Supplementary Materials

ZNF804A Variation May Affect Hippocampal-Prefrontal Resting-State Functional Connectivity in Schizophrenic and Healthy Individuals

Yuyanan Zhang, Hao Yan, Jinmin Liao, Hao Yu, Sisi Jiang, Qi Liu, Dai Zhang, Weihua Yue

Table S1. Regions of significant main effect of diagnosis in resting-state imaging analysis ($P < 0.05$ after FDR correction, cluster size >10)

ROI region	Cortical region	Cluster size	MNI coordinates			F value
			X	Y	Z	
Left Hippocampus	Right Thalamus	26	6	-18	12	24.57
			12	-30	6	23.06
Right Hippocampus	Right Thalamus	28	6	-24	6	29.35
			-3	-9	6	25.17

MNI, Montreal Neurological Institute

Table S2. Regions of significant main effect of genotype in resting-state imaging analysis when the left hippocampus was treated as the seed region ($P < 0.001$ uncorrected, cluster size >10)

Cortical region	Brodmann area	Cluster size	MNI coordinates			F value
			X	Y	Z	
Right dorsolateral superior frontal gyrus	BA9	19	21	42	33	13.43
Right dorsolateral middle frontal gyrus	BA9	14	39	36	33	11.35
Left middle frontal gyrus	BA8, 9	17	-27	24	36	9.45

MNI, Montreal Neurological Institute

Table S3. Significant correlation of the left hippocampal-right dorsolateral middle frontal

resting-state functional connectivity and behavior.

Diagnoses	Genotype	Cognitive performance	PANSS score
SZ	AA genotype	WMS-R	Total
		($r = 0.665, P = 0.005$)	($r = -0.498$，$P = 0.035$)
		CFT	General
		($r = 0.679, P = 0.002$)	($r = -0.518$，$P = 0.028$)

The mean strength of resting-state functional connectivity between the left hippocampus and the right dorsolateral middle frontal region was significantly correlated with different models of cognitive performance and the severity of symptom in patients. The numbers are the Pearson correlation coefficients for the left hippocampus-right DLPFC resting-state functional connectivity and neuropsychological test scores. SZ, schizophrenic patients; HC, healthy controls; WMS-R, Wechsler Memory Scale-Revised; CFT, Category Fluency Test-animal Naming; PANSS, Positive and Negative Syndrome Scale; Total, total PANSS score; Negative, negative symptom scores in PANSS.

Table S4. Significant correlation of left hippocampal-left middle frontal resting-state functional connectivity and behavior.

Diagnosis	Genotype	Cognitive performance
SZ	CA genotype	DSST
		($r = -0.596, P = 0.019$)
	AA genotype	CFT
		($r = 0.556, P = 0.016$)

The mean strength of resting-state functional connectivity between the left hippocampus and the left middle frontal region was significantly correlated with different measures of cognitive performance. The numbers are the Pearson correlation coefficients for left hippocampal-left middle frontal resting-state functional connectivity and neuropsychological test scores. SZ, schizophrenic patients; HC, healthy controls; DSST, Digit Symbol Substitution Test; CFT, scores of Category Fluency Test-animal naming.
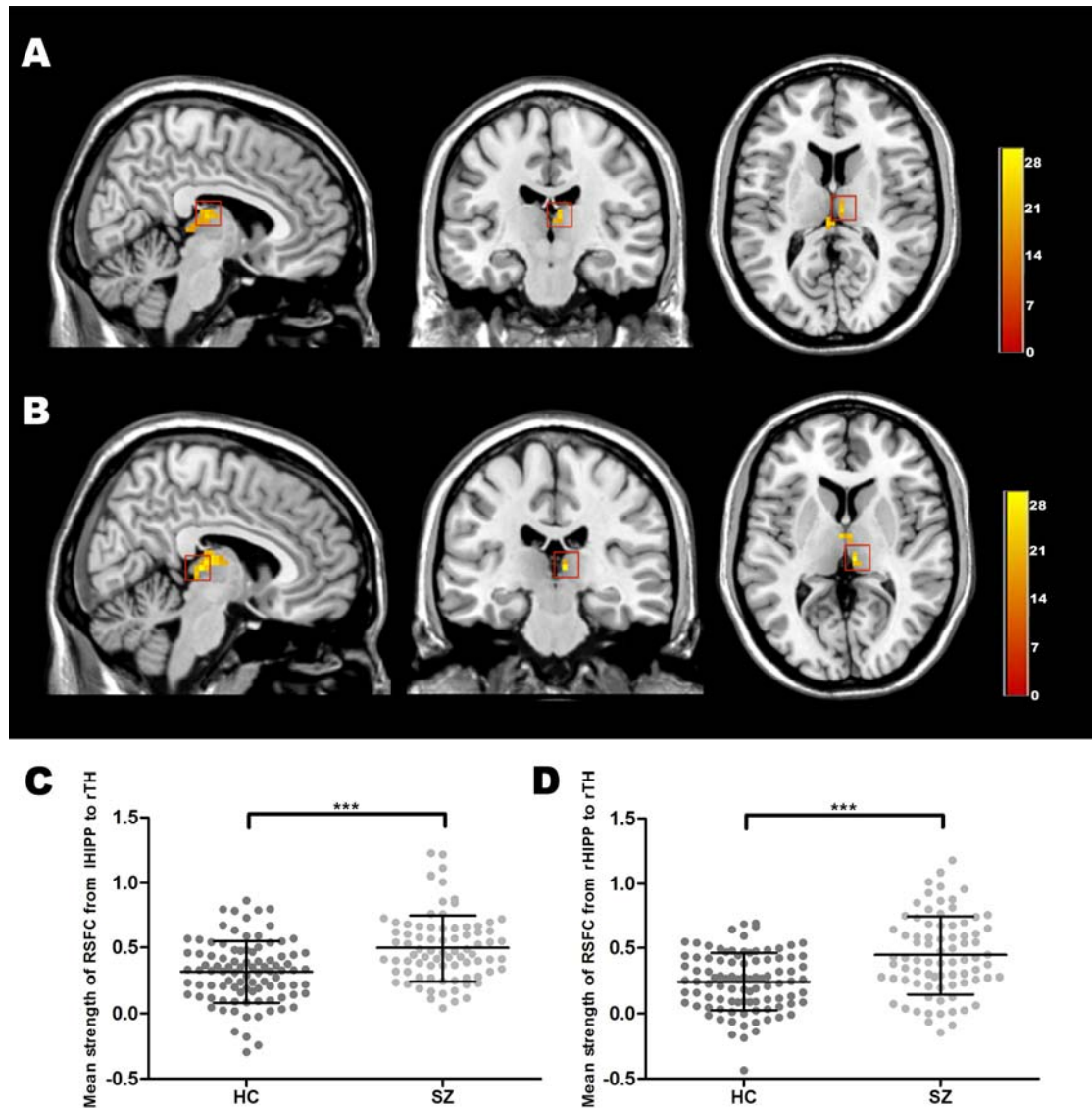
Fig. S1 Main effect of diagnosis on hippocampal-thalamic functional connectivity.
A Region (red box) with a significant diagnosis main effect for functional connectivity from the left hippocampus (lHIPP) to the right thalamus (rTH) (peak MNI coordinates: x = 6, y = -18, z = 12, peak F-score = 24.57, *p* <0.001 after FDR correction, cluster size = 26). **B** Region (red box) with a significant diagnosis main effect for functional connectivity from the right hippocampus (rHIPP) to the right thalamus (rTH) (peak MNI coordinates: x = 6, y = -24, z = 6, peak F-score = 29.35, *p* <0.001 after FDR correction, cluster size = 28). **C** Scatterplot of the mean strength of resting-state functional connectivity (RSFC) (mean ± SD) between the left hippocampus and the spherical region with the peak atlas [6 -18 12] as center and 6 mm as the radius. The Y-axis indicates the Z-score. **D** Scatterplot of the mean RSFC strength (mean ± SD) between rHF and the spherical region with the peak atlas [6 -24 6] as center and 6 mm as the radius. The Y-axis indicates the Z-score. SZ,

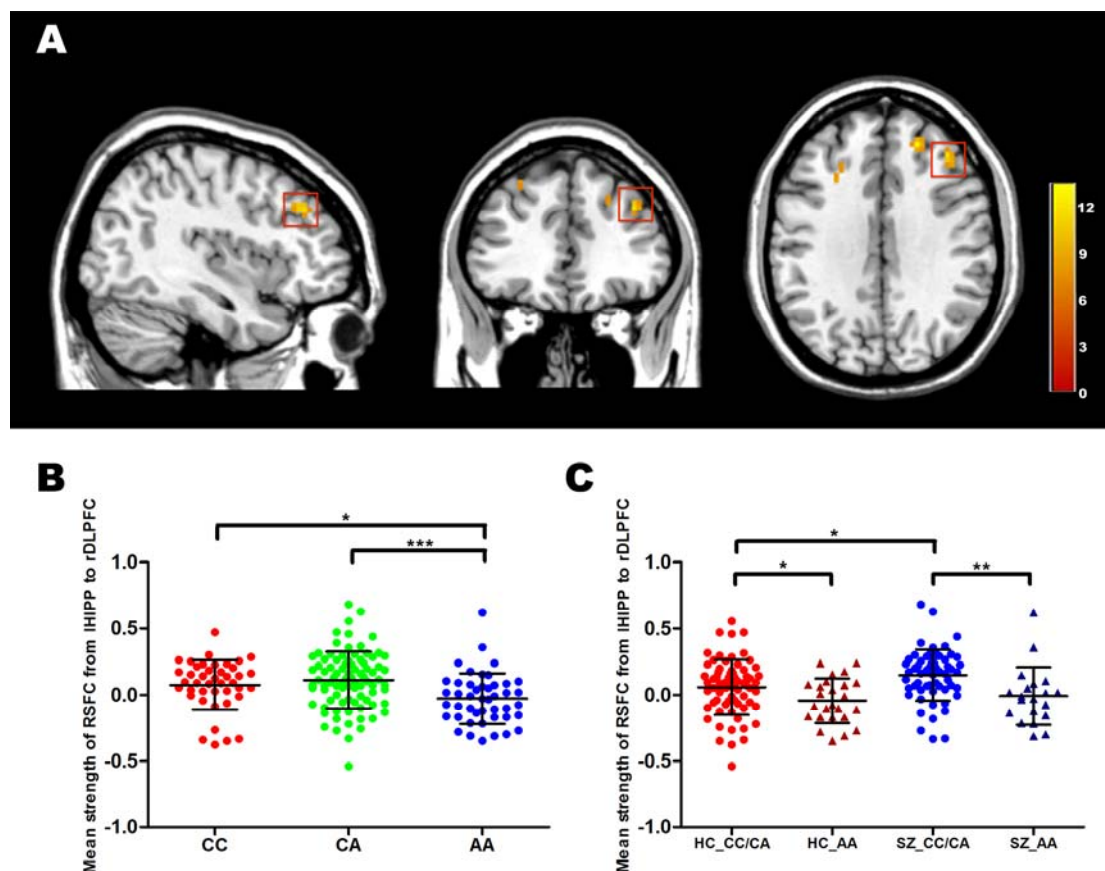schizophrenic patients; HC, healthy controls; ***$P < 0.001$.

Fig. S2 Effects of ZNF804A rs1344704 on left hippocampal-right dorsolateral middle frontal functional connectivity A Another frontal region (red box) with a significant genotype main effect for functional connectivity from the left hippocampus to the right DLPFC (peak MNI coordinates: x = 39, y = 36, z = 33, peak F-score = 11.35, p <0.001, cluster size =14). Color bar indicates F-score. **B** Scatterplot of the mean strength of resting-state functional connectivity (RSFC) (mean ± SD) between the left hippocampus and the spherical region with the peak atlas [39 36 33] as center and 6 mm as the radius in the three genotype groups. The Y-axis indicates the Z-score. **C** Scatterplot of the mean RSFC strength (mean ± SD) from the left hippocampus to the right DLPFC in the genotype groups (CC/CA and AA) in different diagnostic groups. The Y-axis indicates the Z-score. SZ, schizophrenic patients; HC, healthy controls; lHIPP, left hippocampus; rDLPFC, right dorsolateral prefrontal cortex. *$P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.
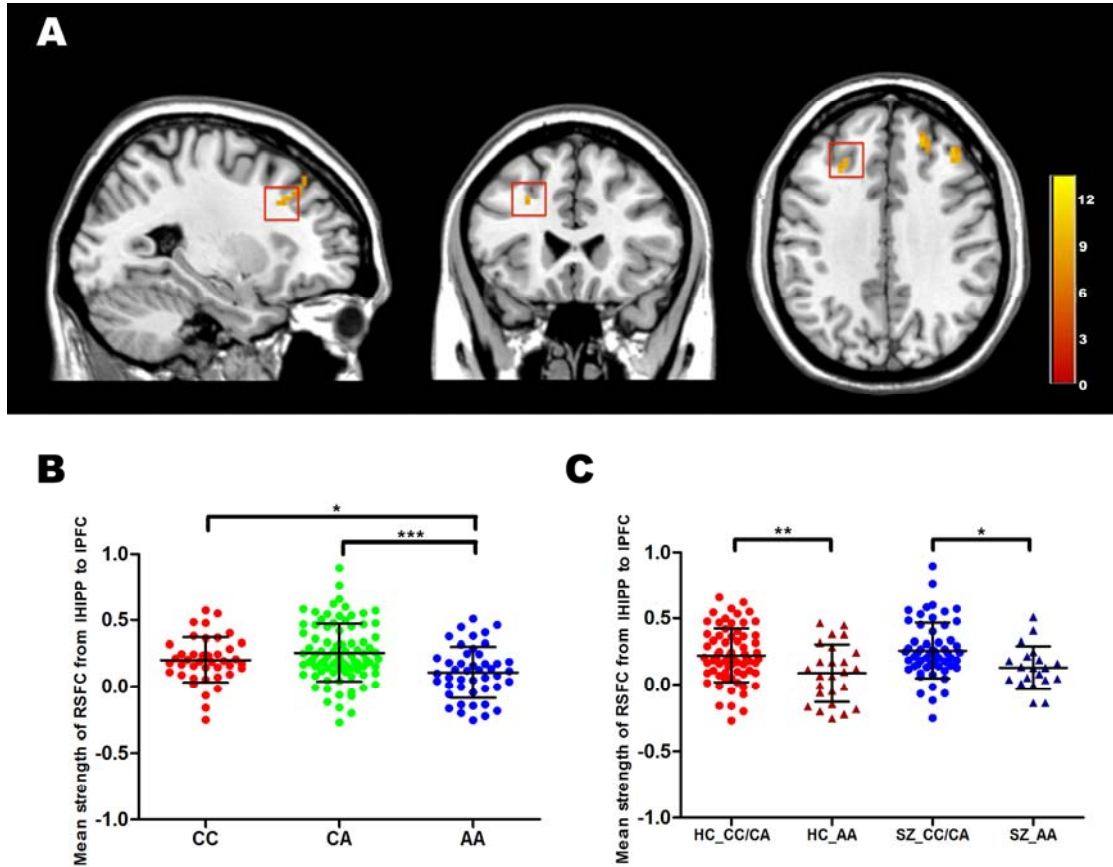
Fig. S3 Effects of ZNF804A rs1344704 on left hippocampal-left middle frontal functional connectivity. **A** A left frontal region (red box) with a significant genotype main effect for functional connectivity from the left hippocampus to the left middle prefrontal cortex (peak MNI coordinates: x = -27, y = 24, z = 36, peak F-score = 9.45, $p < 0.001$, cluster size = 17). Color bar indicates F-score. **B** Scatterplot of the mean strength of resting-state functional connectivity (RSFC) (mean ± SD) between the left hipocampus and the spherical region with peak atlas [-27 24 36] as the center and 6 mm as the radius in the three genotype groups. The Y-axis indicates the Z-score. **C** Scatterplot of the mean RSFC strength (mean ± SD) from the left hippocampus to the left DLPFC in the genotype groups (CC/CA and AA) of different diagnostic groups. The Y-axis indicates the Z-score. SZ, schizophrenic patients; HC, healthy controls; lHIPP, left hippocampus; lPFC, left prefrontal cortex. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.
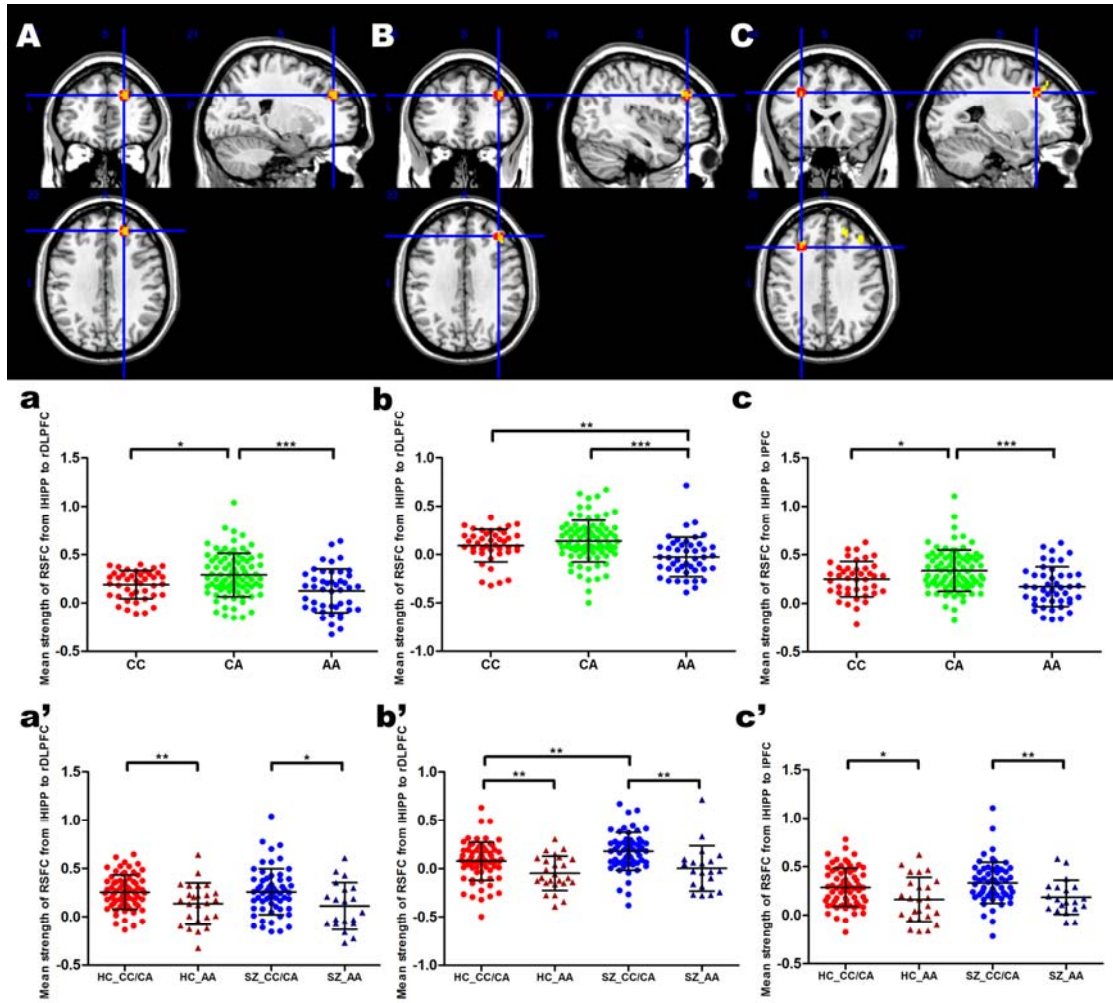
Fig. S4 Comparisons of three spherical regions with the peak atlas as center and 6 mm as the radius and three masks of original regions. A−C Spherical regions in red and original regions in yellow. **a**, **a'** Analysis with peak atlas mask [21 42 33]; **b**, **b'** Analysis with peak atlas mask [39 36 33]; **c**, **c'** Analysis with peak atlas mask [-27 24 36]; *P < 0.05, **P < 0.01, ***P < 0.001.