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ORIGINAL ARTICLE

Corpus callosum organization and its implication to core and co-occurring symptoms of Autism Spectrum Disorder

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Abstract

Autism Spectrum Disorder (ASD) is characterized by social interaction and communication deficits, repetitive behavior and often by co-occurring conditions such as language and non-verbal IQ development delays. Previous studies reported that those behavioral abnormalities can be associated with corpus callosum organization. However, little is known about the specific differences in white matter structure of the corpus callosum parts in children with ASD and TD peers and their relationships to core and co-occurring symptoms of ASD. The aim of the study was to investigate the volumetric and microstructural characteristics of the corpus callosum parts crucially involved in social, language, and non-verbal IQ behavior in primary-school-aged children with ASD and to assess the relationships between these characteristics and behavioral measures. 38 children (19 with ASD and 19 typically developing (TD) controls) were scanned using diffusion-weighted MRI and assessed with behavioral tests. The tractography of the corpus callosum parts were performed using Quantitative Imaging Toolkit software; diffusivity and volumetric measurements were extracted for the analysis. In the ASD group, fractional anisotropy (FA) was decreased across the supplementary motor area and the ventromedial prefrontal cortex, and axial diffusivity (AD) was reduced across each of the corpus callosum parts in comparison to the TD group. Importantly, the AD decrease was related to worse language skills and more severe autistic traits in individuals with ASD. The microstructure of the corpus callosum parts differs between children with and without ASD. Abnormalities in white matter organization of the corpus callosum parts are associated with core and co-occurring symptoms of ASD.

Keywords Corpus callosum · Tractography · Social interaction · Language abilities · Non-verbal IQ · Autism spectrum disorder

Introduction

Autism Spectrum Disorder (ASD) is a highly heterogeneous group of neurodevelopmental conditions characterized by permanent communication deficits, social interaction problems, and repetitive behavior/restricted interests (American Psychiatric Association 2013), as well as some co-occurring symptoms, such as intellectual delay, language impairment, attention deficit, etc. (Mayes & Calhoun 2001; Oeseburg et al. 2011; Schwartz & Neri 2012; Polyak et al. 2015). A range of the previous studies have revealed atypical white matter integrity in individuals with ASD (Travers et al. 2015; Nickel et al. 2017; Martino et al. 2017; Haigh et al. 2020; Chandran et al. 2021). As the corpus callosum (CC) is the largest white matter pathway that connects two hemispheres of the brain and coordinates information between them, its structural abnormalities can result in cognitive impairments

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in ASD leading to both core and co-occurring symptoms of this disorder (Alexander et al. 2007; Zhang et al. 2022).

A number of studies comparing the characteristics of CC between children with and without ASD have identified multiple abnormalities in the ASD group, such as the reduction of the tract's volume (Frazier et al. 2012), higher radial diffusivity (RD) (Temur et al. 2019), higher apparent diffusion coefficient (ADC) (Hong et al. 2011), lower fractional anisotropy (FA) (Temur et al. 2019), higher mean diffusivity (MD) (Travers et al. 2015), and reduced fiber density (FD) (Dimond et al. 2019). Although some studies showed a total reduction in the volume of CC in ASD (Boger-Megiddo et al. 2006; Alexander et al. 2007), others indicated that specific areas are lower in volume including anterior (Vidal et al. 2006; Kilian et al. 2007), midbody (Kilian et al. 2007), and posterior (Just et al. 2007) parts. In addition to CC volume, lower FA was found specifically in the genu (Barnea-Goraly et al. 2004; Travers et al. 2015), rostral body (Barnea-Goraly et al. 2004), body (Travers et al. 2015), and splenium (Alexander et al. 2007; Travers et al. 2015); lower axial diffusivity (AD) was revealed in midbody, isthmus, and splenium (Sui et al. 2018), and increased AD was found in the posterior CC (Travers et al. 2015); increased MD was found in the posterior CC (Travers et al. 2015).

Some studies have examined the relationships between both core and co-occurring symptoms of ASD and the microstructure and volume of the whole CC and its parts (Prigge et al. 2013; Lau et al. 2013). For example, it has been demonstrated that the lower communicative skills of children with ASD measured with Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) (Lord et al. 2012) were associated with a lower volume of the mid-posterior and anterior-middle parts of the CC as well as the whole CC (Zhang et al. 2022). However, Bakhtiari et al. (2012) did not show any associations between FA values in body, splenium, and genu of the CC and the severity of the autistic traits assessed by the Autism Quotient (AQ) self-report questionnaire (Baron-Cohen et al. 2001; Woodbury-Smith et al. 2005) in individuals with ASD. Additionally, it has been shown that a lower total volume of the CC, higher MD, and lower FA and RD were related to a lower non-verbal IQ in individuals with ASD (Alexander et al. 2007), while higher volumes of the mid-posterior, anterior-middle parts of the CC and the whole CC were associated with lower verbal IQ (Zhang et al. 2022). Although there are no studies in ASD investigating the relationships between language abilities and CC characteristics, studies of other neurodevelopmental conditions indicated better verbal fluency to be associated with a higher volume of the whole CC (Narberhaus et al. 2008; Kontis et al. 2009; Nosarti et al. 2004).

In the present research, the microstructure and volume characteristics of the CC were investigated in primary-school-aged children with ASD. The purpose of the study was twofold: first, to examine possible differences in the microstructure and volume of the CC parts between children with ASD and age-matched typically developing (TD) controls; second, to assess the relationships between behavioral measures (language skills, non-verbal IQ, and the severity of autistic traits) and characteristics of the CC parts in children with ASD. While a range of the previous studies investigated the relationships between non-verbal IQ (Alexander et al. 2007), the severity of autistic symptoms (Zhang et al. 2022), and characteristics of the CC parts in children with ASD, we aimed, for the first time, to reveal the associations between all of these core/co-occurring symptoms and the characteristics of the CC parts in the same group of children with ASD. We also addressed the relationship between language abilities of children with ASD and the structure of the CC parts. Although it has been shown that vocabulary development and verbal fluency can be associated with CC organization in very preterm adolescents (Nosarti et al. 2004; Narberhaus et al. 2008), there is a lack of studies investigating the relationship between language abilities and structure of the CC parts in individuals with ASD. Of note, each behavioral domain was assessed by standardized tests and scored using criterion-referenced score interpretations.

Methods

Participants

A total of 38 native Russian-speaking children participated in the study: 19 children with ASD (5 girls, age range 8.01–14.01 years, $M_{age} = 9.9$, $SD = 1.7$) and 19 TD children as a control group (7 girls, age range 7.08–12.03 years, $M_{age} = 9.7$, $SD = 1.5$). TD children were recruited through advertising on social media. Exclusion criteria for TD children was the previous history of psychiatric and neurodevelopmental problems. Children with ASD were recruited from the Federal Resource Center for Organization of the Comprehensive Support to Children with Autism Spectrum Disorders (Moscow, Russia). Participants of both groups had no hearing or vision problems. The diagnosis of ASD was based on the International Classification of Diseases, ICD-10, and 17 out of 19 children also were assessed by a licensed psychiatrist using ADOS-2 (Lord et al. 2012). Additionally, parents of both ASD and TD groups of children were asked to fill in the Russian version of the Autism Spectrum Quotient: Children's Version, AQ (Auyeung et al. 2008), where the questions were divided into 5 scales associated with autism and broader phenotypes: social skills, attention switching, attention to details, communication, and imagination. The demographic information is provided in Table 1.

Table 1 Demographic information

Characteristics	ASD ($N=19$)	TD ($N=19$)	t	p
Sex (female/male)	5/14	7/12	0.68	0.50
Age (years)	9.9 ± 1.7	9.7 ± 1.5	0.48	0.64
AQ score: social skills	15.7 ± 6.5	7.8 ± 3.1	4.87	**< 0.001***
AQ score: attention switching	16.4 ± 4	12.2 ± 3	4.19	**< 0.002***
AQ score: attention to details	15.1 ± 5	13.9 ± 4.6	1.51	0.14
AQ score: communication	21 ± 4.3	8.8 ± 4.7	9.23	**< 0.001***
AQ score: imagination	15.9 ± 6.8	9 ± 3	3.83	**< 0.005***
Mean language score	0.75 ± 0.22	0.95 ± 0.03	− 3.87	**< 0.004***

The significance is labeled with $*p < 0.05$, $**p < 0.01$, $***p < 0.001$ and highlighted in bold

Behavioral measurements

The non-verbal intelligence of TD children was assessed with Raven's Colored Progressive Matrices (Raven 2000; 2004), and the non-verbal IQ of children with ASD was measured with the Kaufman Assessment Battery for Children, K-ABC II (Kaufman & Kaufman 2004), or Wechsler Intelligence Scale for Children—Third Edition, WISC-III (1991), performance IQ score. Language abilities were comprehensively evaluated with the Russian Child Language Assessment Battery (RuCLAB) consisting of tests that assess phonological, lexical, morphosyntactic, and discourse levels in both the expressive and receptive domains (Arutiunian et al. 2022).

MRI data acquisition and processing

Magnetic resonance imaging (MRI) data were acquired using a 1.5 T Siemens Magnetom Avanto scanner. Diffusion-weighted imaging (DWI) was performed using a single-shot echo-planar imaging sequence with the following parameters: one non-diffusion-weighted image, 64 non-collinear diffusion directions, b value 1000 s/mm^2, TR 6800 ms, TE 97 ms, voxel size 2.5 × 2.5 × 2.5 mm. The sequence was repeated twice with opposite phase-encoding directions (anterior–posterior, AP, and posterior-anterior, PA). In addition, two short sequences were acquired with opposite phase-encoding directions (AP and PA), containing two non-diffusion-weighted images and 12 diffusion directions. Four subjects from the ASD group were scanned with only PA phase-encoding and one short sequence (AP) was acquired for them.

DWI data were corrected for eddy-current-induced distortions and subject motion using the 'eddy' function implemented in the FSL (Jenkinson et al. 2012). Quantitative Imaging Toolkit software (QIT) was used to perform whole-brain tractography using the hybrid probabilistic-deterministic approach (Cabeen et al. 2018). For each child, FA, MD, AD, FD, and volume were extracted for the CC parts projecting to the dorsomedial prefrontal cortex (dmPFC), superior parietal lobule (SPL), supplementary motor area (SMA), and ventromedial prefrontal cortex (vmPFC). We based this on the parcellation approach implemented in the QIT (Cabeen et al. 2018) where the CC is divided into 17 parts on the basis of fiber terminations and chose four of them projecting to the crucial parts of the cortex for language and social skills (Burin et al. 2014; Hiser & Koenigs 2018; Quirarte et al. 2021; Banaszkiewicz et al. 2021).

Statistical analysis

First, to provide between-group comparisons in each metrics of CC (AD, MD, FA, FD, and volume), we fitted linear mixed-effects models with nested effects, including the main effect of the part (dmPFC, SPL, SMA, and vmPFC), the effect of group (TD vs. ASD) nested within each part separately as fixed effects, and participants as a random intercept. The structure of the model was as follows: lmer(metrics ~ 1 + Part/Group + (1 | ID), data = data, control = lmerControl(optimizer = "bobyqa"). Second, to assess the relationships between the metrics of CC and behavioral measures in children with ASD, we fitted linear models included metrics as dependent variables and eight measures (age, non-verbal IQ, mean language score, and five AQ scores), according to the formula: lm(metrics ~ 1 + Age + Mean_language_score + IQ + AQ_social + AQ_attention_to_detail + AQ_attention_switching + AQ_imagination + AQ_communication, data = data).

The analysis was performed in R (R Core Team 2019) with the *lme4* package (Bates et al. 2015). The tables for model outcomes were built with the *sjPlot* package (Lüdecke 2020), and the data were plotted with *ggplot2* (Wickham 2016). The correction for multiple comparisons (false discovery rate, FDR) was applied in R (function *p.adjust.methods = "fdr"*), so that all reported *p* values are FDR-corrected. Supplementary file 1 provides all the R codes used in the analysis and visualization with the structures/formulae for each model.

Results

Behavioral assessment

To explore the differences in children's behavioral measures, we compared the ASD and TD groups. There was significantly higher language performance in TD children: $M_{ASD} = 0.75$ ($SD = 0.22$) vs. $M_{TD} = 0.95$ ($SD = 0.03$), $t(36) = -3.87$, $p < 0.001$. There were also significant differences in four out of five AQ scales between groups of children with ASD and TD children: *social skills,* $M_{ASD} = 15.7$ ($SD = 6.5$) vs. $M_{TD} = 7.8$ ($SD = 3.1$), $t(36) = 4.87$, $p < 0.001$; *attention switching*, $M_{ASD} = 16.4$ ($SD = 4.0$) vs. $M_{TD} = 12.2$ ($SD = 3.0$), $t(36) = 4.19$, $p = 0.002$; *communication,* $M_{ASD} = 21$ ($SD = 4.3$) vs. $M_{TD} = 8.8$ ($SD = 4.7$), $t(36) = 9.23$, $p = 0.001$; *imagination*, $M_{ASD} = 15.9$ ($SD = 6.8$) vs. $M_{TD} = 9$ ($SD = 3.0$), $t(36) = 3.83$, $p = 0.005$. Hence, the severity of autistic symptoms was higher in the ASD group, according to AQ scores.

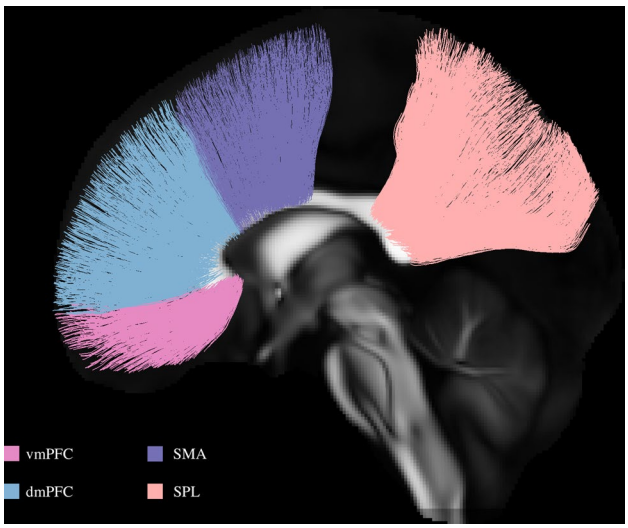

Fig. 1 An illustration of the corpus callosum parts projecting to the dorsomedial prefrontal cortex (dmPFC), superior parietal lobule (SPL), supplementary motor area (SMA), and ventromedial prefrontal cortex (vmPFC)

Between-group comparisons in CC structure

An illustration of the parts of CC investigated in the study can be seen in Fig. 1.

Between-group comparisons showed significantly lower AD values in the ASD group across all parts of the CC (Fig. 2, Table 2): *dmPFC,* $M_{TD} = 0.0013$ ($SD = 3.79$) vs. $M_{ASD} = 0.0010$ ($SD = 3.67$), $Est = 0.00$, $SE = 0.00$, $t = 2.49$, $p = 0.024$; *SPL,* $M_{TD} = 0.00141$ ($SD = 3.76$) vs. $M_{ASD} = 0.00138$ ($SD = 3.94$), $Est = 0.00$, $SE = 0.00$, $t = 2.26$, $p = 0.024$; *SMA,* $M_{TD} = 0.00132$ ($SD = 4.07$) vs. $M_{ASD} = 0.00129$ ($SD = 3.37$), $Est = 0.00$, $SE = 0.00$, $t = 2.37$, $p = 0.024$; *vmPFC*, $M_{TD} = 0.0013$ ($SD = 3.34$) vs. $M_{ASD} = 0.0012$ ($SD = 3.93$), $Est = 0.00$, $SE = 0.00$, $t = 2.77$, $p = 0.024$. We also found that FA values are significantly lower in children with ASD across SMA and vmPFC

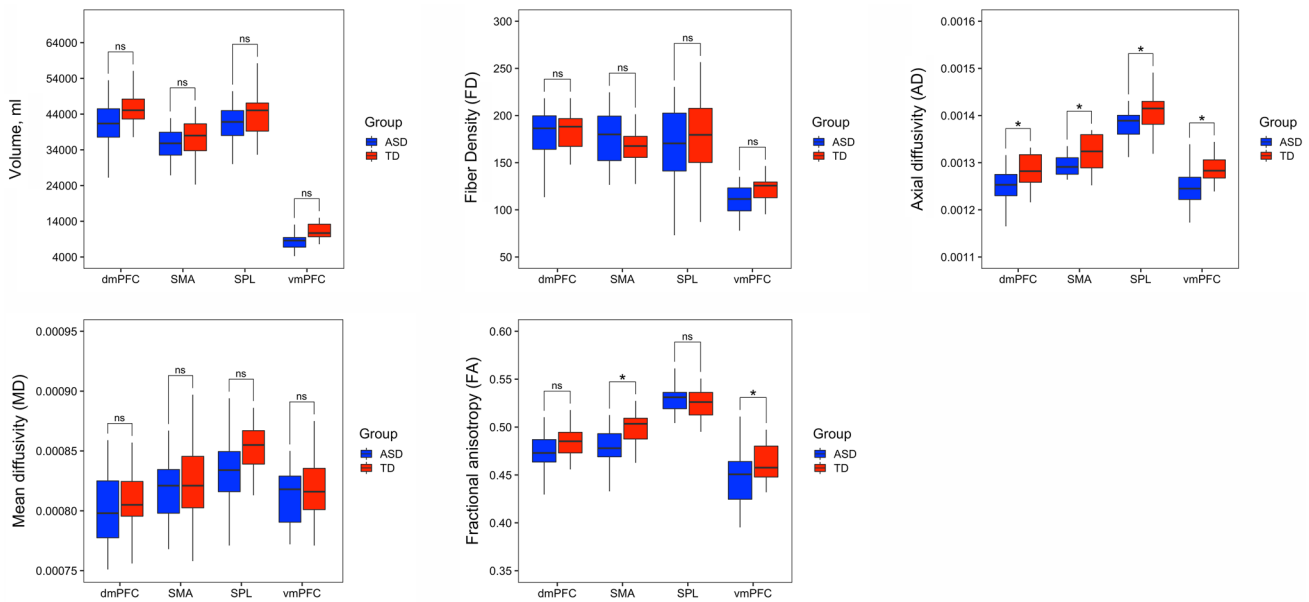

Fig. 2 Between-group (ASD vs. TD) comparisons on each metrics in the CC parts

Table 2 Between-group comparison (TD vs. ASD) in the axial diffusivity of the parts of CC

Predictors	Axial diffusivity (AD)			
	Estimate	Standard error	*t*	*p*
(Intercept)	0.00	0.00	179.46	**< 0.001***
SPL	− 0.00	0.00	− 9.00	**< 0.001***
SMA	0.00	0.00	19.21	**< 0.001***
vmPFC	− 0.00	0.00	− 0.45	0.651
dmPFC:TD_group	0.00	0.00	2.49	**0.024***
SPL:TD_group	0.00	0.00	2.26	**0.024***
SMA:TD_group	0.00	0.00	2.37	**0.024***
vmPFC:TD_group	0.00	0.00	2.77	**0.024***
Random effects				
σ^2	0.00			
$\tau_{00\ ID}$	0.00			
ICC	0.61			
$N_{\ ID}$	38			
Observations	152			
Marginal R^2/conditional R^2	0.688/0.878			

The significance is labeled with $*p < 0.05$, $**p < 0.01$, $***p < 0.001$ and highlighted in bold

parts (Fig. 2, Table 3): *SMA*, $M_{TD} = 0.4981$ ($SD = 0.02$) vs. $M_{ASD} = 0.4804$ ($SD = 0.03$), $Est = 0.02$, $SE = 0.01$, $t = 2.41$, $p = 0.050$; *vmPFC*, $M_{TD} = 0.4624$ ($SD = 0.02$) vs. $M_{ASD} = 0.4460$ ($SD = 0.03$), $Est = 0.02$, $SE = 0.01$, $t = 2.24$, $p = 0.050$. Other metrics did not differ between groups of children (Fig. 2, Tables 4, 5 and 6).

The relationships between CC structure and behavioral measures in ASD

To analyze how a pathological decrease of AD and FA in the CC parts in children with ASD was related to behavioral/clinical measures, we fitted linear models (see details in *Statistical analysis*) with tract's metrics as a dependent variable and children's individual characteristics (age, language score, non-verbal IQ, and AQ scores) as predictors. The analysis showed that a lower AD in the part of the CC projecting to SMA was associated with worse language skills: $Est = 0.00$, $SE = 0.00$, $t = 3.55$, $p = 0.042$. A lower AD in the same structure was also related to higher scores in the AQ scale (attention to details) and, thus, more severe impairments in this domain of functioning: $Est = -0.00$, $SE = 0.00$, $t = -3.07$, $p = 0.048$ (Table 7). Other relationships were not significant.

Discussion

The aim of this study was to investigate the structural characteristics (AD, MD, FA, FD, and volume) of the parts of CC in primary-school-aged children with ASD and reveal the relationships between these characteristics and behavioral measures (language abilities, non-verbal IQ, and the severity of autistic symptoms) in these children. Our results showed that AD and FA values are decreased in the CC parts in children with ASD compared to their TD peers. We also showed that the pathological decrease of AD across the SMA part is related to worse language scores and a higher severity of the autistic traits in individuals with ASD.

The between-group comparisons showed decreased AD across all parts of the CC in children with ASD. The AD metric represents the magnitude of diffusion along the principal diffusion direction (Gibbard et al. 2013). There is an evidence that axial diffusivity can be decreased during the white matter development due to reduction in a water content of the brain and an increase in membrane density (Dubois et al. 2008). Additionally, number of studies linked decreased AD to axonal damage (Winklewski et al. 2018) and altered axonal integrity (Tu et al. 2016). Thus, our results might assume either axonal injuries of CC's fibers in the ASD group including caliber reduction, a less coherent and less symmetrical orientation of the axons of CC in children with ASD compared to TD controls (Takahashi et al. 2000; Winklewski et al. 2018) or slower CC development in ASD rather than in TD children (Gao et al. 2009). Our results are in line with Sui et al. (2018) who found reduced

Table 3 Between-group comparison (TD vs. ASD) in the fractional anisotropy of the parts of CC

Predictors	Fractional anisotropy (FA)			
	Estimate	Standard error	*t*	*p*
(Intercept)	0.48	0.00	109.44	**< 0.001***
SPL	− 0.01	0.00	− 3.29	**0.001***
SMA	0.05	0.00	16.72	**< 0.001***
vmPFC	− 0.00	0.00	− 0.48	0.631
dmPFC:TD_group	0.01	0.01	1.67	0.125
SPL:TD_group	− 0.00	0.01	− 0.45	0.651
SMA:TD_group	0.02	0.01	2.41	**0.050***
vmPFC:TD_group	0.02	0.01	2.24	**0.050***
Random effects				
σ^2	0.00			
$\tau_{00\ ID}$	0.00			
ICC	0.62			
$N_{\ ID}$	38			
Observations	152			
Marginal R^2/conditional R^2	0.584/0.844			

The significance is labeled with $*p < 0.05$, $**p < 0.01$, $***p < 0.001$ and highlighted in bold

Table 4 Between-group comparison (TD vs. ASD) in the volume of the parts of CC

Predictors	Volume			
	Estimate	Standard error	*t*	*p*
(Intercept)	31,497.72	996.23	31.62	**< 0.001***
SPL	9895.54	981.16	10.09	**< 0.001***
SMA	9403.12	981.16	9.58	**< 0.001***
vmPFC	3704.17	981.16	3.78	**< 0.001***
dmPFC:TD_group	4898.21	1977.45	2.48	0.052
SPL:TD_group	2951.16	1977.45	1.49	0.262
SMA:TD_group	1955.63	1977.45	0.99	0.323
vmPFC:TD_group	2552.95	1977.45	1.29	0.262
Random effects				
σ^2	24,387,805.17			
$\tau_{00\ ID}$	12,759,998.32			
ICC	0.34			
$N_{\ ID}$	38			
Observations		152		
Marginal R^2/conditional R^2	0.838/0.894			

The significance is labeled with $*p < 0.05$, $**p < 0.01$, $***p < 0.001$ and highlighted in bold

AD in midbody, isthmus, and splenium and with Andrews et al. (2019) who found lower AD across body, genu, and splenium in males with ASD compared to TD males. The findings of the Andrews et al.'s (2019) study support the results of the current study, not only confirming but also validating them, since the sample size of their study is greater than in ours (85 males with ASD, 42 TD males). However, our findings on AD decrease across the corpus callosum parts are controversial to Travers et al. (2015) who showed that AD is increased in splenium. Additionally, Alexander et al. (2007) found no significant difference in AD between children with and without ASD in genu, body, and splenium.

In line with Barnea-Goraly et al. (2004) and Alexander et al. (2007) who demonstrated reduced FA in body and genu of the CC and Travers et al. (2015) who showed lower FA across genu, body, splenium, we found a significant decrease in FA values of the CC across SMA and vmPFC parts between the two groups. The FA metric is a measure of the directionality of diffusion anisotropy. It has been shown that decreased FA can be connected to axonal

Table 5 Between-group comparison (TD vs. ASD) in the mean diffusivity of the parts of CC

Predictors	Mean diffusivity (MD)			
	Estimate	Standard error	*t*	*p*
(Intercept)	0.00	0.00	147.10	**< 0.001***
SPL	− 0.00	0.00	− 4.33	**< 0.001***
SMA	0.00	0.00	4.29	**< 0.001***
vmPFC	0.00	0.00	0.60	0.547
dmPFC:TD_group	0.00	0.00	0.87	0.738
SPL:TD_group	0.00	0.00	1.99	0.184
SMA:TD_group	0.00	0.00	0.27	0.785
vmPFC:TD_group	0.00	0.00	0.59	0.738
Random effects				
σ^2	0.00			
$\tau_{00\ ID}$	0.00			
ICC	0.59			
$N_{\ ID}$	38			
Observations	152			
Marginal R^2/conditional R^2	0.199/0.669			

The significance is labeled with $*p < 0.05$, $**p < 0.01$, $***p < 0.001$ and highlighted in bold

Table 6 Between-group comparison (TD vs. ASD) in the fiber density of the parts of CC

Predictors	Fiber density			
	Estimate	Standard error	*t*	*p*
(Intercept)	157.65	4.89	32.25	**< 0.001***
SPL	21.70	4.97	4.37	**< 0.001***
SMA	8.78	4.97	1.77	0.077
vmPFC	17.73	4.97	3.57	**< 0.001***
dmPFC:TD_group	4.66	9.86	0.47	0.637
SPL:TD_group	11.80	9.86	1.20	0.231
SMA:TD_group	− 10.70	9.86	− 1.09	0.278
vmPFC:TD_group	12.80	9.86	1.30	0.194
Random effects				
σ^2	625.77			
$\tau_{00\ ID}$	297.49			
ICC	0.32			
$N_{\ ID}$	38			
Observations	152			
Marginal R^2/conditional R^2	0.431/0.615			

The significance is labeled with $*p < 0.05$, $**p < 0.01$, $***p < 0.001$ and highlighted in bold

damages including dysmyelination or reduced axonal myelination, lower axon density and diameter (Le Bihan 2003; Winston 2012), higher proportion of crossing fibers (Jones et al. 2013), and disorganization of fibers (Aung et al. 2013). Therefore, we can conclude that diffusion in the CC's fibers projecting to SMA and vmPFC cortices are more isotropic in the ASD group compared to the TD group. Although, as in the previous study on investigating FA values in depressed patients (Meinert et al. 2019), we did not measure myelination directly, there is evidence that reduced FA can be explained by the hypersecretion of glucocorticoids (Frodle & O'Keane 2013) leading to altered oligodendrocyte functioning and potentially reduced myelination (Jauregui-Huerta et al. 2010).

The analysis revealed that MD, RD values and volume of the CC parts did not differ between the two groups. These results are not consistent with those reporting higher MD of the posterior CC in ASD (Travers et al. 2015) and lower volume in anterior (Vidal et al. 2006; Kilian et al. 2007), midbody (Kilian et al. 2007), and posterior (Just et al. 2007)

Table 7 Brain-behavioral relationships in children with ASD (summary of model outcomes)

Predictors	dmPFC (AD)		SMA (AD)		SPL (AD)		vmPFC (AD)		SMA (FA)		vmPFC (FA)	
	t	*p*	*t*	*p*	*t*	*p*	*t*	*p*	*t*	*p*	*t*	*p*
(Intercept)	16.99	**<0.001***	21.33	**<0.001***	15.69	**<0.001***	13.00	**<0.001***	8.23	**<0.001***	5.03	**<0.001***
Age	− 1.69	0.194	− 2.27	0.103	− 1.58	0.389	− 1.05	0.319	1.05	0.365	0.27	0.789
Mean language score	2.28	0.121	3.55	**0.042***	1.63	0.389	1.01	0.338	2.17	0.212	1.17	0.268
Non-verbal IQ	− 2.04	0.138	− 1.89	0.140	− 1.98	0.389	0.38	0.711	− 1.05	0.365	− 0.34	0.739
AQ_social	− 0.50	0.720	− 1.00	0.402	0.53	0.813	0.65	0.527	− 2.43	0.212	− 1.02	0.332
AQ_attention_switching	1.07	0.410	− 0.40	0.699	− 0.07	0.945	0.38	0.708	− 1.21	0.365	− 0.98	0.348
AQ_imagination	2.39	0.121	2.21	0.103	1.25	0.401	0.95	0.364	1.95	0.212	1.30	0.220
AQ_communication	− 0.23	0.823	0.98	0.402	0.24	0.933	− 0.32	0.755	1.32	0.365	0.60	0.558
AQ_attention_to_detail	− 2.90	0.122	− 3.07	0.048*	− 1.22	0.401	− 1.61	0.139	− 0.88	0.399	− 0.66	0.523
Observations	19		19		19		19		19		19	
R^2/R^2 adjusted	0.561/0.210		0.667/0.401		0.460/0.028		0.437/− 0.127		0.630/0.335		0.375/− 0.123	

The significance is labeled with *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ and highlighted in bold

parts of the CC. These differences can be caused by various tractography techniques, parcellation approaches and the highly heterogeneous nature of the ASD population.

The investigation of how the pathological reduction of AD and FA values in the CC parts is related to behavioral measures in ASD showed that the lower AD in the part of the CC projecting to SMA is associated with poorer language performance and more impaired attention to details in children with ASD. While previous studies showed that the severity of autistic traits is related to the lower volume of the CC and its parts (Prigge et al. 2013; Zhang et al. 2022), we demonstrated that a decreased AD is also associated with more severe autistic traits. Although it has been shown that language impairment can be related to the pathology of the volume of the CC parts in adolescents who were born very preterm (Nosarti et al. 2004; Narberhaus et al. 2008), we found that the volume of the CC parts is not related to language abilities in children with ASD. However, we demonstrated that the decrease of AD across the SMA part is associated with poorer language performance in children with ASD. These differences can be explained by the specificity of the autistic brain organization and the types of language tests used in previous studies. Our findings also showed that there are not any links between FA values of SMA and vmPFC parts of the CC and the behavioral characteristics of ASD. These results are in line with Bakhtiari et al. (2012) who also showed that a reduction of FA in the CC parts is not related to the severity of autistic traits.

Implications

It is important to note that the parts of the CC analyzed in the previous studies differed from those we chose. However, we conclude that reduced AD and FA are specific for the CC parts in individuals with ASD, as our work and some other studies (Barnea-Goraly et al. 2004; Keller et al. 2007; Travers et al. 2015; Sui et al. 2018; Temur et al. 2019) showed decreased values of these metrics. This result contributes to the understanding of white matter organization in children with ASD pointing out that there are specific diffusion differences in the CC of the autistic brain associated with core and co-occurring symptoms of this disorder.

Limitations and future research

There are several potential limitations associated with this study. First, we measured the severity of autistic traits indirectly, using a parental questionnaire. It may be more appropriate in future to assess each behavioral characteristic using

more direct tests. Second, the sample size of the current study was moderate, which could affect statistical power.

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Author contributions AM: methodology, investigation, data curation, formal analysis, writing—original draft, and writing—review and editing. ED: investigation. DP: investigation. AS: investigation. ST: investigation. UM: investigation. KD: investigation. OD: methodology, formal analysis, writing—review and editing, resources. VA: conceptualization, methodology, investigation, data curation, formal analysis, writing—review and editing, and project administration. All authors read and approved the final manuscript.

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Data availability The datasets generated and analyzed during the current study are not publicly available as it is human data but are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare that the study was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethical approval The approval for this study was obtained from the HSE University Committee on Interuniversity Surveys and the Ethical Assessment of Empirical Research (for the TD group) and the local ethics committee of the Moscow State University of Psychology and Education (for the ASD group). The study was conducted in accordance with the Declaration of Helsinki.

Consent to participate A parent of each child signed a written consent form.

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