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Abnormalities in brain complexity in children with autism spectrum disorder: a sleeping state functional MRI study

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Abstract

Background and Objective The theory of complexity loss in neurodivergent brain is widely acknowledged. However, the findings of autism research do not seem to align well with this theory. We aim to investigate the brain complexity in children with ASD (Autism Spectrum Disorders) compared with the TD (Typical Developed) children in sleeping state.

Method 42 ASD children and 42 TD children were imaged using sleep-state functional magnetic resonance imaging (ss-fMRI), and brain complexity was analyzed by employing sample entropy (SampEn) and transfer entropy (TE). For the ASD group, we also investigated the relationship of symptom severity with SampEn and with TE.

Results In compared with TD group, ASD group showed significant increased SampEn in the right inferior frontal gyrus. However, in the group of TD, 13 pairs of brain regions exhibit higher TE compared to the ASD group. In the ASD group, the TE of 5 pairs of brain regions is higher than in the TD group.

Conclusion This sleeping-state fMRI study provide evidence that ASD children exhibited aberrant brain complexity in compare with the TD children. The complexity of the autistic brain is composed of aberrant randomness in brain activity and anomalous information transmission between brain regions. We believe that brain complexity in ASD is a highly valuable area of research. Differences in the entropy of local brain regions, as well as in the transfer entropy between brain regions, may be related to the brain complexity observed in children with ASD.

Keywords Autism spectrum disorder, Brain complexity, Sample entropy, Transfer entropy, Sleeping state fMRI

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Introduction

Autism spectrum disorder (ASD) is a lifelong neurodevelopmental condition affecting around 2.3% children aged 8 years. It involves difficulties in social interaction, communication and by repetitive behaviors or restricted interests [1]. Emerging evidence suggests that individuals with ASD often exhibit altered intrinsic brain activity and functional connectivity [2–4]. Studies have demonstrated that these alterations in brain activity and functional connectivity can be characterized by local overconnectivity and long-range underconnectivity, which may contribute to the corresponding behavioral impairments [5, 6].

The human brain is a sophisticated system distinguished by its dynamic neural communications within functionally specialized assemblies and extensive long-range mutual interactions across these assemblies [7, 8]. Focusing solely on abnormal local brain activity or changes in brain activity may be in sufficient given the current understanding of human brain. Neurophysiologic signals obtained from electroencephalography (EEG), magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI) exhibit complex temporal fluctuations that reflects the state of neural activity [9, 10]. Increasing studies reveals the atypical dynamic connectivity patterns in early autism brain and established some reliable findings [11–14]. For example, in compare with typical developed brain, autistic brain exhibits lower temporal variance in default mode network (DMN) and lower dynamic functional connectivity between precuneus and precentral gyrus [11]. While some studies showed higher temporal variability functional connectivity between precuneus/ post cingulate gyrus and temporal pole [14]. These studies also revealed that symptom severity is associated with the variance of dynamic functional connectivity. Although some fruitful results have been obtained, previous studies seem to have overlooked the complexity of brain activity.

The complexity of the human brain increases progressively throughout its developmental trajectory [15]. The autistic brain, however, shown abnormal early overgrowth occurs during the first 2 year of life. By age 2 to 4, the most pronounced overgrowth is observed in structures that underlie high-order cognitive, emotional, social, and language functions [16]. Such overgrowth may inevitably result in aberrations in brain activity, thereby compromising the complexity of brain signals. However, the findings regarding the complexity of brain signals during development stage exhibit inconsistencies across different studies. For example, Takahashi et al. explored MEG signal variability between ASD children and typical developed (TD) children. They found increased signal variability in ASD children [12]. On the contrary, Bosl et al. explored EEG signal variability between high-risk ASD infants (confirmed family history of ASD) and TD infants. They found decreased EEG signal variability in high-risk ASD infants [17]. While, fMRI studies reported inconsistence results as well. A study recruit resting-state fMRI signal complexity as features and using support-vector machine to distinguish ASD patients from TD individuals. It revealed lower signal complexity in ASD patients compare to TD individuals [18]. Another study examining the resting-state fMRI signal complexity in children with and without ASD and found both increase and decrease signal complexity in occurring specific brain regions [19]. These results appear to be incongruent with the theory "loss of brain complexity hypothesis". The measure of complexity, as posited by this theory, encompasses not only the system's randomness but also its quantity of transmitted information [20]. The existing studies on brain complexity in autism, however, appear to overlook the consideration of information transmission.

Entropy indicates system complexity. In the context of neurophysiological signals, by utilizing approximate entropy or sample entropy (SampEn), we can assess the regularity and predictability of fluctuations within a time series, by quantifying the probability that similar patterns of observations will not be succeeded by additional similar observations [21]. SampEn has been successfully applied to various neurodivergent conditions, including ASD [22–24]. On the other hand, by utilizing transfer entropy (TE), we can measure the amount of directed (time-asymmetric) information flow between two random processes, by quantifying the how much the state of one variable uniquely contributes to the future state of another variable, beyond what is already contained in the past of the affected variable [25]. It is worth noting that there are various entropy algorithms that can evaluate the complexity of neurophysiological signals. For example, the utilization of multiscale entropy, which developed based on SampEn, is prevalent in EEG researches, and the utilization of permutation entropy in MEG research [26, 27]. Multiscale entropy can be used to evaluate the complexity and dynamics of brain signals at multiple time scale. However, permutation entropy is particularly advantageous for real-time analysis and for cases where the data length is limited. Since our objective is to assess the flow of information among different brain regions, TE is a suitable option.

The TE is widely recognized for evaluating effective connectivity, distinguishing itself from dynamic causal modeling (DCM) by its ability to assess the directional influence between two brain regions, it determines whether a causal relationship exists [28, 29]. Signal transmission between brain regions exhibit linearity or nonlinearity [30]. In compared with Granger causality (GC), TE is more appropriate for analyzing nonlinear causality [31]. The purpose here does not aim to determine whether GC or TE is superior in terms of effective

connectivity. A previous study employed both of the methods on the adult ASD patients, we observed that while GC exhibited strong performance in detecting linear causal connections, it demonstrated limited efficacy in detecting non-linear causal connections. In contrast, TE displayed a relatively balanced ability to detect both linear and non-linear causal connections compared to GC [32].

The symptoms of ASD in boys typically manifest between the ages of 12 and 36 months. While, the onset of symptoms in girls tends to occur later than in boys [33]. However, little is known about the changes of brain characteristics during this stage. That's because it is extremely difficult to conduct fMRI studies in children at this developmental stage. In the early 2000s, "sleep fMRI" was initially employed to characterize brain functionality in typically developing infants and toddlers [34, 35]. The previous fMRI studies on autism research have mainly focused on high-functioning autistic subjects who are highly cooperative and older subjects, which may introduce bias due to the specific sample selection [36]. Although those bias can be eliminated by "sleep fMRI", fMRI scanning in the natural sleep state is still very difficult and require adaptive training [37].

In this study, we investigated the differences in brain complexity between children with ASD and TD children in sleeping-state. We opted to investigate the fMRI of children with ASD during natural sleep due to emerging evidence suggesting intricate associations between sleep and ASD [38]. Moreover, the sleeping state may be the most sensitive period for detecting neurodevelopmental conditions in children, potentially revealing abnormalities even before they manifest behaviorally [39]. Therefore, we intended to investigate brain complexity in children with ASD during sleep, although this is a challenging study.

Methodology

Participants

In total of 84 subjects, including 42 ASD children and 42 TD children, age 12–36 months, were recruited in Shenzhen Children's hospital in China. All of ASD children meet the DSM-5 criteria for clinical interviews, administered by clinicians with reliable research background, ensuring adherence to standardized diagnostic procedures. All of the children with ASD were carried out scan before treatment. Exclusion criteria for ASD group included other neurological diseases (e.g., seizure, tuberous sclerosis, brain palsy, brain trauma) or family history of psychiatric disorder, hematological-system diseases, abnormalities on MRI. Exclusion criteria for TD group included any personal or family history (first degree relatives) of ASD or other heritable psychiatric disorder, abnormalities on MRI. Furthermore, this study exclusively included participants who successfully completed the fMRI scan.

The study was approved by Review Board of Shenzhen Children's Hospital Committee of Medical Ethics. Written informed consent was obtained from each subject's parents after providing them with a comprehensive description of study. Clinical trial number: not applicable.

Clinical and behavioral assessments

The ASD group screened with completed the Developmental Scale for Children Aged 0–6 years (DSCA 0-6Y) [40]. The Developmental Scale for Children Aged 0–6 years is a scale released by the National Health Commission of the People's Republic of China in 2017 to assess the developmental behavior of children aged 0–6 years. Childhood Autism Rating Scale (CARS) [41] and Autism Behavior Checklist (ABC). The use of these clinical assessment scales has been widely documented in previous studies. As for DSCA 0-6Y, it composed of five items: gross motor, fine motor, ability to adapt, language skills and social skills. The CARS was administered by a team expert pediatricians and psychiatrists, comprising 15 items on the rating scale. Each item was assessed on a scale from 1 to 4, with a maximum total score of 60. The classification criteria were as follows: a total score < 30 was categorized as non-ASD, a total score ranging from 30 to 36 indicated mild to moderate ASD, a total score > 36 denoted severe ASD. This assessment scale is applicable for children aged two years and above. The ABC scale is suitable for individuals aged from 8 months to 28 years of age. A total score of 30–67 suggests the potential presence of symptoms associated with ASD, while total score of ≥ 67 indicates the definite presence of ASD symptoms.

Data acquisition

The following section provides only an introduction to the scanning parameters of MRI, while the specific sleep adaptive training for children's magnetic resonance environment can be found in the supplemental material.

The MRI datasets were acquired with a 16-channel head coil on a 3.0T Siemens Skyra scanner at the Radiology Department of Shenzhen Children's Hospital. The parents were instructed to ensure their child was asleep prior to MR scan and maintain their sleep throughout the duration of the scan. A T2-weighted gradient echo planar imaging was acquired to measure brain oxygenation level-dependent (BOLD) signal, and the parameters were as follows: repetition time /echo time = 2000ms/ 30ms, slice thickness = 3.6 mm, slice gap = 0.72 mm, matrix = 64 × 64, field of view (FOV) = 230 mm ×230 mm, flip angle = 90°, interleaved scanning, axial slice were distributed approximately along the anterior commissure- posterior commissure (AC-PC) line, and 240 volumes were

obtained in about 8 min. 176 sagittal slice T1-weighted structural images (T1WI) covering the entire brain using a 3D magnetization-prepared rapid acquisition gradient echo (MPRAGE) sequence was obtained, and the parameters were as follows: repetition time / echo time = 2300ms / 2.26ms, TI = 900ms, flip angle = 8°, matrix = 256 × 256, FOV = 256 mm × 256 mm, slice thickness = 1 mm, inter-slice gap = 0.5 mm. T2-FLAIR images were obtained to exclude asymptomatic lesion.

Data preprocessing

The preprocessing procedures were implemented using Statistical Parametric Mapping (SPM12, https://www.fil.ion.ucl.ac.uk/spm/software/spm12/). Including following steps: the first 10 volumes were discarded, slice-timing correction, head motion correction excluding subjects exhibiting 1 mm axial displacement and 1° rotation angle, normalize and deformation to the Montreal Neurological Institute space. In this step, we collected data from 150 typically developing participants aged 12 to 36 months and used the Computational Anatomy Toolbox 12 (https://neuro-jena.github.io/cat/) to create a DARTEL brain template, which was then normalized to the MNI space. The template resolution is 1 mm. And then, the data were re-slicing to achieve a voxel dimension of 3 × 3 × 3 isotropic, remove covariates such as white matter, spinal fluid, and head motion parameters (Friston 24), band-pass filtering (0.01 ~ 0.1 Hz), and the data were smoothed with 8 mm full-width at half-maximum Gaussian kernel before further calculating TE.

Sample entropy calculation

To compute the entropy for each voxel, we utilized brain entropy mapping toolbox (BENtbx, https://www.cfn.upenn.edu/zewang/BENtbx.php), developed by Wang et al. [42]. SampEn, an enhancement over Approximate Entropy, measures the temporal coherence of a time series. This is achieved by calculating the "logarithmic likelihood" that a small data segment (within a window of length 'm') will continue to exhibit similarity with other segments as the window length increases by one unit. A "match" is defined by a threshold less than r times standard deviation of the entire time series. The window length was set to 3, with a cut-off threshold of 0.6. The entropy values across all voxels were then aggregated to formed the BEN map, which was subsequently smoothed using an isotropic Gaussian kernel (FWHM = 8 mm) to minimize the structural brain difference between individuals that may not be fully aligned during spatial normalization of each brain into the MNI space.

Transfer entropy calculation

Each subject's fMRI data were parcellated into 116 ROI time series, by using the auto anatomical labelling (AAL) atlas. A combination of home-made Matrix Laboratory (Matlab version 2017b) code (see supplementary material 1) and Java Information Dynamics Toolkit (JIDT, https://github.com/jlizier/jidt) were used to investigate the directional information flow between brain regions [43]. We employed Kozachenko-Leonenko and Kraskov-Stögbauer-Grassberger (KSG) estimator to calculate transfer entropy. KSG estimator is a non-parametric method used to estimate the mutual information between multidimensional random variables [44]. It leverages the k-neighbors (KNN) approach to estimate mutual information (MI) efficiently and effectively, especially in high-dimensional spaces. Although there are multiple algorithms can be u sed to estimate TE for continues data, KSG estimator was regarded as the "best of breed solution".

The KSG estimator for mutual information $I(X; Y)$ between two random variables X and Y is given by:

$$I(X;Y) = \psi(k) + \psi(N) - \frac{1}{k} - \frac{1}{N}\sum_{i=1}^{N}[\psi(n_x(i)+1) + \psi(n_y(i)+1)]$$

ψ stand for the digamma function, $\psi(x) = \frac{d}{dx}\ln\Gamma(x)$, which adjusts for bias in the estimation process. k is the number of nearest neighbors, which is 4 in this study. N is the samples size of the data, which is 230 time-point. When using the KSG estimator in JIDT, by setting the source history length "k", the target history length "l" and the delay "τ", we can use the KSG estimator to calculate the transfer entropy:

$$TE_{X\to Y} = (X_{t-\tau}; Y_t | Y_{t-1})$$

We calculated a 116 × 116 matrix for each subject. Since the TE is a directed metric, the TE matrix can be described as a directed graph. Since the KSG algorithm is an estimator associated with variance, the estimated TE can be negative when the true TE between processes approaches or equals zero [43]. However, according to the theoretical principles of TE, it cannot be negative [45]. Therefore, measured negative TE would indicate a measurement error. Consequently, we can exclude negative TE by setting them to zero.

Statistical analysis

Two-sample t-tests were used to compare age differences, SampEn maps, and TE maps between the two groups. The two-sample t-test in SampEn maps and TE matrices, covariates include age and head motion (mean Framewise displacement Jenkinson, mean FD Jenkinsen) [46], and false discovery rate (FDR) correction was used for the multiple comparison correction, and the significant level was $p < 0.05$. The SampEn maps and TE

Table 1 Demographic and clinical data of ASD group and TD group

	ASD	TD	*p*-value
Age (Month)	26.93 ± 5.77	24.88 ± 6.99	0.15
Sex (Male/Female)	(34/8)	(34/8)	-
ABC total score	70.83 ± 15.02	-	-
CARS total score	33.61 ± 1.80	-	-
DSCA total score	54.12 ± 9.12	-	-
ABC Sub-scale			
Sensory	10.21 ± 5.22	-	-
Relating	18.58 ± 4.25	-	-
Language	15.51 ± 3.10	-	-
Stereotype and object use	13.37 ± 3.47	-	-
Self-help and social	13.24 ± 2.33	-	-
DSCA 0-6Y Sub-scale			
Gross motor	68.01 ± 11.32	-	-
Fine motor	50.97 ± 10.28	-	-
Ability to adapt	66.34 ± 11.43	-	-
Language	48.70 ± 13.17	-	-
Social skills	54.15 ± 8.16	-	-
Head motions			
Mean FD Jenkinson	0.051 ± 0.028	0.048 ± 0.021	0.12

Note: ASD, Autism spectrum disorder; TD, Typical developed; Autism Behavior Checklist, ABC; Childhood Autism Rating Scale, CARS; Developmental Scale for Children Aged 0–6 years, DSCA 0-6Y; Mean framewise Jenkinson, mean FD Jenkinson; The age of the two groups of subjects was assessed in months, and the disparity in age between the two groups was evaluated using a two-sample *t* test

maps showed group difference was selected to perform Pearson's correlation analysis with the clinical variables including the CARS, ABC, DSCA 0-6Y total scores, and subscales scores of ABC and DSCA 0-6Y. Age and head motion (mean FD Jenkinson) were included as covariates. The significant level was $p < 0.05$. Due to the large number of p-values generated from correlation analysis. Applying the Bonferroni correction may result in excessive adjustments and an increased risk of type II errors; therefore, we propose using the Holm-Bonferroni method cautiously.

Result

No significant difference was observed in age. Demographic and clinical data was presented in Table 1.

In analyzing the whole brain SampEn, group differences were found only in the right frontal lobe as we presented in the Fig. 1 and there is a boxplot in the supplement material. The ASD group showed significant elevated SampEn in compare with the TD group in the right inferior frontal gyrus (see Table 2. for effect sizes and *t*-values) in sleeping state. In addition, there was no significant statistical relationship between SampEn and clinical indicator.

Figure 2. shows group difference in TE matrix. Figure 3. shows brain regions and information flow with significant group differences. In general, a total of 13 pairs of brain regions exhibited higher TE values in the TD group compared to the ASD group, while only 5 pairs showed

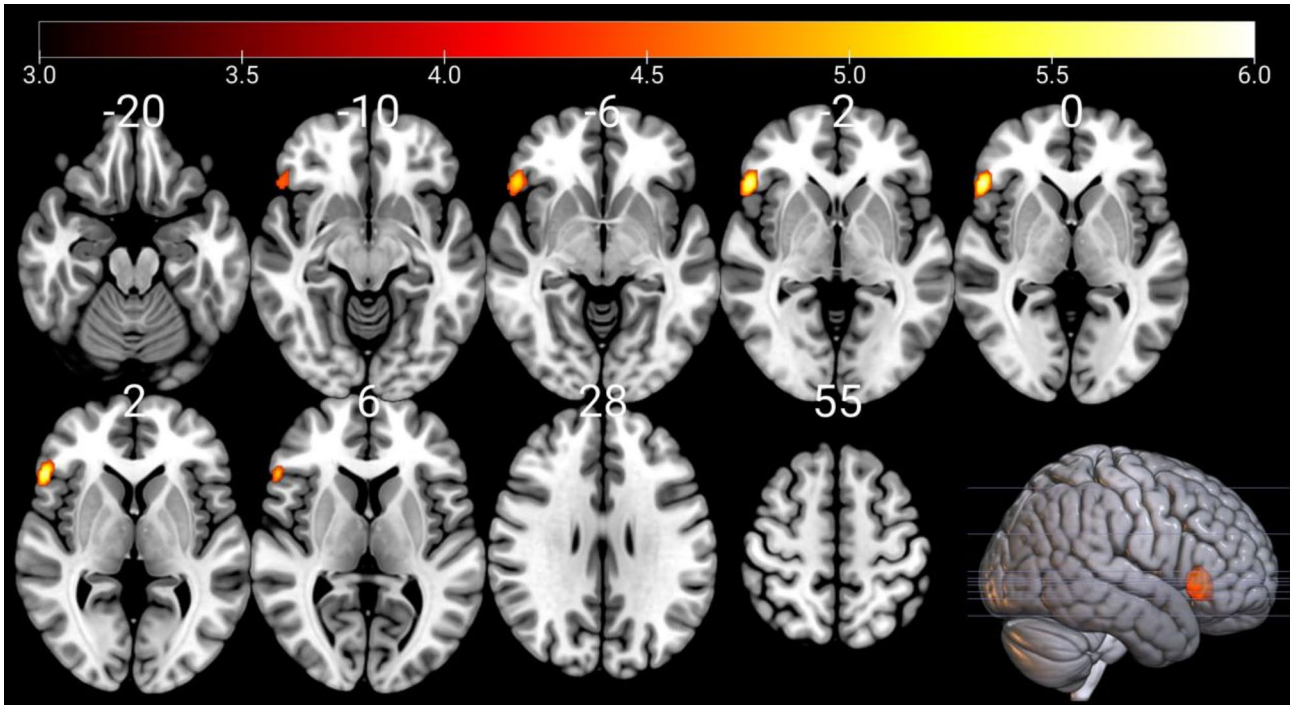

Fig. 1 Note: Brain region showing increased SampEn in the right inferior frontal gyrus in the ASD group compared with the TD group. The color bar indicated the *t* value. This image is presented in the MNI space at 1 mm resolution. This image was rendered by using MRIcroGL (https://github.com/rordenlab/MRIcroGL)

Table 2 Brain regions showing significant sampen information and corresponding *t*-value

Brain regions	AAL	MNI peak voxel Coordinates			Voxel size	t-value
		x	y	z		
Right Inferior frontal Gyrus	Frontal_Inf_Tri_R	52	24	0	318	5.943

Note: The *t*-value indicates the significant increased SampEn in the ASD group. The template resolution is 1 mm. MNI, Montreal Neurological Institute; AAL, anatomical automatic labeling

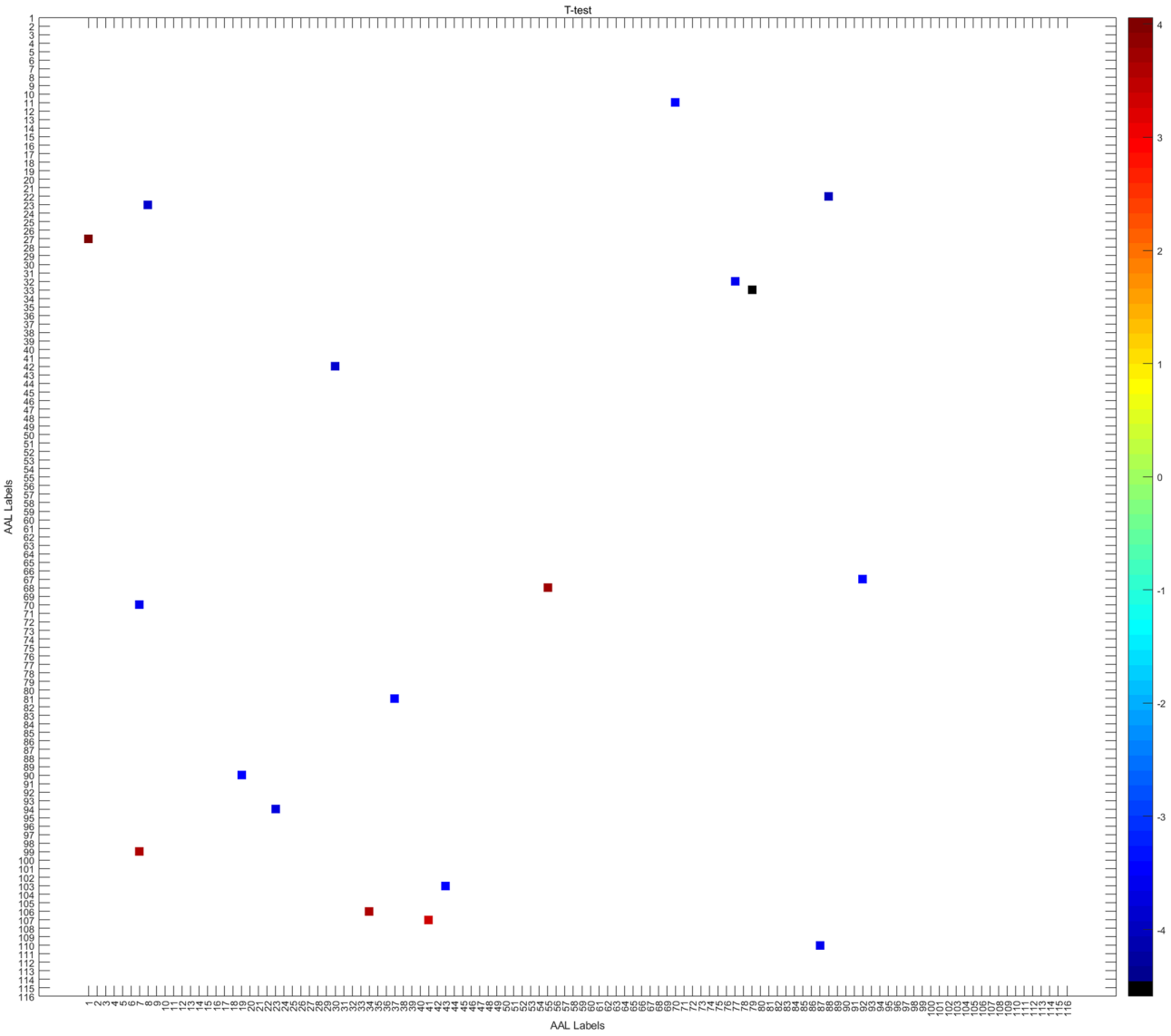

Fig. 2 Note: This figure illustrates the regions where there are differences in Transfer Entropy (TE) between the ASD and TD groups. The x-axis and y-axis represent the 116 brain regions in the AAL atlas. Each point in the matrix corresponds to the TE value between a pair of brain regions. If a diagonal line is drawn from the coordinate (1,1) to (116,116) across the matrix, the two coordinates symmetric about this diagonal represent the two different directions of TE transmission between a pair of brain regions. In other words, the brain regions on the x-axis can be considered the "source" of the information flow, whereas those on the y-axis represent the "target."

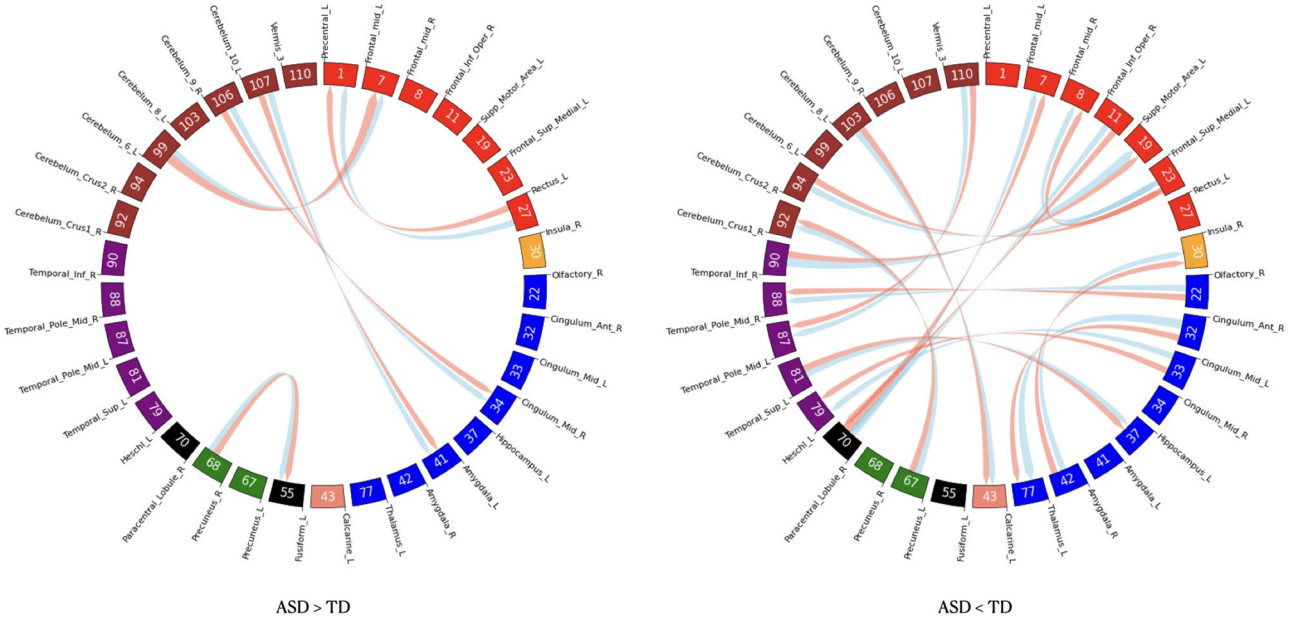

Fig. 3 Note: The chord diagram illustrates the TE connections between different brain regions. We presented the ASD > TD and TD > ASD separately. Different colored sectors represent different brain structures: Red- Frontal lobe, Orange- I nsula, Blue- limbic system, salmon- Occipital lobe, purple- Temporal lobe, brown- Cerebellum. The black sectors represent the regions situated between two lobes

higher values in the ASD group. In compare with the TD group the ASD group showed significant higher TE from cerebellum to the frontal lobe and limbic system. However, the TD group showed significant increased TE in multiple brain regions. After applying multiple comparison correction, we did not observe any significant correlation between clinical scales and TE in the ASD group after multiple comparison correction.

Discussion

In this study, we employed SampEn and TE to analyze the complexity of brain activity in young children with ASD during nature sleep state. In compare with TD group, significant increased SampEn was found in the right inferior frontal gyrus of ASD group. However, ASD group showed more decreased TE than increased TE in compare with TD group. Furthermore, our findings indicate a higher level of information flow in the ASD group compared to the TD group mainly originating from the cerebellum.

Previous studies have shown that a significant portion of the frontal cortex exhibits early enlargement in individuals with autism [47]. Our participants fall within the age range corresponding to the early stages of brain development in autism. Therefore, it is unsurprising that the frontal lobe was the sole region in our study to exhibit significant group differences as indicated by SampEn. However, notable disparities appear to exist between our study and prior SampEn research. For example, Jose O et al. found abnormal SampEn in four brain regions, including the superior frontal gyrus, angular gyrus, superior parietal gyrus, and inferior temporal gyrus. Conversely, the ASD group exhibited lower SampEn values only in the superior frontal gyrus compared to the TD group [19]. The possible explanation to this may be attributed to the researchers investigating various age group. Their study included a cohort of ASD patients aged between 9 and 11 years. However, the ASD patients recruited in our study were between 1 and 3 years. In other words, the autistic brains sampled in our study may be in a phase of overgrowth. We employed the voxel-based morphometry (VBM) method to validate this and discovered that the volume of certain brain regions in autistic children is significantly larger than that in typically developing children (see supplementary material 1). Conversely, the autistic brains in Jose's study appear to be in an arrested growth phase [16, 19]. As the brain develops, the brain complexity become more sophisticated [48]. The higher brain SampEn observed in ASD group in this study may be attributed to this factor. Other factors, such as participant state, data processing methods, and head motion, may also contribute to differences in the results. Unfortunately, no significant correlation was observed between the SampEn and clinical scales in the ASD group.

In terms of information transmission, we observed a significantly reduced TE in the ASD group compared to the TD group. The TE values were found to be significantly higher in 13 pairs of brain regions within the TD group compared to the ASD group. The present findings

are consistent with previous studies, indicating that individuals with ASD demonstrate comparatively weaker brain connections and/ or impaired information transmission among various brain regions compare to those without autism [49, 50]. The results of a previous study on TE also produced a similar outcome [32]. Conversely, some studies have reported instances of hyperconnectivity in ASD [51, 52]. This suggests that brain connectivity in ASD may be highly complex. Therefore, we believed that the entropy of local brain activity may not adequately capture the complexity of the brain. The existing body of evidence has demonstrated aberrant in both functional and structural connectivity among children diagnosed with ASD [53, 54]. Therefore, it is reasonable to suggest that there is abnormal transmission of information between different regions in the young autistic brain.

Previous effective connectivity research has demonstrated that children with ASD exhibit significant aberrations in the effective connectivity both between and within brain networks, with the most pronounced abnormality observed in the social brain network [55–57]. Although relevant brain networks were not the focus of our study, the results of TE in this study also exhibit certain systematic characteristics. The most prominent findings in the TE results include differences in information transmission within the frontal lobe, temporal lobe, cerebellum, and limbic system. The limbic system plays a pivotal role in regulating emotions especially in facial expressions processing [58]. However, the participants in this study were all asleep during the MR scans, thus implying no discernible impact on emotional processing. One possible explanation for this is that some neurotransmitters may affect the neural activity of the limbic system in autistic brain. Some evidence suggests that around third of ASD patients whole blood serotonin level increased significantly [59, 60]. And a previous study found reduced serotonin receptor in the limbic system and neocortical region in autistic brain [61]. Therefore, we speculated that altered emotional processing in autistic brain only represent an aspect of disrupted neural activity of the limbic system. A previous fMRI study indicated that serotonin affect the neuro activity of the limbic system in autistic brain, leading to abnormalities in the homeostatic control of the limbic system [62]. And the homeostatic control is associated with impaired sleep quality in ASD patients [63].

To our astonishment, the ASD group exhibited higher values of TE in certain brain regions compared to the TD group. The abnormally elevated TE predominantly originates from the cerebellar hemisphere. Earlier studies have shown a significant decrease density of Purkinje cells in the cerebellum [64]. Furthermore, alterations in the cerebellar volume, morphology, and connectivity have also been observed among ASD patients [65]. The involvement of the cerebellum in ASD remains a subject of debate [66]. However, the cerebellum has been implicated in numerous studies as playing a crucial role in cognition, emotion, and various other aspects [67]. It is thought that the cerebellum may guide the development of remote nonmotor neural circuitry and influence cognitive development in autistic brain [68]. In the present study, the ASD group showed increased TE between the cerebellum and amygdala compared with the TD group. Since the amygdala is one of the key regions in the limbic system, we believe that this atypical TE could be associated with the aberrant cerebellum-limbic system in autistic brain. Animal experiments have shown that the amygdala is a key region receiving signals from the cerebellum to the limbic system [69]. There is evidence that the cerebellum and amygdala might interact in shaping social and affective behavior [70]. Therefore, we postulated that the aberrant transmission of signals between the cerebellum and amygdala may associated with the different progression during the early stages of the condition.

The present study had several limitations. First, the sleep state of human is divided into two main stages: rapid eye movement (REM) sleep and non-rapid eye (NREM) sleep, but we can't monitor what stage of sleep the subjects are in during the MRI scan. This factor may have the potential to influence the results. Secondly, we employ the AAL template for brain analysis; however, this particular template is unsuitable for studying brain networks. Therefore, we will employ a more sophisticated template in our subsequent studies of information transfer in autistic brain. Thirdly, we used a Chinese autism diagnostic scale (the Developmental Scale for Children aged 0–6 years), which is widely used in China, but there is no official English version, which may not be friendly to researchers in non-Chinese speaking regions. We have decided to collaborate with other Chinese autism researchers to translate the scale and aim to make it available to researchers in other regions as quickly as possible. Fourth, the relatively small sample size in our study may have resulted in limited statistical power. Additionally, the predominance of male participants could have introduced bias into the results. In future studies, we plan to increase the sample size and balance the gender distribution of participants to obtain more accurate and reliable findings.

Conclusion

This study found significant differences in brain complexity between autistic children and TD children during sleep. The present study offers empirical support for the presence of abnormalities in brain complexity during early stages of autism. The complexity of brain signals in autism may itself be a highly intricate phenomenon. The

randomness of brain activity within local regions alone may not adequately capture the full extent of brain complexity in autism. In the early stages of autism, the complexity of brain may be related to the signal randomness of neural activity and the transfer of information between brain regions.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12888-025-06689-4.

Supplementary Material 1

Author contributions

Shishun Fu wrote the main manuscript text, and Xiang Wang prepared all the figures. Ziwei Chen wrote the supplement material. The Matlab code for this study was collaboratively developed by Shishun Fu and Zengfa Huang. The data collection and inspection task were carried out by Yin Feng and Yuanliang Xie. The text and figures were reviewed by Chunlan Yang. The study was designed by Shoujun Xu and Shishun Fu, Shoujun Xu also serves as the corresponding author.

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Data availability

The fMRI data and behavioral scales data available on request from the corresponding author (Shoujun Xu) by request. Code is available from the first author (Shishun Fu) by request or you can vistit https://github.com/biophilia007/Transfer-Entropy/.

Declarations

Ethics approval and consent to participate

The study was approved by Review Board of Shenzhen Children's Hospital Committee of Medical Ethics.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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