Supplementary material

Brain-wide analysis of functional connectivity in first-episode and chronic stages of schizophrenia

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Methods S1 Data scrubbing and global signal removal

Data scrubbing

We carried out a careful volume scrubbing movement correction recommended by Power et al (1) so that head-motion artifacts do not influence observed effects. The mean framewise displacement (FD) was computed with the FD threshold for displacement being 0.5 mm. In addition to the frame corresponding to the displaced time point, 1 preceding and 2 succeeding time points were also deleted to reduce the 'spill-over' effect from head movements. Thirdly, we discard subjects with >10% displaced frames from the analysis as it is likely that such a high level of movement would have had an influence on several volumes. Finally, the mean displacements after scrubbing were computed as the root-mean-square of the translation parameters and rotation parameters (computed as the average of the absolute value of the Euler angle of the rotation of each brain volume as compared to the previous volume) (2). The total root mean square displacements between the 2 groups in the overall sample did not show significant differences. Furthermore we used the root mean square displacement as a covariate when comparing the 2 groups for a t-test.

Global signal removal

Currently there is no consensus in the neuroimaging field whether to remove global signal when computing functional connectivity. Global signal removal has been shown to reduce physiological noise and movement-related effects (3), thus improving its reliability (3-5), although it can increase the number of negative functional connectivities (6). The major argument against global signal removal is the introduction of spurious correlations. In our study we are interested in only the difference between control and patient groups in terms of their functional connectivity strength, irrespective of the sign of the functional connectivity. Global signals in both

groups are regressed using an identical approach thus reducing the possibility of introducing spurious group differences. Therefore we believe that removing global signals will have little effect in the statistical test between two groups. Moreover, though global signal removal can increase the frequency of pairwise negative correlation coefficients, we consider negative correlation only on relative terms rather than anticorrelations, which is consistent with Murphy et al (12).

Though there is still controversy about global signal removal in group-wise analysis (13), the key functional connectivity changes we identified are clearly consistent among different datasets belonging to the same stage, see Table 2 in the MS. Importantly, the most significant functional-connectivity changes found in Broca's area for first-episode patients are consistent with Crow's hypothesis that the price paid for emergence of language in Homo sapiens is schizophrenia. Future investigations are needed to access systematically the impact of global signal.

Methods S2 Imaging acquisition

Dataset 1#: BOLD fMRI was acquired parallel to the anterior commissure - posterior commissure line on a 3T Siemens MRI scanner with a 32-channel head coil (TR/TE 2000ms/ 24ms; FOV 256 × 256 mm^2; matrix 64 × 64; slice-thickness 3 mm; flip angle 90°).

Dataset 2# : BOLD fMRI was obtained with a 3T General MRI system (EXCITE) using a gradient–echo echo-planar imaging (EPI) sequence (TR/TE: 2000/30 ms, flip angle 90°, slice-thickness 5 mm (no gap), in-plane resolution 3.75×3.75 mm^2, matrix size 64×64, FOV 240×240 mm^2, slices 30).

Dataset 3#: BOLD fMRI was obtained axially using a 1.5T Siemens MRI scanner (TR/TE: 2000/40 ms, thickness 5 mm, gap 1 mm, FOV 24 ×24 mm^2, resolution 64× 64, flip angle 90 °, slices 20).

Dataset 4#: BOLD fMRI was obtained by single-shot full k-space EPI with ramp sampling correction using the inter-commissural line (AC-PC) as a reference (TR/ TE: 2000/29 ms, matrix size: 64×64, voxel size: 3 × 3 × 4 mm^3; FOV = 256×256 mm^2, slices 32).

Dataset 5#: BOLD fMRI was obtained using a 3T Siemens MRI scanner (TR/TE: 2000/25 ms, Flip angle=90°, thickness=5mm, matrix size: 64*64; FOV=240mm^2, slices=32, measurements=170).

Dataset 6# : BOLD fMRI were acquired on a GE Signa HDX 3.0T MR scanner with a 12-channel head coil([TR/TE] = 2000/30 ms, FOV= 24 × 24 cm^2, acquisition matrix = 64 × 64, flip angle = 90°, 35 slices 3 mm thickness without gap).

Text S1 Information for Dataset 1# (UHR subjects-prodromal stage)

Eighteen subjects at ultra-high risk of psychosis (UHR) were recruited from the Shanghai Mental Health Center in 2011. The recruiting and diagnosis procedures have been described elsewhere (9). The Structured Interview for Prodromal Symptoms (SIPS) and Scale of Prodromal Syndromes (SOPS, thus SIPS/SOPS) (10) were used to determine whether subjects met criteria for a putatively prodromal syndrome (CHR

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status) or the Presence of a Psychotic Syndrome (POPS). The SIPS/SOPS (Version 5) was translated into Chinese according to the strict international translation standard (9). Among 18 UHR subjects included in the present study, one met the criteria of Brief Intermittent Psychotic Syndrome (BIPS), 14 met the criteria of Attenuated Positive Symptom Syndrome (APSS) and 3 met the criteria of Genetic Risk and Deterioration Syndrome (GRDS). The final UHR diagnosis was made by panel discussion of the prodromal research group.

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Table S1 Functional connectivity differences in high-risk subjects of psychosis (prodromal stage). As the number of subjects is quite small (17 prodromal subjects and 23 controls), we used FDR correction q=0.05 here. Here Pearson correlation is used as the measure of functional connectivity.

Functional connectivity		Control	Patient	P value
Frontal_Inf_Orb_L	Angular_R	-0.1392	0.2072	1.21*1e-5
Frontal_Inf_Tri_L	Precuneus_R	-0.3671	-0.1668	1.46*1e-5
Frontal_Sup_Medial_L	Temporal_Inf_R	0.0649	-0.1764	1.89*1e-5

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Table S2 Functional connectivity differences from controls for first-episode schizophrenia patients revealed by meta-analysis using datasets 2#, 3# and 6#. The sign of z-score comes from mean(FC_control)- mean(FC_patient), i.e., a positive z score indicates that the mean functional connectivity in patients is smaller than in controls. P_fix indicates p values from a fixed-effect model, while P_random indicates p values from a random-effects model. P_Hete represents the p value of Cochran's Q test that evaluates effect-size across datasets. We divided the total of 82 links into the following 3 categories for clarity: **(a)** links associated with the inferior frontal gyrus (including opercular and triangular parts, i.e., Broca's area; and the orbital part) that are increased in patients. **(b)** links associated with the inferior frontal gyrus that are decreased in patients. **(c)** The remaining links, i.e., those links in the 82 links except the links in (a) and (b). Note that because the inferior frontal cortex has the largest number of altered functional connectivity links, we listed the altered links according to their association with opercular, triangular and orbital part of the inferior frontal gyrus.

(a) Altered links of inferior frontal gyrus (including opercular and triangular parts, i.e., Broca's area; and the orbital part) that are increased in patietns.

Functional connectivity increases in patients		P_fix	P_random	z score	P_Hete
Broca's area (opercular and triangular parts of the inferior frontal gyrus)					
Frontal_Inf_Oper_L	Temporal_Pole_Mid_R	5.84E-09	0.013358	-5.8211	0.0204
Frontal_Inf_Oper_L	Frontal_Sup_L	1.36E-07	9.19E-06	-5.2701	0.2349
Frontal_Inf_Oper_L	Temporal_Mid_L	1.86E-07	8.88E-07	-5.213	0.4002
Frontal_Inf_Oper_R	Frontal_Sup_Medial_L	6.36E-07	0.000963	-4.9799	0.9351
Frontal_Inf_Oper_R	Temporal_Mid_R	6.42E-07	0.00011	-4.9782	0.2283
Frontal_Inf_Oper_R	Cingulate_Ant_L	7.52E-07	0.000815	-4.9473	0.8389
Frontal_Inf_Oper_R	Temporal_Pole_Mid_R	7.91E-07	0.064284	-4.9377	0.0102
Frontal_Inf_Oper_R	Cingulate_Ant_R	2.15E-06	0.000956	-4.739	0.8520
Frontal_Inf_Oper_L	Temporal_Pole_Mid_L	6.90E-06	0.004422	-4.4967	0.1251
Frontal_Inf_Oper_L	Precuneus_L	7.86E-06	0.001853	-4.4689	0.7334
Frontal_Inf_Tri_L	Frontal_Sup_L	7.15E-08	7.94E-06	-5.3875	0.5308
Frontal_Inf_Tri_R	Frontal_Sup_L	1.26E-07	0.00031	-5.2842	0.8668
Frontal_Inf_Tri_R	Cingulate_Ant_L	1.77E-07	9.79E-05	-5.2224	0.6608
Frontal_Inf_Tri_R	Cingulate_Ant_R	2.17E-07	1.82E-06	-5.1842	0.3219
Frontal_Inf_Tri_R	Frontal_Sup_Medial_L	2.49E-07	0.000783	-5.1582	0.9864
Frontal_Inf_Tri_L	Cingulate_Ant_L	2.67E-07	0.001343	-5.1451	0.9289
Frontal_Inf_Tri_L	Cingulate_Ant_R	2.86E-07	0.000956	-5.1325	0.8857
Frontal_Inf_Tri_L	Temporal_Pole_Mid_L	6.64E-07	9.11E-05	-4.9717	0.2605
Frontal_Inf_Tri_R	Frontal_Sup_Medial_R	1.97E-06	0.001439	-4.7562	0.9976
Frontal_Inf_Tri_L	Cingulate_Post_L	2.11E-06	0.000101	-4.7429	0.2758

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Frontal_Inf_Tri_R	Frontal_Med_Orb_L	3.39E-06	0.018484	-4.6456	0.0169
Frontal_Inf_Tri_L	Frontal_Med_Orb_R	5.02E-06	0.000592	-4.5638	0.7035
Frontal_Inf_Tri_L	Precuneus_L	1.08E-05	0.004683	-4.4006	0.9289
Orbital part of the inferior frontal gyrus					
Frontal_Inf_Orb_R	Frontal_Sup_L	1.20E-12	1.44E-06	-7.1054	0.1365
Frontal_Inf_Orb_L	Cingulate_Post_R	1.19E-11	0.041912	-6.7813	0.0031
Frontal_Inf_Orb_L	Precuneus_R	1.71E-10	0.208942	-6.3851	0.0001
Frontal_Inf_Orb_L	Cingulate_Post_L	2.72E-10	0.020546	-6.314	0.0128
Frontal_Inf_Orb_R	Frontal_Sup_R	1.53E-09	3.44E-05	-6.0417	0.1206
Frontal_Inf_Orb_L	Precuneus_L	2.15E-09	0.134664	-5.9857	0.0015
Frontal_Inf_Orb_R	Frontal_Sup_Medial_R	4.01E-09	4.25E-06	-5.8836	0.2260
Frontal_Inf_Orb_R	Frontal_Sup_Medial_L	8.14E-09	1.04E-05	-5.7656	0.6096
Frontal_Inf_Orb_L	Frontal_Sup_R	1.68E-08	5.82E-05	-5.6419	0.8446
Frontal_Inf_Orb_L	Frontal_Sup_Medial_R	8.80E-07	0.000825	-4.9168	0.8565
Frontal_Inf_Orb_L	Frontal_Sup_L	3.94E-06	5.48E-05	-4.6144	0.4887
Frontal_Inf_Orb_L	Frontal_Mid_R	1.09E-05	0.000833	-4.3985	0.6935

(b) Altered links associated with the inferior frontal gyrus that are decreased in patients.

Functional connectivity decreases in patients		P_fix	P_random	z score	P_Hete
Broca's area (opercular and triangular parts of the inferior frontal gyrus)					
Frontal_Inf_Oper_R	Parietal_Inf_R	5.19E-10	2.71E-08	6.2131	0.3037
Frontal_Inf_Oper_R	Frontal_Inf_Tri_L	1.96E-09	6.32E-05	6.0014	0.1643
Frontal_Inf_Oper_R	Parietal_Inf_L	4.22E-08	7.85E-07	5.4814	0.4415
Frontal_Inf_Oper_L	Frontal_Inf_Tri_L	1.06E-05	0.000158	4.4043	0.2897
Frontal_Inf_Oper_R	Frontal_Inf_Tri_L	1.96E-09	6.32E-05	6.0014	0.1643
Frontal_Inf_Tri_L	Precentral_R	5.84E-09	2.33E-06	5.8211	0.5140
Frontal_Inf_Tri_R	Parietal_Inf_L	1.66E-06	5.85E-05	4.7908	0.2390
Frontal_Inf_Tri_L	Postcentral_L	1.96E-06	0.000219	4.7574	0.5441
Frontal_Inf_Tri_L	Rolandic_Oper_L	4.25E-06	0.024833	4.5989	0.0337
Frontal_Inf_Tri_L	Precentral_L	4.78E-06	0.028484	4.5741	0.0992
Frontal_Inf_Tri_R	Precentral_L	5.67E-06	8.28E-06	4.5384	0.3765
Frontal_Inf_Tri_L	Rolandic_Oper_R	7.33E-06	0.000184	4.4838	0.4948
Frontal_Inf_Oper_L	Frontal_Inf_Tri_L	1.06E-05	0.000158	4.4043	0.2897
Frontal_Inf_Tri_R	SupraMarginal_R	1.09E-05	0.000153	4.3978	0.5242
Orbital part of the inferior frontal gyrus					
Frontal_Inf_Orb_L	Postcentral_L	2.05E-07	0.000619	5.1947	0.9198
Frontal_Inf_Orb_L	Postcentral_R	2.57E-07	1.43E-05	5.1529	0.4711
Frontal_Inf_Orb_L	Precentral_R	1.38E-06	0.001016	4.8286	0.7662
Frontal_Inf_Orb_R	Rolandic_Oper_L	1.06E-05	2.55E-05	4.4044	0.3959

(c) The remaining links.

Functional connectivity: other		P_fix	P_random	z score	P_Hete
Rectus_R	Temporal_Pole_Mid_R	4.32E-10	6.61E-09	6.2418	0.4232
Rectus_L	Angular_R	2.34E-09	8.73E-07	-5.9725	0.4808
Rectus_L	Temporal_Pole_Mid_R	2.52E-08	7.05E-05	5.572	0.7560
Olfactory_L	Temporal_Pole_Mid_R	3.48E-08	0.000149	5.5152	0.9574
Rectus_R	Angular_R	8.77E-08	2.00E-05	-5.3506	0.2561
ParaHippocampal_R	Temporal_Pole_Mid_L	2.13E-07	0.000207	5.1878	0.1278
Olfactory_L	Fusiform_R	2.64E-07	0.000302	5.1474	0.8735
Frontal_Mid_Orb_L	Cingulate_Post_R	4.09E-07	0.036744	-5.0649	0.0345
Rectus_L	Fusiform_R	4.69E-07	0.000635	5.0386	0.8920
Olfactory_R	Temporal_Pole_Mid_R	5.24E-07	0.000729	5.0173	0.9561
Frontal_Sup_Medial_L	Frontal_Mid_R	6.41E-07	0.000601	-4.9785	0.7807
Frontal_Mid_R	Cingulate_Ant_L	7.42E-07	9.75E-05	-4.9499	0.6128
Rectus_R	Temporal_Pole_Mid_L	1.06E-06	5.11E-05	4.8794	0.5105
Olfactory_L	Angular_R	1.21E-06	0.043904	-4.854	0.0275
Rectus_L	Fusiform_L	1.95E-06	0.001461	4.7582	0.9443
Rectus_L	Temporal_Pole_Mid_L	2.01E-06	7.58E-05	4.7526	0.2908
Precentral_L	Cingulate_Post_L	2.61E-06	0.00384	-4.6992	0.0431
Olfactory_L	Fusiform_L	2.81E-06	0.000169	4.6841	0.6011
Frontal_Mid_Orb_L	Cingulate_Post_L	3.05E-06	0.023746	-4.6677	0.0588
Frontal_Mid_Orb_R	Frontal_Sup_Medial_R	4.24E-06	0.000438	-4.5994	0.6599
Rectus_R	Frontal_Mid_L	4.30E-06	1.03E-05	-4.5965	0.3383
Frontal_Sup_Medial_L	Frontal_Sup_Orb_R	4.66E-06	0.026427	-4.5795	0.0318
Temporal_Pole_Mid_L	Amygdala_R	4.68E-06	0.002683	4.5787	0.0721
Olfactory_R	Fusiform_R	5.49E-06	9.73E-05	4.5452	0.4843
Frontal_Sup_Medial_L	Frontal_Mid_Orb_R	5.54E-06	6.91E-05	-4.5431	0.4523
Parietal_Inf_L	Frontal_Mid_R	7.58E-06	0.001858	4.4767	0.0984
Olfactory_L	Frontal_Mid_R	7.66E-06	0.000506	-4.4744	0.6843
Temporal_Mid_L	Calcarine_L	8.62E-06	0.006944	4.4491	0.0817
Rectus_R	Fusiform_R	8.85E-06	0.001224	4.4436	0.7657
Temporal_Mid_L	Fusiform_R	1.09E-05	7.90E-05	4.3995	0.3215
Rectus_L	Frontal_Mid_L	1.16E-05	0.003055	-4.3845	0.0861

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Table S3. Functional connectivity differences from controls for chronic stage schizophrenia patients revealed by meta-analysis integrating Datasets 4#,5# and 6#. We divided the total of 162 links into **(a)** links associated with the thalamus, **(b)** links associated with the cingulate cortex (ACC, MCC and PCC), and **(c)** the remaining links. Conventions as in Table S2.

(a) Links involving the thalamus.

Functional connectivity		P_fix	P_random	z score	P_Hete
Frontal_Mid_R	Thalamus_L	1.24E-19	4.89E-06	9.0651	0.0175
Frontal_Mid_R	Thalamus_R	2.93E-17	4.53E-05	8.4492	0.0122
Postcentral_L	Thalamus_R	9.73E-15	6.74E-05	-7.7427	0.0270
Postcentral_R	Thalamus_R	3.98E-14	2.33E-06	-7.5617	0.0823
Postcentral_R	Thalamus_L	4.59E-14	8.24E-06	-7.5432	0.0571
Postcentral_L	Thalamus_L	8.25E-13	0.000647	-7.1570	0.0131
Frontal_Mid_L	Thalamus_R	4.09E-12	0.000202	6.9342	0.0227
Fusiform_R	Thalamus_R	1.64E-10	0.000145	-6.3921	0.0507
Lingual_L	Thalamus_R	4.35E-10	0.00017	-6.2409	0.0569
Frontal_Mid_L	Thalamus_L	5.09E-10	2.67E-05	6.2162	0.1021
Precentral_R	Thalamus_R	5.11E-10	1.08E-05	-6.2156	0.1358
Temporal_Mid_L	Thalamus_L	6.47E-10	1.41E-06	-6.1785	0.1904
Fusiform_L	Thalamus_R	9.00E-10	0.000572	-6.1262	0.0387
Fusiform_R	Thalamus_L	1.64E-09	1.14E-07	-6.0299	0.2735
Precentral_R	Thalamus_L	1.74E-09	1.81E-05	-6.0204	0.1359
Lingual_L	Thalamus_L	2.91E-09	4.52E-05	-5.9369	0.1111
Fusiform_L	Thalamus_L	3.36E-09	5.96E-05	-5.9131	0.1060
Lingual_R	Thalamus_R	6.51E-09	0.00018	-5.8030	0.0922
Temporal_Sup_R	Thalamus_R	8.45E-09	0.006842	-5.7593	0.0140
Temporal_Mid_L	Thalamus_R	1.60E-08	0.000129	-5.6509	0.1154
Heschl_L	Thalamus_R	1.66E-08	3.56E-08	-5.6446	0.3512
Rolandic_Oper_R	Thalamus_R	3.92E-08	3.44E-05	-5.4944	0.1793
Angular_R	Thalamus_R	5.25E-08	8.26E-06	5.4427	0.2270
Angular_R	Thalamus_L	5.29E-08	2.03E-06	5.4412	0.2655
Frontal_Sup_R	Thalamus_L	8.42E-08	0.007178	5.3579	0.0114
Precentral_L	Thalamus_L	1.24E-07	6.72E-06	-5.2877	0.2550
Temporal_Mid_R	Thalamus_R	1.27E-07	0.02597	-5.2834	0.0036
Cingulate_Ant_R	Thalamus_R	1.45E-07	0.000106	5.2584	0.1807
Heschl_L	Thalamus_L	1.50E-07	1.86E-07	-5.2531	0.3626
Cingulate_Ant_R	Thalamus_L	1.89E-07	2.04E-06	5.2096	0.4385
Paracentral_Lobule_L	Thalamus_L	2.60E-07	2.09E-05	-5.1501	0.2467
Precentral_L	Thalamus_R	2.93E-07	8.70E-06	-5.1276	0.2758
Temporal_Mid_R	Thalamus_L	3.93E-07	0.005479	-5.0723	0.0320
Heschl_R	Thalamus_R	3.93E-07	2.16E-05	-5.0722	0.2469

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Parietal_Inf_R	Thalamus_L	5.44E-07	1.70E-06	5.0100	0.3329
Frontal_Mid_Orb_R	Thalamus_L	8.62E-07	0.003202	4.9208	0.0481
Temporal_Sup_R	Thalamus_L	9.13E-07	0.014084	-4.9096	0.0198
Frontal_Sup_R	Thalamus_R	1.30E-06	0.016299	4.8405	0.0102
Cingulate_Mid_R	Thalamus_R	1.48E-06	0.010016	4.8145	0.0130
Calcarine_R	Thalamus_R	1.51E-06	0.000321	-4.8095	0.7471
Lingual_R	Thalamus_L	1.61E-06	6.45E-05	-4.7967	0.2411
ParaHippocampal_R	Thalamus_L	1.70E-06	0.000545	-4.7863	0.1748
Paracentral_Lobule_L	Thalamus_R	1.80E-06	2.09E-05	-4.7747	0.2966
Frontal_Sup_Medial_R	Thalamus_R	2.05E-06	0.031741	4.7488	0.0185
Occipital_Sup_R	Thalamus_R	2.23E-06	7.89E-06	-4.7316	0.3294
Frontal_Sup_Medial_R	Thalamus_L	2.56E-06	0.05479	4.7029	0.0073
Rolandic_Oper_R	Thalamus_L	2.72E-06	0.000109	-4.6906	0.2315
Frontal_Mid_Orb_R	Thalamus_R	2.73E-06	0.003727	4.6898	0.0574
Parietal_Inf_R	Thalamus_R	3.01E-06	0.002701	4.6700	0.0771
Frontal_Inf_Orb_R	Thalamus_R	3.66E-06	0.004674	4.6299	0.0591
Rolandic_Oper_L	Thalamus_R	3.78E-06	0.000333	-4.6230	0.7053
Rolandic_Oper_L	Thalamus_L	4.85E-06	0.000102	-4.5712	0.2525
Cingulate_Mid_R	Thalamus_L	5.37E-06	0.014116	4.5498	0.0143
ParaHippocampal_R	Thalamus_R	6.44E-06	0.000182	-4.5115	0.5676
Frontal_Inf_Orb_R	Thalamus_L	7.05E-06	0.010954	4.4923	0.0386
Heschl_R	Thalamus_L	7.70E-06	0.000268	-4.4734	0.2327
Angular_L	Thalamus_R	8.31E-06	0.039678	4.4569	0.0048
Cingulate_Ant_L	Thalamus_R	1.22E-05	0.002885	4.3748	0.1328

(b) Links involving the cingulate cortex

Functional connectivity		P_fix	P_random	z score	P_Hete
Cingulate_Mid_R	Occipital_Sup_L	7.63E-12	0.000159	-6.8454	0.0432
Cingulate_Post_R	Calcarine_R	3.54E-10	1.35E-06	-6.2732	0.7200
Cingulate_Post_R	Lingual_R	4.85E-10	1.66E-06	-6.2240	0.1801
Cingulate_Post_R	Lingual_L	1.11E-09	0.000102	-6.0931	0.0817
Cingulate_Post_L	Cuneus_L	1.22E-09	3.25E-07	-6.0770	0.2540
Cingulate_Mid_R	Putamen_R	1.53E-09	0.002824	6.0408	0.0105
Cingulate_Post_R	Cuneus_L	2.70E-09	2.52E-08	-5.9490	0.4170
Cingulate_Mid_R	Occipital_Sup_R	2.96E-09	1.66E-08	-5.9336	0.3329
Cingulate_Mid_L	Occipital_Sup_L	5.86E-09	0.003288	-5.8206	0.0204
Cingulate_Post_R	Calcarine_L	7.39E-09	1.73E-05	-5.7818	0.8047
Cingulate_Mid_R	Pallidum_R	1.36E-08	0.007732	5.6783	0.0077
Cingulate_Mid_R	Pallidum_L	1.97E-08	0.007088	5.6144	0.0098
Cingulate_Mid_L	Occipital_Mid_L	2.80E-08	0.00011	-5.5536	0.1261
Cingulate_Mid_R	Putamen_L	3.94E-08	0.00407	5.4934	0.0189
Cingulate_Mid_R	Occipital_Mid_L	4.62E-08	7.09E-08	-5.4653	0.3574
Cingulate_Post_R	Fusiform_R	5.58E-08	0.036586	-5.4318	0.0017

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Cingulate_Post_R	Occipital_Mid_L	7.37E-08	0.000128	-5.3819	0.8919
Cingulate_Post_L	Calcarine_R	1.06E-07	9.96E-05	-5.3154	0.8711
Cingulate_Post_R	Occipital_Sup_R	1.18E-07	1.63E-05	-5.2962	0.6143
Cingulate_Mid_R	Olfactory_L	1.33E-07	0.029191	5.2745	0.0016
Cingulate_Post_L	Calcarine_L	1.34E-07	6.59E-05	-5.2736	0.7727
Cingulate_Ant_R	Thalamus_R	1.45E-07	0.000106	5.2584	0.1807
Cingulate_Post_R	Cuneus_R	1.57E-07	1.21E-06	-5.2442	0.3168
Cingulate_Mid_L	Putamen_R	1.74E-07	0.024588	5.2255	0.0027
Cingulate_Ant_R	Thalamus_L	1.89E-07	2.04E-06	5.2096	0.4385
Cingulate_Mid_L	Putamen_L	3.87E-07	0.012084	5.0753	0.0117
Cingulate_Post_L	Lingual_L	3.96E-07	0.001829	-5.0709	0.0700
Cingulate_Mid_R	Olfactory_R	4.02E-07	0.028092	5.0678	0.0024
Cingulate_Post_R	Occipital_Sup_L	7.45E-07	0.00032	-4.9493	0.8862
Cingulate_Mid_L	Occipital_Sup_R	8.94E-07	0.000563	-4.9136	0.1325
Cingulate_Mid_L	Pallidum_L	9.15E-07	0.024382	4.9090	0.0058
Cingulate_Post_R	Occipital_Mid_R	9.35E-07	0.000118	-4.9049	0.6365
Cingulate_Mid_R	Frontal_Inf_Orb_R	1.19E-06	0.003278	4.8570	0.0571
Cingulate_Mid_R	Thalamus_R	1.48E-06	0.010016	4.8145	0.0130
Cingulate_Mid_R	Amygdala_R	2.23E-06	0.008539	4.7312	0.0381
Cingulate_Mid_R	Cuneus_L	2.43E-06	0.000666	-4.7139	0.8951
Cingulate_Post_R	Fusiform_L	3.48E-06	0.032756	-4.6405	0.0126
Cingulate_Mid_L	Amygdala_R	3.86E-06	0.032891	4.6189	0.0064
Cingulate_Post_L	Lingual_R	4.13E-06	2.26E-05	-4.6047	0.3048
Cingulate_Ant_R	Occipital_Sup_R	4.95E-06	0.013732	-4.5670	0.0322
Cingulate_Mid_R	Thalamus_L	5.37E-06	0.014116	4.5498	0.0143
Cingulate_Mid_L	Olfactory_L	6.01E-06	0.013029	4.5262	0.0328
Cingulate_Post_L	Occipital_Mid_L	7.18E-06	0.000462	-4.4883	0.6606
Cingulate_Mid_L	Pallidum_R	7.75E-06	0.074213	4.4721	0.0009
Cingulate_Mid_L	Cuneus_L	8.38E-06	0.000176	-4.4553	0.5450
Cingulate_Mid_R	Amygdala_L	9.41E-06	0.034606	4.4302	0.0116
Cingulate_Mid_R	Cuneus_R	1.08E-05	2.31E-05	-4.4009	0.3387
Cingulate_Post_R	Frontal_Mid_L	1.12E-05	0.021487	4.3928	0.0442
Cingulate_Ant_L	Thalamus_R	1.22E-05	0.002885	4.3748	0.1328

(c) The remaining links. (26 links are related to subcortical areas such as Putamen, Caudate and Pallidum).

Functional connectivity		P_fix	P_random	z score	P_Hete
SupraMarginal_R	Putamen_R	2.62E-11	1.38E-06	6.6666	0.8742
SupraMarginal_R	Pallidum_R	7.90E-11	4.10E-10	6.5024	0.3993
SupraMarginal_R	Putamen_L	3.59E-10	8.51E-07	6.2709	0.6720
Postcentral_R	Temporal_Mid_R	6.20E-10	5.65E-07	6.1853	0.2350
Temporal_Pole_Mid_L	Caudate_R	1.09E-08	0.005309	-5.7155	0.0141

SupraMarginal_R	Pallidum_L	1.14E-08	2.25E-07	5.7086	0.2962
Supp_Motor_Area_R	Putamen_R	3.05E-08	6.48E-05	5.5385	0.1370
Postcentral_L	Temporal_Mid_R	3.60E-08	0.000126	5.5097	0.1477
Parietal_Inf_R	Putamen_L	4.85E-08	7.35E-06	5.4569	0.5989
Caudate_L	Temporal_Pole_Mid_L	6.41E-08	0.008238	-5.4071	0.0269
Occipital_Mid_L	Precuneus_R	6.89E-08	0.000116	-5.3939	0.9441
Temporal_Mid_L	Pallidum_L	1.05E-07	1.14E-06	-5.3183	0.3031
Occipital_Mid_R	Precuneus_R	1.51E-07	0.00024	-5.2513	0.9910
Amygdala_L	Parietal_Inf_R	1.59E-07	9.47E-05	5.2418	0.8280
Occipital_Inf_L	Temporal_Pole_Mid_L	1.74E-07	5.94E-06	5.2256	0.2611
Occipital_Sup_R	Angular_R	1.83E-07	0.016707	-5.2159	0.0062
Frontal_Mid_R	Pallidum_L	2.12E-07	0.01583	5.1884	0.0070
Amygdala_L	SupraMarginal_R	2.13E-07	4.27E-07	5.1874	0.3491
Temporal_Pole_Mid_R	Caudate_L	2.93E-07	0.009093	-5.1282	0.0307
SupraMarginal_L	Putamen_L	3.10E-07	1.16E-05	5.1170	0.5325
Parietal_Inf_R	Pallidum_R	3.34E-07	9.70E-06	5.1032	0.5170
Cuneus_L	Lingual_L	3.53E-07	0.043584	5.0927	0.0445
Frontal_Mid_R	Putamen_L	4.00E-07	0.023055	5.0688	0.0043
Frontal_Mid_R	Pallidum_R	4.03E-07	0.018957	5.0677	0.0078
Occipital_Mid_L	Precuneus_L	4.09E-07	1.95E-05	-5.0645	0.5605
Temporal_Mid_R	Pallidum_R	4.54E-07	0.002733	-5.0450	0.0823
SupraMarginal_L	Putamen_R	5.09E-07	9.33E-05	5.0229	0.7065
Temporal_Mid_L	Pallidum_R	5.55E-07	3.30E-06	-5.0064	0.3134
Occipital_Inf_L	Temporal_Pole_Mid_R	8.37E-07	1.28E-06	4.9265	0.3798
Postcentral_L	Caudate_R	9.74E-07	9.05E-05	-4.8969	0.2017
Parietal_Sup_L	Temporal_Pole_Mid_L	1.07E-06	0.000136	4.8783	0.7026
Cuneus_R	Angular_R	1.28E-06	0.004219	-4.8422	0.0555
Occipital_Sup_R	Parietal_Inf_R	1.60E-06	2.81E-05	-4.7981	0.5026
Parietal_Inf_R	Pallidum_L	1.62E-06	0.000231	4.7954	0.7450
Occipital_Sup_L	Angular_R	1.86E-06	0.013587	-4.7681	0.0283
Occipital_Sup_R	SupraMarginal_R	2.19E-06	8.71E-05	-4.7355	0.5681
Occipital_Sup_R	Fusiform_R	3.14E-06	0.000913	4.6615	0.1318
Lingual_L	Occipital_Sup_L	3.63E-06	0.000399	4.6314	0.6437
Temporal_Sup_L	Temporal_Mid_R	3.65E-06	5.57E-05	4.6304	0.2804
Parietal_Sup_R	Temporal_Pole_Mid_L	3.72E-06	0.000185	4.6265	0.6032
Supp_Motor_Area_L	Putamen_R	4.31E-06	0.000668	4.5959	0.1559
Cuneus_L	Angular_R	4.40E-06	0.001308	-4.5916	0.1309
Frontal_Mid_R	Occipital_Sup_R	5.11E-06	0.002749	-4.5601	0.1078
Occipital_Sup_L	Angular_L	5.30E-06	0.072507	-4.5525	0.0017
Parietal_Inf_R	Putamen_R	5.99E-06	0.00015	4.5269	0.5684
Postcentral_R	Temporal_Mid_L	7.39E-06	0.000784	4.4820	0.1862
Frontal_Inf_Tri_R	Insula_L	7.57E-06	0.001147	4.4769	0.8657
Frontal_Mid_L	Caudate_R	8.04E-06	0.000134	4.4640	0.2501

Temporal_Pole_Mid_R	Putamen_L	8.16E-06	0.042503	-4.4610	0.0113
Occipital_Sup_L	SupraMarginal_L	8.26E-06	0.000658	-4.4584	0.7595
Temporal_Pole_Mid_R	Pallidum_R	8.43E-06	0.009148	-4.4541	0.0525
Occipital_Sup_L	Fusiform_R	8.72E-06	0.000146	4.4466	0.2592
Cuneus_R	Lingual_R	1.00E-05	0.002306	4.4166	0.6655
Hippocampus_R	Lingual_L	1.02E-05	0.045341	-4.4132	0.0059
Occipital_Sup_R	Fusiform_L	1.02E-05	0.001616	4.4124	0.1421
Cuneus_L	Lingual_R	1.04E-05	0.002797	4.4096	0.2035
Occipital_Mid_R	Angular_R	1.12E-05	0.012774	-4.3927	0.0426
Lingual_L	Putamen_R	1.13E-05	0.007367	-4.3900	0.0447
Supp_Motor_Area_R	Postcentral_L	1.20E-05	0.000614	-4.3777	0.6787
Amygdala_L	SupraMarginal_L	1.22E-05	0.001454	4.3733	0.8783

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Table S4 Correlations between symptoms and significantly altered functional connectivities in **(a)** first-episode and **(b)** chronic patients. The results were integrated by meta-analysis. For the chronic stage, as dataset 6[#] has only BPRS scores, while datasets 4[#]and 5[#] have PANSS score, we used PANSS scores in the correlation analysis using datasets 4[#]and 5[#]. Bonferroni correction is used for both the sum scores and subscores. Since there are 3 sum scores (positive, negative and general scores) and 30 sub scores, the corresponding thresholds are 0.017(0.05/3) and 0.0017 (0.05/30), respectively.

(a) First-episode

Sum score				
Functional connectivity		Symptom	P val	corr
Fusiform_R	Temporal_Mid_L	Positive	0.0016	-0.2703
Frontal_Mid_R	Cingulate_Ant_L	Positive	0.0035	0.2464
Frontal_Sup_Orb_R	Frontal_Sup_Medial_L	Positive	0.0042	0.2471
Frontal_Mid_R	Olfactory_L	positive	0.0148	0.2114
Frontal_Inf_Oper_R	Temporal_Mid_R	Positive	0.0148	0.2097
Frontal_Inf_Tri_R	Frontal_Sup_Medial_R	Negative	0.0061	0.2318
Frontal_Inf_Oper_R	Frontal_Sup_Medial_L	Negative	0.0062	0.2243
Frontal_Mid_Orb_R	Frontal_Sup_Medial_R	Negative	0.0122	0.2084
Frontal_Inf_Orb_L	Precuneus_R	General	0.0085	0.2260
Frontal_Mid_Orb_R	Frontal_Sup_Medial_R	sum of all	0.0158	0.1980
Sub scores (positive)				
Frontal_Mid_R	Olfactory_L	Excitement	0.0016	0.2681
Sub scores (negative)				
Frontal_Mid_Orb_R	Frontal_Sup_Medial_R	Difficulty in abstract thinking	0.0013	0.2707
Sub scores (general)				
Frontal_Mid_Orb_R	Frontal_Sup_Medial_L	Uncooperativeness	0.0001	0.3421
Frontal_Mid_Orb_R	Frontal_Sup_Medial_R	Uncooperativeness	0.0001	0.3378
Frontal_Inf_Orb_L	Frontal_Sup_Medial_R	Lack of judgment & insight	0.0003	0.3111
Frontal_Mid_R	Frontal_Sup_Medial_L	Uncooperativeness	0.0015	0.2725
Frontal_Sup_R	Frontal_Inf_Orb_L	Lack of judgment & insight	0.0016	0.2704
Frontal_Inf_Orb_L	Cingulate_Post_L	Lack of judgment & insight	0.0016	0.2715

(b) Chronic

Sum score				
Functional connectivity		symptom	P val	corr
Cingulate_Post_R	Fusiform_L	Sum	0.00002	0.3876
Frontal_Mid_L	Thalamus_L	Sum	0.0007	-0.3130
Frontal_Sup_Medial_R	Thalamus_R	Sum	0.0007	-0.3088
Frontal_Sup_Medial_R	Thalamus_L	Sum	0.0008	-0.3076
Frontal_Sup_Medial_R	Thalamus_R	P	0.0001	-0.3485

Postcentral_R	Thalamus_R	P	0.0005	0.3173
Frontal_Mid_L	Thalamus_L	P	0.0008	-0.3028
Cingulate_Post_R	Fusiform_L	P	0.0011	0.2982
Postcentral_R	Thalamus_L	P	0.0015	0.2898
Cingulate_Post_R	Fusiform_R	N	0.0002	0.3345
Cingulate_Post_R	Occipital_Sup_R	N	0.0003	0.3260
Cingulate_Post_R	Fusiform_L	N	0.0004	0.3227
Cingulate_Post_R	Occipital_Mid_L	N	0.0015	0.2947
Cingulate_Post_R	Fusiform_L	G	0.0009	0.3075
Sub scores (positive)				
Postcentral_R	Thalamus_L	Delusions	0.00004	0.3714
Frontal_Sup_Medial_R	Thalamus_R	Delusions	0.0001	-0.3545
Frontal_Mid_L	Thalamus_L	Delusions	0.0001	-0.3390
Postcentral_R	Thalamus_R	Delusions	0.0002	0.3419
Frontal_Sup_Medial_R	Thalamus_L	Delusions	0.0004	-0.3224
Precentral_R	Thalamus_L	Delusions	0.0008	0.3103
Frontal_Sup_Medial_R	Thalamus_R	Hallucinations	0.0002	-0.3462
Caudate_R	Temporal_Pole_Mid_L	Hallucinations	0.0013	0.2973
Frontal_Sup_Medial_R	Thalamus_R	Suspiciousness	0.0004	-0.3226
Frontal_Mid_R	Thalamus_R	Suspiciousness	0.0006	-0.3172
Frontal_Sup_R	Thalamus_R	Suspiciousness	0.0007	-0.3113
Lingual_L	Occipital_Sup_L	Suspiciousness	0.0009	-0.3031
Cingulate_Mid_R	Thalamus_L	Suspiciousness	0.0013	0.2950
Sub scores (negative)				
Cingulate_Post_L	Lingual_R	B1unted affect	0.0012	0.2975
Cingulate_Post_R	Occipital_Sup_R	B1unted affect	0.0013	0.2946
Cingulate_Post_R	Fusiform_R	B1unted affect	0.0015	0.2920
Frontal_Mid_Orb_R	Thalamus_L	Passive / pathetic social withdrawal	0.0004	-0.3250
Cingulate_Post_R	Fusiform_L	Passive / pathetic social withdrawal	0.0007	0.3073
Parietal_Inf_R	Putamen_L	Passive / pathetic social withdrawal	0.0012	-0.2979
Cingulate_Post_R	Occipital_Sup_R	Passive / pathetic social withdrawal	0.0012	0.2865
Occipital_Sup_R	Parietal_Inf_R	Difficulty in abstract thinking	0.0003	0.3360
Pallidum_R	Temporal_Pole_Mid_R	Difficulty in abstract thinking	0.0014	0.2765
Cingulate_Mid_R	Amygdala_R	Lack of spontaneity and flow of conversation	0.0007	-0.2997
Sub scores (general)				

Cingulate_Post_R	Fusiform_L	Motor retardation	0.0007	0.3014
Parietal_Inf_R	Pallidum_L	Motor retardation	0.0013	-0.2938
Parietal_Sup_L	Temporal_Pole_Mid_L	Uncooperativeness	0.0008	-0.3084
Cingulate_Post_R	Fusiform_L	Disturbance of volition	0.0003	0.3218
Cingulate_Post_R	Fusiform_R	Disturbance of volition	0.0013	0.2980
Cingulate_Post_L	Occipital_Mid_L	Preoccupation	0.0010	0.3015
Cingulate_Post_R	Fusiform_L	Preoccupation	0.0013	0.2956
Cingulate_Mid_R	Occipital_Sup_L	Active social avoidance	0.0015	-0.2929

Table S5 Correlations between illness duration and significantly altered functional connectivities in chronic patients. The results were integrated by meta-analysis using datasets 4[#]and 5[#]. We list the functional connectivity links that have p values smaller than 0.001. The first 2 can survive Bonferroni correction.

Functional connectivity		P val	Corr. Coef.
Precuneus_L	Occipital_Mid_L	0.0000807	0.3422
Putamen_R	Cingulum_Mid_L	0.0003132	-0.3189
Precuneus_R	Occipital_Mid_L	0.0008562	0.2967
Pallidum_L	Cingulum_Mid_L	0.0008941	-0.2956

Table S6 Common links identified for first-episode (FE) and chronic patients using FDR correction (q=0.05) by comparing FE and chronic patients with their matched controls. 505 significant links were identified for first episode patients and 820 links for the chronic patients. The first episode and chronic stage schizophrenia patients have 70 links in common, and we show here the 21 links which have a *p* value smaller than 0.0025 in both stages.

Functional connectivity		P (FE)	P(Chronic)
Frontal_Mid_L	Frontal_Med_Orb_R	0.00042	0.000736
Frontal_Mid_R	Frontal_Inf_Orb_R	0.001227	0.000244
Frontal_Inf_Oper_L	Precuneus_L	8.78E-07	0.000444
Frontal_Inf_Tri_R	SupraMarginal_R	2.07E-05	0.001141
Frontal_Inf_Tri_R	Temporal_Pole_Mid_R	4.14E-05	0.00114
Frontal_Inf_Orb_R	SupraMarginal_R	0.000655	0.000138
Supp_Motor_Area_L	Putamen_L	0.000375	0.000386
Supp_Motor_Area_R	Putamen_L	0.000291	2.17E-05
Supp_Motor_Area_R	Putamen_R	3.25E-05	3.05E-08
Olfactory_R	Fusiform_R	1.75E-05	0.001944
Insula_L	Putamen_R	0.000107	0.000119
Insula_R	Putamen_R	0.001184	0.000957
Cingulate_Ant_L	Temporal_Pole_Mid_R	8.65E-06	0.00119
Cingulate_Ant_R	Temporal_Pole_Mid_R	0.000277	0.000379
Cingulate_Post_R	Cuneus_L	0.001996	2.70E-09
Cingulate_Post_R	Cuneus_R	0.002197	1.57E-07
Amygdala_R	Parietal_Inf_R	0.001055	0.000525
Calcarine_L	Thalamus_L	0.002232	0.002465
Fusiform_L	Temporal_Pole_Mid_R	8.19E-05	0.001528
Fusiform_R	Temporal_Mid_L	5.54E-06	0.002013
Parietal_Inf_R	Pallidum_R	0.002307	3.34E-07

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Table S7 Functional connectivity differences from controls for **drug-naive** first-episode schizophrenia patients revealed by meta-analysis using datasets 2#, 3# and 6#. A positive z score indicates that the mean functional connectivity in controls is larger than that of patients. P_fix indicates p values from a fixed-effect model, while P_random indicates p values from a random-effects model. P_Hete represents the p value of Cochran's Q test that evaluates effect-size across datasets. We divided the total of 62 links into (a) links associated with the inferior frontal gyrus (including opercular, triangular part, i.e., Borca's area, and orbital part) that are increased in patients. (b) links associated with the inferior frontal gyrus (including opercular, triangular and orbital part) that are decreased in patients. (c) The remaining links. Compared with Table S2 (i.e., using all first-episode patients) there are 50 connectivity in common.

(a) Links associated with the inferior frontal gyrus that are increased

Functional connectivity		P_fix	P_random	Zscore	P_Hete
Broca's area (opercular and triangular parts of the inferior frontal gyrus)					
Frontal_Inf_Oper_L	Temporal_Pole_Mid_R	9.90E-09	0.057104	-5.7325	0.0235
Frontal_Inf_Oper_R	Cingulate_Ant_L	5.36E-08	3.44E-06	-5.4390	0.4607
Frontal_Inf_Oper_R	Frontal_Sup_Medial_L	1.79E-07	3.77E-05	-5.2198	0.5303
Frontal_Inf_Oper_R	Temporal_Pole_Mid_R	2.48E-07	0.078772	-5.1590	0.0304
Frontal_Inf_Oper_R	Cingulate_Ant_R	5.79E-07	0.000453	-4.9980	0.1452
Frontal_Inf_Oper_L	Temporal_Mid_L	6.31E-07	0.000171	-4.9815	0.5122
Frontal_Inf_Oper_L	Precuneus_L	3.34E-06	0.00268	-4.6485	0.8906
Frontal_Inf_Oper_R	Frontal_Sup_L	3.93E-06	8.38E-06	-4.6151	0.3550
Frontal_Inf_Oper_R	Temporal_Mid_R	8.04E-06	0.000145	-4.4640	0.3129
Frontal_Inf_Tri_L	Cingulate_Ant_L	2.40E-08	3.68E-07	-5.5806	0.3359
Frontal_Inf_Tri_R	Cingulate_Ant_L	3.97E-08	0.000114	-5.4921	0.1565
Frontal_Inf_Tri_L	Cingulate_Ant_R	4.20E-08	4.44E-06	-5.4824	0.4543
Frontal_Inf_Tri_R	Frontal_Sup_L	6.28E-08	0.000131	-5.4105	0.6949
Frontal_Inf_Tri_R	Frontal_Sup_Medial_L	2.01E-07	0.000533	-5.1980	0.7757
Frontal_Inf_Tri_R	Cingulate_Ant_R	2.92E-07	0.000548	-5.1284	0.1210
Frontal_Inf_Tri_L	Cingulate_Post_L	1.49E-06	0.010442	-4.8128	0.0777
Frontal_Inf_Tri_L	Frontal_Sup_L	2.59E-06	0.001075	-4.7009	0.6893
Frontal_Inf_Tri_L	Temporal_Pole_Mid_L	6.15E-06	0.138358	-4.5212	0.0339
Frontal_Inf_Tri_L	Precuneus_L	6.76E-06	0.006358	-4.5011	0.9589
Frontal_Inf_Tri_R	Frontal_Sup_Medial_R	8.46E-06	0.003939	-4.4532	0.8749
Orbital part of the inferior frontal gyrus					
Frontal_Inf_Orb_L	Precuneus_R	8.16E-13	0.059784	-7.1584	0.0095
Frontal_Inf_Orb_L	Cingulate_Post_R	9.15E-12	0.038639	-6.8192	0.0137
Frontal_Inf_Orb_L	Precuneus_L	2.05E-11	0.004634	-6.7028	0.0899

Frontal_Inf_Orb_L	Cingulate_Post_L	3.91E-10	0.007309	-6.2574	0.0765
Frontal_Inf_Orb_R	Frontal_Sup_L	1.23E-08	7.63E-05	-5.6952	0.5906
Frontal_Inf_Orb_R	Frontal_Sup_R	2.20E-06	0.000263	-4.7338	0.5555
Frontal_Inf_Orb_R	Frontal_Sup_Medial_L	3.98E-06	0.000813	-4.6123	0.2729
Frontal_Inf_Orb_R	Precuneus_L	4.14E-06	0.14514	-4.6044	0.0448
Frontal_Inf_Orb_R	Cingulate_Post_L	4.17E-06	0.388088	-4.6029	0.0056
Frontal_Inf_Orb_R	Cingulate_Post_R	5.97E-06	0.314269	-4.5275	0.0159
Frontal_Inf_Orb_R	Frontal_Sup_Medial_R	8.00E-06	0.001135	-4.4653	0.4916

(b) Links associated with the inferior frontal gyrus that are decreased

Functional connectivity		P_fix	P_random	Zscore	P_Hete
Broca's area (opercular and triangular parts of the inferior frontal gyrus)					
Frontal_Inf_Oper_R	Frontal_Inf_Tri_L	4.85E-08	0.000201	5.4567	0.5496
Frontal_Inf_Oper_R	Parietal_Inf_R	3.19E-07	0.002678	5.1120	0.1404
Frontal_Inf_Oper_R	Parietal_Inf_L	1.23E-05	3.25E-05	4.3721	0.3526
Frontal_Inf_Tri_L	Precentral_R	1.86E-08	0.000264	5.6248	0.7900
Frontal_Inf_Tri_L	Frontal_Inf_Oper_R	4.85E-08	0.000201	5.4567	0.5496
Frontal_Inf_Tri_L	Precentral_L	1.23E-06	7.11E-05	4.8501	0.4250
Frontal_Inf_Tri_L	Postcentral_L	7.18E-06	0.002946	4.4882	0.2151
Frontal_Inf_Tri_L	Postcentral_R	8.65E-06	0.002062	4.4485	0.6319
Orbital inferior frontal gyrus					
Frontal_Inf_Orb_L	Postcentral_R	2.24E-07	0.001238	5.1782	0.8136
Frontal_Inf_Orb_L	Precentral_R	4.49E-06	0.008825	4.5875	0.9281

(c) Other links

Functional connectivity		P_fix	P_random	Zscore	P_Hete
Olfactory_L	Fusiform_R	1.08E-07	2.67E-06	5.3133	0.3041
Olfactory_L	Temporal_Pole_Mid_R	1.73E-07	1.37E-06	5.2258	0.3315
Rectus_L	Angular_R	2.26E-07	0.025788	-5.1763	0.0868
Rectus_R	Temporal_Pole_Mid_R	4.83E-07	1.37E-06	5.0329	0.3850
Frontal_Mid_Orb_L	Cingulate_Post_R	5.46E-07	0.009174	-5.0093	0.1638
Olfactory_R	Temporal_Pole_Mid_R	5.86E-07	6.07E-07	4.9957	0.3684
Rectus_L	Temporal_Pole_Mid_R	7.50E-07	0.001159	4.948	0.6636
Cingulate_Ant_L	Temporal_Pole_Mid_R	1.09E-06	0.004606	4.8748	0.1774
Olfactory_L	Angular_R	1.40E-06	0.022615	-4.8254	0.1340
Frontal_Mid_R	Frontal_Sup_Medial_L	1.63E-06	0.00025	-4.7948	0.2630
Olfactory_R	Fusiform_R	1.94E-06	0.000351	4.7595	0.2059
Frontal_Mid_L	Temporal_Sup_L	1.98E-06	0.046173	-4.7553	0.0430
Rectus_R	Angular_R	4.18E-06	0.004258	-4.602	0.2112
Frontal_Mid_R	Cingulate_Ant_L	6.53E-06	4.66E-05	-4.5084	0.3255
Rectus_L	Fusiform_R	6.68E-06	0.000154	4.5038	0.4354
Supp_Motor_Area_L	Precuneus_L	6.82E-06	0.000381	-4.4991	0.5109

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Caudate_L	Caudate_R	7.52E-06	0.033942	-4.4784	0.1424
Precentral_L	Temporal_Pole_Mid_R	8.36E-06	3.04E-05	-4.4559	0.3492
Frontal_Mid_Orb_L	Cingulate_Post_L	8.96E-06	0.02324	-4.4408	0.1406
Temporal_Pole_Sup_R	Temporal_Inf_R	9.55E-06	0.002675	-4.4272	0.7120
Cingulate_Ant_R	Temporal_Pole_Mid_R	9.97E-06	1.74E-05	4.4179	0.3756
Fusiform_R	Temporal_Mid_L	1.14E-05	0.002772	4.3881	0.5956

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Table S8 Influence of medication

(a) First episode patients: p values for different functional connectivity from controls in first episode schizophrenia (see Table S2) obtained by comparing medicated patients and drug-naïve patients in Datasets 3# and 6#. As can be seen, only 4 out of 82 links were significantly different as a result of the medication p<0.05 (uncorrected), providing some evidence that the influence of medication on the functional connectivities is not a major factor in accounting for the differences between the first episode and chronic patients. Here Pearson correlation is used as the measure of functional connectivity.

Functional connectivity		P value	medicated	drug-naive
Dataset 3#			25	14
Calcarine_L	Temporal_Mid_L	0.013	0.2405	0.1837
Frontal_Inf_Tri_R	SupraMarginal_R	0.010	0.2085	0.0838
Dataset 6#			22	22
Angular_R	Postcentral_L	0.035	-0.1435	-0.086
Frontal_Sup_Medial_R	Cingulate_Post_L	0.039	0.2609	0.1986

(b) Chronic stage: Correlation coefficients between the altered functional connectivities in chronic schizophrenia (see Table S3) and the dosage of medication of patients in Dataset 4#. As can be seen, only 3 out of 162 functional connectivities were correlated with the medication dosage (p<0.05, uncorrected), and these links do not include those that are important in making our main conclusion. (For chronic Datasets 5# and 6#, medication dosage information is not available.)

Brain region	Brain region	Corr coef	P value
SupraMarginal_R	Pallidum_L	-0.3297	0.0182
Cuneus_R	Angular_R	0.2845	0.0430
Frontal_Mid_L	Caudate_R	0.4066	0.0031

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Table S9 The names and abbreviations of the regions in the AAL atlas (11).

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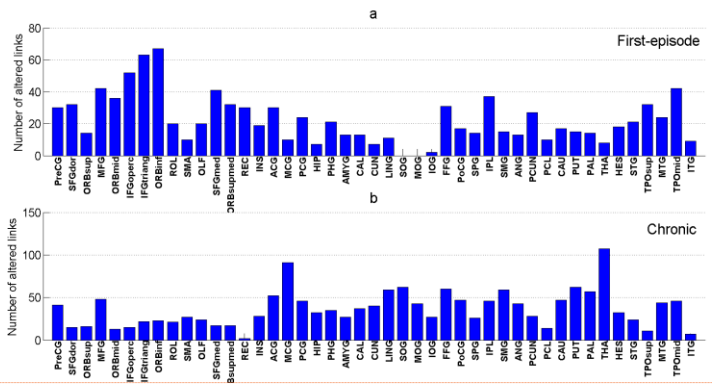
NO.	Regions	Abbr.	NO.	Regions	Abbr.
1, 2	Precentral gyrus	PreCG	47, 48	Lingual gyrus	LING
3, 4	Superior frontal gyrus, dorsolateral	SFGdor	49, 50	Superior occipital gyrus	SOG
5, 6	Orbitofrontal cortex, superior part	ORBsup	51, 52	Middle occipital gyrus	MOG
7, 8	Middle frontal gyrus	MFG	53, 54	Inferior occipital gyrus	IOG
9, 10	Orbitofrontal cortex, middle part	ORBmid	55, 56	Fusiform gyrus	FFG
11, 12	Inferior frontal gyrus, opercular part	IFGoperc	57, 58	Postcentral gyrus	PoCG
13, 14	Inferior frontal gyrus, triangular part	IFGtriang	59, 60	Superior parietal gyrus	SPG
15, 16	Orbitofrontal cortex, inferior part	ORBinf	61, 62	Inferior parietal	IPL
17, 18	Rolandic operculum	ROL	63, 64	Supramarginal gyrus	SMG
19, 20	Supplementary motor area	SMA	65, 66	Angular gyrus	ANG
21, 22	Olfactory cortex	OLF	67, 68	Precuneus	PCUN
23, 24	Superior frontal gyrus, medial	SFGmed	69, 70	Paracentral lobule	PCL
25, 26	Orbitofrontal cortex, superior medial	ORBsupmed	71, 72	Caudate nucleus	CAU
27, 28	Gyrus rectus	REC	73, 74	Lenticular nucleus, putamen	PUT
29, 30	Insula	INS	75, 76	Lenticular nucleus, pallidum	PAL
31, 32	Anterior cingulate & paracingulate gyri	ACG	77, 78	Thalamus	THA
33, 34	Cingulate & paracingulate gyri	DCG	79, 80	Heschl gyrus	HES
35, 36	Posterior cingulate gyrus	PCG	81, 82	Superior temporal gyrus	STG
37, 38	Hippocampus	HIP	83, 84	Temporal pole: superior	TPOsup
39, 40	Parahippocampal gyrus	PHG	85, 86	Middle temporal gyrus	MTG
41, 42	Amygdala	AMYG	87, 88	Temporal pole: middle	TPOmid
43, 44	Calcarine fissure & surrounding cortex	CAL	89, 90	Inferior temporal gyrus	ITG
45, 46	Cuneus	CUN			

Figure S1. The numbers of significantly different functional connectivity links from controls associated with each brain region for **(a)** first-episode and **(b)** chronic stage schizophrenia patients (for each pair of symmetric region, we added the number of links of the left and right hemispheres for the corresponding regions) by FDR correction (q=0.05). 505 links were identified for first-episode and 820 links were identified for chronic schizophrenia.



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