# Abnormal Mechanisms of Spontaneous Brain Activity Dynamics and Its Integration in Autism Spectrum Disorder

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## Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental disorder of unknown etiology with a high prevalence. Currently, most resting-state functional magnetic resonance imaging (resting-state fMRI, R-fMRI) studies have only examined the static characteristics of brain activity in ASD patients, neglecting dynamic features. Recent studies have found that there is consistency among the dynamic properties of different R-fMRI local metrics. Based on a public ASD database, this study systematically calculated the dynamics of mainstream R-fMRI local metrics and the consistency dynamic features between R-fMRI local metrics for 480 ASD patients and 539 typical control (TC) subjects using the sliding time window method, and examined the relationship between these metrics and ASD behavioral indicators. We found that ASD patients exhibited significantly increased dynamics in the lateral frontal lobe, a phenomenon that was manifested in the dynamics of both amplitude of low-frequency fluctuations (ALFF) and degree centrality (DC). We also found that the dynamics of ALFF, DC, and regional homogeneity (ReHo) showed decreases in visual-related brain regions, such as the fusiform gyrus, calcarine sulcus, and lingual gyrus. After further examining the consistency dynamic features among these metrics, we found that the consistency dynamic features of ASD patients were significantly lower than those of the TC group, demonstrating significantly reduced functional integration capacity. Our results indicate that ASD patients exhibit abnormalities in the dynamics of spontaneous brain activity and its integration.

## Full Text

# Aberrant Dynamics of Spontaneous Brain Activity and Its Integration in Autism Spectrum Disorder

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## Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental disease with high prevalence but unclear etiology. Most resting-state functional magnetic resonance imaging (R-fMRI) studies have only examined static features of brain activity in ASD patients, neglecting dynamic characteristics. Recent research has revealed concordance among the dynamics of different R-fMRI regional metrics. Based on publicly available ASD databases, this study systematically calculated the dynamics of mainstream R-fMRI regional metrics and the concordance among these metrics in 480 ASD patients and 539 typical control (TC) participants using a sliding-window approach, and investigated the relationship between these indices and ASD behavioral measures. We found significantly elevated dynamics in the lateral frontal cortex of ASD patients, manifested in both the amplitude of low-frequency fluctuations (ALFF) and degree centrality (DC). We also observed decreased dynamics of ALFF, DC, and regional homogeneity (ReHo) in visual-related brain regions such as the fusiform gyrus, calcarine sulcus, and lingual gyrus. Upon further examining the dynamic concordance among these metrics, we found that ASD patients exhibited significantly lower concordance than TC participants, indicating impaired functional integration capacity. Our results demonstrate aberrant dynamics of spontaneous brain activity and its integration in ASD patients.

**Keywords**: autism, resting-state fMRI, regional metrics, dynamics, concordance

## 1. Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental condition that manifests in early childhood, characterized primarily by impairments in social interaction and communication, as well as restricted and repetitive patterns of behavior and interests [?]. Epidemiological studies in the United States have reported that in 2012, the estimated prevalence among 8-year-old children was 1 in 68, with a rate of 1 in 42 for boys and 1 in 188 for girls [?]. In China, the prevalence of ASD is 5.49 per 10,000 people, and 16.1 per 10,000 for individuals under 15 years of age [?]. Currently, the etiology and pathogenesis of autism remain unclear, and diagnosis relies solely on symptomatic observation and clinical judgment. There is an urgent need to identify objective biological markers to guide clinical diagnosis and treatment. In recent years, researchers have increasingly employed functional magnetic resonance imaging (fMRI) to investigate abnormal brain mechanisms and potential biomarkers in ASD. Resting-state fMRI (R-fMRI) offers several advantages including safety, non-invasiveness, high spatial and temporal resolution, and ease of implementation, making it a promising technique for characterizing disturbances in spontaneous brain activity in ASD.

Resting-state fMRI studies have demonstrated that ASD is associated with abnormalities in spontaneous brain activity. Patients with ASD exhibit atypical functional connectivity (FC) between different brain regions, with both hypo-connectivity [?] and hyper-connectivity [?, ?] reported in previous studies. Additionally, ASD has been linked to abnormalities in R-fMRI regional metrics, including altered amplitude of low-frequency fluctuations (ALFF) and fractional ALFF (fALFF) [?, ?], regional homogeneity (ReHo) [?], degree centrality (DC) [?], and voxel-mirrored homotopic connectivity (VMHC) [?]. However, these findings have been inconsistent, likely due to the small sample sizes employed in these studies [?]. Di Martino et al. [?] conducted a large-scale study with 360 ASD patients and 403 TC participants, revealing widespread hypo-connectivity across the brain in ASD patients, while hyper-connectivity was limited to specific subcortical nuclei and primary sensorimotor cortices. Regarding R-fMRI regional metrics, ASD was associated with elevated fALFF and ReHo in the frontal lobe, and reduced DC and VMHC in the temporal lobe.

Nevertheless, most R-fMRI studies in ASD have focused exclusively on static features of brain activity, overlooking its dynamic temporal characteristics. Research indicates that the human brain responds to internal and external stimuli through dynamic integration and adjustment across multiple timescales [?]. In recent years, the sliding-window method has enabled investigation of the dynamic mechanisms of spontaneous brain activity in humans [?] and non-human primates [?]. In clinical contexts, sliding-window FC has effectively revealed abnormalities in brain functional dynamics across various neuropsychiatric disorders, including schizophrenia [?], Alzheimer' s disease [?], major depressive disorder [?], and idiopathic generalized epilepsy [?]. In ASD research, Zhang et al. [?] employed sliding-window FC to examine the relationship between ASD and dynamic variability of brain activity, finding abnormally increased dynamic

variability in frontal brain regions of ASD patients. Chen et al. [?] calculated whole-brain dynamic FC in ASD patients using a large public dataset, identifying widespread increases in long-range dynamic functional connectivity variability. However, focusing solely on FC dynamics is insufficient, as high spatiotemporal resolution imaging has revealed substantial fluctuations in local neural activity itself [?]. While numerous studies have explored the temporal dynamics of regional R-fMRI metrics [?, ?], no systematic investigation has examined voxel-level dynamic features of regional metrics in ASD.

Different R-fMRI metrics reflect distinct aspects of spontaneous brain activity, and the concordance among these metrics represents the degree of integration across different functional dimensions [?]. Our previous research [?] found strong voxel-wise and volume-wise concordance among the dynamic features of resting-state regional metrics (e.g., ReHo, ALFF), which declines with age. Fu et al. [?] discovered concordance between dynamic ALFF and dynamic FC over time, with differences between schizophrenia patients and healthy controls. Whether concordance among R-fMRI regional metrics is abnormal in ASD remains an unexplored question.

Despite numerous small-sample studies characterizing static mechanisms of aberrant spontaneous brain activity in autism using various metrics, no study has systematically examined the dynamic features of R-fMRI regional metrics or their inter-metric concordance. This study utilized the publicly available "Autism Brain Imaging Data Exchange" (ABIDE I and II, accessible at http://fcon_{1000}.projects.nitrc.org/indi/abide/) dataset to analyze brain imaging data from 480 ASD patients and 539 TC participants. Using a sliding-window approach, we systematically calculated differences in dynamic features of multiple mainstream R-fMRI metrics between ASD patients and TC participants. We further computed the concordance among R-fMRI metrics and its dynamic characteristics, exploring the potential application of inter-metric concordance dynamics in discriminating ASD patients from TC participants. Finally, we examined the correlation between inter-metric concordance dynamics and ASD symptom severity.

## 2. Methods

### 2.1 Participants

All data used in this study were obtained from the publicly available ABIDE/ABIDE II datasets. Inclusion criteria for imaging data analysis were as follows: (1) male participants only (given the strong gender effect in autism and the fact that male participants comprise 90% of the entire ABIDE sample); (2) complete structural images with good registration quality; (3) mean framewise displacement (FD) [?] $< 0.2$ mm; (4) translational and rotational movement in X, Y, and Z directions between adjacent time points $< 3$ mm and $3°$ (maximum head motion: X translation: 2.41 mm; Y translation: 2.91 mm; Z translation: 3.00 mm; X rotation: 2.99°; Y rotation: 1.89°; Z rotation: 2.61°); (5) no

obvious abnormalities in dynamic regional metric calculations; (6) availability of intelligence quotient (IQ) standard scores; and (7) after applying these exclusion criteria, each site had more than 10 participants in both ASD and TC groups. We ultimately selected 1,019 participants from 21 sites (480 ASD patients and 539 TC participants). There was no significant age difference between the two groups (t = -0.037, p = 0.82).

### 2.2 Data Preprocessing

All preprocessing was performed using the "Data Processing Assistant for Resting-State fMRI" (DPARSF [**?**], http://rfmri.org/DPARSF), which is based on the Statistical Parametric Mapping software (SPM8, http://www.fil.ion.ucl.ac.uk/spm) and the "Data Processing & Analysis for Brain Imaging" toolbox (DPABI [**?**], http://rfmri.org/DPABI). The preprocessing pipeline included: (1) removal of the first 10 time points from each participant' s R-fMRI time series to ensure data were acquired after the participant had adapted to the scanning environment and the magnetic field had stabilized; (2) slice timing correction to eliminate temporal phase differences resulting from interleaved scanning; (3) head motion correction using a six-parameter rigid-body linear transformation to align functional images to the first time point and then to the mean functional image; (4) structural image alignment, where each participant' s T1-weighted image was aligned to the mean functional image using a six-degree-of-freedom linear transformation; (5) tissue segmentation of structural images into gray matter, white matter, and cerebrospinal fluid; (6) nuisance regression, as recent studies [**?**] have shown that subtle head motion during MRI scanning can introduce artifacts into resting-state functional metrics. Therefore, we only included participants with minimal head motion (mean FD $<$ 0.2 mm, maximum translation and rotation $<$ 3 mm or 3°). Recent research also indicates that higher-order models better remove motion effects [**?**, **?**], so we used the Friston 24-parameter model (six motion parameters, their values from the previous time point, and the squares of these 12 parameters) to regress out motion effects from aligned functional images. Motion effects were further controlled in group-level analyses by including mean FD as a covariate. Additionally, white matter and cerebrospinal fluid signals were regressed out to reduce physiological noise from respiration and cardiac activity. To account for low-frequency drift in the blood oxygen level-dependent (BOLD) signal, linear trends were removed. Given ongoing controversies surrounding global signal regression (GSR) [**?**] and evidence that GSR can introduce negative FC and alter FC distributions, we did not apply GSR; (7) registration to MNI152 standard space using DARTEL (diffeomorphic anatomical registration through exponentiated lie algebra) based on spatial transformation information from step 5, with resampling to 3 mm $\times$ 3 mm $\times$ 3 mm voxels.

### 2.3 Resting-State fMRI Metrics Calculation

To investigate whether ASD patients exhibit abnormalities in the dynamic features of spontaneous brain activity, we calculated six R-fMRI metrics using a sliding-window approach to characterize dynamic changes in regional features and inter-metric concordance in both ASD patients and TC participants. For each time window, we computed the following six metrics:

1. **ALFF/fALFF**: We used ALFF and fALFF to measure the intensity of local spontaneous brain activity. ALFF was calculated as the mean amplitude of the frequency spectrum within a specific frequency range (0.01–0.1 Hz in this study) after Fourier transformation of a voxel' s time series. Since ALFF is sensitive to noise in white matter and ventricular regions, we also calculated fALFF, defined as the ratio of the sum of amplitudes in a specific frequency band (0.01–0.1 Hz) to the sum of amplitudes across the entire frequency spectrum. ALFF measures the intensity of low-frequency oscillations in spontaneous brain activity, while fALFF characterizes the relative contribution of specific frequency oscillations to the entire frequency domain.

2. **ReHo**: ReHo quantifies regional consistency/synchronization of fMRI time series. It is defined as Kendall' s coefficient of concordance (Kendall' s W) between the time series of a given voxel and its nearest neighbors (26 voxels in this study).

3. **VMHC**: VMHC measures functional connectivity between mirrored voxels in the left and right hemispheres, calculated as the Pearson correlation coefficient between the BOLD time series of a voxel and its counterpart in the contralateral hemisphere. To achieve more precise correspondence between hemispheric symmetric voxels, we first registered each participant' s MNI-space functional image to a more symmetric space. This was accomplished by computing the average T1 structural image across all participants in MNI space, creating a group-level symmetric template by averaging this image with its mirrored version, and then registering each participant' s MNI-space T1 structural image (which is co-registered with their functional image) to this symmetric template. The resulting transformation was applied to the MNI-space functional images. Given that precise correspondence between hemispheric symmetric voxels cannot be perfectly achieved, we applied smoothing (4 mm full width at half maximum, FWHM) to reduce discrepancies and enhance inter-hemispheric consistency [**?**]. For VMHC calculation, we used a symmetrically expanded group-level mask (the union of the original group mask and its mirrored version) as the analysis space (inter-metric concordance calculations used the original group-level mask consistent with other metrics).

4. **DC**: DC represents the number or weighted sum of voxels across the whole brain that have functional connectivity with a given voxel above a specific threshold. In this study, we calculated voxel-wise functional connectivity

between each voxel and all other voxels in the brain, then computed the weighted sum of positive connections exceeding the threshold ($r > 0.25$) to generate whole-brain DC maps.

5. **GSCorr**: GSCorr was calculated by first computing the average time series of all voxels within the group-level mask as the global signal, then calculating the Pearson correlation coefficient between this global signal and each voxel' s time series within the mask. Power et al. [**?**] found that the spatial distribution of GSCorr aligns with that of end-tidal pCO2-BOLD signal correlations, suggesting a potential link between GSCorr and respiration rate, with cerebral blood flow regulation also contributing to the GSCorr spatial pattern. All GSCorr values were Fisher-Z transformed before further analysis.

### 2.4 Dynamic R-fMRI Metrics

To quantify the dynamic characteristics of spontaneous brain activity in patients, we employed a sliding-window approach to calculate dynamic regional metrics [**?**]. First, a Hamming window with a width of 32 TRs and a step size of 4 TRs was applied to the whole-brain BOLD signal time series (each window contained 32 time points, with each successive window starting 4 TRs later than the previous one). Within each window, we calculated the six R-fMRI metrics described above (ALFF, fALFF, ReHo, VMHC, DC, and GSCorr). To quantitatively characterize the temporal dynamics of each metric, we computed the standard deviation (SD) of each metric over time for every voxel across the brain. The resulting SD maps were Z-standardized within the group mask (subtracting the whole-brain mean and dividing by the whole-brain SD) and smoothed (FWHM = 4 mm) for all metrics except VMHC (which was already smoothed during preprocessing) to improve signal-to-noise ratio. All dynamic metrics were calculated using the temporal dynamic analysis module in DPABI. To ensure our findings were not dependent on window width, we repeated all analyses with window widths of 48 and 64 TRs, obtaining highly consistent results (see Supplementary Materials).

### 2.5 Statistical Analyses

**2.5.1 Analysis of Dynamic Regional Metric Differences** We performed two-sample t-tests to examine differences in the SD of six dynamic R-fMRI regional metrics between ASD patients and TC participants. Although the two groups were matched for age, we included age as a covariate in the regression model to exclude any potential effects. Site and head motion were also included as covariates to reduce site effects and motion artifacts. To control for multiple comparisons, we applied permutation testing with threshold-free cluster enhancement (TFCE [**?**], $p < 0.05$, 1,000 random permutations) using DPABI. Our recent research has shown that TFCE-based permutation testing is a stringent multiple comparison correction method that maintains low false positive rates while achieving high reproducibility [**?**].

**2.5.2 Dynamic Concordance Among R-fMRI Regional Metrics** Based on our previous study [**?**], we calculated the dynamic concordance among R-fMRI metrics (volume-wise concordance) by computing Kendall' s coefficient of concordance across the spatial patterns of five metric maps (ALFF, ReHo, DC, VMHC, and GSCorr) for each time window. Kendall' s coefficient is a non-parametric statistic that does not assume a specific population distribution and is insensitive to differences in absolute values among R-fMRI metrics. Due to the high similarity between fALFF and ALFF in both definition and results, we included only ALFF in concordance calculations to avoid artificially inflating consistency. ALFF was selected because it is highly sensitive to brain activity abnormalities in neuropsychiatric disorders [**?**, **?**] and showed numerous significant dynamic abnormalities in ASD, whereas fALFF dynamics did not differ between groups after statistical correction. We then performed two-sample t-tests on the mean and SD of the concordance time series between ASD and TC groups to assess the average level and stability of functional integration, with age, head motion, and site included as covariates.

**2.5.3 Correlation Between Concordance Dynamics and ASD Symptom Severity** To investigate the relationship between R-fMRI metric concordance characteristics and behavioral measures in ASD, we calculated partial correlations between concordance features (mean and SD) and scores from the Autism Diagnostic Observation Schedule (ADOS), controlling for age and head motion. Data from 241 ASD patients were included in this analysis, with the following ADOS subscales: total score (ADOS_{TOTAL}), communication score (ADOS_{COMM}), social score (ADOS_{SOCIAL}), and stereotyped behavior and restricted interests score (ADOS_{{{STEREO}}_{{BEHAV}}}). Partial correlation coefficients were corrected for false discovery rate (FDR) using MATLAB' s mafdr function ($q < 0.05$).

## 3. Results

### 3.1 Abnormal Dynamics of Regional Metrics in ASD

We performed two-sample t-tests to compare the temporal dynamic variability (SD) of spontaneous brain activity metrics between ASD patients and TC participants. After controlling for head motion, age, and site effects, the results revealed that ASD patients showed increased dynamics in the prefrontal cortex but decreased dynamics in posterior medial brain regions compared to TC participants.

Regarding the frequency-domain characteristics of regional spontaneous activity, ASD patients exhibited widespread ALFF dynamic abnormalities. Specifically, ASD patients showed increased ALFF dynamics in bilateral lateral prefrontal cortex, bilateral orbital frontal cortex, and medial prefrontal cortex, while demonstrating decreased ALFF dynamics in bilateral calcarine sulcus, fusiform gyrus, lingual gyrus, and posterior cingulate cortex (see [Figure 1: see

original paper] and ). For network centrality, ASD patients displayed significantly higher DC dynamic variability in the right middle frontal gyrus and posterior thalamus compared to controls (see [Figure 1: see original paper] and ). For local activity consistency, ASD patients showed reduced ReHo dynamics in bilateral calcarine sulcus, fusiform gyrus, lingual gyrus, and parahippocampal regions compared to TC participants (see [Figure 1: see original paper] and ). The ReHo and DC results further supported the ALFF findings.

[Figure 1: see original paper] shows brain regions with significant group differences in R-fMRI dynamic indices (SD) between ASD and TC groups: (a) ALFF; (b) DC; (c) ReHo. Notably, no significant group differences were observed for fALFF, GSCorr, or VMHC.

lists brain regions showing significant group differences in R-fMRI dynamic indices (SD) between ASD and TC groups, including Brodmann areas, MNI coordinates, peak T-values, and cluster sizes for regions such as the lingual gyrus, cuneus, calcarine sulcus, posterior cingulate cortex, fusiform gyrus, middle occipital gyrus, precuneus, middle frontal gyrus, superior frontal gyrus, inferior frontal gyrus, orbital frontal gyrus, thalamus, parahippocampal gyrus, and midbrain. Regions with fewer than 10 voxels were not reported.

### 3.2 Abnormal Concordance Among R-fMRI Metrics

We calculated the concordance among R-fMRI metrics by computing, for each participant and each time window, the spatial concordance across metric maps, yielding a concordance time series for each participant. As illustrated in Figure 2: see original paper, a typical ASD patient showed lower concordance than a TC participant in both average level and variability. Statistical comparisons revealed that both the mean (T = -2.32, p = 0.0203) and SD (T = -2.05, p = 0.0404) of the concordance time series were significantly lower in the ASD group compared to the TC group Figure 2: see original paper(c).

[Figure 2: see original paper] shows differences in R-fMRI metric concordance between ASD and TC participants: (a) concordance time series for a typical ASD patient and TC participant; (b) two-sample t-test of mean concordance; (c) two-sample t-test of concordance SD. The displayed mean and SD values are fitted after regressing out head motion, age, and site effects. * indicates significance level $p < 0.05$.

### 3.3 Correlation Between Concordance Dynamics and Disease Severity

We further examined partial correlations between R-fMRI metric concordance dynamics and ADOS scores in ASD patients, controlling for age and head motion, with FDR correction. As shown in [Figure 3: see original paper], the mean concordance level was significantly negatively correlated with ADOS_{COMM} (r = -0.2111, p = 0.0082), whereas the variability of inter-metric concordance (SD) showed no significant correlation with any of the four ADOS subscales.

[Figure 3: see original paper] shows correlations between the mean/SD of R-fMRI metric concordance and ADOS subscale scores. ADOS scores displayed are fitted values after regressing out head motion and age effects. ADOS_{COMM}: communication total subscore of the classic ADOS. ** indicates significance level $p < 0.01$.

## 4. Discussion

This study comprehensively examined abnormalities in the dynamic features of regional metrics of spontaneous brain activity in ASD patients. We found significantly elevated dynamics in the lateral frontal cortex, observed in both ALFF and DC metrics. Concurrently, ASD patients showed significantly reduced dynamics in visual regions, consistently across ALFF, DC, and ReHo metrics. We further investigated the concordance among these dynamic metrics and found that both the mean and SD of inter-metric concordance were significantly lower in ASD patients than in TC participants, indicating impaired functional integration capacity. Finally, we examined the relationship between functional integration abnormalities and disease severity, revealing a negative correlation between the average level of functional integration and ADOS_{COMM} scores, which illuminates the nature of dynamic functional integration deficits in ASD.

We found that ALFF dynamics showed the most extensive abnormalities in the ASD group, consistent with previous findings that ALFF is highly sensitive to brain activity abnormalities in neuropsychiatric disorders [**?**, **?**]. ASD patients exhibited elevated ALFF dynamics in bilateral dorsolateral prefrontal cortex, right anterior cingulate cortex, and medial prefrontal cortex, while showing decreased ALFF dynamics in the lingual gyrus, calcarine sulcus, fusiform gyrus, and posterior cingulate cortex. These abnormal regions have been reported in previous studies. For instance, Supekar et al. [**?**] found that children with ASD showed significantly higher FC and ALFF in most brain regions, including the lateral frontal cortex, suggesting an excitation/inhibition imbalance in local neural circuits. Guo et al. [**?**] also reported significant ALFF decreases in medial prefrontal cortex, middle occipital gyrus, and precuneus. Itahashi et al. [**?**] found reduced fALFF in the fusiform gyrus, lingual gyrus, and inferior occipital gyrus in ASD patients. Lai et al. [**?**] used the Hurst exponent, another metric of local activity intensity, to examine spontaneous brain activity oscillations in ASD and similarly found reduced local activity intensity in the fusiform gyrus, lingual gyrus, precuneus, and posterior cingulate cortex.

In addition to ALFF, DC abnormalities were also concentrated in the lateral frontal cortex, showing elevated dynamics. Di Martino et al. [**?**] conducted a large-scale multi-site study based on the ABIDE database and found that ASD patients showed significantly higher fALFF, ReHo, and DC in the dorsolateral prefrontal cortex compared to controls, suggesting this region is important in the pathological circuitry of autism. While these studies focused on static brain activity analyses, our study extends previous work by employing a sliding-window approach to analyze brain activity dynamics. Our findings enhance

understanding of the neural basis of executive control deficits in autism. The dorsolateral prefrontal cortex is a critical component of the executive control network [**?**], and abnormal activity in this region may indicate disruption of the control execution system and impairment of relevant cognitive functions. Specifically, the significantly greater temporal variability of activity in the dorsolateral prefrontal cortex in ASD patients suggests functional deficits in this region, with patients unable to stably control their cognitive processes. Numerous behavioral studies have documented executive control deficits in ASD and their strong correlation with repetitive behaviors [**?**, **?**], providing supportive evidence for our interpretation.

Another notable DC dynamic abnormality in ASD patients was elevated dynamics in the thalamus. Cheng et al. [**?**] conducted a comprehensive voxel-level large-sample study (including 419 ASD patients and 509 controls) and found significantly increased functional connectivity between the medial thalamus and cortex in ASD patients, suggesting abnormal degree centrality in the thalamus. Additionally, Doyle-Thomas et al. [**?**] found that thalamic choline concentration was negatively correlated with ADI-R communication total scores and restricted/repetitive behavior scores, indicating possible metabolic abnormalities in the thalamus of ASD patients. The elevated DC dynamics in the thalamus observed in our study (i.e., excessive variability in degree centrality) suggest that the thalamus, as a sensory relay station, is unstable in transmitting sensorimotor information to the cortex.

In contrast to the widespread dynamic elevation in the dorsolateral prefrontal cortex, we found consistent dynamic decreases in ALFF, DC, and ReHo in the calcarine sulcus, fusiform gyrus, and lingual gyrus, further suggesting functional abnormalities in visual brain regions in ASD. Numerous behavioral and EEG studies have indicated that impaired face processing abilities in children with ASD may underlie their social cognitive deficits [**?**]. Task-based fMRI studies have shown that ASD patients exhibit significantly lower activation in inferior temporal regions (e.g., fusiform gyrus) responsible for face processing during facial emotion judgment [**?**] and perceptual discrimination tasks [**?**] compared to controls. In R-fMRI studies, Keown et al. [**?**] found widespread abnormal increases in local degree centrality in the fusiform gyrus, lingual gyrus, and calcarine sulcus of ASD patients, with local degree centrality positively correlated with ADOS_{SOCIAL} and ADOS_{{{STEREO}}_{{BEHAV}}} scores. Maximo et al. [**?**] used local connectivity metrics such as ReHo and local degree centrality to identify significant local over-connectivity in visual regions of ASD patients. Cheng et al. [**?**, **?**] also reported functional connectivity abnormalities in brain regions involved in face processing. Using R-fMRI with a sliding-window approach, our study similarly identified reduced dynamics in visual regions, particularly the fusiform gyrus, indicating inflexibility. This lack of flexibility aligns with behavioral observations that ASD patients have difficulty making efficient judgments and short-term memory for face and expression information. Notably, studies have shown abnormal reductions in functional connectivity between the fusiform gyrus [**?**] and calcarine sulcus [**?**] and the

dorsolateral prefrontal cortex in ASD, suggesting a physiological link between decreased visual region dynamics and increased dorsolateral prefrontal dynamics. The abnormal reduction in visual region dynamics in ASD patients may represent the neural basis for their inability to efficiently and rapidly process and memorize fleeting facial expression information.

As the repertoire of resting-state metrics continues to expand, examining concordance among multiple metrics has gained research attention and may develop into a new imaging biomarker. Building upon the dynamic features of spontaneous brain activity, we further investigated concordance among different R-fMRI metrics. Since different metrics reflect distinct aspects of brain activity, their concordance can measure integration across functional dimensions. Fu et al. [**?**] measured the similarity between dynamic ALFF in the cuneus and dynamic functional connectivity between this region and the lingual gyrus, finding that this similarity was significantly negatively correlated with working memory span. Our previous work [**?**] calculated concordance among multiple R-fMRI metrics and found that inter-metric concordance negatively correlated with age. Healthy brain function should demonstrate high-level yet flexible integration across multiple dimensions. However, our study found that ASD patients showed reduced inter-metric concordance compared to TC participants, manifested as both lower average levels (reduced mean) and insufficient flexibility (reduced SD), indicating deficits in multi-faceted brain functional integration that may relate to cognitive decline in ASD [**?**]. Consistently, within the ASD group, the mean temporal concordance was significantly negatively correlated with ADOS-COMM scores, suggesting that lower average inter-metric concordance is associated with poorer communication abilities. We interpret this as indicating that ASD patients have deficits in integrating multiple brain functions, with inflexible integration and switching among different functional domains.

This study has several limitations. First, while we used multiple metrics to reflect different functional aspects of spontaneous brain activity, some metrics (e.g., seed-based FC, independent component analysis, Hurst exponent) were not included due to heterogeneity in selection (e.g., inability to unify seed selection for FC). Second, this study used a publicly available multi-site large-sample database, and differences in MRI scanners and scanning parameters across sites introduced site effects. Although we controlled for site as a covariate in analyses of dynamic regional metrics, limitations inherent to the general linear model mean that site effects may still influence statistical results. While we have entered the era of big data, establishing single large-sample databases remains challenging. Therefore, multi-site large-sample data will continue to be a primary resource for psycho-brain-behavior mechanism research, early diagnosis of mental disorders, and medical imaging deep learning studies. Developing linear mixed models that more effectively control site effects could better advance R-fMRI research in the big data era. Third, we used SD as a quantitative index of spontaneous brain activity dynamics, but since SD positively correlates with mean (larger mean values tend to have larger SD), and the mean of dy-

namic regional metrics calculated via sliding windows shares some similarity with static regional metrics, this may artificially inflate concordance between dynamic and static metrics. Future research should develop more effective statistical indices for quantifying spontaneous brain activity dynamics. Fourth, due to the lack of large-sample resting-state fMRI datasets for other neuropsychiatric disorders, we could not verify whether reduced inter-metric concordance is specific to autism or common across multiple mental disorders. Future studies should examine the sensitivity and specificity of inter-metric concordance as a biomarker in other neuropsychiatric conditions.

## 5. Conclusion

Using a sliding-window approach, this study systematically calculated the dynamics of mainstream R-fMRI regional metrics and the concordance among these metrics in ASD patients and TC participants, and examined their relationship with ASD. The results demonstrated that ASD patients exhibited increased dynamics in lateral frontal cortex in both ALFF and DC metrics, and decreased dynamics in visual-related regions including the calcarine sulcus, fusiform gyrus, and lingual gyrus across ALFF, DC, and ReHo metrics. Both the average level and variability of inter-metric concordance were lower in ASD patients compared to the TC group. The average inter-metric concordance was negatively correlated with communication symptom severity in ASD. These findings suggest that ASD patients exhibit aberrant dynamics of spontaneous brain activity and its integration.

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