

1 **Observational *in-vivo* axon development in children with autism and**
2 **developmental disability using MRI**

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Supplementary Results 1. The sensitivity of NODDI metrics to white matter development

We examined the sensitivity of NODDI metrics to white matter development across early childhood using partial Pearson correlation analyses, including sex and head motion during the MRI scan as covariates. Our results revealed that the NDI increased rapidly with age (TD: $r=0.765$, ASD with DD/ID: $r=0.767$, ASD without DD/ID: $r=0.601$, DD: $r=0.500$, all groups' P values <0.001). Moreover, the ODI exhibited a plateau pattern with no age effects (TD: $r=-0.030$, ASD with DD/ID: $r=0.111$, ASD without DD/ID: $r=0.069$; DD: $r=-0.024$, all groups' P values >0.4) throughout early childhood (Supplementary Fig. 2). This observation suggested that the NDI, a marker of axon density in white matter derived from NODDI, is sensitive to the white matter developmental process in early childhood.

Supplementary Results 2. Validation analyses

To evaluate the reliability of our findings, we performed a split-half validation analysis. Due to the limited sample sizes in the ASD without DD/ID and DD/ID groups, the validation analyses were only performed in the ASD with DD/ID and TD groups. Specifically, we divided 105 ASD with DD/ID and 160 TD children into two validation populations: 1) Validation Population 1, 53 ASD with DD/ID children (7 females) and 80 TD children (41 females); 2) Validation Population 2, 52 ASD with DD/ID children (6 females) and 80 TD children (39 females). We applied the hybrid hierarchical clustering algorithm and curve fitting to these four validation groups separately. For the clustering analyses, most results of the validation populations were consistent with the main findings except for those of 2 white matter regions (right fornix (cres) and/or stria terminalis and left tapetum). In the TD group of Validation Population 1, the right fornix (cres) and/or stria terminalis was clustered into the A-S Cluster, which belonged to the P-I Cluster in the main clustering findings. In the TD and ASD with DD/ID groups of Validation Population 2, the left tapetum was clustered into the A-S Cluster instead of the P-I Cluster in the main clustering findings. Given that our analyses in the main findings included 36 regions in total, alterations in only 2 white matter regions in the clustering outcomes were still acceptable. Moreover, the developmental curves for all validation populations were almost consistent with the main results (Supplementary Fig. 4 and 5). The only exception was that the developmental curve of the P-I Cluster of ASD with DD/ID children in Validation Group 1 tended to be linear, suggesting a stronger similarity with the DD/ID population.

In addition, we conducted another validation analysis with male-only samples for all groups to explore the potential sex effects of ASD. A total of 250 male participants were included (79 TD, 37 DD/ID, 42 ASD without DD/ID, and 92 ASD with DD/ID). We applied the hybrid hierarchical clustering algorithm and curve fitting to all four male-only groups. For clustering analyses and developmental curves, the results across the four groups were also mostly consistent with the main findings. A minor change was observed in the developmental curve of the A-S Cluster for the DD/ID group, whose growth rates were still very slow but showed mild staging features (Supplementary Fig. 6 and 7).

Supplementary Table 1. The list of cerebral white matter regions in each white matter cluster

Abbreviations of white matter clusters	Full spell of white matter clusters	Abbreviations of White matter regions	Full spell of white matter regions
CC Cluster	Corpus Callosum Cluster	GCC	Genu of corpus callosum
		BCC	Body of corpus callosum
		SCC	Splenium of corpus callosum
		ALIC R&L	Right and left anterior limb of internal capsule
		PLIC R&L	Right and left posterior limb of internal capsule
A-S Cluster	Anterior-Superior Cluster	ACR R&L	Right and left anterior corona radiata
		SCR R&L	Right and left superior corona radiata
		CGC R&L	Right and left cingulum (cingulate gyrus)
		SLF R&L	Right and left superior longitudinal fasciculus
		SFOF R&L	Right and left superior fronto-occipital fasciculus
		RLIC R&L	Right and left retrolenticular part of internal capsule
		FXS L	Left fornix (cres) / Stria terminalis
		FX	Fornix
P-I Cluster	Posterior-Inferior Cluster	PCR R&L	Right and left posterior corona radiata
		PTR R&L	Right and left posterior thalamic radiation
		SS R&L	Right and left sagittal stratum
		CGH R&L	Right and left cingulum (cingulate gyrus)
		UCF R&L	Right and left uncinate fasciculus
		EC R&L	Right and left external capsule
		TAP R&L	Right and left tapetum
		FXS R	Right fornix (cres) / Stria terminalis

89 **Supplementary Table 2. Participants for creating group templates.**

	ASD			TD		
	Numb er	Age, mean (SD), years	Male	Number	Age, mean (SD), years	Male
Age 1	6	1.88(0.09)	6	6	1.59(0.21)	3
Age 2	6	2.61(0.32)	3	6	2.47(0.28)	2
Age 3	6	3.53(0.22)	4	6	3.52(0.28)	2
Age 4	6	4.57(0.30)	3	6	4.65(0.29)	3
Age 5	5	5.21(0.18)	5	5	5.49(0.25)	3
Age 6	5	6.69(0.35)	5	5	6.51(0.32)	1
Age 7	5	7.53(0.37)	4	5	7.47(0.43)	1

90 ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical
91 developing. SD, standard deviation.

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Supplementary Table 3. Smoothing parameters, EDF, R² and AIC of GAM.

		TD	ASD without DD/ID	ASD with DD/ID	DD/ID
CC Cluster	R ² (adjusted)	0.611	0.567	0.29	0.204
	AIC	-608.3954	-209.1697	-374.6034	-168.1454
	k	6	4	4	3
	EDF	3.34	2.84	2.04	1
A-S Cluster	R ² (adjusted)	0.741	0.672	0.489	0.291
	AIC	-653.1693	-207.2286	-402.3139	-160.5951
	k	6	5	5	3
	EDF	4.43	2.72	2.05	1
P-I Cluster	R ² (adjusted)	0.661	0.613	0.388	0.206
	AIC	-704.248	-237.704	-451.0292	-185.0031
	k	6	5	4	3
	EDF	4.14	2.21	1.75	1

EDF, effective degrees of freedom. The value of EDF formed by the general additive model refers to the degree of curvature of the relationship. R², coefficient of determination. AIC, Akaike information criterion. k, smoothing parameter, setting the upper limit on the degrees of freedom. CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing. SD, standard deviation.

Supplementary Table 4. Two timepoints for defining stages of early white matter development

		TD	ASD without DD/ID	ASD with DD/ID	DD/ID
CC Cluster	Point1 (Years)	3.84	2.80	4.21	n.a.
	Point2 (Years)	5.00	4.71	6.07	n.a.
A-S Cluster	Point1 (Years)	3.84	4.24	4.21	n.a.
	Point2 (Years)	4.76	5.60	7.89	n.a.
P-I Cluster	Point1 (Years)	3.84	4.24	4.21	n.a.
	Point2 (Years)	4.72	6.13	7.89	n.a.

n.a., not applicable. CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing.

Supplementary Table 5. Group comparisons of NDI growth rates

Developmental stage	Group comparisons	CC Cluster		A-S Cluster		P-I Cluster	
		β	p	β	p	β	p
The fast stage	ASD without DD/ID v.s. TD	0.013371	5.9E-28	-0.00817	2.05E-07	-0.01173	2.23E-33
	ASD with DD/ID v.s. TD	-0.01902	1.44E-59	-0.01808	3.29E-32	-0.01698	6.19E-63
	ASD with DD/ID v.s. ASD without DD/ID	-0.03239	2.37E-67	-0.0099	4.79E-10	-0.00525	7.71E-11
The moderate-slow stage	ASD without DD/ID v.s. TD	0.001831	0.110961	0.004671	2.85E-05	0.001906	0.003639
	ASD with DD/ID v.s. TD	0.001239	0.272652	0.0056	3E-08	0.003477	8.97E-09
	ASD with DD/ID v.s. ASD without DD/ID	-0.00059	0.669282	0.000928	0.465322	0.001571	0.039301
The entire age range	ASD without DD/ID v.s. TD	0.004264	0.018743	0.001585	0.352232	-0.00265	0.01951
	ASD with DD/ID v.s. TD	-0.00773	9.58E-08	-0.00339	0.011666	-0.00563	7.27E-10
	DD/ID v.s. TD	-0.00366	0.050808	-0.00327	0.063838	-0.00505	2.13E-05
	ASD with DD/ID-ASD without DD/ID	-0.01199	1.23E-09	-0.00497	0.006308	-0.00297	0.014001
	DD/ID v.s. ASD without DD/ID	-0.00793	0.000565	-0.00486	0.0242	-0.00239	0.09483
	ASD with DD/ID v.s. DD/ID	-0.00406	0.043429	-0.00011	0.952008	-0.00058	0.64376

The moderate and slow developmental stages were combined as the moderate-slow stage. **The bold numbers:** False discovery rate (FDR) correction with Benjamini-Hochberg procedure for multiple comparisons, $p < 0.05$. CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing.

Supplementary Table 6. Comparisons of mean NDI between fast and moderate-slow stage in ASD and TD respectively

	CC Cluster		A-S Cluster		P-I Cluster	
	β	p	β	p	β	p
ASD without DD/ID	0.037016	0.033264	0.004874	0.797557	0.006428	0.630792
ASD with DD/ID	-0.00311	0.841027	-0.00075	0.95576	0.001141	0.913201
TD	0.044741	0.000504	0.043795	0.000113	0.024447	0.006569

The moderate and slow developmental stages were combined as the moderate-slow stage. **The bold numbers:** False discovery rate (FDR) correction with Benjamini-Hochberg procedure for multiple comparisons, $p < 0.05$. CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing.

Supplementary Table 7. Group comparisons of mean NDI

		CC Cluster		A-S Cluster		P-I Cluster	
		β	p	β	p	β	p
The fast stage	ASD without DD/ID v.s. TD	0.00972169	0.341139	0.006671	0.39742	0.002484	0.695992
	ASD with DD/ID v.s. TD	0.00898923	0.2456229	0.004804	0.455921	0.002233	0.667381
	ASD with DD/ID v.s. ASD without DD/ID	-0.0007325	0.9439742	-0.00187	0.798973	-0.00025	0.966231
The moderate-slow stage	ASD without DD/ID v.s. TD	-0.01379	0.071415	-0.00555	0.46457	-0.00585	0.348602
	ASD with DD/ID v.s. TD	-0.00038	0.960276	0.001719	0.806759	-0.00244	0.672649
	ASD with DD/ID v.s. ASD without DD/ID	0.013406	0.131341	0.00727	0.404186	0.003406	0.633898
The entire age range	ASD without DD/ID v.s. TD	-0.0043	0.529346	-3.9E-06	0.9995	-0.00213	0.658298
	ASD with DD/ID v.s. TD	0.011951	0.032302	0.008525	0.094227	0.003514	0.369966
	DD/ID v.s. TD	-0.01432	0.040434	-0.01225	0.054773	-0.01208	0.014155
	ASD with DD/ID v.s. ASD without DD/ID	0.016254	0.021106	0.008529	0.184217	0.005644	0.254019
	DD/ID v.s. ASD without DD/ID	-0.01001	0.229888	-0.01225	0.108183	-0.00995	0.090418
	ASD with DD/ID v.s. DD/ID	0.026267	0.000384	0.020777	0.002062*	0.015595	0.002682

The moderate and slow developmental stages were combined as the moderate-slow stage. **The bold numbers:** False discovery rate (FDR) correction with Benjamini-Hochberg procedure for multiple comparisons, $p < 0.05$. CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing. NDI, neurite density index.

Supplementary Table 8. Correlations of behavioural measurements and NDI in ASD with DD/ID during the fast stage

	CC Cluster		A-S Cluster		P-I Cluster	
	r	p	r	p	r	p
CARS Sum	-0.01144	0.927926	0.108917	0.387781	-0.04646	0.71325
CARS Human Relatedness	0.07686	0.54283	0.186803	0.136228	0.09213	0.465439
CARS Imitation	0.045134	0.721091	0.16454	0.190273	0.100506	0.425683
CARS Affect	0.048967	0.698494	0.095548	0.448979	-0.00382	0.975938
CARS Use Of Body	0.084734	0.502154	0.194712	0.120118	0.049378	0.696085
CARS Relation To Objects	0.266373	0.031968	0.296667	0.016409	0.237051	0.057265
CARS Adaptation To Change	-0.04861	0.700572	-0.03837	0.761568	-0.06785	0.591247
CARS Visual Responsiveness	0.002153	0.986422	0.116438	0.355648	-0.01249	0.921346
CARS Auditory Responsiveness	-0.0373	0.768025	0.090797	0.471948	-0.08736	0.488949
CARS Near Receptor Responsiveness	-0.1798	0.151807	-0.05516	0.662537	-0.12289	0.329455
CARS Anxiety Reaction	0.021013	0.868042	0.05314	0.674185	-0.07692	0.54253
CARS Verbal Communication	-0.03774	0.765335	0.022125	0.861129	0.02671	0.832727
CARS Nonverbal Communication	-0.00272	0.98285	0.122528	0.330874	0.04609	0.715433
CARS Activity Level	-0.07132	0.572396	0.022075	0.861437	-0.07125	0.572742
CARS Intellectual Consistency	0.053753	0.675646	0.127948	0.317633	0.119347	0.351516
CARS Global Impression	0.00119	0.992496	0.121256	0.335955	0.017499	0.889963
ADOS_SA_CSS	0.034999	0.778578	0.027953	0.822335	-0.00546	0.965027
ADOS_RRB_CSS	-0.14883	0.260588	-0.15253	0.2488	-0.16623	0.208295
Gross Motor DQ	-0.07149	0.574546	-0.1108	0.383398	-0.14535	0.251801
Fine Motor DQ	-0.25306	0.142445	-0.44326	0.007656	-0.365	0.031086
Adaptive DQ	-0.12852	0.311504	-0.25157	0.044931	-0.34292	0.005538
Language DQ	-0.12302	0.332811	-0.15319	0.226852	-0.09268	0.466352
Personal-Social DQ	-0.07973	0.534474	-0.08364	0.514604	-0.11309	0.377521
Average DQ	-0.19145	0.129652	-0.2976	0.01693	-0.31344	0.011668

The moderate and slow developmental stages were combined as the moderate-slow stage. **The bold numbers:** False discovery rate (FDR) correction with Benjamini-Hochberg procedure for multiple comparisons, $p < 0.05$. CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing. ADOS, Autism Diagnostic Observation Schedule. SA-CSS, social affect calibrated severity score. RRB-CSS, restricted and repetitive behaviours calibrated severity score. CARS, Childhood Autism Rating Scale. DQ, developmental quotient. NDI, neurite density index.

Supplementary Table 9. Correlations of behavioural measurements and NDI in ASD with DD/ID during the moderate-slow stage

	CC Cluster		A-S Cluster		P-I Cluster	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
CARS Sum	-0.30811	0.097627	-0.2923	0.117017	-0.25532	0.173285
CARS Human Relatedness	-0.3293	0.075578	-0.33459	0.070721	-0.35272	0.055903
CARS Imitation	-0.0014	0.994146	-0.126	0.507028	-0.02098	0.912393
CARS Affect	-0.08053	0.672267	-0.1025	0.589886	-0.03488	0.854805
CARS Use Of Body	-0.10097	0.595488	0.124306	0.512811	0.116877	0.538506
CARS Relation To Objects	-0.24829	0.185846	-0.08615	0.650798	-0.01726	0.927859
CARS Adaptation To Change	-0.09439	0.61979	-0.13059	0.491553	-0.11452	0.54679
CARS Visual Responsiveness	-0.12513	0.517776	-0.23768	0.214418	-0.18154	0.345942
CARS Auditory Responsiveness	-0.15229	0.430328	-0.065	0.737623	-0.00022	0.99908
CARS Near Receptor Responsiveness	-0.30309	0.109991	-0.07963	0.681341	-0.22749	0.235291
CARS Anxiety Reaction	-0.21122	0.27139	-0.06768	0.727203	-0.13679	0.479216
CARS Verbal Communication	-0.37975	0.042167	-0.212	0.26957	-0.22967	0.230722
CARS Nonverbal Communication	-0.28278	0.137184	-0.33793	0.072983	-0.24656	0.197269
CARS Activity Level	-0.24963	0.191564	-0.05714	0.76843	-0.12469	0.519281
CARS Intellectual Consistency	0.272963	0.159907	-0.06394	0.746524	0.130074	0.509434
CARS Global Impression	-0.20844	0.277894	-0.26042	0.172449	-0.12971	0.50245
ADOS_SA_CSS	-0.1999	0.29849	-0.20207	0.293158	-0.21833	0.255202
ADOS_RRB_CSS	-0.11557	0.550523	-0.05496	0.777033	0.038302	0.843623
Verbal IQ	0.321566	0.10192	0.379859	0.050657	0.355578	0.068725
Performance IQ	0.204194	0.306955	0.300344	0.127964	0.156585	0.435409
Full IQ	0.326711	0.09625	0.3511	0.072542	0.318771	0.105102
SRS Total	-0.00697	0.970842	0.168889	0.372302	0.082227	0.665761
SRS Social Awareness	-0.09765	0.607716	0.202682	0.28275	0.021678	0.909474
SRS Social Cognition	0.132666	0.484636	0.277928	0.136997	0.251827	0.179447
SRS Social Communication	-0.07606	0.689528	-0.05859	0.758423	-0.083	0.662792
SRS Social Motivation	-0.0082	0.965681	0.048109	0.800689	0.018566	0.922426
SRS Autistic Mannerisms	0.03958	0.835496	0.301013	0.106007	0.183085	0.33284

The moderate and slow developmental stages were combined as the moderate-slow stage. CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing. ADOS, Autism Diagnostic Observation Schedule. SA-CSS, social affect calibrated severity score. RRB-CSS, restricted and repetitive behaviours calibrated severity score. SRS, Social Responsiveness Scale. CARS, Childhood Autism Rating Scale. IQ, intelligence quotient.

Supplementary Table 10. Correlations of behavioural measurements and NDI in ASD without DD/ID during the fast stage

	CC Cluster		A-S Cluster		P-I Cluster	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
CARS Sum	-0.39239	0.184779	-0.23257	0.310331	0.074039	0.749762
CARS Human Relatedness	-0.00363	0.990605	-0.19626	0.393856	-0.01593	0.945345
CARS Imitation	-0.2911	0.334569	-0.19718	0.3916	0.182717	0.427923
CARS Affect	-0.2676	0.376749	-0.06108	0.792551	0.258085	0.258669
CARS Use Of Body	-0.71105	0.006432	-0.25068	0.27307	-0.31926	0.158341
CARS Relation To Objects	-0.34883	0.242739	-0.06843	0.768205	0.110304	0.634088
CARS Adaptation To Change	0.129774	0.672621	0.118821	0.607961	0.09115	0.69436
CARS Visual Responsiveness	-0.04137	0.893243	-0.18542	0.420997	0.101489	0.661578
CARS Auditory Responsiveness	-0.12931	0.673726	-0.06841	0.768267	-0.05691	0.806437
CARS Near Receptor Responsiveness	-0.39818	0.177814	0.051041	0.82609	0.067758	0.770419
CARS Anxiety Reaction	0.035284	0.908894	-0.18829	0.413723	-0.04344	0.851691
CARS Verbal Communication	-0.24279	0.424151	-0.2663	0.24328	-0.14696	0.524974
CARS Nonverbal Communication	-0.22518	0.459496	-0.1562	0.498961	-0.11304	0.625653
CARS Activity Level	-0.06465	0.833804	0.100068	0.666049	0.175658	0.446282
CARS Intellectual Consistency	0.39988	0.175793	0.157807	0.494492	0.273381	0.230494
CARS Global Impression	-0.5259	0.064895	-0.35759	0.111504	0.041943	0.856746
ADOS_SA_CSS	-0.14299	0.641202	-0.211	0.358565	0.000293	0.998996
ADOS_RRB_CSS	-0.38327	0.196108	-0.26971	0.237058	-0.10099	0.66316
Gross Motor DQ	0.451978	0.104694	0.459009	0.048059	0.456201	0.049621
Fine Motor DQ	0.339764	0.306648	0.307422	0.357767	0.240566	0.476121
Adaptive DQ	0.379356	0.180979	0.191481	0.432284	0.198951	0.41419
Language DQ	-0.05172	0.860618	-0.23546	0.331844	-0.31291	0.192095
Personal-Social DQ	-0.00196	0.994686	-0.15723	0.52033	-0.05175	0.833355
Average DQ	0.295943	0.304267	-0.01359	0.955965	0.005914	0.980829

The moderate and slow developmental stages were combined as the moderate-slow stage. CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing. ADOS, Autism Diagnostic Observation Schedule. SA-CSS, social affect calibrated severity score. RRB-CSS, restricted and repetitive behaviours calibrated severity score. CARS, Childhood Autism Rating Scale. DQ, developmental quotient.

Supplementary Table 11. Correlations of behavioural measurements and NDI in ASD without DD/ID during the moderate-slow stage

	CC Cluster		A-S Cluster		P-I Cluster	
	r	p	r	p	r	p
CARS Sum	0.123744	0.522476	0.117084	0.613253	0.236143	0.302754
CARS Human Relatedness	0.217323	0.257449	0.272756	0.231604	0.395822	0.075703
CARS Imitation	-0.04439	0.819146	0.080938	0.727265	0.147515	0.523401
CARS Affect	-0.07752	0.689394	-0.31554	0.163514	-0.12748	0.581857
CARS Use Of Body	0.015509	0.936357	0.034984	0.880335	0.056969	0.806243
CARS Relation To Objects	-0.12405	0.521437	0.020246	0.930588	0.095433	0.680711
CARS Adaptation To Change	-0.16766	0.384657	-0.01447	0.950362	0.11483	0.620149
CARS Visual Responsiveness	0.12971	0.502458	0.285677	0.209357	0.287554	0.206249
CARS Auditory Responsiveness	0.216471	0.259365	-0.08382	0.717928	0.076572	0.741478
CARS Near Receptor Responsiveness	-0.14593	0.450043	-0.27937	0.220035	-0.12606	0.586116
CARS Anxiety Reaction	-0.12277	0.525779	0.584998	0.005343	0.563182	0.007853
CARS Verbal Communication	0.168148	0.383259	0.22184	0.333813	0.278486	0.221555
CARS Nonverbal Communication	0.030868	0.873704	-0.06081	0.793445	0.19401	0.399411
CARS Activity Level	-0.13369	0.489329	0.21621	0.346537	0.070688	0.760763
CARS Intellectual Consistency	0.352134	0.066102	0.54913	0.012153	0.341323	0.140802
CARS Global Impression	-0.02574	0.894557	0.042247	0.855719	0.194798	0.39746
ADOS_SA_CSS	-0.06132	0.751997	0.164869	0.475121	0.213452	0.352871
ADOS_RRB_CSS	-0.29277	0.123249	-0.01389	0.952365	-0.28761	0.20616
Verbal IQ	-0.50964	0.018275	-0.32861	0.183056	-0.53279	0.022814
Performance IQ	0.324774	0.150874	0.514375	0.028963	0.371603	0.12892
Full IQ	-0.13083	0.571907	0.150832	0.550227	-0.12605	0.618223
SRS Total	-0.23185	0.299174	-0.12526	0.609375	-0.2297	0.344146
SRS Social Awareness	-0.5652	0.006124	-0.473	0.040826	-0.47918	0.037909
SRS Social Cognition	-0.12994	0.564375	-0.10339	0.673619	-0.00913	0.970412
SRS Social Communication	-0.17502	0.435954	0.010011	0.967556	-0.13158	0.591305
SRS Social Motivation	0.091237	0.686358	0.082519	0.736986	-0.11594	0.636467
SRS Autistic Mannerisms	-0.26721	0.229294	-0.18176	0.456442	-0.28515	0.236688

The moderate and slow developmental stages were combined as the moderate-slow stage. **The bold numbers:** False discovery rate (FDR) correction with Benjamini-Hochberg procedure for multiple comparisons, $p < 0.05$. CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing. ADOS, Autism Diagnostic Observation Schedule. SA-CSS, social affect calibrated severity score. RRB-CSS, restricted and repetitive behaviours calibrated severity score. SRS, Social Responsiveness Scale. CARS, Childhood Autism Rating Scale. IQ, intelligence quotient.

Supplementary Table 12. Correlations of behavioural measurements and NDI in ASD without DD/ID across the entire age

	CC Cluster		A-S Cluster		P-I Cluster	
	r	p	r	p	r	p
CARS Sum	-0.06234	0.68065	-0.00872	0.954155	0.170067	0.258491
CARS Human Relatedness	-0.0121	0.936369	0.027664	0.855191	0.107243	0.478081
CARS Imitation	-0.06107	0.686815	0.07801	0.606334	0.215696	0.14996
CARS Affect	-0.19586	0.192067	-0.16965	0.259693	0.051471	0.734075
CARS Use Of Body	-0.18988	0.206252	-0.05822	0.70072	-0.07173	0.635691
CARS Relation To Objects	-0.11801	0.434743	-0.05521	0.715564	0.070218	0.642857
CARS Adaptation To Change	-0.10076	0.505212	-0.11265	0.456043	0.012642	0.933544
CARS Visual Responsiveness	0.114324	0.449331	0.109533	0.468679	0.214351	0.152581
CARS Auditory Responsiveness	0.028775	0.849443	-0.09993	0.508746	-0.09888	0.513263
CARS Near Receptor Responsiveness	-0.16255	0.280438	-0.09053	0.549623	0.03938	0.794987
CARS Anxiety Reaction	-0.13756	0.361955	0.067532	0.655649	0.168376	0.263326
CARS Verbal Communication	0.014427	0.924189	-0.01069	0.94377	0.082956	0.583627
CARS Nonverbal Communication	-0.23667	0.113287	-0.23363	0.118125	-0.06033	0.690412
CARS Activity Level	0.003951	0.979207	0.098148	0.51639	0.107766	0.475927
CARS Intellectual Consistency	0.272204	0.07046	0.292091	0.051539	0.201672	0.184017
CARS Global Impression	-0.22649	0.130121	-0.16564	0.271262	0.089128	0.555837
ADOS_SA_CSS	-0.15379	0.307533	-0.08927	0.555195	0.073748	0.6262
ADOS_RRB_CSS	-0.37021	0.011327	-0.21176	0.157724	-0.20144	0.179459
Gross Motor DQ	0.399549	0.080927	0.456531	0.043032	0.454227	0.044231
Fine Motor DQ	0.339764	0.306648	0.307422	0.357767	0.240566	0.476121
Adaptive DQ	0.321875	0.166377	0.208055	0.378735	0.19454	0.411143
Language DQ	-0.19438	0.411537	-0.26761	0.254007	-0.30067	0.197711
Personal-Social DQ	0.027903	0.90704	-0.12431	0.60155	-0.05543	0.816467
Average DQ	0.143831	0.545196	-0.01102	0.963216	0.00558	0.981374
Verbal IQ	-0.50964	0.018275	-0.36535	0.1034	-0.54457	0.010695
Performance IQ	0.324774	0.150874	0.423124	0.055985	0.268423	0.239398
Full IQ	-0.13083	0.571907	0.050017	0.829529	-0.20603	0.370248
SRS Total	-0.23185	0.299174	-0.06123	0.786637	-0.09739	0.666339
SRS Social Awareness	-0.5652	0.006124	-0.37979	0.081266	-0.30731	0.164162
SRS Social Cognition	-0.12994	0.564375	-0.06906	0.760063	0.08807	0.696735
SRS Social Communication	-0.17502	0.435954	0.05782	0.798274	-0.03027	0.89361
SRS Social Motivation	0.091237	0.686358	0.115912	0.607477	-0.01026	0.963856
SRS Autistic Mannerisms	-0.26721	0.229294	-0.12782	0.570799	-0.20115	0.369387

The moderate and slow developmental stages were combined as the moderate-slow stage. **The bold numbers:** False discovery rate (FDR) correction with Benjamini-Hochberg procedure for multiple comparisons, $p < 0.05$. CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing. ADOS, Autism Diagnostic Observation Schedule. SRS, Social Responsiveness Scale. CARS, Childhood Autism Rating Scale. IQ, intelligence quotient.

Supplementary Table 13. Correlations analyses of ASD with DD/ID across the entire age

	CC Cluster		A-S Cluster		P-I Cluster	
	r	p	r	p	r	p
CARS Sum	-0.06944	0.494616	0.024163	0.812347	-0.09785	0.335257
CARS Human Relatedness	-0.04156	0.682951	0.008087	0.93668	-0.06714	0.509072
CARS Imitation	0.028235	0.781453	0.125661	0.215214	0.059572	0.558061
CARS Affect	0.00837	0.934465	0.042434	0.676651	-0.02831	0.780886
CARS Use Of Body	0.028943	0.776118	0.146898	0.146796	0.040926	0.687534
CARS Relation To Objects	0.098334	0.332879	0.176486	0.080558	0.102592	0.312263
CARS Adaptation To Change	-0.04571	0.653225	-0.05328	0.600442	-0.08747	0.389306
CARS Visual Responsiveness	0.001112	0.99133	0.051256	0.61621	-0.06729	0.5103
CARS Auditory Responsiveness	-0.01474	0.885483	0.075371	0.460752	-0.0903	0.376558
CARS Near Receptor Responsiveness	-0.23142	0.021864	-0.11887	0.243693	-0.15862	0.118755
CARS Anxiety Reaction	-0.05576	0.585549	-0.00415	0.967669	-0.0493	0.629752
CARS Verbal Communication	-0.09745	0.339781	-0.02398	0.814678	-0.03573	0.726851
CARS Nonverbal Communication	-0.01931	0.850346	0.062292	0.542301	-0.03521	0.730693
CARS Activity Level	-0.08278	0.41771	-0.02146	0.83386	-0.07631	0.455162
CARS Intellectual Consistency	0.050477	0.627122	0.114575	0.268899	0.092379	0.373259
CARS Global Impression	-0.01403	0.890975	0.051198	0.616611	-0.04701	0.645756
ADOS_SA_CSS	-0.02009	0.842759	-0.02914	0.7735	-0.07215	0.47565
ADOS_RRB_CSS	-0.16232	0.122128	-0.09685	0.358419	-0.13607	0.195912
Gross Motor DQ	-0.08784	0.479645	-0.1108	0.383398	-0.14535	0.251801
Fine Motor DQ	-0.25306	0.142445	-0.44326	0.007656	-0.365	0.031086
Adaptive DQ	-0.1321	0.2866	-0.25157	0.044931	-0.34292	0.005538
Language DQ	-0.1658	0.179963	-0.15319	0.226852	-0.09268	0.466352
Personal-Social DQ	-0.103	0.410507	-0.08364	0.514604	-0.11309	0.377521
Average DQ	-0.21881	0.075247	-0.2976	0.01693	-0.31344	0.011668
Verbal IQ	0.323374	0.087055	0.360169	0.054956	0.385929	0.038663
Performance IQ	0.200312	0.297471	0.1458	0.450451	0.278509	0.143475
Full IQ	0.320301	0.090273	0.305919	0.106545	0.333985	0.076612
SRS Total	-0.05847	0.734803	0.016175	0.9254	0.152188	0.375574
SRS Social Awareness	-0.09809	0.569251	-0.01136	0.947568	0.193235	0.258824
SRS Social Cognition	0.080959	0.638797	0.165324	0.335251	0.238078	0.162037
SRS Social Communication	-0.10624	0.537441	-0.10097	0.557901	-0.0162	0.925303
SRS Social Motivation	-0.05602	0.745549	-0.01393	0.935752	0.078648	0.648431
SRS Autistic Mannerisms	-0.03492	0.839781	0.090083	0.601333	0.234852	0.167971

The moderate and slow developmental stages were combined as the moderate-slow stage. **The bold numbers:** False discovery rate (FDR) correction with Benjamini-Hochberg procedure for multiple comparisons, $p < 0.05$. CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing. ADOS, Autism Diagnostic Observation Schedule. SRS, Social Responsiveness Scale. CARS, Childhood Autism Rating Scale. DQ, developmental quotient. IQ, intelligence quotient.

186 **Supplementary Table 14. Correlations of behavioural measurements and NDI in DD/ID across the**
187 **entire age**

	CC Cluster		A-S Cluster		P-I Cluster	
	r	p	r	p	r	p
CARS Sum	0.126581	0.412915	0.262585	0.085068	0.136254	0.377827
CARS Human Relatedness	-0.16424	0.286736	-0.04637	0.765008	-0.01235	0.936568
CARS Imitation	0.241413	0.114403	0.300669	0.047351	0.070556	0.649029
CARS Affect	0.186555	0.225312	0.253521	0.096812	0.179865	0.242685
CARS Use Of Body	-0.03728	0.810124	0.067339	0.664063	0.049637	0.74899
CARS Relation To Objects	0.103956	0.501879	0.180935	0.239849	0.138552	0.369758
CARS Adaptation To Change	0.082617	0.593928	0.191297	0.213531	0.057433	0.711154
CARS Visual Responsiveness	0.099946	0.518602	0.13411	0.385447	0.058108	0.70791
CARS Auditory Responsiveness	-0.20843	0.174549	-0.09965	0.519847	-0.05883	0.704435
CARS Near Receptor Responsiveness	0.205875	0.180011	0.290704	0.055573	0.213248	0.164573
CARS Anxiety Reaction	0.235977	0.123049	0.118322	0.444299	0.188611	0.220152
CARS Verbal Communication	-0.02211	0.886723	0.028972	0.851906	0.02001	0.897419
CARS Nonverbal Communication	0.056952	0.716794	0.119827	0.444052	0.060146	0.701626
CARS Activity Level	0.25441	0.095607	0.11848	0.443686	0.071618	0.644098
CARS Intellectual Consistency	-0.05152	0.739791	0.016445	0.915624	0.050285	0.74582
CARS Global Impression	0.241406	0.114415	0.311203	0.03976	0.209139	0.173055
ADOS_SA_CSS	0.202371	0.187701	0.300855	0.047207	0.317337	0.03582
ADOS_RRB_CSS	0.146787	0.341703	0.175904	0.253388	0.107158	0.488725
Gross Motor DQ	0.597944	0.089002	0.747946	0.020477	0.500181	0.170291
Fine Motor DQ	-0.50637	0.493627	0.936648	0.063352	0.601103	0.398897
Adaptive DQ	-0.07748	0.842955	0.066858	0.864304	-0.09494	0.808033
Language DQ	-0.51228	0.158529	-0.54962	0.125293	-0.51653	0.154521
Personal-Social DQ	-0.71834	0.029259	-0.72248	0.027904	-0.48395	0.186828
Average DQ	-0.18755	0.628952	-0.05192	0.89446	-0.23904	0.535624
Verbal IQ	-0.13187	0.487288	-0.13132	0.489122	-0.11817	0.533976
Performance IQ	-0.22128	0.239948	-0.23892	0.203551	-0.29613	0.112077
Full IQ	-0.34946	0.05837	-0.3663	0.046494	-0.43105	0.017402
SRS Total	-0.0208	0.926805	-0.09956	0.659356	-0.07086	0.754014
SRS Social Awareness	0.102327	0.650453	-0.01457	0.948698	-0.02888	0.898476
SRS Social Cognition	0.169786	0.450013	0.051292	0.820668	0.013921	0.950973
SRS Social Communication	-0.13475	0.549928	-0.18957	0.398139	-0.16118	0.473626
SRS Social Motivation	0.030698	0.892128	-0.0311	0.89073	0.104288	0.64418
SRS Autistic Mannerisms	-0.1771	0.430443	-0.20464	0.360953	-0.18203	0.417511

188 The moderate and slow developmental stages were combined as the moderate-slow stage. CC Cluster,
189 Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster.
190 ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical
191 developing. ADOS, Autism Diagnostic Observation Schedule. SA-CSS, social affect calibrated severity
192 score. RRB-CSS, restricted and repetitive behaviours calibrated severity score. SRS, Social
193 Responsiveness Scale. CARS, Childhood Autism Rating Scale. IQ, intelligence quotient.

Supplementary Table 15. Demographics and clinical measurements of children with ASD in longitudinal data.

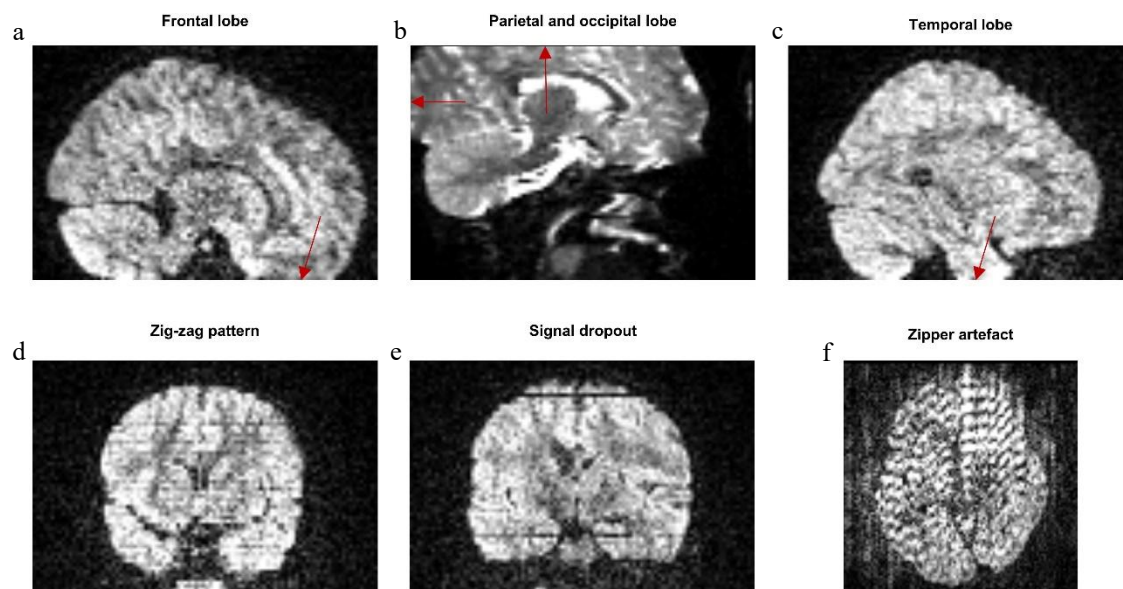
Scan times	Sample	Age, (years, mean $\pm$ sd)	Sex, (M/F)	ADOS_SA (mean $\pm$ sd)	ADOS_RRB (mean $\pm$ sd)	CARS_Sum (mean $\pm$ sd)	SRS_Sum (mean $\pm$ sd)	Average DQ (mean $\pm$ sd)	Full IQ (mean $\pm$ sd)
Time1	22	4.3 $\pm$ 2.0	19/3	8.3 $\pm$ 1.6	6.1 $\pm$ 2.1	36.7 $\pm$ 3.8	85.5 $\pm$ 26.9	68.0 $\pm$ 10.4	74.6 $\pm$ 25.5
Time2	22	5.5 $\pm$ 2.0	19/3	8.3 $\pm$ 1.1	4.2 $\pm$ 2.9	34.8 $\pm$ 4.2	72.1 $\pm$ 37.6	71.9 $\pm$ 12.5	70.1 $\pm$ 23.9
Time3	4	6.2 $\pm$ 3.1	3/1	8.8 $\pm$ 1.5	7.5 $\pm$ 0.6	37.4 $\pm$ 2.87	94.8 $\pm$ 9.7	/	55.5 $\pm$ 15.8
Time4	1	6.05	0/1	10	8	38	107	/	45

ASD, autism spectrum disorder. ADOS, Autism Diagnostic Observation Schedule. ADOS_SA, The ADOS calibrated severity scores of social affects. ADOS_RRB, The ADOS calibrated severity scores of restricted, repetitive behaviour. SRS, Social Responsiveness Scale. CARS, Childhood Autism Rating Scale. DQ, developmental quotient. IQ, intelligence quotient.

Supplementary Table 16. Significant associations between metabolites and the mean NDI of each white matter cluster.

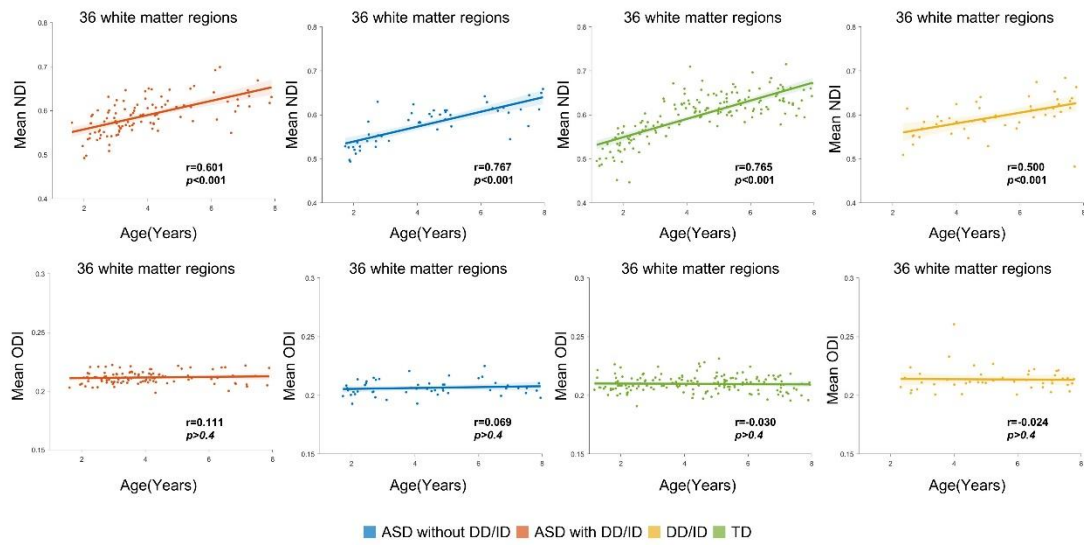
Metabolites	WM clusters	beta	pval
Creatine	A-S Cluster	0.02	0.01
3-Hydroxyanthranilic acid	A-S Cluster	0.04	0.00
Alloxan	P-I Cluster	0.02	0.01
p-Hydroxymandelic acid	P-I Cluster	0.03	0.00
Pelargonin	P-I Cluster	0.01	0.01
3-Hydroxyanthranilic acid	P-I Cluster	0.03	0.00

CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. NDI, neurite density index. WM, white matter.



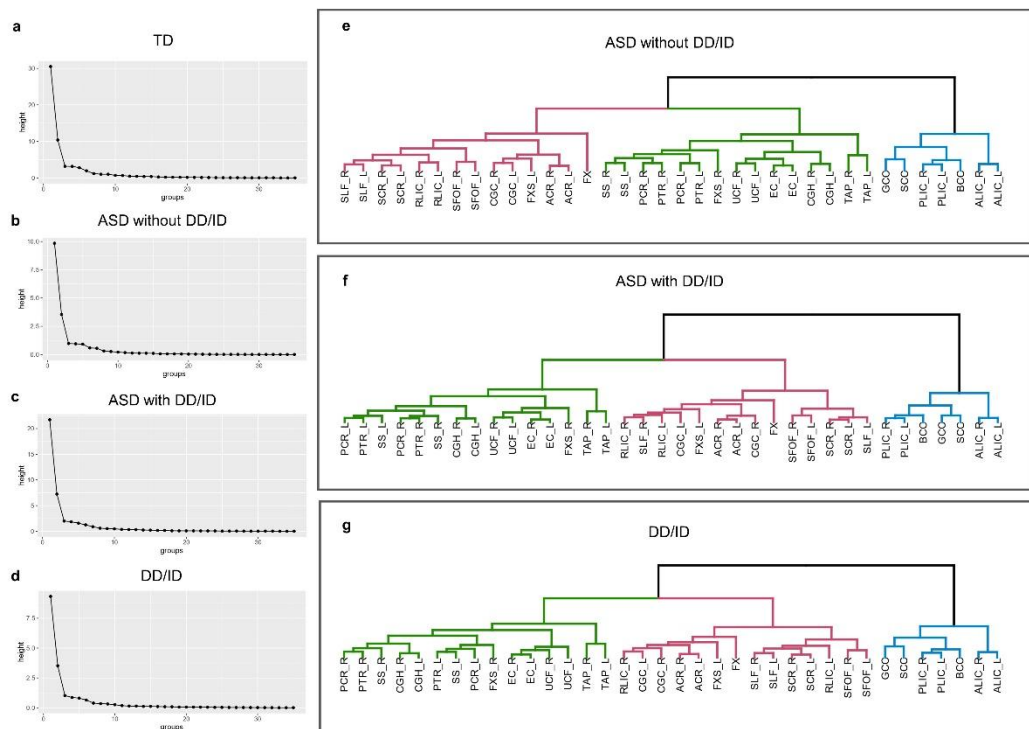
Supplementary Fig. 1. Images with the incomplete coverage, signal dropout, zig-zag pattern and zipper artefact

Incomplete cerebral coverage in the frontal (a), parietal and occipital (b), and temporal lobes (c) (red arrows indicate affected areas). Artifacts from head motion producing zig-zag patterns (d), signal dropout from motion (e), and zipper artifacts from radio frequency (RF) breakthrough (f).



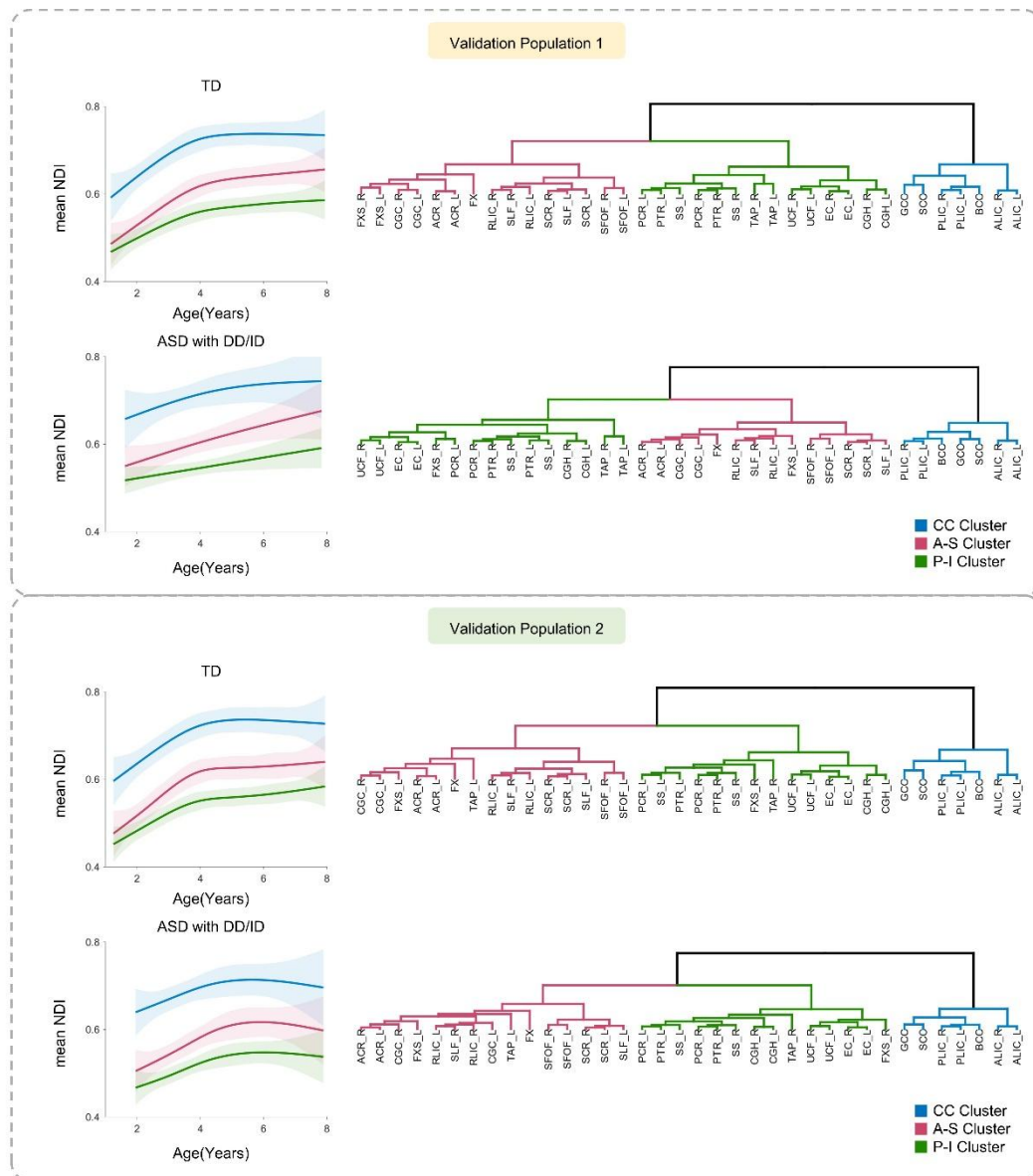
Supplementary Fig. 2. The evolution of NODDI metrics across the early childhood

ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability. TD, typical developing. ODI, orientation dispersion index. NDI, neurite density index.



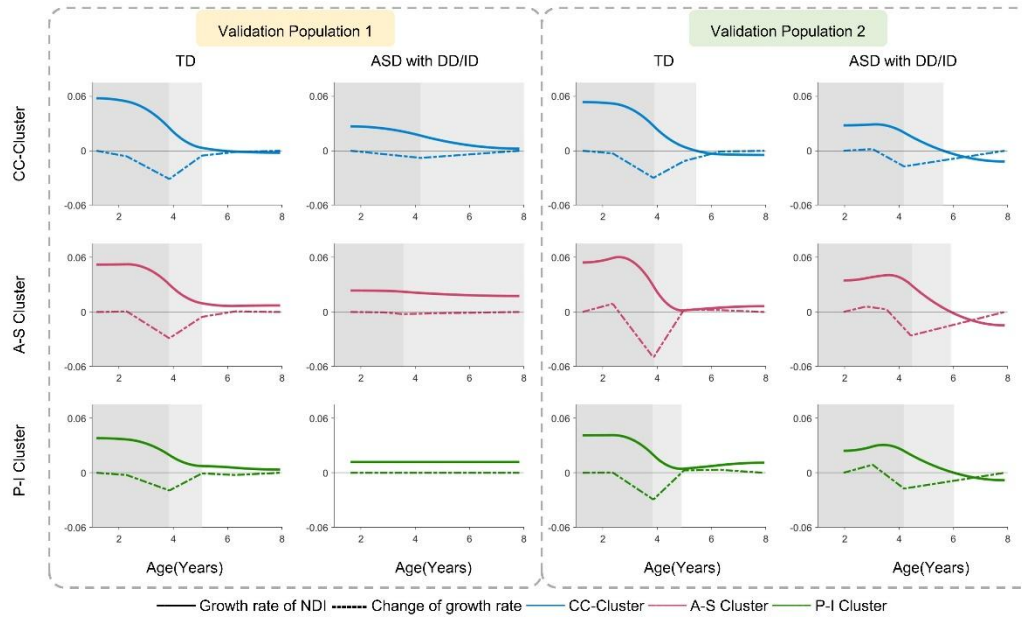
Supplementary Fig. 3. Knee plots of inter-cluster Euclidean distances and hierarchical dendrograms.

hybrid hierarchical clustering analysis was conducted using the mean NDI value of the 36 core white matter regions into clusters for all four groups. For each group, the optimal number of clusters was chosen as the “knee point” on the inter-cluster distance vs. the number of cluster plots (the left column). The clustering results were consistent in all four groups. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability. TD, typical developing.



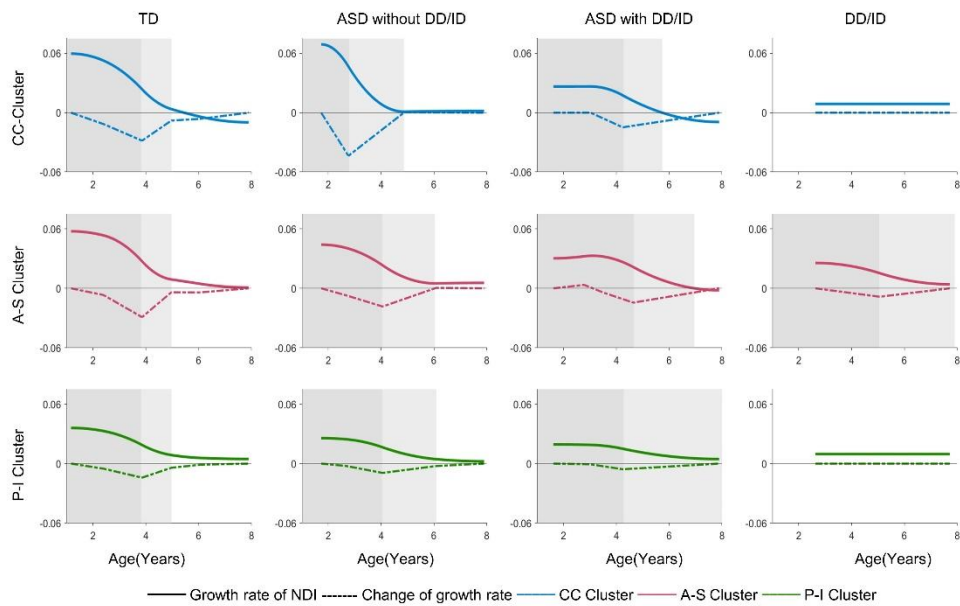
Supplementary Fig. 4. Clustering results and developmental curves of each validation group in Splitting analyses

Due to the limited sample size, the split-half validation analyses were only performed in the ASD with DD/ID and TD groups. we divided 105 ASD with DD/ID and 160 TD children into two validation populations: 1) Validation Population 1, 53 ASD with DD/ID children (7 females) and 80 TD children (41 females); 2) Validation Population 2, 52 ASD with DD/ID children (6 females) and 80 TD children (39 females). For the clustering analyses, most results of the validation populations were consistent with the main findings except for those of 2 white matter regions (right fornix (cres) and/or stria terminalis and left tapetum). ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability. TD, typical developing.



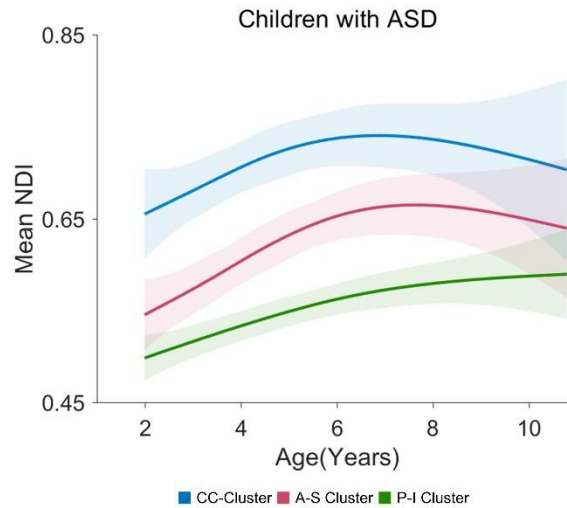
Supplementary Fig. 5. Growth rates and developmental stages of each validation group in Splitting analyses

Due to the limited sample size, the split-half validation analyses were only performed in the ASD with DD/ID and TD groups. we divided 105 ASD with DD/ID and 160 TD children into two validation populations: 1) Validation Population 1, 53 ASD with DD/ID children (7 females) and 80 TD children (41 females); 2) Validation Population 2, 52 ASD with DD/ID children (6 females) and 80 TD children (39 females). The developmental curves for all validation populations were almost consistent with the main results. The only exception was that the developmental curve of the P-I Cluster of ASD with DD/ID children in Validation Group 1 tended to be linear. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability. TD, typical developing.



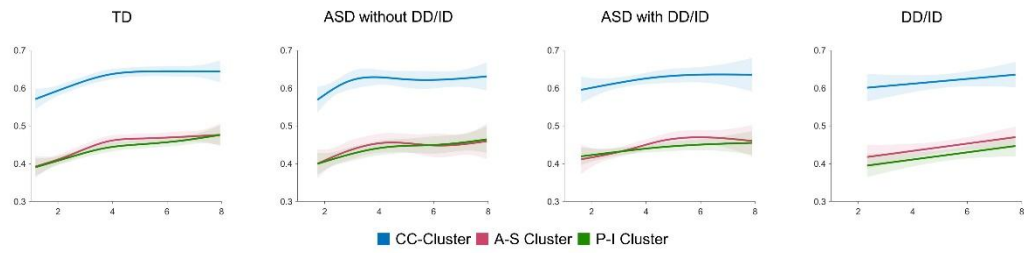
Supplementary Fig. 7. Growth rates and developmental stages in male-only sample

We applied the curve fitting to all four male-only groups (79 TD, 37 DD/ID, 42 ASD without DD/ID, and 92 ASD with DD/ID). The results across the four groups were also mostly consistent with the main findings. A minor change was observed in the developmental curve of the A-S Cluster for the DD/ID group, whose growth rates were still very slow but showed mild staging features. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability. TD, typical developing.

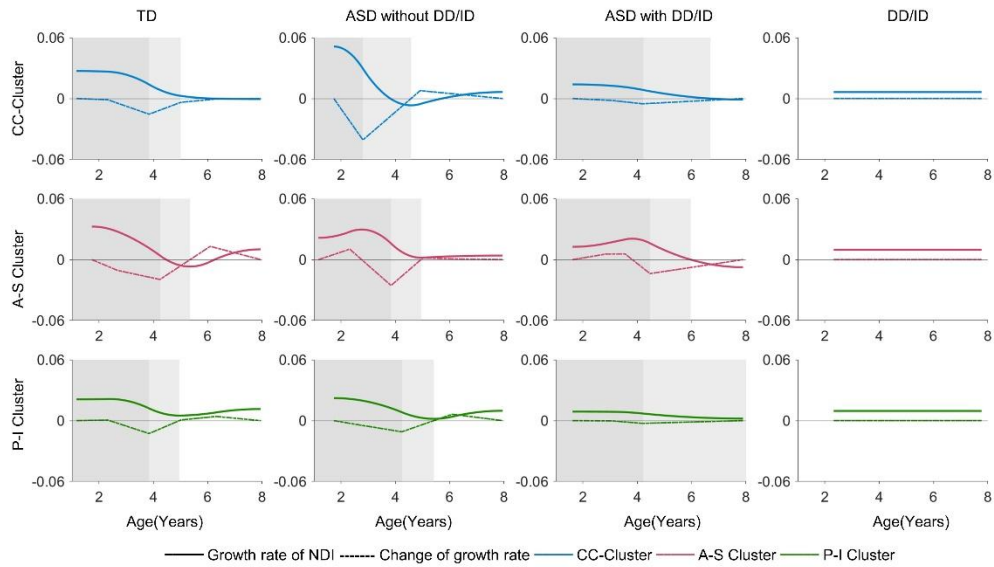


Supplementary Fig. 8. Developmental curves of NDI in white matter clusters of the longitudinal sub dataset in ASD.

CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing. ASD, autism spectrum disorder. NDI, neurite density index.



Supplementary Fig. 9. Developmental curves of FA in white matter clusters of each group
 Developmental trajectories of FA in the three white matter clusters were delineated using the cross-section dataset. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability. TD, typical developing. CC Cluster, Corpus Callosum Cluster. A-S Cluster, Anterior-Superior Cluster. P-I Cluster, Posterior-Inferior Cluster. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability, TD, typical developing.



Supplementary Fig. 10. Growth rates of early white matter maturation based on FA

Developmental trajectories of FA in the three white matter clusters were delineated using the cross-section dataset. The growth rates of FA were calculated by the first derivative of developmental curves (solid line). The changes of rates were represented by the derivative of growth rate (dotted line). According to the changes of rates for all white matter clusters, three developmental stages were defined: fast, moderate and slow stages (shadow areas) except DD/ID group. ASD, autism spectrum disorder. DD/ID, developmental delay/intellectual disability. TD, typical developing.