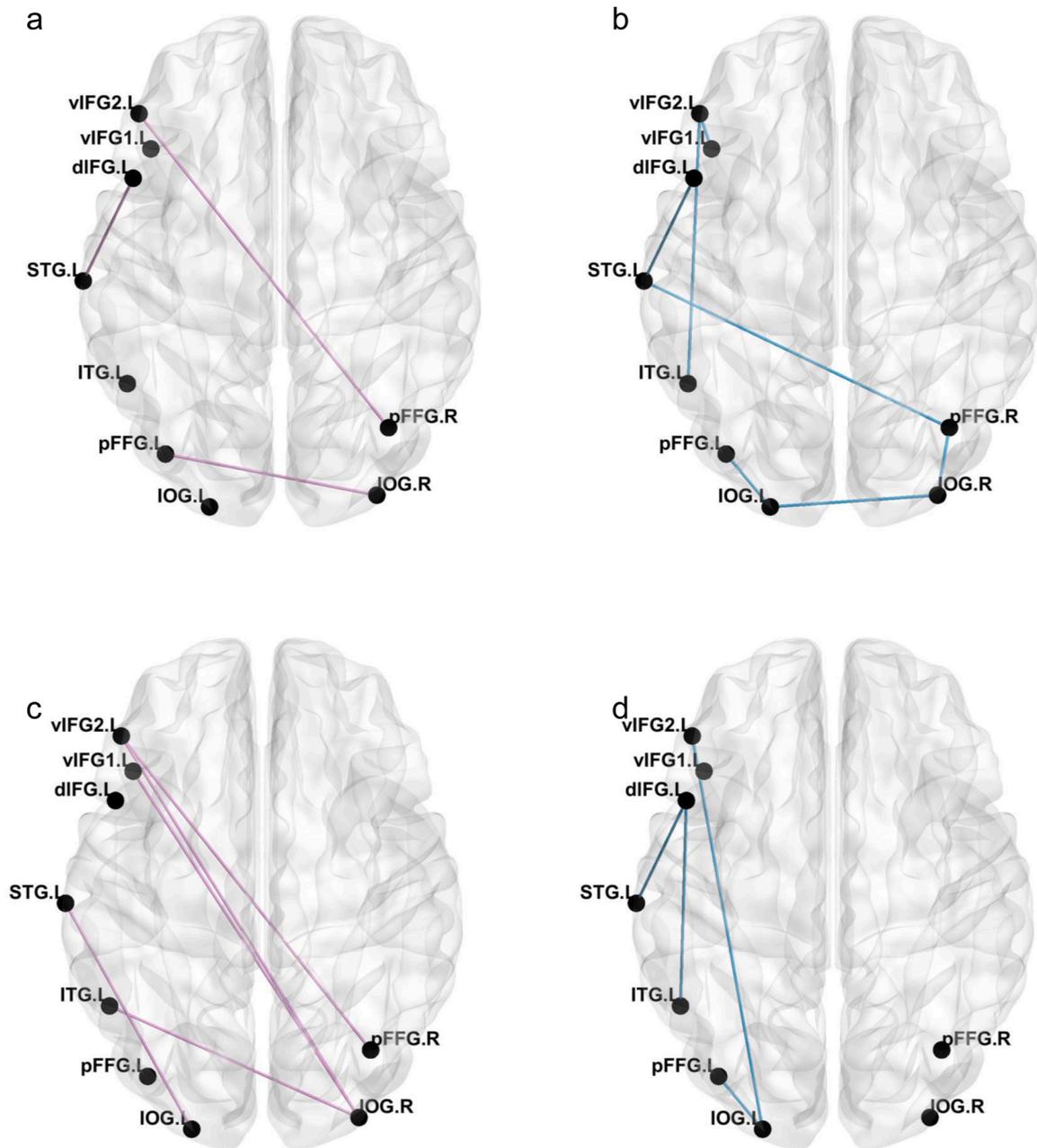
#### 4. Discussion

In the current study, we investigated sex differences in the resting-state reading-related neural network. We mainly found 1) greater strength of girls than boys in the RSFC between the left dIFG and the right IOG, and this connection strength increased with age in boys but stabilised with age in girls. 2) Several RSFCs mainly between the visual orthographic area and the other brain regions showed significant age-sex-interaction effects, with almost all of these RSFCs increasing with age in girls and decreasing in boys. 3) In relationship between reading neural circuit and behaviour, there were stable sex differences independent of age. Specifically, the most important RSFCs predicting reading performance in boys mainly include intrahemispheric connections, while the most important RSFCs predicting reading performance in girls display more interhemispheric inclination than that in boys. Moreover, RSFCs in the phonological route may contribute more to boys' reading performance than girls'. We will interpret and discuss these results from a developmental perspective.

##### 4.1. The interaction between sex and age in resting-state reading-related neural circuits

Our results showed that there was a restricted main effect of sex in the RSFC. However, when we considered the effect of the interaction between age and sex, RSFCs of broad brain regions showed significant results. Previous studies have demonstrated that sex differences in reading behaviour and neural circuits may be different at a wide range of ages (Etchell et al., 2018; Wallentin, 2009). Of note, most of the connections showing the interaction effect are located between the visual orthographic area and other brain areas in the reading neural circuit. This is consistent with a previous study arguing that females have higher flexibility in the occipital cortex, which may reflect female's potential in visual processing (Nini et al., 2017). Moreover, Marcela Perrone-Bertolotti and partners reported that the connections between visual orthographic areas and other language areas support orthographic information transfer (Perrone-Bertolotti et al., 2017). A study on sex and grapheme-to-phoneme conversion (GPC) shows that women perform better than men in recognising simple GPC stimuli, reflecting their advantages in visual language information conversion (Perrone-Bertolotti et al., 2011). Further, Wang et al. (2012) found that the speed of Chinese single word reading is positively correlated with the connection strength the left inferior occipital gyrus and left superior parietal lobule, as well as the connection strength between the right posterior fusiform gyrus and right superior parietal lobule. Similarly, our study found that reading comprehension fluency is related to the connection between visual regions and other brain regions no matter for boys or girls. Both Wang's and our study may suggest that the connections between visual orthographic regions and other reading-related regions may play an important role in automatic reading process. Our finding that girls rely more on connections of visual orthographic regions with other regions might suggest more automatic visual orthography processing in girls than boys.

Besides, the RSFC of the left dIFG with the right IOG, whose strength is higher in girls than boys, showed an increasing trend with age for boys, while kept relatively stable with age for girls. The result may suggest that the development of this connection for girls is stabilised in a relatively mature pattern, while its development in boys is still in progress. And this is supported by a previous study suggesting that this connection is related to a more mature automatic reading process (Liu



**Fig. 4.** The locations of the most important RSFCs predicting reading performances for the boys and the girls separately. The black nodes represent the locations of ROIs. The pink edges represent the RSFCs for girls. And the blue edges represent the RSFCs for boys. **a)** shows the most important RSFCs predicting reading accuracy for the girls. **b)** shows the most important RSFCs predicting reading accuracy for the boys. **c)** shows the most important RSFCs predicting reading comprehension for the girls. **d)** shows the most important RSFCs predicting the reading comprehension for the boys.

et al., 2012).

To our knowledge, our study is the first to report the interaction between age and sex in the resting-state reading networks of children and adolescents. This study might expand our understanding of the changing sex differences in the reading networks of children and adolescents.

#### 4.2. Different RSFCs predicting reading performance in girls and boys

The results of the prediction model imply that the boy and girl brain connections that most relate to reading behaviour are different. First, girls seemed to require fewer connections than boys in reading accuracy network (Fig. 4a–b). Studies of dyslexic groups have found that children who performed better were most likely to recruit fewer neural circuits

(Edwards et al., 2018; Morken et al., 2017). Our results may reflect a more mature and effective network model in girls. Second, we found that compared with boys, girls have a higher proportion of interhemispheric connections, which may reflect interhemispheric connections play a more important role in girls' than boys' reading network. Our finding is aligned with previous studies on sex differences in brain lateralisation in reading (Hill et al., 2006; Jaeger et al., 1998; Spironelli et al., 2010; Bitan et al., 2010; Shaywitz et al., 1995). However, there are also some studies arguing that sex differences in brain lateralisation do not exist (Sommer et al., 2008; Eliot, 2013). The inconsistency between previous studies may be due to the age differences of the subjects. And some studies demonstrate that the sex difference in lateralisation is related to age. Hirnstein et al. found that sex differences in lateralisation during dichotic listening tasks only existed in 16- to 49-year-old adults,

which was not observed in children and elder adults (Hirnstein et al., 2013). By controlling for the influence of age, we still found sex differences in the pattern of RSFC, with girl RSFCs being more bilateralized. Therefore, our results may indicate that when considering the relationship between brain and behaviour, stable sex differences independent of age might exist in brain lateralisation in the resting-state neural network in the 8–15 age group.

For a long time, studies on reading have shown that the reading network is left lateralized; however, an increasing number of studies have found that the right hemisphere of the brain also plays an important role in the process of reading (Waldie and Mosley, 2000; Jung-Beeman, 2005; Xu et al., 2005; Tan et al., 2001). A study on the development of the Chinese reading brain indicated that adults show more activation in the right middle occipital gyrus during visual word processing than children (Cao et al., 2009). This may be because adults rely more on visual orthographic processing in reading than children and adolescents. Also, a functional connectivity study on Chinese reading found a similar pattern by showing that adults had stronger connectivities between orthographic regions and other language regions in visual word processing (Liu et al., 2018). The trend of girl brain bilateralization in the process of reading may also occur for the same reason, which partly presents the similarity between girls and adults. In particular, the trend that girls show inter-hemispheric RSFCs is more obvious in the prediction model of reading comprehension than in that of reading accuracy. This may be because the reading comprehension task in the current study is a more complex task than word reading accuracy, including additional processing for semantics and syntax. The present study perhaps provides additional evidence with respect to sex differences in the neural basis of reading comprehension at the sentence level.

In addition, our results showed that connections in the phonological route (e.g., the connections between the right pFFG and the left STG, the left dIFG and the left STG, the left dIFG and the left ITG) may contribute more to boys' reading performance. dIFG is thought to be involved in phonological processing in reading, while vIFG is thought to be involved in semantic processing (Liu et al., 2009; Perrone-Bertolotti et al., 2017). In our study, both vIFG and dIFG played a role in boys' reading comprehension, but only connections with vIFG not dIFG seemed to be associated with girls' reading comprehension, which implied the important role of phonological route for boy' reading comprehension. This is in line with a previous study which reported that the connection between the left vIFG and other reading-related brain regions in female was higher than that in male (Wang et al., 2012). Previous research suggests that during language processing across both visual and auditory modalities, compared with boys, girls may be less restricted by sensory information processing and more likely to rely on higher-level language-related brain regions, such as the IFG (Burman et al., 2008). Our results are consistent with this study by showing that boy reading is more associated with phonological processing regions (e.g., left STG, left dIFG). Although the reading process of different languages has some specificities, such as more activities in the right fusiform gyrus during Chinese reading (Wu et al., 2012; Wang et al., 2015), reading in different languages and their development trends also have commonalities. Previous studies have shown that the development of reading occurs by eliminating phonological processing. This trend is reflected in both the development of alphabetic (e.g., English) and logographic (e.g., Chinese) reading (Bitan et al., 2007; Liu et al., 2018; Zhou et al., 2021). Consequently, the different connections related to reading performance between boys and girls in the current study might reflect the different developmental stages of intrinsic reading networks. That is, the girl resting-state reading network may be closer to maturity level, using both direct (orthographic-semantic) and indirect (orthographic-phonetic-semantic) reading routes, while the boy resting-state reading network seems to be more dependent on phonological processing (orthographic-phonetic-semantic route).

Our results are consistent with previous research (Burman et al.,

2008) arguing that there seems to be a bottleneck in the process of boys transmitting visual and auditory information to the language processing area, which may be related to the relatively lagging development of boy brains. As early as the 20th century, some researchers examined a series of cognitive abilities of males and females, which suggests that sex differences in language may be due to different maturation rates of men and women brains (Cohn, 1991). The research of Burman also supports this point of view, to a certain extent. However, some studies have not found differences in the rate of brain development between men and women (Wierenga et al., 2019). Research using grey matter volume to predict reading performance has found sex differences in both children and adults (Cui et al., 2018), which seems to contradict the idea that sex differences may come from differences in the development rate. Nevertheless, the sex differences found in the current study may reflect the different stages of reading development between boys and girls, at least from childhood to adolescence.

Alternatively, the different role of phonological loop between boys and girls might reflect their different cognitive Strategies. Some studies have shown that boys and girls may use different cognitive strategies in completing language tasks, both in L1 (Burman et al., 2013) and L2 (Sugiura et al., 2015). Behavioural research also showed that boys are more likely to use phonological strategies than girls in reading (Brian Thompson, 1987).

In fact, gender differences may be the result of complex interaction of biological, environmental, social and cultural factors (Rinaldi et al., 2021). Biological factors such as brain differences will affect the way individuals choose the environment, and these environmental factors will lead to further biological development (Miller and Halpern, 2014). For our research, boys and girls may have different rates of development in reading related brain regions. This asynchrony perhaps promotes boys and girls to use different cognitive strategies in the same task.

Our study has one limitation. Since the IQ of all the participants in our study were above the 50th percentile, it may be unsafe to generalise our results to the population of lower IQ. Actually, a previous study has reported that in groups with higher IQ or language skills, the size of sex differences tends to be larger (Burman et al., 2013). It is worthy to further investigate the influence of IQ on sex differences in language processing in the future.

## 5. Conclusion

Sex differences in the resting-state reading network were age-related in 8- to 15-year-old Chinese children and adolescents to a large extent, suggesting that sex differences in the brain reading circuit may be partly due to different reading developmental trajectories. Meanwhile, stable sex differences independent of age in the RSFCs for predicting reading performance were found, specifically, with girl reading circuits being more interhemispheric and more visually based but boy reading circuits being more intrahemispheric and more phonologically based. This may be due to different ways of information processing preferred by boys and girls or due to different maturation states of reading brain circuits, with girls closer to the maturation state. Taken together, this study provides more evidence for sex differences in the development of reading circuits.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data statement

Data are available on request to the authors.

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## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.dcn.2022.101098](https://doi.org/10.1016/j.dcn.2022.101098).

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