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Abnormalities of intrinsic regional brain activity in first episode and chronic schizophrenia: a meta-analysis of resting-state functional MRI

Supplementary materials

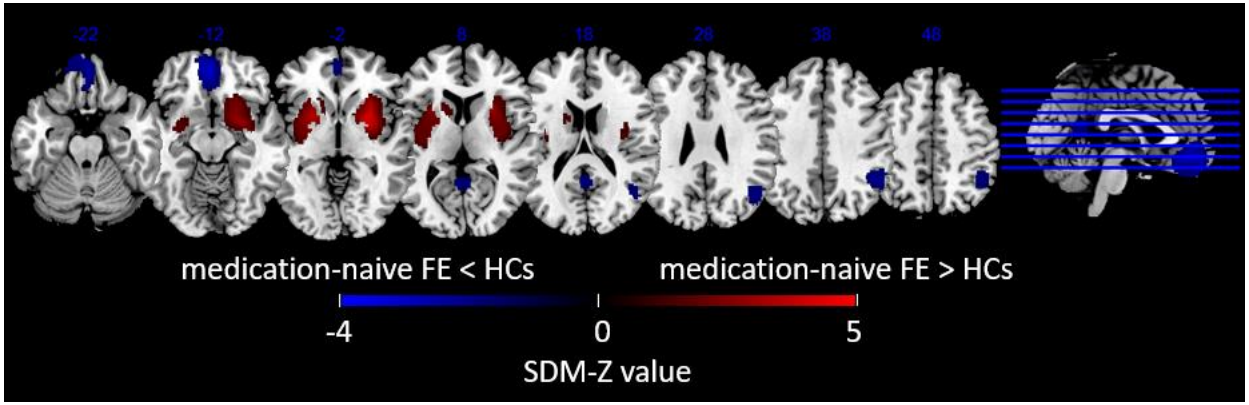

Figure S1. Alterations in ALFF in medication-naive FE patients with SZ compared to HCs. Areas with decreased ALFF relative to controls are displayed in blue, and areas with increased ALFF are displayed in red. The color bar indicates the maximum and the minimum SDM-Z values.

Abbreviations: FE = first episode; SZ = schizophrenia; HCs = healthy controls; ALFF = amplitude of low-frequency fluctuations; SDM = seed-based d mapping.

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Table S1 Quality assessment checklist (score 0/0.5/1 per item; total score out of 10)*

Category 1: Participants

1. Patients were evaluated prospectively, specific diagnostic criteria were applied, and demographic data were reported.

2. Healthy comparison participants were evaluated prospectively, psychiatric and medical illnesses were excluded.

3. Important variables (e.g., age, sex, illness duration, onset, medication status, comorbidity, severity of illness) were checked either by stratification or statistically.

4. Sample size per group > 10.

Category 2: Methods for image acquisition and analysis

5. Whole brain analysis was automated with no a priori regional selection.

6. Coordinates reported in a standard space.

7. The imaging technique used was clearly described so that it could be reproduced.

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8. Measurements were clearly described so that they could be reproduced.

Category 3: Results and conclusions

9. Statistical parameters for significant and important nonsignificant differences were provided.

10. Conclusions were consistent with the results obtained and the limitations were discussed.

*When criteria were partially met, 0.5 points were awarded.

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Table S2. Clusters of ALFF differences in medication-naive FE patients with SZ

	Cluster	Anatomical label	Peak MNI coordinate (x, y, z)	No. of voxels	SDM-Z value	*p* value
FE > control	1	Right putamen	26, 6, -4	2749	5.148	$< 1.0 \times 10^{-6}$
	2	Left putamen	-22, 8, 2	1870	4.451	$< 1.0 \times 10^{-6}$
FE < control	3	Left mPFC, BA 11	-2, 48, -12	1551	-3.191	$< 1.0 \times 10^{-6}$
	4	Right angular gyrus/IPG, BA 39	48, -60, 26	853	-2.107	0.000253
	5	Right precuneus	4, -54, 16	281	-2.072	0.000304

Abbreviations: ALFF = amplitude of low-frequency fluctuations; FE = first episode; SZ = schizophrenia; BA = Brodmann area; MNI = Montreal neurological institute; SDM = seed-based d mapping; mPFC = medial prefrontal cortex.

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Table S3. Heterogeneity of ALFF alterations in FE, chronic patients with SZ, and total patients with SZ

Anatomical label	Peak MNI coordinate (x, y, z)	No. of voxels	SDM-Z value	Heterogeneity	*p* value
Total patients with SZ					
Left putamen	-26, -2, 8	491	3.906	No	$< 1.0 \times 10^{-6}$
Right precentral gyrus, BA 6	52, -8, 42	307	1.792	No	0.000470
Right ITG, BA 20	60, -34, -18	182	2.208	No	0.000201
Right putamen	28, -2, 12	150	2.393	Yes	0.000134
Left gyrus rectus, BA 11	-8, 50, -20	131	2.148	No	0.000248
Right ACC	14, 14, 4	92	1.672	Yes	0.000635
Left MOG, BA 19	-36, -84, -2	67	1.604	No	0.000717
Left MTG, BA 21	-54, 0, -30	30	1.195	No	0.001646
Left SFG, BA 10	-18, 66, 4	29	1.141	No	0.001806
Right SOG, BA 19	26, -84, 32	30	1.274	Yes	0.001388
FE patients with SZ					
Left gyrus rectus, BA 11	-8, 50, -20	327	3.152	No	0.000031
Left putamen	-24, 0, 8	243	3.985	Yes	$< 1.0 \times 10^{-6}$
Right putamen	26, 0, 10	249	3.321	Yes	0.000026
Right putamen	20, 14, -6	99	1.841	Yes	0.000981
Right IPG, BA 40	44, -54, 50	41	1.536	Yes	0.001780

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Left MFG, BA 8	-24, 8, 58	29	1.660	No	0.001373
Right precuneus	8, -46, 40	16	1.574	Yes	0.001672
Chronic patients with SZ					
Right ITG, BA 20	60, -34, -18	273	3.870	No	0.000062
Right caudate	14, 14, 4	121	3.201	No	0.000299
Left MTG, BA 21	-54, 0, -28	87	2.995	No	0.000470
Left MOG, BA 19	-36, -84, 0	60	3.006	No	0.000459
Left SFG, BA 10	-18, 66, 4	62	2.798	Yes	0.000748
Right SOG, BA 19	28, -84, 32	25	2.632	Yes	0.001182
Left heschl gyrus, BA 48	-42, -18, 6	20	2.000	No	0.004278
Left IPG, BA 39	-56, -56, 36	19	2.178	No	0.003076
Right IFG, triangular part	48, 42, 0	12	2.115	Yes	0.003416
Left precuneus, BA 7	-8, -62, 66	10	2.073	Yes	0.003762

Abbreviations: ALFF = amplitude of low-frequency fluctuations; FE = first episode; SZ = schizophrenia; BA = Brodmann area; No. = number; MNI = Montreal neurological institute; SDM = seed-based d mapping; MFG = middle frontal gyrus; ITG = inferior temporal gyrus; MTG = middle temporal gyrus; MOG = middle occipital gyrus; SFG = superior frontal gyrus; SOG = superior occipital gyrus; IPG = inferior parietal gyri; IFG = inferior frontal gyrus; ACC = anterior cingulate cortex.

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Table S4 Meta-regression analyses: factors affecting ALFF in studies of patients with SZ

	Anatomical label	Peak MNI coordinate (x, y, z)	No. of voxels	SDM-Z value	*p* value
Total patients with SZ					
Effects of PANSS positive score	ALFF alterations in studies with higher PANSS positive score				
	Left precuneus, BA 7	-10, -64, 68	18	-4.068	0.000041
	Right precuneus, BA 29	4, -42, 6	86	4.934	0.000015
Effects of PANSS negative score	ALFF alterations in studies with higher PANSS negative score				
	Left precuneus, BA 7	-10, -64, 68	18	-4.417	0.000046
	Right precuneus, BA 29	4, -42, 6	59	5.169	$< 1.0 \times 10^{-6}$
Effects of PANSS general psychopathology score	ALFF alterations in studies with higher PANSS general psychopathology score				
	Right putamen	32, 0, 4	364	3.548	$< 1.0 \times 10^{-6}$
	Right IFG, BA 45	48, 40, -4	380	-3.458	0.000015
	Right IFG, BA 48	52, 16, 20	73	-2.847	0.000134
	Right ACC, BA 32	8, 42, 26	46	-2.834	0.000144
	Left ITG, BA20	-50, -24, -24	38	-2.663	0.000299

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FE patients with SZ					
Effects of PANSS positive score	ALFF alterations in studies with higher PANSS positive score				
	Right IPG, BA 40	44, -54, 50	218	3.848	$< 1.0 \times 10^{-6}$
	Right precuneus	6, -54, 14	116	3.740	$< 1.0 \times 10^{-6}$
	Left mPFC	-24, 10, 58	29	3.113	0.000062
Effects of PANSS negative score	ALFF alterations in studies with higher PANSS negative score				
	Right putamen	22, 14, -10	13	-2.685	0.000222
Effects of PANSS general psychopathology score	ALFF alterations in studies with higher PANSS general psychopathology score				
	None				
Chronic patients with SZ					
Effects of PANSS positive score	ALFF alterations in studies with higher PANSS positive score				
	Left SFG, BA 10	-18, 64, 4	29	5.226	$< 1.0 \times 10^{-6}$
	Left precuneus, BA 7	-10, -64, 68	19	-4.804	0.000005
Effects of PANSS negative score	ALFF alterations in studies with higher PANSS negative score				
	Left precuneus, BA 7	-10, -64, 68	18	-4.674	0.000015
Effects of PANSS	ALFF alterations in studies with higher PANSS general psychopathology score				

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general psychopathology score					
	Right ACC, BA 32	8, 42, 26	181	-3.282	0.000046
	Left ITG, BA 20	-50, -26, -24	172	-3.067	0.000077
	Right IFG, BA 47	44, 36, -6	73	-2.744	0.000144

Abbreviations: ALFF = amplitude of low-frequency fluctuations; FE = first episode; SZ = schizophrenia; BA = Brodmann area; MNI = Montreal neurological institute; SDM = seed-based d mapping; PANSS = Positive and Negative Syndrome Scale; IFG = inferior frontal gyrus; ACC = anterior cingulate cortex; ITG = inferior temporal gyrus; IPG = inferior parietal gyri; mPFC = medial prefrontal cortex; SFG = superior frontal gyrus.

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Table S5. Clusters of ALFF differences between FE and chronic patients with SZ compared to controls.

	Cluster	Anatomical label	Brain network	Peak MNI coordinate (x, y, z)	No. of voxels	SDM-Z value	*p* value
FE > Chronic							
	1	Left postcentral gyrus, BA 4	SMN	-52, -12, 38	1036	2.903	0.000036
	2	Left precuneus, BA 7	DMN	-6, -58, 62	717	3.620	$< 10^{-6}$
	3	Right precentral gyrus, BA 4	SMN	50, -14, 42	479	2.056	0.001063
	4	Left putamen		-28, 0, 0	132	1.860	0.002297
	5	Right putamen		28, 0, 4	22	1.786	0.002921
Chronic > FE							
	1	Right PCC	DMN	4, -46, 10	400	-2.765	0.000268
	2	Left SFG, BA 10		-18, 64, 4	69	-2.079	0.002369

Abbreviations: ALFF = amplitude of low-frequency fluctuations; FE = first episode; SZ = schizophrenia; BA = Brodmann area; MNI = Montreal neurological institute; SDM = seed-based d mapping; PCC = posterior cingulate cortex; SFG = superior frontal gyrus.

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Table S6. Clusters of ALFF differences between chronic SZ patients and HCs after FDR correction ($p < 0.05$).

	Anatomical label	Brain network	Peak MNI coordinate (x, y, z)	No. of voxels	SDM-Z value	*p* value	Egger's test (*p* value)	JK
Chronic < HCs	Right postcenral gyrus, BA 4	SMN	46, -20, 44	2517	-5.160	$< 1.0 \times 10^{-6}$	0.591	15/15

Abbreviations: ALFF = amplitude of low-frequency fluctuations; SZ = schizophrenia; HCs = healthy controls; BA = Brodmann area; MNI = Montreal neurological institute; SDM = seed-based d mapping; JK = Jackknife sensitivity analysis; SMN = sensorimotor network.