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ORIGINAL PAPER

Facial emotion recognition function and white matter microstructural alterations in drug-naive, comorbidity-free autism

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Abstract

Individuals with autism spectrum disorder have deficits in facial emotion recognition and white matter microstructural alterations. Nonetheless, most previous studies were confounded by different variables, such as psychiatric comorbidities and psychotropic medications used by ASD participants. Also, it remains unclear how exactly FER deficits are related to white matter microstructural alterations in ASD. Accordingly, we aimed to investigate the FER functions, white matter microstructure, and their relationship in drug-naive and comorbidity-free ASD individuals. 59 ASD individuals and 59 typically developed individuals were included, where 46 ASD and 50 TD individuals completed FER tasks. Covariance analysis showed scores were lower in both basic and complex FER tasks in the ASD group. Tract-Based Spatial Statistics showed FA values in widespread white matter fibers were lower in the ASD group than in the TD group, including forceps major and forceps minor of the corpus callosum, anterior thalamic radiation, corticospinal tract, cingulum, inferior frontal-occipital fasciculus, inferior longitudinal fasciculus, superior longitudinal fasciculus. Moreover, in the TD group but not the ASD group, the performance in the complex FER task was negatively correlated with the FA value in some white matter fibers, including forceps major of the corpus callosum, ATR, CT, cingulum, IFOF, ILF, SLF. Our study suggests children with ASD may experience deficits in facial emotion recognition and exhibit alterations in white matter microstructure. More importantly, our study indicates that white matter microstructural alterations may be involved in FER deficits in children with ASD.

Keywords Autism spectrum disorder · Facial emotion recognition · White matter microstructure · Tract-based spatial statistics

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Abbreviations

ASD	Autism spectrum disorder
CC	Corpus callosum
CR	Corona radiate
DTI	Diffusion tensor imaging
FER	Facial emotion recognition
TBSS	Tract-based spatial statistics
FA	Fractional anisotropy
fMRI	Functional magnetic resonance imaging
IFOF	Inferior frontal-occipital fasciculus
ILF	Inferior longitudinal fasciculus
MRI	Magnetic resonance imaging
SLF	Superior longitudinal fasciculus
TBSS	Tract-based spatial statistics
TD	Typically developed
ts-FMRI	Task-state functional magnetic resonance imaging

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Background

Background Autism Spectrum Disorder is a neurodevelopmental disorder that occurs in the early developmental period. It is characterized by impairments in social communication and interaction, limited interests, and repetitive behaviors [1]. The prevalence of ASD has been steadily increasing globally [2]; however, its etiology and pathogenesis remain unclear. Facial emotion recognition (FER) refers to a person's perception of a particular emotional state through the interpretation of facial features [3]. Previous studies demonstrated that ASD individuals have deficits in FER [4], impairing social interaction, social adaption, and social function [5, 6]. Yet, the features of FER function and underlying mechanisms remain unclear, so investigation of them is of significant importance for finding more effective therapies for ASD.

Facial emotions in people can be categorized as basic or complex emotions, which differ in their characteristics. Basic emotions, such as happiness, sadness, fear, anger, surprise, and disgust [7], are cross-culturally expressed and recognized [8]. On the other hand, complex emotions like depression, pride, jealousy, and flirting [9, 10] are more culture and context-dependent [11]. Additionally, complex FER is associated with other cognitive functions [9]. Therefore, when studying the functions and mechanisms of FER in individuals with ASD, it is important to distinguish between basic and complex emotions.

Previous studies on FER function in individuals with ASD have primarily focused on basic FER, with limited attention given to complex FER. These studies have yielded incongruent results, with some demonstrating deficits in both basic [12–14] and complex [15–17] FER in children and adults with ASD, while others have found no difficulties with recognizing basic [18–20] and complex [18, 21] facial emotions. Possible reasons for the inconsistent findings may be due to the varying task paradigms and study populations used. For instance, many studies include participants with comorbidities, such as Attention-Deficit/Hyperactivity Disorder (ADHD), which can confound results as it is known to be associated with FER deficits [22–24]. However, previous studies did not always exclude individuals with comorbidities, making it difficult to determine whether FER function is impacted by ASD or other psychiatric disorders. Therefore, further exploration is needed to better understand FER function in individuals with ASD who do not have other medical conditions, taking into account potential confounds and inconsistent results.

The mechanism of FER deficit in individuals with ASD is still unclear. The FER deficits may be similar to other cognitive symptoms, which are related to changes in microstructures of white matter [25]. White matter is the structural basis for connections between neural networks [26], and its histopathology can be investigated by Diffusion tensor imaging technique [27]. DTI is a magnetic resonance imaging technique based on quantification of the random Brownian motion of water molecules that allows for evaluation of the spatial organization of tissues with specific orientations [28, 29]. Fractional anisotropy, which is the normalized variance of diffusion along the three orthogonal axes, is most widely used [30] in DTI studies and has been considered an indicator of white matter integrity [31, 32]. Many previous studies have found that ASD individuals of all ages present altered FA in extensive white matter fibers [33] (i.e.,: corpus callosum, corona radiata, superior longitudinal fasciculus, inferior longitudinal fasciculus, inferior frontal-occipital fasciculus and uncinate fasciculus [34–36]. Two studies have investigated the relationship between FER deficits and white matter microstructural alterations in ASD individuals. One study found no correlation between white matter changes and FER ability in children with ASD [37]. On the other hand, the other study found that FER was associated with the white matter structure of the ventral occipital complex region, superior temporal/parietal association areas, and forceps major of the CC in the ASD adults [38]. However, some participants in these two studies have comorbidities or were taking psychotropic drugs, which could have affected their white matter microstructure [35, 39–42] and influenced the results. Furthermore, the FER tasks utilized in both studies were limited to basic facial expressions. As a result, it is crucial to conduct further research on the relationship between white matter microstructure and basic and complex FER abilities in medication-naïve and comorbidity-free ASD individuals.

The aim of the present study was to explore the FER function, the white matter microstructure, and the relationship between FER deficits and white matter microstructure alterations in medication-naive and comorbidity-free ASD participants. We recruited ASD and TD children and adopted FER task consists both basic and complex emotions. As an exploratory study, tract-based spatial statistics were utilized to compare the white matter microstructure between these two groups. This analysis can examine main white matter fiber tracts simultaneously and produce more rigorous results [43]. To reduce the influence of confounding factors, two groups were age- and IQ (Intelligence Quotient)-matched, and ASD children were medication-naïve and comorbidity-free. Our predictions were that the ASD group would perform worse on FER measures, have decreased FA values of white matter, and show atypical correlation between FER measures and FA values compared to the TD group.

Methods

Participants

Through the outpatient clinic at Peking University Sixth Hospital, a group of 62 ASD individuals between the ages of 6 and 18 were enrolled in the study. Two experienced child and adolescent psychiatrists diagnosed them using the DSM-V [1]. Additionally, 59 TD participants between the ages of 6 and 18 were recruited through advertising. All participants were of Han ethnicity, right-handed, and had an IQ score greater than 70 as measured by either the Chinese-Wechsler Intelligence Scale for Children [44] or the Wechsler Adult Intelligence Scale-Revised in China [45]. Individuals with major physical or neurological diseases, current or previous psychiatric diagnoses (other than the autistic disorder in the ASD group), and those who take psychotropic medication were excluded from both groups through the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version [46].

Given that motion introduces artifacts in DTI metrics, participants with excessive head movement (head motion index was the mean absolute intervolume displacement with respect to the first image of each run; root-mean-square deviation was calculated using FSL (the FMRIB Software Library) rmsdiff) were also excluded. We only included data with a mean absolute RMS > 2 mm and passing visual inspection. Four individuals, three with ASD and one TD individual, were excluded due to excessive head movement or poor data quality. We ultimately included 59 children with ASD and 59 TD individuals with reliable MRI data. Among them, 13 ASD and nine TD participants were unable to complete the FER task due to lack of time. As a result, 46 ASD and 50 TD participants completed the FER task. Demographic data did not significantly differ between those who completed the FER task and those who did not (Additional file 1).

The procedure was approved by the Ethics Committee of Peking University Sixth Hospital. For participants < 8 years old, written informed consent was obtained from their parents/legal guardians; for participants > 8 years old, written informed consent was obtained from both participants and their parents/legal guardians.

FER task

This task was the full facial version of "reading the mind with the eyes," created by Simon Baron-Cohen [47]. It consisted of 20 photographs displaying various emotions–10 basic and 10 complex. Each photograph had two words below it describing the emotion, with one being correct and the other a foil. For example, a photo of a happy expression might have the words “happy” and “surprise” beneath it. In another instance, a photo of a guilty expression might have the words "arrogant" and "guilt" below it.

Participants completed the FER task on the day of their MRI scanning. During the task, they were seated comfortably in a chair in front of a desk, and were presented with photographs on the desk. They were asked to focus their attention on the photograph, and then select the word which is more suitable for the emotion in the photograph from two words below. Ten basic emotion photographs and 10 complex emotion photographs were presented in sequence, the number of correct answers for basic emotion and complex emotion were being recorded as scores of these two categories (0–10).

MRI acquisition

MRI scans were acquired on a GE-Discovery 750 3.0 T scanner with an eight-channel head coil at the Peking University Sixth Hospital, using a diffusion-weighted echoplanar imaging sequence [repetition time = 8090 ms, echo time = 92 ms, field of view = 240 × 240 mm, flip angle = 90°, voxel size = 2 × 2 × 2 mm, 64 noncollinear diffusion directions, uniformly distributed around a unit sphere with b value of 1000 s/mm2, 8 images with no diffusion weighting]. During scanning, subjects were required to keep their head as still as possible.

Preprocessing

Functional Magnetic Resonance Imaging of the Brain Software Library(http://www.fmrib.ox.ac.uk) was used to conduct analyses [48]. Quality assurance involved eddy current and motion corrections, as well as the removal of nonbrain tissue. Our head motion index was the mean absolute intervolume displacement with respect to the first image of each run; root-mean-square (RMS) deviation was calculated using FSL (the FMRIB Software Library) rmsdiff.

Tract-based spatial statistics

First, nonlinear registration to a common space was conducted by aligning each participant’s FA image to the Montreal Neurologic Institute 152 space template, after which a mean FA image and a mean FA skeleton of the aligned images were created. Voxelwise analyses were subsequently conducted for skeleton areas with an FA of at least 0.2. To examine the main influence of diagnosis on DTI metrics, a general linear model was performed using FSL Randomize. Age, sex, IQ, and head motion were included as nuisance covariates. Statistical significance was set at threshold-free

cluster enhancement $P < 0.05$ to control for familywise error (FWE) rate ($\alpha = 0.05$). The JHU White-Matter Tractography Atlas was utilized to display the location and composition of each cluster with significant differences in FA values between groups. Subsequently, the FA values of these clusters were extracted for further analysis.

Statistical analysis

Shapiro Wilk test was used to test the normality of continuous variables. In case of normal distribution, the results were presented as (mean ± standard deviation), and the t-test was used for comparisons among groups. When dealing with non-normal distribution variables, the data was presented as median (minimum, maximum), and group comparisons were performed using the Wilcoxon test. Categorical variables were reported by proportions, and the Chi-square test was used for comparison. In order to compare the differences in basic and complex FER between the ASD group and the TD group while minimizing the influence of age, sex, and IQ, analysis of covariance (ANCOVA) was performed with these factors as covariates. A comparison of FA values of white matter was conducted using TBSS between the ASD group and the TD group (see Tract-Based Spatial Statistics part for more details), resulting in the identification of some white matter clusters that have significantly different FA values between the two groups. Partial correlation analysis, which can control for confounding variables and assess the relationship between the two main variables more accurately, were performed to explore the relationship between the FA values and the scores of FER tasks. In the partial analysis, the FA values were averaged from the significant clusters and used for the correlation with the scores of both basic and complex FER tasks, while adjusting for sex, age, IQ, and head motion. To investigate whether there was difference in partial correlation between the ASD group and the TD group, we applied the Fisher's exact test to compare the between-group difference of the coefficient. SPSS 20.0 was used for data analysis, and the significance level was defined as $P < 0.05$; the R package was used for FDR correction of the results.

Results

Demographic data

The two groups had no significant differences in age, full scale IQ (FSIQ), verbal IQ and head motion. In the subgroup with available FER data, the ASD group had a lower FSIQ than the TD group, while age and head motion were not significantly different. The TD group had more female participants in both the full group and subgroup with FER data, as shown in Table 1. Demographic data did not differ significantly between subjects with and without FER data. (Additional File 1).

The facial emotion recognition task

We conducted ANCOVA to compare the ability to recognize basic and complex emotions between individuals with ASD and TD individuals. The results showed that individuals with ASD had lower scores on both basic (ASD group mean score: 7.72 ± 1.515, TD group mean score: 8.74 ± 1.121) and complex emotion recognition (ASD group mean score: 6.41 ± 1.240, TD group mean score: 7.40 ± 1.107) compared to TD individuals. This difference cannot be attributed to age, sex, or IQ, as shown in Table 2.

Measures of water diffusion along white matter fibers

Results from the randomization and TFCE methods revealed that the ASD group had significantly lower FA values than the TD group in 4 clusters, including extensive white matter (see Fig. 1 and Table 3; four clusters are shown respectively in Additional File 2). Furthermore, to verify the result in

Table 1 Participant demographics

Variables	DTI				FER			
	ASD(59)	TD(59)	t/F	*P*-value	ASD(46)	TD(50)	t/F	*P*-value
AGE	12.38 ± 2.99	13.10 ± 2.49	–1.423(2, 116)	0.158	13.00 ± 2.86	12.94 ± 2.53	0.109 (2, 94)	0.913
Gender(M/F)	54/5	37/22	13.880(1)	0.000	43/3	31/19	13.439 (1)	0.000
FSIQ	105.59 ± 21.877	112.17 ± 15.781	-1.873(2, 116)	0.326	102.98 ± 21.328	112.18 ± 16.480	-2.376 (2, 94)	0.020
V-IQ	107.98 ± 23.536	113.34 ± 21.117	-1.3012, 116)	0.196	105.39 ± 23.714	114.34 ± 22.222	-1.909 (2, 94)	0.059
RMD	0.21(0.10, 1.69))	0.23(0.06, 0.90))	0.987(2, 116)	0.326	0.21(0.10, 1.69))	0.23(0.06, 0.90))	0.906 (2, 94)	0.380

ASD autism spectrum disorder; *TD* typically developing; *DTI* children who have dti data; *FER* children who have facial emotion recognition data; *FSIQ* full-scale intelligence quotient; *V-IQ* verbal intelligence quotient; *RMD* relative motion displacement.

Table 2 ANCOVA results of basic and complex FER tasks between ASD and TD

	F	*p*	η2/partialη2
Basic FER			
Group	6.47 (1, 91)	0.013	0.066
Group*age	1.02 (1, 91)	0.317	0.011
Group*gender	1.16 (1, 91)	0.284	0.013
group*IQ	3.49 (1, 91)	0.065	0.038
Complex FER			
Group	8.50 (1, 91)	0.004	0.085
Group*age	0.21 (1, 91)	0.647	0.002
Group*gender	0.39 (1, 91)	0.537	0.004
Group*IQ	2.17 (1, 91)	0.144	0.024

the subgroup with FER data, the FA values of the 4 clusters were extracted and ANCOVA was used to compare the FA values between the ASD subgroup and the TD subgroup, adjusting for age, sex, IQ and head motion. The results were consistent with those of the full group (see Table 4). In addition, we repeated the ANCOVA for all male participants in the subgroup with FER data, adjusting for age, IQ and head movement, and found consistent results (see Additional File 3).

Associations between white matter and FER measures

We used partial correlation analysis to investigate the connection between mean FA values of significant clusters identified in the previous step and FER scores in the subgroup with FER data. We found that complex FER scores were negatively correlated with mean FA values in cluster 3 (Anterior thalamic radiation (ATR) (L); Corticospinal tract (L); forceps major of the CC; IFOF (L); ILF (L); SLF (L); SLF (temporal part) (L)) and cluster 4 (ATR (R); Corticospinal tract (R); Cingulum (cingulate gyrus) (R); Cingulum (hippocampus) (R); Forceps major of the CC; IFOF (R); ILF (R); SLF (R); SLF (temporal part) (R)) after FDR correction in the TD group but not in the

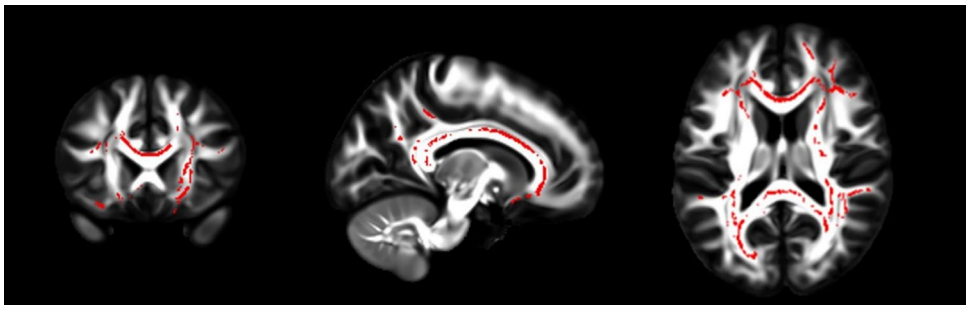

Fig. 1 Brain white matter structural differences on TBSS analysis between the ASD and the TD group. Adjusted for sex, age, FSIQ, and head motion, the map revealed that the ASD group had lower FA than the TD group. The red color indicates lower FA values of the white matter fibers, including Corpus callosum; Cingulum; Anterior thalamic radiation; Corticospinal tract; Forceps major; Inferior frontal-occipital fasciculus; Inferior longitudinal fasciculus; Superior longitudinal fasciculus; Superior longitudinal fasciculus (temporal part), in the ASD group

Table 3 Clusters whose tracts showed lower FA in the ASD group compared to the TD group

Cluster index	White matter tracts	voxels	MNI coordinate of the peak voxel (x, y, z)	*p*-value
1	The forceps major of the corpus callosum	89	(–1, –37, 16)	0.042
2	Cingulum (cingulate gyrus) (L); forceps minor of the corpus callosum	440	(10, 23, 17)	0.040
3	Anterior thalamic radiation (L); corticospinal tract (L); forceps major; Inferior frontal-occipital fasciculus (L); Inferior longitudinal fasciculus (L); Superior longitudinal fasciculus (L); Superior longitudinal fasciculus (temporal part) (L);	672	(–26, –27, 24)	0.040
4	Anterior thalamic radiation (R); Corticospinal tract (R); Cingulum (cingulate gyrus) (R); Cingulum (hippocampus) (R); Forceps major; Inferior frontal-occipital fasciculus (R); Inferior longitudinal fasciculus (R); Superior longitudinal fasciculus (R); Superior longitudinal fasciculus (temporal part) (R)	717	(31, -48, 16)	0.033

Table 4 Group differences of the mean FA in 4 clusters in subgroup with FER data

index	ASD(n = 46)	Control (n = 50)	F	*P*-value	η2	pfdr
Cluster1	0.8378 ± 0.033	0.8648 ± 0.031	13.904 (1, 90)	0.000	0.134	0.002
Cluster2	0.7179 ± 0.033	0.7456 ± 0.027	12.450 (1, 90)	0.001	0.122	0.002
Cluster3	0.5343 ± 0.032	0.5572 ± 0.027	10.657 (1, 90)	0.002	0.106	0.002
Cluster4	0.5137 ± 0.030	0.5348 ± 0.027	10.090 (1, 90)	0.002	0.101	0.002

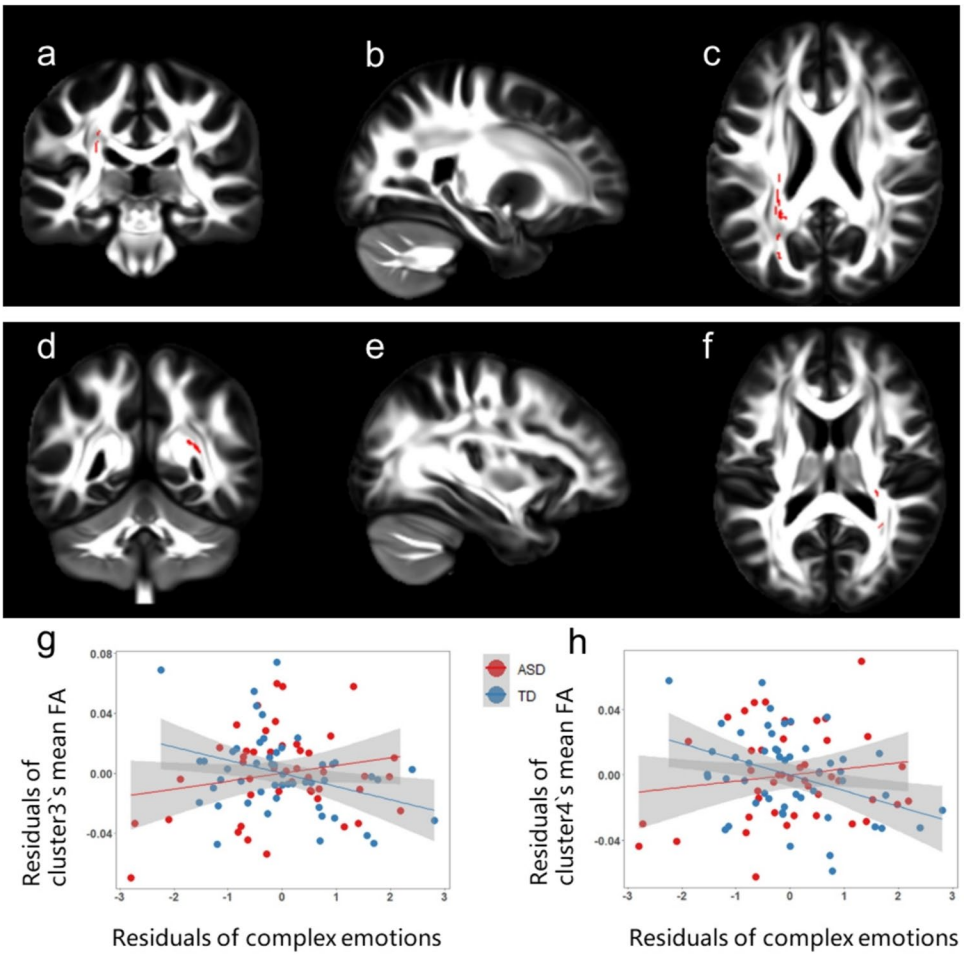

Fig. 2 Partial correlation of FA values and complex FER scores. **a–c** The red color indicates voxels of cluster 3 from the coronal, sagittal, and horizontal planes. The ASD group had lower FA values in the voxels of cluster 3, which included the Anterior thalamic radiation (L); Corticospinal tract (L); Forceps major; Inferior frontal-occipital fasciculus (L); Inferior longitudinal fasciculus L; Superior longitudinal fasciculus (L); Superior longitudinal fasciculus (temporal part) (L), compared to the TD group. Similarly, **d–e** The red color indicates voxels of cluster 4 from the coronal, sagittal, and horizontal planes. The ASD group had lower FA values in the voxels of cluster 4, which included the Anterior thalamic radiation (R); Corticospinal tract (R); Cingulum (cingulate gyrus) (R); Cingulum (hippocampus) (R); Forceps major; Inferior frontal-occipital fasciculus (R); Inferior longitudinal fasciculus (R); Superior longitudinal fasciculus (R); Superior longitudinal fasciculus (temporal part) (R), compared to the TD group. **g** The scatter plot shows the residuals of the mean FA of cluster 3 on the vertical axis and the residuals of the FER score on the horizontal axis. **h** The scatter plot shows the residuals of the mean FA of cluster 4 on the vertical axis and the residuals of the FER score on the horizontal axis

ASD group (Fig. 2, Table 5). However, we did not observe a significant correlation between basic FER scores and FA values in either group, as shown in Table 5. Furthermore, We repeated the partial correlation analysis for male participants in this subgroup adjusting for sex, IQ, and head motion, and found a similar pattern (Additional File 4). Additionally, Fisher's exact test was used for further examination of the difference of the correlation coefficient between ASD and TD group, significant differences were found in the correlation coefficients of FA values

Table 5 The partial correlation of FA value and FER scores in ASD and TD

	Cluster1			Cluster2			Cluster3			Cluster4		
	r	*p*	pfdr	r	*p*	pfdr	R	*p*	pfdr	r	*p*	pfdr
Basic(ASD)	-0.147	0.354	0.906	-0.238	0.129	0.845	-0.032	0.84	0.958	0.055	0.731	0.952
Complex(ASD)	0.024	0.880	0.960	0.058	0.716	0.951	0.202	0.199	0.845	0.151	0.341	0.903
Basic(TD)	0.124	0.411	0.430	-0.009	0.955	0.637	0.02	0.896	0.622	0.171	0.256	0.350
Complex(TD)	-0.104	0.492	0.475	-0.128	0.396	0.424	-0.347	0.018	0.046	-0.382	0.009	0.046

ASD autism spectrum disorder; *TD* typically developing.

Table 6 Fisher's exact test to compare the between-group differences in partial correlation

	basic	Fisher's exact test	*p*-Values	complex	Fisher's exact test	*p*-Values
Cluster1(ASD)	–0.147	–0.998	0.322	0.024	0.736	0.466
Cluster1(TD)	0.124			–0.104		
Cluster2(ASD)	–0.238	–0.181	0.858	0.058	0.936	0.352
Cluster2(TD)	–0.009			-0.009		
Cluster3(ASD)	–0.032	–0.168	0.872	0.202	2.674	0.008
Cluster3(TD)	0.020			–0.347		
Cluster4(ASD)	0.055	–1.120	0.262	0.151	2.896	0.004
Cluster4(TD)	0.171			–0.382		

ASD autism spectrum disorder; *TD* typically developing.

and complex FER scores, both in cluster 3 and cluster 4 (Table 6).

Discussion

Our study aimed to investigate the differences in basic and complex FER function between individuals with ASD and TD individuals. Additionally, we explored the variations in white matter microstructure and the correlation between FER function and white matter microstructure in these two groups. Our findings revealed that children with ASD exhibited impairments in both basic and complex FER and showed changes in white matter microstructure compared to the TD group. In addition, our findings indicate that there is a connection between FER performance and the microstructure of white matter in TD group. However, no such relationship was observed in the ASD group. These results suggest that alterations of white matter microstructure may involve in FER deficits in ASD children.

As predicted, ASD children had lower scores in basic and complex FER tasks, indicating that they have basic and complex FER deficits. This finding is in line with the majority of previous studies [12, 49], including a recent meta-analysis [50]. However, this finding is inconsistent with some studies, which have reported that ASD children do not have problems with basic FER [18]. This inconsistency could be attributed to variations in task paradigms and participants, further research is needed to clarify these variations. In our study, we found that children with ASD who have not taken psychotropic medication and do not have other conditions still show deficits in both basic and complex facial emotion recognition, indicates the deficits may be the common characteristic of ASD individuals. Although our study showed ASD individuals have FER deficits, it can not demonstrate whether these deficits are the mechanism or the results of ASD symptoms. More rigorously designed studies are needed to clarify the causality.

Secondly, we found lower FA of white matter in the ASD group, suggesting extensive white matter microstructural alterations in ASD children, including the ATR, corticospinal tract, forceps major, cingulum, IFOF, ILF, SLF. These results are consistent with previous studies. E.g. in their study, Aoki et al. [35] found lower FA in CC, Fitzgerald et al.[36] found lower FA in CC, corona radiata, and SLF. In this study, we addressed the confounding factors affecting white matter microstructure [35, 39–42] by excluding participants with comorbidities and the use of psychotropic medication, and we also controlled for participants' head movements [51], which can affect the accuracy of the data. In the end, our findings indicate that medication-naïve and comorbidity-free ASD children have widespread alterations in white matter microstructure, contributing to understanding more clarity on changes in white matter microstructure in ASD. However, our study could not prove whether white matter microstructure alteration causes or is a consequence of ASD, requiring further investigations.

Based on the findings above, we delved deeper into the correlation between the microstructure of white matter, which differs significantly between individuals with ASD and TD individuals, and FER functions. The study revealed that among the TD group, the FA values of various regions such as the SLF, ILF, and IFOF were correlated to complex FER scores. These findings align with previous studies showed that these white matter fibers connect grey matter regions responsible for face processing, and are regions involved in face processing [52, 53]. It is worth noting that the FA values of these regions are negatively correlated with complex FER scores, which means lower FA values in these regions are correlated with better FER function, which is unexpected as higher FA values usually indicate higher myelinization levels and better cognitive function[54]. Nevertheless, our findings are consistent with some other studies that suggest lower FA values can predict better cognition[55, 56]. The correlation between cognitive function and FA values is complex and heterogeneous. This may be due to the sensitivity of FA to white matter structure, but its lack of specificity. Both lower FA values[57, 58] and higher FA can be necessary for optimal cognitive function[54, 59], and thus FA values can be both positively and negatively correlated with cognitive functions. In our study, we found regions where FA values are negatively associated with FER function. This highlights the importance of white matter in cognition among TD individuals. Similarly, causality and underlying mechanisms need further investigation.

Another noteworthy point is that, unlike the TD group, our study did not find a significant relationship between the FA value and the FER function in the ASD group. Further, similar results were found in subgroup analysis in males, which indicates this pattern can not be interpreted by the gender difference between these two groups. Similar phenomenon has also been reported in schizophrenia, one study has found that better general cognitive ability was correlated with lower FA in some white matter fibers in healthy subjects, but not in schizophrenia patients[55]. The lack of association suggests the white matter fibers involved in FER function in TD children may not subserve the FER function in the ASD group [52, 53]. Given that white matter connectivity may be related to functional organization[60], and that microstructural alterations exist in these fibers in ASD, we speculate that white matter microstructural alterations may be involved in complex FER deficits in children with ASD. However, this does not necessarily imply a causal relationship, that is, our results cannot determine whether the white matter microstructure alterations observed in the ASD group reflect the primary pathophysiology of or the consequence of the FER deficits. In addition, ASD is characterized by multifaceted conditions, involving genes, metabolism and even peripheral systems [61–64], our study can not determine whether there is a third factor mediating changes in these two variables too. Therefore, further studies are needed to fully understand the mechanism that links the white matter microstructure alterations and the FER deficits.

Finally, we found that the scores of basic FER were not correlated with the FA of white matter fibers in either group. This is consistent with Li et al.' study, they found no relationship between white matter microstructure and basic FER function in both ASD and TD children when adjusting for IQ and age [37]. Nonetheless, Yasuno et al. found that basic FER function in ASD adults was correlated with white matter microstructures in some regions (ventral occipital complex region, superior temporal/parietal association areas, and forceps major of the corpus callosum) [38]. These differing results may relate to different ages of subjects and the different FER paradigms used in these studies. In their study, Yasuno et al. asked subjects to identify emotional expressions from faces in pictures moving behind a narrow vertical and horizontal slit and all subjects were adults, while in our and Li's study, the subjects only needed to identify the facial emotions of the whole static face and they were children. Also, the former study concentrated more on mechanisms of long-range synchronization function across hemispheres instead of the FER function.

There are some strengths and limitations to this study. In this study, we tightly controlled head movements. Further, we excluded confounding of the comorbidity and the medicine. However, the exclusion of comorbidities and medicines, perhaps, reduces the ecological validity of the study. Further studies with larger sample sizes that include categories of comorbid disorders are needed to test whether these results can be generalized more broadly. In addition, these results need to be carefully considered for the following potential confounding factors remain in our study. First, sex ratio differed between the ASD and TD groups. While previous studies have shown no difference in FER task performance between genders[16], differences in white matter microstructure may exist in individuals of different sexes[65, 66]. Although gender was considered a covariate during analysis and the same analysis was performed in the subgroup of males, however, white matter microstructure may be different in individuals of different sex, it is necessary to match the sex ratio in future studies. Second, the study focused on children aged 6 to 18 years old with an IQ score above 70. However, it is important to note that the white matter microstructure and emotion recognition abilities may undergo changes with development, which could affect the results. Additionally, as the age and IQ range of the participants are limited, the findings may not be applicable to the broader ASD population. To obtain a more comprehensive understanding, future research should involve individuals of all ages and those with intellectual impairments, while taking developmental changes into account. Third, the photographs of the FER task utilized in this study are

other-race. Although our study successfully distinguished FER functions between ASD and TD children, it is possible that other-race faces[67] in this task could affect individual performance. To clarify the generalizability of the current findings, tasks specifically tailored to the particular race should be used in the future study. Fourth, In regards to investigating white matter microstructure, there are various DTI analysis methods available. However, for our study, we solely utilized TBSS which can only match the main white matter fiber bundles according to the DTI map. It's important to note that different partitions of the same white matter fiber bundle may have different functions, but TBSS analysis cannot differentiate between the specific segments. In the future, we suggest utilizing other DTI analysis methods to accurately identify specific white matter tract segments. Most importantly, because of the nature of cross-sectional study, it was not possible to assume causal relationships of white matter, FER function and ASD, longitudinal and prospective studies are needed for deeper investigation.

Conclusions

Our study shows that children with ASD have difficulties in recognizing both basic and complex facial emotions, as well as alterations in the microstructure of their white matter. In TD children, we observed a negative relationship between performance in complex facial expression recognition and FA values of some white matter fibers, but this correlation was not present in children with ASD. These findings can improve the comprehension of the FER deficits of ASD, and highlight the potential of white matter for future studies. Additionally, this study may shed light on using white matter as a biomarker to evaluate the efficacy of treatments and therapies.

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Authors contributions Jing Liu, Xue Li, and Xing Su developed the study concept. All authors contributed to the study design and data collection. Siuching Kat and Xing Su conducted the data processing and Xing Su performed the statistical analysis under the supervision of Siuching Kat, Xue Li, and Jing Liu. Xing Su drafted the paper, and Jing Liu, Siuching Kat, and Xue Li provided critical revisions. All authors approved the final version of the paper for submission.

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Data availability All the clinical data used to support the findings of this study may be released upon application to the data access manager and the corresponding author, who can be contacted at ljyuch@bjmu.edu.cn.

Declarations

Ethical approval and consent to participate This work was approved by the Ethics Committee of Peking University Sixth Hospital.

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