The Atypical Functional Connectivity of Broca Area at Multiple Frequency Bands in Autism Spectrum Disorder

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Abstract

As a developmental disorder, autism spectrum disorder has drawn much attention due to its severe impacts on language capacity. Broca area, an important brain region of language network, has largely involved in language-related functions. Using Autism Brain Image Data Exchange (ABIDE) dataset, a total of 1454 participants (618 ASD and 836 HCs) were included in our research. In order to detect the pathophysiological mechanism of autism spectrum disorder from the perspective of language, we conducted a functional connectivity analysis with Broca as the seed in multiple frequency bands (conventional: 0.01–0.08 Hz; slow-4: 0.027–0.073 Hz; slow-5: 0.01–0.027 Hz). We found that compared with healthy controls, patients with autism spectrum disorder have demonstrated increased functional connectivity in left thalamus, left precuneus, left anterior cingulate and paracingulate gyri, and left medial orbital of the superior frontal gyrus in conventional frequency band (0.01-0.08Hz). The results of slow-5 frequency band (0.01-0.027Hz) presented increased functional connectivity values of left precuneus, left medial orbital of the superior frontal gyrus, right medial orbital of the superior frontal gyrus and right thalamus. No significant cluster was detected in the slow-4 frequency band (0.027-0.073Hz). In conclusion, the abnormal functional connectivity in patients with autism spectrum disorder has frequency-specific properties. Furthermore, the findings of conventional frequency bands (0.01-0.08Hz) were mainly contributed by slow-5 (0.01-0.027Hz). The current study might shed new light on the pathophysiological mechanism of language impairments in autism spectrum disorder.

1. Introduction

Autism spectrum disorder (ASD), a pervasive developmental disorder with high global prevalence (Baio et al., 2018; Levy et al., 2009; Traut et al., 2018), has severely affected patients' language capacities (Elsabbagh et al., 2012; Levy et al., 2009; Lombardo et al., 2015; Lord et al., 2018; Sanchack & Thomas, 2016). Impaired language development places patients with ASD on a disabled trajectory in which deviant neural activity in language affects ASD patients' communicational ability (Bennett et al., 2008; Bookheimer, 2002; Green et al., 2010; Pickles et al., 2014). A variety of neuroimaging researches have demonstrated the abnormal connectivity in ASD patients' language network that may result in the impairments of language-related functions, such as capacities of communication (Levy et al., 2009) and expression (Lai et al., 2014). As one of the prominent brain areas of language network, Broca area has been regarded as a widely known broad-domain region that responded to language processing (Bookheimer, 2002) and has been confirmed as an exclusive speech-production area which is related to language acquisition and production (Nishitani et al., 2005). Further, prior studies have demonstrated that the impairment of Broca might trigger the dysfunction of language fluency (Iwashiro et al., 2016), story listening (Papathanassiou et al., 2000), expressive speech (Bookheimer, 2002), language comprehension (Murdaugh et al., 2015) and speech articulation of language (Trupe et al., 2013), etc. Hence, investigating aberrant activity of Broca is of great importance to the research in detecting language network. As ASD is characterized by dysfunction of language (Elsabbagh et al., 2012; Lai et al., 2014), more attention should

be paid to the alterations of Broca and pathophysiology of ASD and it needs to be further explored by using neuroimaging technique.

Resting state functional magnetic resonance imaging (rs-fMRI) is a non-invasive approach in presenting spontaneous brain activity (B. Biswal et al., 1995; B. B. Biswal, 2012; Fox & Raichle, 2007), and has been regarded as a promising neuroimaging tool to detect the pathophysiology of neural diseases (Eaton et al., 2008; Plante et al., 2017). It can provide insights into memory disorder Alzheimer's disease (AD) (Pasquini et al., 2015), restoration of motor function in stroke (Park et al., 2011) and impairments in social and language abilities in ASD (Boucher, 2012; Gotts et al., 2012; Lai et al., 2014). Characterized by impairments of language network (Gao et al., 2019; Lee et al., 2017), ASD is likely involved in the alterations in connectivity patterns (Ebisch et al., 2011; Gotts et al., 2012). Hence, we attempted to analyze the connectivity patterns of Broca in order to further detect the language impairments of ASD using functional connectivity. As an widely used measure of rs-fMRI, functional connectivity (FC) has been broadly applied in illustrating the relationship of the temporal correlated features of functionally related brain regions (B. Biswal et al., 1995; Fox & Raichle, 2007; Friston, 1994) in neural diseases (Bai et al., 2009; Y. Liu et al., 2020; Pasquini et al., 2015; Zhang et al., 2020), including ASD (Gao et al., 2019; J. Liu et al., 2020). However, the FC results of Broca in ASD patients were inconsistent. One found abnormal connectivity between Broca and bilateral heschl's gyrus and bilateral thalamus respectively (J. Liu et al., 2020); while the other found that of angular gyrus and posterior cingulate cortex (Gao et al., 2019). The possible explanations may be contributed to the small sample size of these studies. As a previous study mentioned that the analyses of a large sample size could provide a more precise and less heterogeneous estimation (Traut et al., 2018), we adopted the data of a multi-center dataset named Autism Brain Image Data Exchange (ABIDE) to assess the language dysfunction of ASD.

Besides, many FC analyses are conducted in the conventional frequency band (0.01-0.08Hz) (Park et al., 2011; Shi et al., 2020; Zhao et al., 2019) since the first rs-fMRI research revealed the neural mechanism in low frequency ($< 0.01\text{Hz}$) (B. Biswal et al., 1995). Further, emerging evidence has provided new insights for the different contributions mainly made by slow-4 (0.027-0.073Hz) and slow-5 (0.01-0.027Hz) frequency bands to conventional frequency band (0.01-0.08Hz) (Buzsáki & Draguhn, 2004; Zuo et al., 2010) in order to deepen the understanding of oscillations in physiological functions (Penttonen & Buzsáki, 2003). Researchers indicated that slow-4 and slow-5 oscillations were prominently observed in grey matter activity (Zuo et al., 2010) and had noteworthy differences in neural diseases (Hu et al., 2020; Wang et al., 2020; Xue et al., 2016). For example, some researchers found altered FC of default mode network (DMN) in Alzheimer's disease (AD) differ between slow-4 and slow-5 (Y. Li et al., 2017). Other studies found that real transcutaneous vagus nerve stimulation (tVNS) increased FC in slow-5 in patients with major depressive disorder (Wang et al., 2018). All these findings indicated the significances of frequency-specific properties of FC in neural diseases. Therefore, it is valuable to investigate the frequency-specific properties of FC in ASD from the perspective of language.

In the current study, we hypothesis that there are frequency-specific alterations of FC in language dysfunction of ASD. To realize this purpose, we conducted a seed-based functional connectivity with

Broca area as the seed to explore the aberrant brain activity related to language network in the different frequency band, namely, conventional (0.01-0.08Hz), slow-4 (0.027-0.073Hz) and slow-5 (0.01-0.027Hz) frequency band. It should be noted that we collected data from a public dataset named ABIDE and perform a mega-analysis to provide more reliable results in order to explore the pathophysiological mechanism of ASD.

2. Materials And Methods

2.1 Participants

Data in the current study were collected from Autism Brain Imaging Data Exchange (ABIDE) dataset, namely ABIDE I (http://fcon_1000.projects.nitrc.org/indi/abide/abide_I.html) (Di Martino et al., 2014) and ABIDE II (http://fcon_1000.projects.nitrc.org/indi/abide/abide_II.html) (Di Martino et al., 2017). A total of 23 cohorts were obtained in this research. Furthermore, these cohorts were divided into 30 groups based on the number of timepoints and slice number. The inclusive criteria were as follows: (1) Participants with corresponding functional image and structural image; (2) The participants' head movements are less than 3 mm in translation and 3° in rotation; (3) Good spatial normalization; (4) Right-handed participants; (5) Cohorts with both ASD and HC participants. Based on this, 1454 participants (618 ASD and 836 HCs) were included in our research. The precise information of the inclusive criteria is demonstrated in the supplementary material. Detailed demographic information about the included participants is shown in Table 1. The scan parameter, promotion of the ethics committee and other relative information are demonstrated at http://fcon_1000.projects.nitrc.org/indi/abide/.

2.2 Resting-state fMRI data preprocessing

The preprocessing of the image data collected in the current study were performed using Resting-State fMRI Data Analysis Toolkit plus (Jia et al., 2019) (RESTplus V1.24, <http://restfmri.net/forum/restplus>), Statistical Parametric Mapping software (SPM12, www.fil.ion.ucl.ac.uk/spm) on Matlab2017b (MathWorks, Natick, MA, USA). To be specific, the following steps were conducted: (1) The first 10 timepoints were discarded for the purpose of magnetization stabilization and participants' adaptation to the scanning circumstance; (2) Slice timing and realignment were performed to ensure that the time differences of acquired functional images and the head motion of the remaining volumes of each participant were corrected; (3) Structural images were co-registered to the mean functional image, and segmented with the New Segment algorithm. Spatial normalization was then conducted within Montreal Neurological Institute (MNI) space and all images were resampled to $3 \times 3 \times 3 \text{ mm}^3$ voxels to suit the scope of brain mask; (4) Smoothing was conducted using a 6 mm with a full width at half maximum (FWHM) Gaussian kernel to remove noise; (5) The linearly increasing trend of the time series was removed to maintain the stability of the signal; (6) Nuisance regression was completed. Namely, polynomial trend and Friston 24 head motion parameter (Friston et al., 1996) were regressed out. Finally, band-pass filtering was conducted in conventional frequency band (0.01–0.08 Hz), slow-4 band (0.027–0.073 Hz), and slow-5 band (0.01–0.027 Hz).

2.3 Functional connectivity analysis

Followed by data preprocessing, we conducted voxel-wise functional connectivity (FC) analysis with Broca area as the seed. According to a previous research (Lurito et al., 2000), we anchored a 6mm-diameter sphere that was centered at (-55, 13, 7) in Talairach space and transformed to (-58, 16, 3) in MNI space as our seed to represent Broca area. To assess FC, we conduct the calculation of Pearson correlation coefficient (r value) between the mean time series of seed and those of the other voxels of the whole brain in different frequency bands (conventional: 0.01–0.08 Hz; slow-4: 0.027–0.073 Hz; slow-5: 0.01–0.027 Hz). Further, Fisher's r -to- z transformation was adopted in three bands respectively to confirm that the r value was transformed to z value.

2.3 Statistical analyses

Two-sample t -tests were performed to clarify the group differences between ASD and HCs groups. Age, gender together with site bias effects were set as covariates and were regressed out to minimize the potential impacts. Statistical significance was assessed with the threshold of voxel-level $p < 0.001$ and cluster-level $p < 0.05$ corrected by Gaussian random field (GRF) correction based on Data Processing & Analysis for Brain Imaging (DPABI_V5.1, <http://rfmri.org/dpabi>) (Yan et al., 2016).

3. Results

3.1. Demographic information

Demographic information of the current study was summarized in Table 1. The 2168 participants were collected. According to the inclusive criteria mentioned above, 228 participants were excluded for excessive head motion (exceeding 3mm or 3°). The 213 participants were deleted for the bad effect of normalization; 14 participants were discarded for the lack of functional image and 16 were excluded for the lack of structural image. The 55 participants were deleted because the cohorts Kul and Nyu2 lacked healthy controls. Additionally, 188 participants were discarded because this study only included the right-handed participants. In the final, 618 ASD patients and 836 HCs were included in this study. Detailed information was demonstrated in the supplementary material.

(Insert Table 1)

3.2. FC analysis results

In the conventional frequency band (0.01-0.08Hz), compared with HC, ASD patients have demonstrated increased FC in the left thalamus, left precuneus, left anterior cingulate and paracingulate gyri and left medial orbital of the superior frontal gyrus. As for slow-5 frequency band (0.01-0.027Hz), ASD patients have shown higher FC values in bilateral medial orbital of the superior frontal gyrus, right thalamus and left precuneus. No significant cluster was demonstrated in the slow-4 frequency band (0.027-0.073Hz) (Figure 1, Table 2).

(Insert Figure 1)

(Insert Table 2)

4. Discussion

This study performed FC analysis which targeted Broca as the seed to investigate its frequency-specific properties at multi-frequency bands (conventional: 0.01–0.08 Hz; slow-4: 0.027–0.073 Hz; slow-5: 0.01–0.027 Hz) between ASD patients and HCs. Compared with HCs, ASD patients showed higher FC values in the left thalamus, left precuneus, left anterior cingulate and paracingulate gyri and left medial orbital of the superior frontal gyrus in the conventional frequency band (0.01-0.08Hz). Two of those, left precuneus and left medial of the superior frontal gyrus, were replicated in the slow-5 frequency band (0.01–0.027). Besides, the increased FC value of right medial orbital of the superior frontal gyrus and right thalamus were also detected in slow-5. No significant cluster was found in slow-4 frequency band. These findings indicated that abnormal FC in ASD patients might be linked to specific frequency bands and may provide new understanding of pathophysiology in ASD.

4.1 Altered FC between Broca area and the whole brain in the conventional frequency band

In the conventional frequency band (0.01-0.08Hz), we found increased FC in the left thalamus, left precuneus, left medial orbital of the superior frontal gyrus and left anterior cingulate and paracingulate gyri among ASD, compared with HCs.

Thalamus is taken as language monitor (Munte & Kutas, 2008) and was activated in semantic and syntactic language tasks (Wahl et al., 2008). Prior research demonstrated the sensitivity of thalamus to language (Munte & Kutas, 2008), and various lines of evidence have observed the activation of thalamus in language-related tasks, such as phonological word retrieval processes (Perani et al., 2003) and verbal and semantic fluency tasks (Rodrigo et al., 2008a). The abnormalities appeared in thalamus among ASD have also been discovered (Ayub, 2021; Tomasi & Volkow, 2019). Our results also revealed the increased FC between left thalamus and Broca area in ASD, indicating that atypical connectivity between Broca and thalamus might connect with the language dysfunction in ASD. Hence, the neural mechanism of language might be related to thalamus.

Located in the posteromedial cortex (Cavanna & Trimble, 2006), precuneus is widely involved in higher-order cognitive functions (Cavanna & Trimble, 2006) and has been proven to relate with semantic processing (Jennings et al., 1997) and social interaction (Cavanna & Trimble, 2006) which might suggest the involvement of precuneus in language processing. Meanwhile, Broca area has been reported to be activated in the similar language-related task (Kepinska et al., 2018). The atypical connectivity between precuneus and Broca might provide a possible proof for the dysfunction of language in ASD. Recent studies have also found the abnormality of bilateral precuneus in ASD (Kitamura et al., 2021; Lukito et al.,

2020). Similar to the prior research (Lukito et al., 2020), our results also showed the increased FC in left precuneus in ASD. This might provide support for the speculation that precuneus could be involved in language processing in ASD.

The anterior cingulate and paracingulate gyri are considered as the center of allocating resources to auditory and visual information (Gennari et al., 2018) and have been proved to be activated in numerous language-related tasks, such as speech sound discrimination (Gennari et al., 2018) and prosody production (Mitchell et al., 2016). These findings provided reasonable explanations for the influence of its alterations on language functions. Recently, a study about ASD proposed that the weaker connectivity of anterior cingulate cortex may result in communicative and linguistic impairment (Kana et al., 2017). However, our results demonstrated the increased FC in anterior cingulate and paracingulate gyri among ASD patients. The possible explanation for this difference might contribute to sample sizes or the methodological difference. Taken together, the anterior cingulate and paracingulate gyri might be regarded as one of the core brain regions which is responsible for language dysfunction.

Bilateral medial orbital of the superior frontal gyrus is located at medial prefrontal cortex (Zhu et al., 2019) which has been posited to serve a variety of social functions (Lieberman et al., 2019). Further, the activation of medial prefrontal cortex has been proved in language-related tasks, such as semantic autobiographical memory (Martinelli et al., 2013) and semantic ambiguity (Bilenko et al., 2009). A Recent study has found attenuated link between medial prefrontal cortex and amygdala in ASD (L. Li et al., 2021). Our results presented the increased FC of medial orbital of the superior frontal gyrus which might provide more evidence for the influence of medial prefrontal cortex in language processing. From this perspective, the abnormal activity of medial orbital of the superior frontal gyrus might contribute to language deficits in ASD.

4.2 Altered FC between Broca area and the whole brain at sub-frequency bands

The current study demonstrated that functional connectivity of Broca among ASD has frequency-dependent characteristics. To be more specific, no significant cluster was found in the slow-4 frequency band (0.027-0.073Hz). While in the slow-5 frequency band (0.01-0.027Hz), there was increased FC in left precuneus, left medial orbital of the superior frontal gyrus which were consistent with those observed in the conventional frequency band (0.01-0.08Hz). Besides, right thalamus and right medial orbital of the superior frontal gyrus which were also detected in slow-5 frequency band did not present significance in the conventional frequency band.

Previous studies have indicated the involvement of the right thalamus (Hervais-Adelman et al., 2015; Rodrigo et al., 2008b) and right medial orbital of the superior frontal gyrus which is located in the medial prefrontal cortex (Gilead et al., 2013; Zhu et al., 2019) in language processing. This might suggest that right thalamus and right medial orbital of the superior frontal gyrus could be regard as potential brain region in language production. The increased FC in right thalamus and right medial orbital of the superior frontal gyrus demonstrated in our research might provide new insights for the involvement of the right

hemisphere in language processing, and enrich the findings of language lateralization (Kleinhans et al., 2008; Nielsen et al., 2014; Rodrigo et al., 2008b). For ASD patients, the involvement of right hemisphere in language processing could be a compensatory mechanism that needs to be further explored.

The results of the present study demonstrated that functional connectivity of Broca was frequency-dependent, especially in slow-5 frequency band (0.01-0.027Hz). According to our findings, slow-5 (0.01-0.027Hz) contributes more to the results of conventional (0.01-0.08Hz) frequency band and is more sensitive than slow-4 (0.027-0.073Hz) in detecting FC of Broca in ASD. According to a prior study, the benefits of slow-5 has also shown relative powerful interpretation than other bands in illustrating decreased FC in adolescents with ASD (Duan et al., 2017). These findings might suggest that frequency-dependent characteristics have potential merits in revealing the language processing mechanism in ASD patients.

5. Conclusions

In the current study, a FC analysis targeted Broca area as the seed was conducted in ASD at conventional (0.01-0.08Hz), slow-4 (0.027-0.073Hz) and slow-5 (0.01-0.027Hz) frequency bands. According to this study, the findings of conventional frequency band might be primarily contributed by slow-5 band, and slow-5 band might provide additional information for aberrant spontaneous brain activity. The selection of proper frequency bands might benefit in exploring the underlying neural language mechanisms. There are some limitations of this study. For example, in order to include as many as participants in the current research, few cohorts we collected have relatively small sample size due to the exclusion of bad normalization or exceeding head motion. Further studies should detect the dysfunction of language deeply and shed more light on the potential pathophysiological mechanism of ASD.

Declarations

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Conflicts of Interest: The authors declare no conflict of interest.

Ethical Approval: All procedures conducted in research involving human subjects were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Detailed information could be obtained at http://fcon_1000.projects.nitrc.org/indi/abide/.

Informed Consent: Informed consent was obtained from all subjects involved in the Autism Brain Image Data Exchange (ABIDE, a public multi-center datasets) on which this research is based. Detailed information could be obtained at http://fcon_1000.projects.nitrc.org/indi/abide/.

Consent for publication: Not applicable.

Availability of data and material: The data used in this study was derived from the ABIDE (http://fcon_1000.projects.nitrc.org/indi/abide/) public database.

Code availability: All data were processed with the legal edition of RESTplus V1.24. All code generated or used during the study are available from the corresponding author by request.

Author Contributions: Conception and study design (Lulu Cheng, Xize Jia and Linlin Zhan), data collection or acquisition (Yanyan Gao, Lina Huang and Hongqiang Zhang), statistical analysis (Jiawei Sun, Guofeng Huang and Yadan Wang), interpretation of results (Mengting Li and Huayun Li), drafting the manuscript work or revising it critically for important intellectual content (Linlin Zhan, Xize Jia and Lulu Cheng) and approval of final version to be published and agreement to be accountable for the integrity and accuracy of all aspects of the work (All authors).

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Tables

Table 1. Demographic information of included healthy controls (HCs) and autism spectrum disorder (ASD) patients.

Cohort name[1]	HCs			ASD		
	Age	Gender (Male/Female)	Sample size	Age	Gender (Male/Female)	Sample size
BNI	36.95 ± 15.20	21/0	21	35.32 ± 15.43	22/0	22
Caltech	28.10 ± 12.22	6/4	10	25.00 ± 8.68	4/0	4
EMC	8.00 ± 0.78	11/3	14	8.38 ± 1.33	10/3	13
ETH	23.42 ± 4.76	19/0	19	21.17 ± 3.97	6/0	6
GU	10.58 ± 1.93	15/16	31	10.91 ± 1.72	20/2	22
IP	17.24 ± 7.96	9/8	17	24.47 ± 11.37	7/8	15
IU	23.80 ± 5.23	11/4	15	25.92 ± 11.83	9/3	12
KKI_1	10.46 ± 1.07	16/12	28	9.77 ± 1.69	9/4	13
KKI_2	10.28 ± 1.27	66/42	108	10.61 ± 1.56	30/11	41
Leuven	18.85 ± 5.25	23/4	27	18.00 ± 5.26	22/2	24
MaxMun_1	33.25 ± 8.97	8/4	12	36.09 ± 11.75	8/3	11
MaxMun_2	26.43 ± 3.74	14/0	14	15.00 ± 9.90	2/0	2
MaxMun_3	9.00 ± 2.83	2/0	2	19.25 ± 13.30	8/0	8
NYU	14.98 ± 6.41	78/20	98	14.39 ± 7.99	55/12	67
OHSU_1	10.31 ± 1.18	13/0	13	11.62 ± 2.22	13/0	13
OHSU_2	10.39 ± 1.70	26/25	51	11.71 ± 2.30	25/6	31
Olin1	17.55 ± 3.96	9/2	11	17.21 ± 3.77	12/2	14
Olin2	24.34 ±	16/13	29	21.50 ±	10/0	10

	3.69			3.95		
Pitt	19.43 ± 6.62	20/3	23	18.95 ± 7.14	19/3	22
SBL	35.50 ± 4.86	10/0	10	35.00 ± 7.43	9/0	9
SDSU	13.83 ± 2.43	34/7	41	13.84 ± 2.98	31/6	37
Stanford_1	10.00 ± 1.59	12/4	16	10.00 ± 1.66	14/3	17
Stanford_2	11.06 ± 1.35	16/2	18	11.00 ± 1.27	16/1	17
Trinity_1	17.57 ± 3.68	23/0	23	17.05 ± 2.68	20/0	20
Trinity_2	16.44 ± 2.79	18/0	18	14.46 ± 3.67	13/0	13
UMIA	9.50 ± 1.69	6/2	8	10.20 ± 1.87	8/2	10
UCD	14.85 ± 1.68	10/3	13	14.94 ± 1.91	12/4	16
UCLA	12.19 ± 2.48	37/10	47	12.98 ± 2.44	45/4	49
UM	15.17 ± 3.60	44/15	59	13.59 ± 2.45	30/7	37
USM	22.65 ± 6.62	38/2	40	22.81 ± 8.18	43/0	43

Footnote: [1] The 23 cohorts collected from Autism Brain Image Data Exchange (ABIDE) were divided into 30 groups based on the number of timepoints and slice number and renamed as cohort name_1 or cohort name_2.

Table 2. FC results between the Broca area and the whole brain in the three frequency bands between ASD patients and HCs.

Brain regions (AAL)	BA	Number of voxels	Peak T value	MNI coordinate		
				x	y	z
Conventional frequency band (0.01-0.08Hz)						
(a)						
L THA		1151	4.9436	-3	-6	3
L PCUN		223				
(b)						
L ACG		233	4.6493	0	45	3
L ORBsupmed		51				
Slow5 frequency band (0.01-0.027Hz)						
(a)						
L ORBsupmed	10	173	4.9233	-3	54	-6
R ORBsupmed		49				
(b)						
R THA		1693	5.3234	15	-9	9
L PCUN		281				

Abbreviation: AAL, automatic labeling; BA, Brodmann Area; MNI, Montreal Neurological Institute Anatomical; L, left; R, right; THA, thalamus; PCUN, precuneus; ACG, anterior cingulate and paracingulate gyri; ORBsupmed, the medial orbital of the superior frontal gyrus. Labels under (a) and (b) are clusters with significant between-group difference. The first label under (a) and (b) denotes a brain region that was located at peak and the second label under (a) and (b) indicated submaximal brain region within the same cluster.

Figures

Figure 1

Functional connectivity (FC) results between the Broca area and the whole brain in the three frequency bands between autism spectrum disorder (ASD) patients and healthy controls (HCs).

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