

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study.

For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a Confirmed

- ☒ The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
- ☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- ☒ The statistical test(s) used AND whether they are one- or two-sided
Only common tests should be described solely by name; describe more complex techniques in the Methods section.
- ☒ A description of all covariates tested
- ☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
- ☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
- ☒ For null hypothesis testing, the test statistic (e.g. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted
Give P values as exact values whenever suitable.
- ☒ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
- ☒ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
- ☒ Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection No software was used in data collection.

Data analysis
 Matlab 2020a
 R 3.6.0
 R 4.2.1
 The hybrid hierarchical clustering algorithm was implemented in the "hybridHclust" package (hybridHclust version 1.0-5); freely available for download on Github (<https://github.com/cran/hybridHclust/blob/master/R/hybridhclust.R>) and implemented in R 3.6.0.
 The generalized additive model was conducted in the "mgcv" package (mgcv version 1.8-41); freely available for download in R on CRAN (<https://cran.r-project.org/web/packages/mgcv/>) and implemented in R 4.2.1.
 MRtrix3 (www.mrtrix.org).
 FSL version 6.0.6 (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSL>).
 NODDI MATLAB toolbox (https://www.nitrc.org/projects/noddi_toolbox).
 NiftyReg (<http://cmictig.cs.ucl.ac.uk/wiki/index.php/NiftyReg>).
 DTI-TK (<https://dti-tk.sourceforge.net/>).

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [guidelines for submitting code & software](#) for further information.

Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

Access to the de-identified participant research data must be approved by the research ethics board on a case-by-case basis, please contact the corresponding authors (feili@shsmu.edu.cn, mcao@fudan.edu.cn, jiajing.zhang@bupt.edu.cn) for assistance in data access request.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender

The ASD with DD/ID sample used in the analyses included N = 105 (ages 1.62-7.89); N_male = 92 male (ages 1.62-7.89); N_female = 13 female (ages 2.07-4.90). The ASD without DD/ID sample used in the analyses included N = 51 (ages 1.73-7.95); N_male = 42 male (ages 1.73-7.90); N_female = 9 female (ages 2.19-7.95). The TD sample used in the analyses included N = 160 (ages 1.17-7.94); N_male = 79 male (ages 1.17-1.89); N_female = 81 female (ages 1.35-7.94). The DD/ID sample used in the analyses included N = 48 (ages 2.32-7.77); N_male = 37 male (ages 2.63-7.72); N_female = 11 female (ages 2.32-7.77).

Reporting on race, ethnicity, or other socially relevant groupings

All of participants in the study are Chinese.

Population characteristics

This study included a sample of 364 participants before 8 years old, comprising 160 TD children (age range: 1.17-7.94 years, 49.4% males), 51 children diagnosed as ASD without DD/ID (age range: 1.73-7.95 years, 82.4% males), 105 children diagnosed as ASD with DD/ID (age range: 1.62-7.89 years, 87.6% males), and 48 children with DD/ID (age range: 2.32-7.77 years, 35.2% males). A total of 40 participants were excluded after MR image quality control. The ADOS SA-CSS and the RRB-CSS, CARS and SRS were used to assess social-related clinical phenotypes. The DQ was assessed by the GDS for children younger than 4 years. The IQ was assessed by the WPPSI for 4- to 6-year-old children and the WISC-R for children older than 6 years. TD children had a higher average DQ and full IQ than all three groups of children with atypical development. There was no significant difference in either the DQ or IQ between the DD/ID and ASD with DD/ID groups. Both of the ASD subgroups had more severe social deficits than the TD and DD/ID groups.

Recruitment

Participants were recruited in the neurodevelopmental project - Shanghai Autism Early Development Cohort (SAED) in Xinhua Hospital affiliated to Shanghai Jiao Tong University.

Ethics oversight

The study was conducted in accordance with the Declaration of Helsinki, with approval from the Ethical Committee of the Xinhua Hospital Affiliated to Shanghai Jiao Tong University, and in compliance with all applicable laws and regulations. All necessary biosecurity and institutional safety protocols were followed during the study.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size

No sample size calculation was performed. Sample size was based on the number of subjects collected in the existing data sets.

Data exclusions

The diffusion-weighted MR images of all participants were visually checked to ensure image quality in this study. We assessed the diffusion-weighted MR images carefully from the following aspects: 1) the coverage of cerebral regions (occipital/parietal/temporal/frontal lobes) was complete; 2) signal dropout due to head motion or zig-zag patterns had occurred; and 3) zipper artefacts, the most common equipment artefacts, were caused by radio frequency (RF) break-through. Images were excluded if they met the following exclusion criteria: 1) more than 3 volumes (more than 5% of all volumes) that exhibited signal dropout, zigzag patterns and/or zipper artefacts; and 2) incomplete coverage of the 36 selected core white matter ROIs. Based on these criteria, a total of 40 participants were excluded, including 16 ASD with DD/ID, 5 ASD without DD/ID, 17 TD and 2 DD/ID children.

Replication

To validate our findings, we performed validation analyses in split-half samples and male-only population and longitudinal data. Across all

Replication

validation groups with cross-sectional data, the clustering results and developmental curves were mostly consistent with the main findings. We fitted the developmental curves of FA (a common metric derived from DTI) in each white matter cluster and found similar growth patterns. Furthermore, the longitudinal data of ASD children was used to assess the reliability of findings on the developmental curves of three white matter clusters. And we observed similar developmental patterns, indicating NDI increased with age before 8 years old, with the highest growth rate observed in the A-S cluster.

Randomization

The authors conducted analysis of an existing dataset, so subject randomization was not applicable.

Blinding

The authors conducted analysis of an existing dataset, so blinding was not applicable.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

- n/a Involved in the study
- ☒ ☐ Antibodies
- ☒ ☐ Eukaryotic cell lines
- ☒ ☐ Palaeontology and archaeology
- ☒ ☐ Animals and other organisms
- ☒ ☐ Clinical data
- ☒ ☐ Dual use research of concern
- ☒ ☐ Plants

Methods

- n/a Involved in the study
- ☒ ☐ ChIP-seq
- ☒ ☐ Flow cytometry
- ☐ ☒ MRI-based neuroimaging

Plants

Seed stocks

No plants involved in the study.

Novel plant genotypes

No plants involved in the study.

Authentication

No plants involved in the study.

Magnetic resonance imaging

Experimental design

Design type

Resting state

Design specifications

For children with high compliance, MR scans were performed without additional preparations. Otherwise, sedation with chloral hydrate orally or by enema before the MR scan, a common preparation strategy for paediatric MR examinations, was given under the supervision and careful guidance of experienced nurses.

Behavioral performance measures

None

Acquisition

Imaging type(s)

diffusion MRI

Field strength

3.0T for all subjects

Sequence & imaging parameters

An echo-planar imaging (EPI) sequence was employed for multi-shell diffusion-weighted MR imaging, and its parameters were as follows: 65 axial slices; echo time (TE) = 84 ms; repetition time (TR) = 14500 ms; field of view (FOV) = 192 mm × 192 mm; voxel size = 2×2×2 mm³.

Area of acquisition

Whole-brain scan was used for all subjects.

Diffusion MRI

☒ Used

☐ Not used

Parameters Two shells with diffusion weighting of $b=1000$ and 2000 s/mm²; 30 directions for each shell; 3 additional b0 images without diffusion weighting ($b = 0$ s/mm²); a posterior-to-anterior phase-encoding direction; and a total acquisition time ~ 15 minutes.

Preprocessing

Preprocessing software	MRtrix3 (www.mrtrix.org) and FSL version 6.0.6 (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSL). More details can be found in the Methods section, 'Diffusion MR image quality control and processing'.
Normalization	The registrations involved were conducted using NiftiReg and DTI-TK. Notably, we chose skeletonized core white matter ROIs here to 1) minimize the potential bias of inaccuracies in registration and 2) avoid the influences of subjective experience on white matter anatomy. For all the participants, their NDI maps were transformed from the native space into the space of the corresponding study-specific age-specific tensor template. The transformation matrix was estimated by registering the tensor maps from the native space into the study-specific, age-specific tensor template.
Normalization template	We first warped the labels of ICBM-DTI-81 white matter atlas into the study-specific group tensor template; 2) we then multiplied the masks of the core white matter ROIs and the white matter skeleton of the whole sample; and 3) finally, we warped the labels of the skeletonized core white matter ROIs into study-specific age-specific tensor templates (one per year, seven in total). The study-specific age-specific tensor templates were created from tensor maps of a selective subset of participants within the same year. Then, the group-specific tensor template was created using these seven age-specific tensor templates and was further used to create the white matter skeleton of the whole sample.
Noise and artifact removal	Diffusion-weighted MR images were first preprocessed using MRtrix3 and FSL version 6.0.6. The preprocessing steps were as follows: 1) denoising; 2) removing the Gibbs ring; 3) eddy-current distortion and motion correction using the FSL eddy; and 4) B1 bias correction using the Ants algorithm.
Volume censoring	None.

Statistical modeling & inference

Model type and settings	We used hybrid hierarchical clustering algorithm to classified white matter clusters and generalized additive model to fit developmental curves.
Effect(s) tested	We computed the mean NDI of the 36 core white matter ROIs for clustering analysis and developmental curves modeling.
Specify type of analysis:	☐ Whole brain ☒ ROI-based ☐ Both
Anatomical location(s)	We chose 36 core white matter ROIs in the cerebrum.
Statistic type for inference (See Eklund et al. 2016)	We computed the mean NDI value of all voxels in each ROI and the mean NDI of the 36 core white matter ROIs for statistic analysis.
Correction	Tukey's honest significant difference criterion was performed for all P values resulting from ANOVA in group comparison of demographics. Benjamini-Hochberg correction of the FDR was performed for all P values resulting from GLM or partial correlation analysis.

Models & analysis

n/a	Involved in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☐	☒ Multivariate modeling or predictive analysis
Multivariate modeling and predictive analysis	We used generalized additive model to fit developmental curves. We included sex and head motion during the MR scan in the GAM. General linear model (GLM) was used to evaluate group differences. Age, sex, and head motion during the MRI scan were included as covariates to account for potential confounding effects. We performed partial correlation analyses between the NDI of white matter clusters and cognitive performance as well as clinical scores. Age, sex, and head motion during the MRI scan were included as covariates to account for potential confounding effects.