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Research article

Brain functional connectivity alterations of Wernicke's area in individuals with autism spectrum conditions in multi-frequency bands: A mega-analysis

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ABSTRACT

Characterized by severe deficits in communication, most individuals with autism spectrum conditions (ASC) experience significant language dysfunctions, thereby impacting their overall quality of life. Wernicke's area, a classical and traditional brain region associated with language processing, plays a substantial role in the manifestation of language impairments. The current study carried out a mega-analysis to attain a comprehensive understanding of the neural mechanisms underpinning ASC, particularly in the context of language processing. The study employed the Autism Brain Image Data Exchange (ABIDE) dataset, which encompasses data from 443 typically developing (TD) individuals and 362 individuals with ASC. The objective was to detect abnormal functional connectivity (FC) between Wernicke's area and other language-related functional regions, and identify frequency-specific altered FC using Wernicke's area as the seed region in ASC. The findings revealed that increased FC in individuals with ASC has frequency-specific characteristics. Further, in the conventional frequency band (0.01–0.08 Hz), individuals with ASC exhibited increased FC between Wernicke's area and the right thalamus compared with TD individuals. In the slow-5 frequency band (0.01–0.027 Hz), increased FC values were observed in the left cerebellum Crus II and the right lenticular nucleus, pallidum. These results provide novel insights into the potential neural mechanisms underlying communication deficits in ASC from the perspective of language impairments.

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1. Introduction

Autism spectrum conditions (ASC)[2], also known as Autism spectrum disorders (ASD), are a series of heterogeneous neurodevelopmental conditions [1–3], and severely impact people's social communication and interaction [4–6], contributing to autism-specific language profiles [7] and language regression [8]. Recent neuroimaging studies attribute ASC's language deficiency to the damage to the brain language network which supports the idea that the communication dysfunction resulting from deviant neural activity of the language network will affect individuals with ASC's language ability greatly [5,9–11]. Hence, detecting atypical brain activity from the perspective of language is of great importance to the neural and pathophysiological studies of ASC. As one of the classical and essential language regions [12–14], Wernicke's area has been proven to be responsible for language comprehension [15] and involved in many language-related tasks, such as interactive verbal communication [16]. Taken together, the abnormalities in Wernicke's area may account for the aberrant language network in ASC and its underlying neural mechanisms should be further explored by advanced neuroimaging techniques.

As a promising non-invasive neuroimaging technology, resting-state functional magnetic resonance imaging (rs-fMRI), which has shed new light on the exploration of pathological patterns and neurophysiological significance of the brain [17,18], is widely employed in the detection of neural diseases, including ASC [19–21]. Among all the metrics in rs-fMRI, functional connectivity (FC) is one of the most commonly used analytical approaches with relatively high reliability [22–26]. It detects temporal correlations between distant brain regions that exhibit functionally related synchronization [23,27,28] and has been utilized to estimate the connectivity pattern of individuals with ASC [29,30]. However, prior studies focusing on the dysfunction of Wernicke's area in individuals with ASC generated inconsistent results. One found the loss of connectivity between Wernicke's area and Broca's area [31], while another research demonstrated the opposite results [32]. This inconsistency might contribute to the small sample size whose low statistical power undermines representativeness and reliability [33]. Therefore, large datasets should have been introduced to the neuroscience field to provide replicated results [33,34].

Collecting over 2000 participants from more than 30 sites, a well-formed public dataset named Autism Brain Image Data Exchange (ABIDE) has been established to detect neurophysiological patterns of ASC [9,35,36] and has the potential to demonstrate novel discovery and reproductive results [37,38]. Furthermore, calculations of data from the multicenter call for large-scale integration methods, such as mega-analysis, to reduce the heterogeneity that results from the scanning parameters or instruments utilized in various cohorts [39]. Mega-analysis, the pooled analysis of individual-level raw data obtained from multiple cohorts [39–43], could integrate a substantial amount of individual data into a single statistical analysis and reduce both false positive and false negative results [40]. With lower standard errors, high sensitivity in revealing significant but small effects, and high statistical power [39,40,42,44], mega-analysis has been widely used in neuroimaging studies to detect potential biomarkers that could be meaningful in guiding interventions in individuals with ASC [45,46]. Therefore, we performed a mega-analysis to examine the FC in ASC from the perspective of Wernicke's area based on the ABIDE database.

Moreover, in addition to conventional frequency bands (0.01–0.08 Hz), some experts have elaborated that sub-frequency bands (including slow-5: 0.01–0.027 Hz and slow-4: 0.027–0.073 Hz) correlate with different brain regions and could reveal different physiological functions and various neural processes [47–49]. Further, findings of sub-frequency bands could provide complementary neural information and an objective neural basis for the understanding of the pathophysiological mechanism [50–52]. For instance, FC in slow-5 was dominant in individuals with major depressive disorder [53], while FC in slow-4 was sensitive in stroke patients at risk of subclinical language deficits [54]. Since the property of frequency dependence has a significant influence on patients' neural functions, the way it affects language dysfunction in individuals with ASC should also be estimated.

Based on previous studies that we have illustrated above, we hypothesized that: (1) individuals with ASC would demonstrate abnormal FC between Wernicke's area and other language-related functional brain areas, compared with TD; and (2) those alterations in FC would exhibit frequency dependence.

2. Method

2.1. Participants

In the current study, image data from a widely used public dataset named ABIDE (http://fcon_1000.projects.nitrc.org/indi/abide/) were recruited. As a large-scale grassroots consortium aimed at data sharing with the broader scientific community [37], ABIDE collects functional and structural imaging data of ASC from laboratories worldwide. Namely, ABIDE I contains 17 sites with 1112 participants (539 individuals with ASC and 573 TD), while ABIDE II includes 19 sites with 1114 participants (521 individuals with ASC and 593 TD). Written informed consent was obtained from all participants. More detailed information, including the scan parameters and the ethics approval statements, can be found at https://fcon_1000.projects.nitrc.org/indi/abide/.

After checking the time points and the slice number of fMRI data, the present study combined ABIDE I and ABIDE II into 34 sites. Detailed descriptions can be found in the supplementary material (Table S1). Following the exclusion criteria presented below: (1) not right-handed participants; (2) maximal head movement exceeding 2 mm in x, y, or z translation or 2° in x, y, or z rotation [55]; (3) the

[2] In the current research, 'autism spectrum conditions (ASC)' are used as a synonym for 'autism spectrum disorders (ASD)' in DSM-5 because ASC are less stigmatizing and more respectful of neurodiversity. Further, ASC could express that individuals with the autism spectrum exhibit variations that encompass both strengths and difficulties, and this term has been widely used in prior researches [1–3].

effect of normalization was not good; (4) participants without either functional images or structural images; (5) cohorts without either individuals with ASC or typical developing (TD) individuals; (6) participants over 45 years old were excluded due to the limited number; (7) considering the high prevalence of ASC males [37,56,57] and a small sample size of females in the ABIDE database, it is hard to obtain a comparable group size of males and females, so only male participants were included in accordance with previous studies [37,45]; and (8) sites with less than 10 participants per group after the above exclusions were excluded [45,55]. There were altogether 362 ASC and 443 TD included in the final analysis. Detailed information about the exclusion criteria has been presented in the supplementary material (Table S2). Demographic information of all involved participants has been recorded in Table 1.

2.2. Data preprocessing

The rs-fMRI data underwent preprocessing using Resting-state fMRI Data Analysis Toolkit plus [58] (RESTplus V1.24, http://restfmri.net/forum/restplus) and Statistical Parametric Mapping software (SPM12, www.fil.ion.ucl.ac.uk/spm) on MATLAB2017b (MathWorks, Natick, MA, USA). The preprocessing steps contained: (1) removing the first ten time points to ensure magnetization stabilization; (2) slice time correction was used to minimize the time difference; (3) realignment for the correction of head motion within individual level [59,60]; (4) normalization in which the structural images were coregistered to the mean functional image, segmented with the New Segment algorithm, and performed in Montreal Neurological Institute (MNI) space; (5) a 6-mm full width at half maximum (FWHM) Gaussian kernel was used in smoothing [61,62]; (6) linear detrending was performed; (7) Friston 24 head motion parameters [63] were regressed out as nuisance signals to control the impact of head movement effects; and (8) three frequency bands, including conventional (0.01–0.08 Hz), slow-5 (0.01–0.027 Hz), and slow-4 (0.027–0.073 Hz) were conducted in filtering [47,51].

2.3. Functional connectivity analysis

The current research utilized RESTplus V1.24 [58] software to calculate FC that assesses correlations between Wernicke's area and all the other voxels of the brain. For FC analysis in the current study, a 6 mm-radius sphere [64–66], which was anchored at ($x = -53$, $y = -31$, $z = 9$) in MNI space, was chosen as the seed representing Wernicke's area according to a prior study [67]. Fig. 1 visualizes the location of Wernicke's area using BrainNet Viewer (V1.62, https://www.nitrc.org/projects/bnv/) [68]. We input the center coordinate of the selected seed into an fMRI dataset (http://beta.neurosynth.org) to ensure that 26 language-related studies also showed activation within approximately 6 mm of our seed. Using Pearson's correlation coefficients, the mean time course of the seed was extracted and correlated with all the other voxels of the whole brain in three frequency bands (conventional: 0.01–0.08 Hz; slow-5: 0.01–0.027 Hz; slow-4: 0.027–0.073 Hz). Moreover, to increase the normality, Fisher's z transformation was conducted based on the correlation coefficients.

2.4. Statistical Framework for mega-analysis

Mega-analysis, which is also acknowledged as the pooled analysis of raw data, can respond primarily to necessities such as the maximization of sample size [40]. By pooling individual data from all sites in one mega-analysis [39,69], this study integrated the data from ABIDE and conducted it in a single statistical analysis. That is, the zFC values of individuals with ASC across all sites were combined into one group and were considered as an 'ASC group', and so did the TD group. The group comparisons were conducted between ASC (n = 362) and TD (n = 443) using RESTplus. Meanwhile, age, mean frame-wise displacement (FD, an index for motion

Table 1
Demographic information of the included individuals with autism spectrum conditions (ASC) and typical developing (TD) individuals.

Center's name	ASC		TD	
	Age	Sample size	Age	Sample size
BNI	22.50 ± 5.97	12	29.30 ± 10.24	13
GU	10.86 ± 1.36	14	10.27 ± 1.65	15
KKI_2	10.14 ± 1.36	14	9.94 ± 1.24	54
Leuven	18.29 ± 5.44	21	19.41 ± 5.19	22
NYU	13.12 ± 6.96	50	13.88 ± 6.35	75
OHSU_1	10.92 ± 2.02	12	9.58 ± 0.95	12
OHSU_2	11.84 ± 2.20	25	10.33 ± 1.75	24
Pitt	20.29 ± 6.87	17	20.29 ± 6.86	17
SDSU	13.39 ± 2.83	28	13.50 ± 2.39	30
Stanford_1	9.27 ± 1.65	11	10.00 ± 1.55	10
Stanford_2	10.29 ± 1.22	14	10.69 ± 1.43	13
Trinity_1	16.79 ± 2.59	19	16.91 ± 3.60	23
Trinity_2	14.17 ± 3.39	12	15.71 ± 2.54	17
UCD	14.36 ± 1.82	11	14.70 ± 1.79	10
UCLA	12.31 ± 2.31	39	11.74 ± 2.22	35
UM	13.37 ± 2.30	27	18.03 ± 3.84	39
USM	22.53 ± 7.22	36	21.53 ± 6.21	34

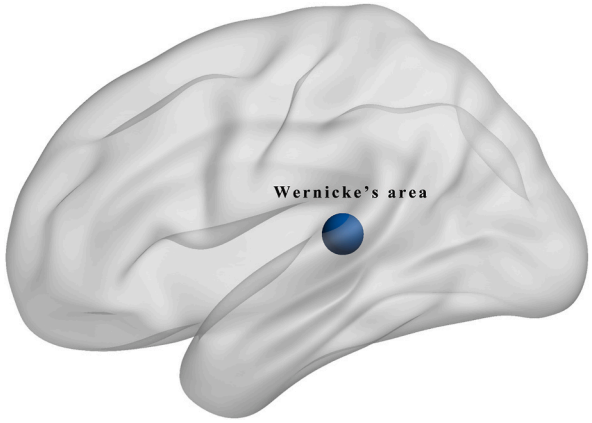

Fig. 1. The location of Wernicke's area.

correction) [70], and site effects were regressed in two-sample *t*-tests. Gaussian random field (GRF) correction with voxel-level $p < 0.001$ and cluster-level $p < 0.05$ was conducted using Data Processing & Analysis for Brain Imaging (DPABI_V5.1, http://rfmri.org/dpabi) [71] across all three frequency bands (conventional: 0.01–0.08 Hz; slow-5: 0.01–0.027 Hz; slow-4: 0.027–0.073 Hz).

2.5. Correlation analysis with symptom severity

Correlation analysis was performed to explore the relationship between altered FC and symptom severity of autism. Considering the inconsistent scale version and incomplete information of some participants, only 175 individuals of ASC with Autism Diagnostic Observation Schedule (ADOS, including social, communication, stereotyped behavior subscales, and total ADOS scores) were included in the correlation analyses. To be specific, FC values of brain regions demonstrating significant differences in 175 individuals with ASC were extracted and ADOS scores of these included individuals with ASC were collected. Further, we conducted Pearson correlations coefficient to examine the correlation between those FC values and ADOS scores.

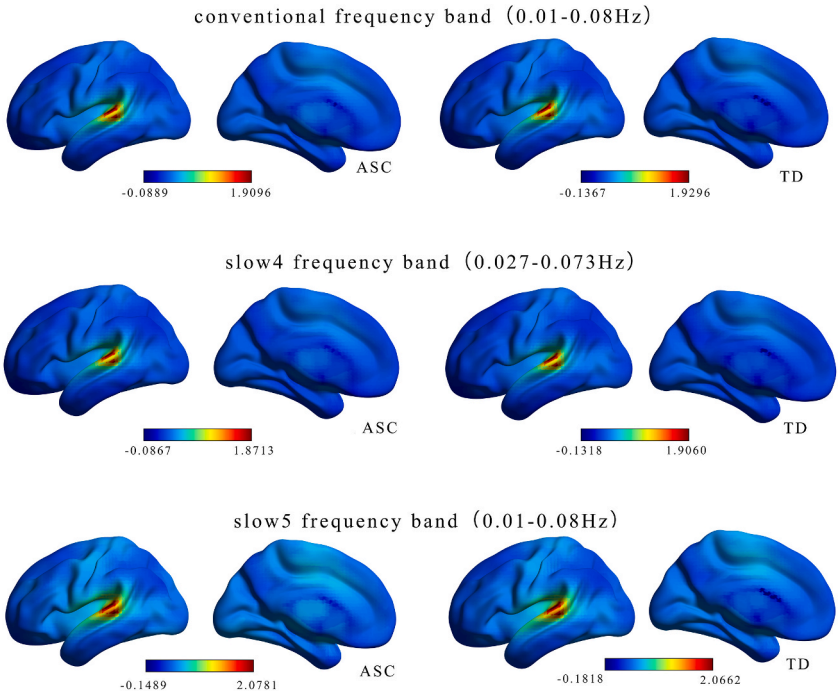

Fig. 2. Intragroup functional connectivity (FC) patterns of the language network in both ASC and TD groups across three frequency bands. The color bar indicates the mean zFC values. Warm colors indicate positive mean zFC values, suggesting positive FC between this region and Wernicke's area; while cool colors indicate negative mean zFC values, suggesting negative FC between this region and Wernicke's area.

3. Results

3.1. Demographic information

The demographic information presented in Table 1 provides detailed information about all included participants. In the current study, a total of 2168 participants from ABIDE were recruited. Among these participants, 131 individuals with ASC and 105 TD were discarded because they were not right-handed. Also, 231 ASC and 195 TD were excluded from further analyses on account of exceeding head motion (more than 2 mm in the x, y, or z translation or 2° in the x, y, or z rotation) [55]. Besides, 72 ASC and 74 TD participants' effects of normalization were not good and were deleted. Meanwhile, 17 ASC and 7 TD were not included due to the lack of functional or structural images. Further, 55 ASC participants were excluded because the sites (KUL and NYU_2) did not include the corresponding TD group. As for the limited number of those aged over 45, 15 ASC and 10 TD were excluded. Moreover, 66 female ASC and 184 female TD were excluded. In addition, 13 sites (83 ASC and 118 TD) were excluded because the number of participants per group after exclusion was less than 10. Based on what has been demonstrated above, 362 individuals with ASC and 443 TD were involved in the present research.

3.2. The mega-analysis of the functional connectivity results

To explore the intragroup FC patterns of the language network, mean FC maps of three frequency bands were established in the ASC and TD groups, separately (Fig. 2). From Fig. 2, a conclusion can be drawn that the language network across three frequency bands showed a little different in both ASC and TD groups. In the current study, these intragroup FC maps were merely for visualizing patterns of language networks in ASC and TD groups.

As for the mega-analysis of FC results, compared with TD, FC increased in the individuals with ASC between Wernicke's area and the right thalamus in the conventional frequency band (0.01–0.08 Hz), and between Wernicke's area and the left cerebellum Crus II and between Wernicke's area and right lenticular nucleus, pallidum in the slow-5 frequency band (0.01–0.027 Hz) (Fig. 3, Table 2).

3.3. Correlation analysis with symptom severity

No results with significant differences ($p < 0.05$) were found in the correlation analysis. The results of the correlation analysis can be found in supplemental material (Table S3).

4. Discussion

In the present study, compared with TD, patients with ASC showed higher FC between Wernicke's area and the right thalamus in the conventional frequency band (0.01–0.08 Hz). For the slow-5 frequency band (0.01–0.027 Hz), ascending FC was found between Wernicke's area and left cerebellum Crus II, and between Wernicke's area and right lenticular nucleus, pallidum. Moreover, no correlations were found between abnormal brain regions and ADOS scales.

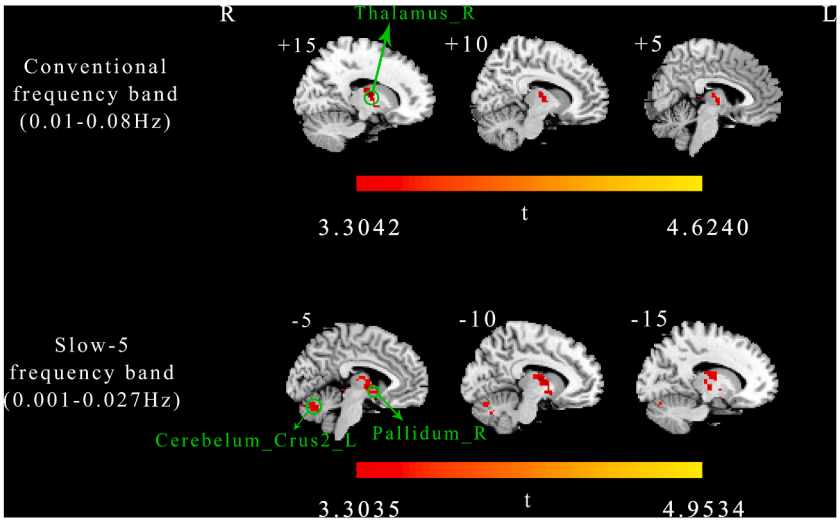

Fig. 3. Mega-analysis of voxel-wise FC results between Wernicke's area and the whole brain in multiple frequency bands between individuals with autism spectrum conditions (ASC) and typically developing (TD) individuals. The current study underwent Gaussian random field (GRF) correction with voxel-level $p < 0.001$ and cluster-level $p < 0.05$. A color bar was used to demonstrate t values of brain regions showing significant differences under GRF correction. Warm colors represent areas with significantly higher FC of brain regions in ASC compared with TD.

Table 2
Mega-analysis of the voxel-wise functional connectivity (FC) results between Wernicke's area and the whole brain in multiple frequency bands between individuals with ASC and TD.

Regions (AAL)	BA	Number of voxels	Peak *T* value	MNI coordinate		
				x	y	z
Conventional frequency band (0.01–0.08 Hz)						
Thalamus_R	–	116	4.624	0	−12	9
Slow-5 frequency band (0.01–0.027 Hz)						
Cerebelum_Crus2_L	–	60	4.0608	−3	−87	−27
Pallidum_R	–	416	4.9534	18	−3	−3

Abbreviations: AAL, anatomical automatic labeling; BA, Brodmann area; MNI, Montreal Neurological Institute; L, left; R, right. The study underwent Gaussian random field (GRF) correction (conventional: two-tailed, voxel-level $p < 0.001$ and cluster-level $p < 0.05$, and cluster size >56 voxels; slow-4: two-tailed, voxel-level $p < 0.001$ and cluster-level $p < 0.05$, and cluster size >51 voxels; slow-5: two-tailed, voxel-level $p < 0.001$ and cluster-level $p < 0.05$, and cluster size >54 voxels).

A variety of evidence reveals the leading contributions of the thalamus to language-related neuropsychological outcomes in individuals with ASC [71,72,73]. For example, researchers found thalamus activation in ASC during language frequency tasks [74], word generation [75], verbal memory [76], and language reading comprehension [73,77]. Therefore, abnormal activity of thalamus may affect ASC individuals' social interaction in daily life. Other research verified correlations between the thalamus and communication scales that might be responsible for the language deficits in ASC [78,79], which further prove the strong links between impaired thalamus and linguistic dysfunctions of social communication in ASC. Meanwhile, the current study presented increased FC in the right thalamus, which corresponds to a previous study focusing on language-related capacities [80]. Therefore, our results indicated that the hyper-connection between the thalamus and Wernicke's area might contribute to language impairments in individuals with ASC and might have relevance with autism symptoms, such as social communication and language regression. Taking previous studies centered on the abnormal activity of thalamus in ASC into consideration [81,82], the thalamus might be a potential biomarker for ASC diagnosis and clinical treatments.

Same as the thalamus, the cerebellum has also been demonstrated aberrant activation/alterations in language fluency tasks [74], language acquisition [78], and reading comprehension in individuals with ASC [79]. Other studies reveal the connection between ASC symptom severity and aberrant activity of the cerebellum [83]. Specifically, the left cerebellum Crus II was regarded as the core region that differentiated early language delay (ELD) and non-ELD ASC and TD children [78]. Similarly, the current research also detected the abnormal FC between the left cerebellum Crus II and Wernicke's area, which reflected the connection between these two spatial distinct brain regions. A possible conclusion could be drawn that cerebellum dysfunction may be responsible for language-related autism symptoms. Therefore, the cerebellum may be considered as a promising biomarker in future research concentrated on language development abilities and might provide new insights for interventions in ASC treatments.

Labeled as one of the subcortical brain regions of the basal ganglia (BG), the lenticular nucleus is composed of the pallidum and putamen [84]. Recently, connections between altered activity of BG (including the lenticular nucleus, pallidum) and language-related hallmarks have been confirmed in individuals with ASC [85]. To be specific, similar to those findings we mentioned in the thalamus and cerebellum, abnormal activity in BG led to communicative impairment [86], dysfunction in word task [87], and metaphor comprehension [76] in ASC. This might indicate that the abnormal activity of BG led to language regression, and further affected ASC individuals' social impairments. In accordance with previous studies listed above, our results detected increased FC between Wernicke's area and the right lenticular nucleus, pallidum. A plausible reason could be that these two linearly correlated brain regions shared a common language-related function and represented functional synergy in individuals with ASC. Therefore, our results may indicate the potential functions pallidum possessed in language development in ASC, which may serve as a promising biomarker in detecting neural patterns in ASC.

As diverse oscillatory waves of the human brain in different frequency bands are related to various neural processes [49] and cognitive functions [75], increased attention has been paid to slow-5 (0.01–0.027 Hz) and slow-4 (0.027–0.073 Hz) frequency bands. In addition to high test-retest reliability, potential significance of these two sub-frequency bands can be summarized as follows: (1) neural activity of gray matter was mainly detected in these two bands [47]; (2) different physiological functions and properties could be revealed by these two bands [53,58]; and (3) these two bands have been proved to be informative in clinical populations and reflect stable trait properties [47,88]. Therefore, to reveal neurophysiological and pathophysiological patterns of the brain from the perspective of frequency range, researchers have attached importance to the slow-5 (0.01–0,027 Hz) and slow-4 (0.027–0.073 Hz) which can provide sensitive and meaningful information in detecting various neural diseases [54,89,90], including ASC [91]. This echoed our results. To be specific, our findings demonstrated that the aberrant FC of Wernicke's area was mainly found in slow-5 rather than slow-4, indicating that slow-5 is more sensitive to detecting language-related brain regions in individuals with ASC. These findings may deepen our understanding of the language processing mechanism of ASC from the perspective of frequency-dependent characteristics and provide new insights into revealing neuropathological patterns of ASC from the perspective of language.

The current study failed to find correlation between brain regions with significant difference and ADOS scales, which may result from individual variability or the heterogeneity of ASC [92,93]. Besides, other factors, such as advanced parental age at offspring birth, parental education level may also impact the autism severity [94,95]. However, relative information was not available in ABIDE. Future studies should take those factors into consideration. Considering that the current research is centered on language dysfunction

in ASC, another possible reason could be that ADOS assesses the severity of ASC symptoms in a comprehensive way, rather than solely focusing on language. Other symptoms that are dominant in ASC might be related to higher scores [96]. Similar to our research, several prior studies also reported no significant correlations between FC values and the severity of ASC [97,98]. Although no significant correlations were detected in the current study, we still have reasons to assume that those abnormal connectivity between Wernicke's area and thalamus and between Wernicke's area and cerebellum and between Wernicke's area and pallidum are closely related to ASC, considering the significant roles those brain regions played in language impairments in ASC [73,78,99,100].

5. Conclusions

The current study conducted a mega-analysis to analyze frequency-specific characteristics of altered FC that targeted Wernicke's area as the seed in individuals with ASC. Specifically, abnormal FC has been found between Wernicke's area and regions with language-related functions, such as the thalamus, left cerebellum Crus II, and right lenticular nucleus, pallidum in ASC. Meanwhile, the slow-5 frequency band (0.01–0.27 Hz) was more sensitive than the slow-4 frequency band (0.027–0.073 Hz) and provided more information than the conventional frequency band (0.01–0.08 Hz).

Thus, our results suggested that the dominance of certain frequency bands might reveal specific physiological patterns and pathological mechanisms of language dysfunctions in ASC. Moreover, brain regions demonstrated in the current study (including the thalamus, cerebellum Crus II, and lenticular nucleus, pallidum) might be useful biomarkers in identifying ASC and contribute to investigating language development in ASC. Further, the current results might be helpful in ASC diagnosis. In addition, the essential mechanistic understandings might hold promise for aiding in the advancement of therapeutic avenues for clinical treatments in ASC.

6. Limitations

Some limitations should be taken into account. First, to maximize the sample size, we only excluded those whose head motion exceeding 2 mm and 2°. Second, to improve statistical power, we only involved male participants. However, considering that the female-specific effects in ASC differ from that of male, further studies should utilize a comparable group size of males and females to provide additional insights into the understanding of autism pathophysiology. Third, no significant correlation was found between FC values and ADOS scales. The possible reason could be contributed to individual variability, the heterogeneity of ASC, other factors (e.g., parental education level) that could impact ASC and the focus of the clinical scales. Future studies should take these factors into consideration and make a more comprehensive study. Last but not least, in order to generate common functional abnormalities across various sites rather than site-specific effects, we regressed site effects as a covariate [69]. And the Bayesian ComBat model [101], a promising approach that could be used to harmonize MRI data across sites [102–104], has not been applied in the current study. Future research should take this model into serious consideration and use this model to reduce site effects and to obtain more reliable results.

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Ethical approval

All participants (or their proxies/legal guardians) provided informed consent to participate in the study. All procedures conducted in research involving human participants 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 can be obtained at http://fcon_1000.projects.nitrc.org/indi/abide/.

Data availability statement

The data used in this study was obtained from the Autism Brain Imaging Data Exchange (ABIDE) (http://fcon_1000.projects.nitrc.org/indi/abide/) public database, where researchers who are interested in autism spectrum conditions could download the relative functional and structural images freely. Also, data will be made available on request.

CRediT authorship contribution statement

Linlin Zhan: Writing – original draft. **Yanyan Gao:** Writing – review & editing. **Lina Huang:** Validation. **Hongqiang Zhang:** Supervision. **Guofeng Huang:** Data curation. **Yadan Wang:** Formal analysis. **Jiawei Sun:** Software. **Zhou Xie:** Software. **Mengting Li:** Investigation. **Xize Jia:** Supervision, Software, Methodology, Conceptualization. **Lulu Cheng:** Conceptualization. **Yang Yu:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e26198.

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