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Appendix 1

Methods

MRI data acquisition

MRI data were acquired in a GE Signa HD 3.0T scanner with a standard 8-channel head coil at the First Affiliated Hospital of China Medical University, Shenyang, China. Functional images were collected with a gradient echo planar imaging (EPI) sequence. The parameters were as follows: TR = 2000ms, TE = 30ms, flip angle = 90°, field of view=240×240mm^2, matrix = 64 × 64. Thirty-five axial slices were collected with 3mm thickness without gap. Participants were instructed to rest with their eyes closed but remain awake during scanning.

Voxel-wise analyses of fALFF values across the diagnostic groups

Four-group (SZ, BD, MDD, and HC) analyses of fALFF values in each band were performed in SPM8 using analysis of covariance (ANCOVA) with diagnostic group as an independent factor, and age and gender as covariates. Statistical significance was determined by a corrected $p < 0.05$. Correction for multiple comparisons was made by combining individual voxel p (uncorrected) < 0.001 with cluster size > 18 voxels for slow-5 and 10 voxels for slow-4, as determined by Monte Carlo simulation [AlphaSim, Analysis of Functional NeuroImages (AFNI)] [1].Post hoc pairwise t-contrasts (SZ vs HC, BD vs HC, and MDD vs HC) were performed to visualize differences between each patient group and HC in the regions showing significant differences among four groups in slow-5 and slow-4. The significant level was set $p < 0.05$ by Monte Carlo simulation.

Data processing

The functional images were processed with Statistical Parametric Mapping 8 (SPM, http://www.fil.ion.ucl.ac.uk/spm) and Data Processing Assistant for R-fMRI (DPARSF, http://www.restfmri.net/forum/DPARSF) toolkits [2]. For each participant, the first 10 volumes of scanned data were discarded due to instability of the initial signal. The remaining data were slice-time corrected and then realigned to the first volume to correct for head motion. Each participant's motion was assessed by means of translation/rotation, and an exclusion criterion (translation > 3 mm, rotation > 3° in each direction) was set. To access the head motion confounder, we compared the mean framewise displacement among the four groups[3, 4]. Head motion comparison showed no significant differences among groups (F=1.355, p = 0.256). The realigned functional data were then normalized to the standard EPI template in Montreal Neurological Institute (MNI) space, and resampled to 3×3×3 mm^3. Images were spatially smoothed with a 6mm full width at half maximum (FWHM) Gaussian kernel. ALFF/fALFF values were calculated in each frequency band: slow-5 (0.01–0.027 Hz) and slow-4 (0.027–0.073 Hz) using linear detrending [5]. Temporal band-pass filtering was

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performed in these bands to reduce the effects of low-frequency drift and high-frequency physiological noise. Nuisance signals, including six head motion parameters, global mean signal, white matter signal and cerebrospinal fluid signal, were regressed out from the data. ALFF at each voxel represents the averaged square root of the power in the above frequency windows normalized by the mean within-brain ALFF value for that subject. fALFF is the ratio of power spectrum of low-frequency (0.01–0.027 Hz &. 0.027-0.073Hz) to that of the entire frequency range (0-0.25Hz).

Results

ALFF across diagnostic groups

There were also significant ALFF differences specific to the frequency bands of interest. In slow-5, significant differences were found in bilateral thalamic (Figure 1A and Table 2). In slow-4, significant differences were shown in right temporal pole, right orbital frontal cortex, bilateral middle occipital gyri, bilateral middle temporal gyri, bilateral inferior occipital gyri, bilateral inferior temporal gyri and right motor cortex (Figure 2A and Table 3).

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fALFF across diagnostic groups

In slow5

The four-group analysis showed significant fALFF differences in slow-5 bands in the bilateral striatum (including the caudate nuclei and putamen), limbic and paralimbic regions (including the left hippocampus, bilateral temporal pole, bilateral insular cortex, bilateral orbitofrontal cortex and bilteral ACC), and heteromodal cortices (including right VPFC, bilateral middle prefrontal cortex, left inferior temporal gyri and left middle temporal gyrus). Significant differences were also seen in the lingual cortices, left fusiform and bilateral thalamus (Figure S1A).

Post hoc analyses found increased fALFF in striatum, limbic and paralimbic regions, heteromodal in the SZ, BD groups when compared to HC (Figures S1B-1C). While increased fALFF found in bilateral orbito frontal cortex, bilateral caudate, right fusiform and left insula in MDD (Figure S1D).

In slow4

The four-group analysis showed significant fALFF differences in slow-4 bands in right orbito frontal cortex, left visual cortex and right occipital cortex (Figures S2A).

Post hoc analyses found common increased fALFF in right orbito frontal cortex in the SZ, BD groups when compared to HC (Figures S1B-1C). While common increased fALFF found in left visual cortex in BD and MDD (Figures S1C-1D). The increased fALFF in right occipital cortex was just seen in BD group (Figure S1B)

Discussion

The effect of fALFF

Fractional ALFF (fALFF) may preferably be used because it standardizes the power spectra and is robust against physiological noise. However, each index has its own pros and cons. For example, fALFF is previously reported to have higher specificity but lower reliability to grey matter signals, vs ALFF [6-8]. Therefore, which would maximize reliability across subjects while providing sufficient specificity to capture interindividual differences [8].

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Clinical Characteristics	ALFF balance ratio in slow-5		ALFF balance ratio in slow-4	
	r-values	p-values	r-values	p-values
BPRS				
BPRS factor 1				
Emotional withdrawal	-0.159	0.017	-0.187	0.005*
Conceptual disorganisation				

Table S1- Correlation between ALFF balance ratios and clinical factors across SZ, BD and MDD in both frequency bands.

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		Motor retardation				
		Blunted affect				
		Disorientation				
	BPRS-factor2					
		Anxiety	0.098	0.142	0.121	0.069
		Guilt BPRS				
		Tension BPRS				
		Depression				
	BPRS-factor3					
		Suspiciousness	-0.160	0.016	-0.138	0.037
		Hallucinations				
		Unusual thought content				
	BPRS-factor4					
		Somatic concern	-0.076	0.253	-0.117	0.078
		Grandiosity				
		Hostility				
		Uncooperativeness				
	BPRS-factor5					
		Mannerisms and posturing	0.029	0.667	-0.013	0.848
		Excitement				
	BPRS-total score		-0.092	0.166	-0.103	0.122
HAMD						
	HAMD-factor1					
		Somatic anxiety	0.102	0.088	0.131	0.028
		Gastrointestinal symptoms				
		General somatic symptoms				
		Genital symptoms				
		Weight loss				
	HAMD-factor2					
		Work and interests	-0.021	0.729	0.027	0.650
		Retardation				
		Agitation				
		Psychic anxiety				
	HAMD-factor3					
		Depressed mood	0.044	0.465	0.081	0.177
		Guilt				
		Suicide				
		Hypochondria				
	HAMD-factor4					
		Early insomnia	0.076	0.206	0.085	0.156
		Middle insomnia				
		Late insomnia				
		Insight				
	HAMD-total score		0.132	0.027	0.146	0.014

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HAMD, Hamilton Depression Scale; BPRS, Brief Psychiatric Rating Scale. *, Significant at $p<0.05$ corrected by false discovery rate correction.

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Table S2-Correlation between ALFF balance ratios and BPRS on the single disorder in both frequency bands.

Clinical Characteristics		ALFF balance ratio in slow-5		ALFF balance ratio in slow-4	
		r-values	p-values	r-values	p-values
SZ					
BPRS	BPRS-factor1	0.068	0.475	0.000	0.999
	BPRS-factor2	0.130	0.173	0.223	0.018
	BPRS-factor3	0.086	0.367	0.133	0.163
	BPRS-factor4	0.045	0.636	0.021	0.825
	BPRS-factor5	0.129	0.176	0.168	0.077
	BPRS-total score	0.119	0.213	0.134	0.160
BD					
BPRS	BPRS-factor1	0.002	0.988	0.049	0.713
	BPRS-factor2	0.163	0.221	0.104	0.436
	BPRS-factor3	0.001	0.992	-0.045	0.738
	BPRS-factor4	-0.069	0.605	-0.204	0.124
	BPRS-factor5	0.023	0.865	-0.211	0.111
	BPRS-total score	0.062	0.641	-0.055	0.680
MDD					
BPRS	BPRS-factor1	0.047	0.733	0.018	0.899
	BPRS-factor2	0.106	0.445	0.088	0.529
	BPRS-factor3	0.061	0.662	0.075	0.588
	BPRS-factor4	-0.105	0.448	-0.113	0.416
	BPRS-factor5	--[#]	--[#]	--[#]	--[#]
	BPRS-total score	0.062	0.654	0.037	0.789

BPRS, Brief Psychiatric Rating Scale. *, Significant at $p<0.05$ corrected by false discovery rate correction.

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Table S3-Correlations between ALFF balance ratios and cognitive function in both frequency bands.

Cognitive Function (WCST)	ALFF balance ratio in slow-5		ALFF balance ratio in slow-4	
	r-values	p-values	r-values	p-values
Correct Responses	0.008	0.917	0.035	0.634
Categories Completed	0.048	0.512	0.083	0.259
Total Errors	0.018	0.810	-0.018	0.802
Perseverative Errors	-0.016	0.827	-0.044	0.547
Non-perseverative Errors	0.007	0.922	0.002	0.977

ALFF, amplitude of low-frequency fluctuation. WCST, Wisconsin Card Sorting Test.

Table S4-Relationship between ALFF balance ratios and clinical characteristics in both frequency bands.

Clinical Characteristics	ALFF balance ratio in slow-5		ALFF balance ratio in slow-4	
	r/t-values	p-values	r/t-values	p-values
Correlations with illness duration	0.016	0.784	-0.013	0.826
Medication (Yes vs.No)	1.110	0.268	1.101	0.272
First episode (Yes vs.No)	0.251	0.802	-0.558	0.607

ALFF, amplitude of low-frequency fluctuation.

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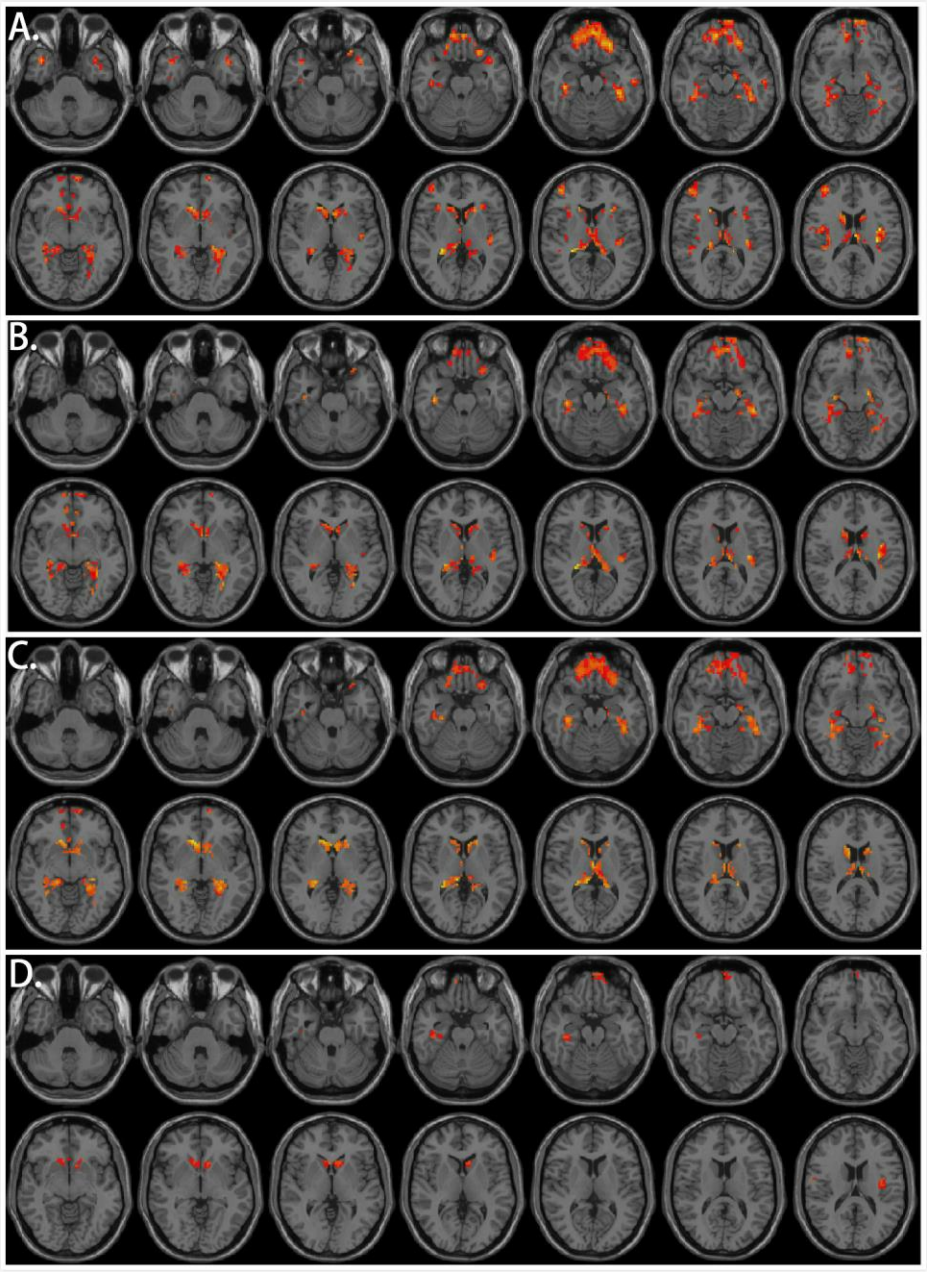

Figure S1. Regions with significant alterations of fALFF values among schizophrenia, bipolar disorder, major depressive disorder and healthy controls in Slow-5. A. Significantly altered regions of fALFF values by ANCOVA. B. Significantly altered regions of fALFF values between SZ and HC. C. Significantly altered regions of fALFF values between BD and HC. D. Significantly altered regions of fALFF values between MDD and HC

Significant at $p<0.05$ corrected for Alphasim correction. fALFF, fractional amplitude of low-frequency fluctuation. ANCOVA, analysis of covariance. SZ, schizophrenia. BD, bipolar disorder. MDD, major depressive disorder.

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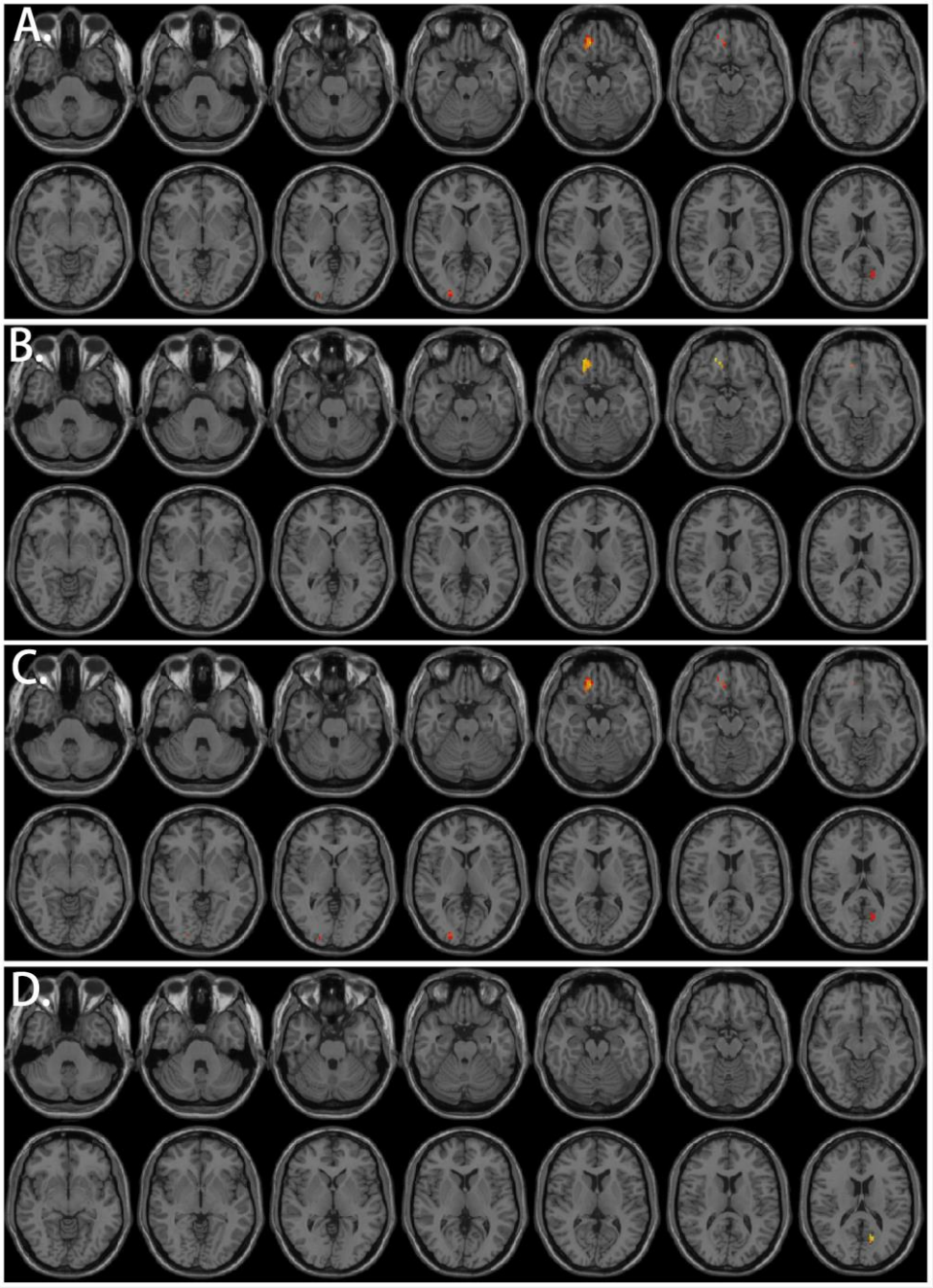

Figure S2. Regions with significant alterations of fALFF values among schizophrenia, bipolar disorder, major depressive disorder and healthy controls in Slow-4. A. Significantly altered regions of fALFF values by ANCOVA. B. Significantly altered regions of fALFF values between SZ and HC. C. Significantly altered regions of ALFF values between BD and HC. D. Significantly altered regions of fALFF values between MDD and HC

Significant at $p<0.05$ corrected for Alphasim correction. fALFF, fractional amplitude of low-frequency fluctuation. ANCOVA, analysis of covariance. SZ, schizophrenia. BD, bipolar disorder. MDD, major depressive disorder.

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