

Doi:10.32604/chd.2025.072242





ARTICLE

A Comprehensive Brain MRI and Neurodevelopmental Dataset in Children with Tetralogy of Fallot

Yang Xu^{1,#}, Yaqi Zhang^{2,#}, Meijiao Zhu³, Pengcheng Xue⁴, Siyu Ma¹, Di Yu¹, Liang Hu¹, Yuxi Zhang¹, Wei Peng¹, Jirong Qi¹, Xuyun Wen⁴, Ming Yang³ and Xuming Mo^{1,2,5,*}

Received: 22 August 2025; Accepted: 31 October 2025; Published: 30 November 2025

ABSTRACT: Background: The life-course management of children with tetralogy of Fallot (TOF) has focused on demonstrating brain structural alterations, developmental trajectories, and cognition-related changes that unfold over time. Methods: We introduce an magnetic resonance imaging (MRI) dataset comprising TOF children who underwent brain MRI scanning and cross-sectional neurocognitive follow-up. The dataset includes brain three-dimensional T1-weighted imaging (3D-T1WI), three-dimensional T2-weighted imaging (3D-T2WI), and neurodevelopmental evaluations using the Wechsler Preschool and Primary Scale of Intelligence–Fourth Edition (WPPSI-IV). Results: Thirty-one children with TOF (age range: 4–33 months; 18 males) were recruited and completed corrective surgery at the Children's Hospital of Nanjing Medical University, Nanjing, China. Aiming to promote the neurodevelopmental outcomes in children with TOF, we have meticulously curated a comprehensive dataset designed to dissect the complex interplay among risk factors, neuroimaging findings, and adverse neurodevelopmental outcomes. Conclusion: This article aims to introduce our open-source dataset on neurodevelopment in children with TOF, which covers the data types, data acquisition and processing methods, the procedure for accessing the data, and related publications.

KEYWORDS: Tetralogy of Fallot; neurodevelopment; dataset; congenital heart disease

1 Introduction

Congenital heart disease (CHD) is one of the most common birth defects worldwide, with an incidence rate of approximately 9.41 per 1000 births. Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart disease (CCHD) in Asia, accounting for 7–10% of CHD [1]. Over the past decade, advances in surgical techniques for CHD have enabled an increasing number of children with TOF to reach adulthood and even geriatrics [2]. Studies have found that 50% of children with CCHD may experience neurodevelopmental disorders (NDDs) at different stages of their life cycles [3]. The primary manifestations include cognitive and attentional impairments [4,5], motor and communication deficits [6,7], as well as delays in executive function [8]. These symptoms can emerge as early as infancy and may persist through adolescence and beyond [9,10]. There has been increased focus on the NDDs and mental health of patients with these conditions [11]. The American Heart Association has identified addressing neurodevelopmental dysfunction in children with CHD as one of the most critical challenges of the 21st century [12]. Therefore, the



¹Department of Cardiothoracic Surgery, Children's Hospital of Nanjing Medical University, Nanjing, 210008, China

²Nanjing Children's Hospital, Clinical Teaching Hospital of Medical School, Nanjing University, Nanjing, 210008, China

³Department of Radiology, Children's Hospital of Nanjing Medical University, Nanjing, 210008, China

⁴College of Artificial Intelligence, Nanjing University of Aeronautics and Astronautics, Jiangning District, Nanjing, 211106, China

⁵State Key Laboratory of Reproductive Medicine and Offspring Health, Nanjing Medical University, Nanjing, 210008, China

^{*}Corresponding Author: Xuming Mo. Email: mohsuming15@sina.com

^{*}These authors contributed equally to this work as joint the first author

identification and intervention of NDDs become particularly crucial. The relationship between risk factors, imaging findings, and adverse neurodevelopmental outcomes in children with TOF remains a significant unresolved issue. Therefore, we have established this dataset to provide support for improving their neurodevelopmental outcomes.

Brain magnetic resonance imaging (MRI) changes in children with CHD are closely associated with NDDs. These changes are currently known to be related to chronic preoperative cerebral hypoxia, perioperative inflammatory responses, intraoperative reperfusion, and rapid changes in body temperature leading to brain injury [8,13]. During the perioperative period, children experience significant hemodynamic alterations due to anesthesia and surgery, which may represent a critical window for intervention. Advancements in neuroimaging technology have broadened our understanding of NDDs in the context of CCHD. The common risk factors are concentrated in the perioperative period, mainly including cardiopulmonary bypass, cerebral perfusion during bypass [14], postoperative arrhythmias, low cardiac output, and prolonged mechanical respiratory support [15-17]. These factors are all associated with adverse neurodevelopmental outcomes, but the specific mechanisms remain unclear. Total brain volume, white matter volume, cortical volume, and deep gray matter volume are smaller in patients with CCHD [18,19]. Structural MRI studies have detected a correlation between larger hippocampal volume and better memory in children with CCHD [20]. Additionally, symmetry of brain sulci and increased brain volume are associated with better neurodevelopmental outcomes in adolescents with CCHD, including intelligence quotient (IQ), executive function, and attention [21-24]. Compared to structural brain abnormalities, the relationship between microstructural changes in the brains of children with CCHD and functional outcomes is more consistent. Early alterations in brain structure and function may arise from subsequent remodeling of microstructural integrity and functional network organization [25]. However, neuroimaging findings remain fragmented across the research. In addition, the complete pattern of brain changes and developmental trajectories in children with TOF remain unclear. These findings are hard to integrate into detailed mechanistic research or routine clinical practice., necessitating long-term developmental monitoring and follow-up. Therefore, establishing a dataset that includes imaging and clinical information is crucial for the prediction and early diagnosis of adverse neurodevelopmental outcomes.

Here, we introduce a comprehensive knowledgebase pertaining to children with TOF, which addresses the paucity of CHD neurodevelopmental databases within the international scientific community. The dataset is intended to facilitate the prediction and early auxiliary diagnosis of poor neurodevelopmental outcomes, enable researchers to replicate previous findings, and provide an empirical basis for mapping the evolving structural and functional trajectories of the developing brain in TOF children. Moreover, it serves as a small-sample benchmark for artificial intelligence algorithms in children with TOF, thereby promoting algorithm optimization and external validation.

2 Methods

2.1 Overall Design

The aim of our study is to build a representative, multidimensional dataset focusing on the neurodevelopmental outcomes of children with TOF following surgical intervention. Our dataset is single-center, covering children with TOF who underwent surgery between 2019 and 2023 at the Children's Hospital of Nanjing Medical University. Children with TOF are at a higher risk for NDDs. Our long-term goal is to expand this dataset to cover a broader population and geographic area to better understand the impact of TOF on neurodevelopment (Fig. 1).

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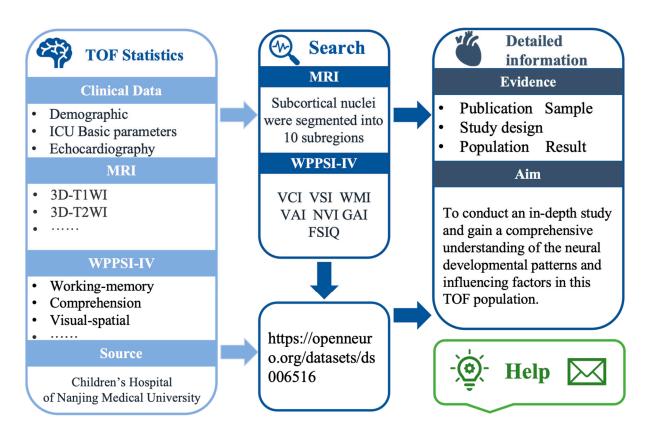


Figure 1: Overview of the framework of CHDbase. TOF, Tetralogy of Fallot; ICU, Intensive Care Unit; MRI, Magnetic Resonance Imaging; WPPSI-IV, Wechsler Preschool and Primary Scale of Intelligence–Fourth Edition; VCI, verbal comprehension index; VSI, visual-spatial index; WMI, working memory index; VAI, vocabulary acquisition index; NVI, non-verbal index; GAI, general ability index.

2.2 Participants

Thirty-one children (18 males, aged 4 to 33 months) recruited for the study were admitted for treatment at the Cardiac Center of the Children's Hospital of Nanjing Medical University from January 2019 to December 2023. The inclusion criteria are as follows: children aged 0–3 years with a confirmed diagnosis of TOF who underwent corrective surgery and completed scheduled postoperative neurodevelopmental assessments. The exclusion criteria are as follows: (1) Presence of diseases in other organs/systems; (2) History of traumatic brain injury or prior use of psychotropic medications; (3) Cardiopulmonary bypass (CPB) surgeries performed after the age of three years; (4) Incomplete corrective surgery for TOF; (5) Inability to meet the requirements for the Wechsler Preschool and Primary Scale of Intelligence–Fourth Edition (WPPSI-IV) testing; and (6) Loss to follow-up. All children with TOF underwent neurodevelopmental assessments and brain MRI scans during postoperative follow-up. All data collected were meticulously cross-verified with the information provided by the caregivers of the participants to ensure accuracy.

2.3 Clinical and Demographic Metrics

The data collection process encompassed multiple facets that could potentially influence neurodevelopmental outcomes. Key clinical variables extracted from electronic medical records included: age, male, preoperative resting oxygen saturation, history of hypoxic spells, and degree of cyanosis. Body mass index, McGoon index, aortic override, pulse oxygen saturation, ventricular septal defect (VSD), CPB time, aortic cross-clamp time, and duration of hospital stay, were extracted from electronic medical records.

Questionnaires were used to assess maternal education and family annual income, as these factors are known to influence neurodevelopment.

3 Neurodevelopmental Assessment

Children with TOF underwent a neurodevelopmental assessment of WPPSI-IV after discharge from the hospital. The WPPSI-IV testing was conducted by specifically trained personnel. Testing was carried out by two examiners, one administering and one observing, while parents waited outside. The assessors were professionally trained and qualified to conduct this evaluation. After a 5-min acclimation period in a standardized room, each child was assessed using the age-appropriate record form. Brief rapport and comfort checks (e.g., hunger, discomfort) were performed before testing began. According to the participant's age, two different scoring books were applied: one for children aged 2 years 6 months to 3 years 11 months, and the other for those aged 4 years to 6 years 11 months. Younger children (aged 2 years 6 months to 3 years 11 months) completed seven subtests. Results yielded the full-scale IQ (FSIQ) along with three primary composite scores—verbal comprehension index (VCI), visual-spatial index (VSI), and working memory index (WMI)—and three ancillary composite scores: vocabulary acquisition index (VAI), non-verbal index (NVI), and general ability index (GAI). Older children (aged 4 years to 6 years 11 months) completed thirteen subtests. From these, the fluid reasoning index (FRI) and processing speed index (PSI) were added as primary composite scores, and the cognitive efficiency index (CEI) was also derived as an ancillary composite score.

All raw scores from the subtests were converted to standardized scores based on the age-specific norms provided in the WPPSI-IV manual. The primary outcome metric was the FSIQ, which has a population mean of 100 and a standard deviation of 15. The primary index scores were also analyzed to identify potential domain-specific cognitive weaknesses. According to the test's standardized classification system:

Scores ≥90 are classified as Average to High Average.

Scores between 80-89 are classified as Low Average.

Scores between 70-79 are classified as Borderline.

Scores ≤69 are classified as Extremely Low.

3.1 MRI Acquisition and Processing

3.1.1 Acquisition

Philips Ingenia 3.0T MR (Ingenia 3.0, Philips Healthcare, Best, Netherlands) scanner, head 16-channel coil, with parental consent, Children < 3 years old were sedated with 5% chloral hydrate (1 mL/kg) 20 min before scanning, and earplugs and foam were used to reduce scanning noise and head movement noise, respectively, after sleeping. Scanning sequence: three-dimensional T1-weighted (3D-T1WI) images high-resolution structural image (ultra-fast gradient Echo sequence): TE = 3.5 ms, TR = 7.9 ms, FOV = 200 \times 200 \times 200 mm, slice thickness 1 mm, acquisition time = 4 min 24 s; Axial three-dimensional T2-weighted (3D-T2WI) (fast spin echo): TE = 110 ms, TR = 4000 ms, FOV = 200 \times 200 \times 119 mm, section thickness 5 mm, acquisition time = 1 min 28 s; Two experienced pediatric neuroradiologists, blinded to each participant's medical history, independently reviewed all images. In cases where there was a difference of opinion, a consensus was reached through discussion.

3.1.2 3D-T1WI Processing

3D-T1WI images were processed with FreeSurfer v6.0 (https://surfer.nmr.mgh.harvard.edu, accessed on 22 August 2025) using the automated recon-all pipeline, and the quality of the preprocessed images was verified. The subcortical nuclei were segmented into 7 subregions (Fig. 2): left thalamus proper nucleus

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(LTHA), left amygdala nucleus (LAM), right thalamus proper nucleus (RTHA), right caudate nucleus (RCAU), right putamen nucleus (RPU), right pallidum nucleus (RPA), and right amygdala nucleus (RAM).

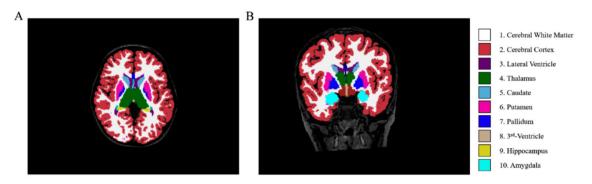


Figure 2: Schematic diagram of brain region segmentation results processed by FreeSurfer. (A) (axial view) and (B) (coronal view) display a 3D T1-weighted MRI scan with segmented subcortical structures. The color codes are as follows: cerebral white matter (1), cerebral cortex (2), lateral ventricle (3), thalamus (4), caudate (5), putamen (6), pallidum (7), third ventricle (8), hippocampus (9), and amygdala (10).; Note: Adapted from Ref. [19].

3.1.3 Data Records

The dataset is available at Open Neuro (https://openneuro.org/datasets/ds006556, accessed on 22 August 2025). The database comprises neurodevelopmental data from 31 children who have undergone surgery for TOF. To protect participant privacy, all data were de-identified prior to analysis. Personal identifying information was removed, and data were anonymized to ensure that no individual could be identified. The "DATA" folder contains 31 subfolders labeled with de-identified participant ID numbers (e.g., sub-01, sub-02). Each folder contains subfolders labeled "anat" which include T1WI and T2WI structural images. The T1WI and T2WI imaging data of each subject are stored in NIfTI format (.nii.gz), while the corresponding metadata are stored in JSON format (.json). We have provided a flowchart for data download, facilitating quick access to the data for users (Fig. 3).

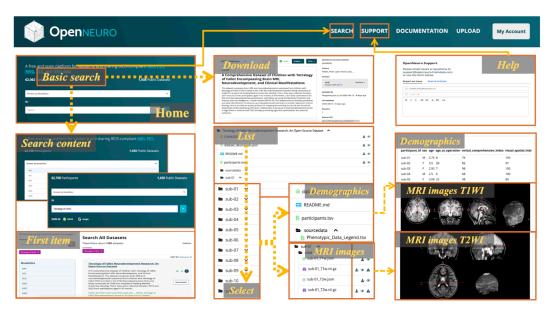


Figure 3: The web interface of OpenNeuro TOF dataset. The major components of the web interface of OpenNeuro are shown.

4 Results

Table 1 exhibits the individual and clinical characteristics of children with TOF. A total of 31 children with TOF were enrolled (age 4–33 months; 18 males). Assessment of preoperative hypoxia status revealed that no patient had a history of hypoxic spells. The median preoperative resting oxygen saturation was 100% (98%, 100%). The median hospital stay was 26 (20, 29) days, and the McGoon index was 1.71 \pm 0.33. Table 2 presents the specific numerical values measured by MRI for subcortical nuclei volume. The subcortical nuclei volumes were segmented into the basal ganglia (caudate: 3491.20 \pm 409.66 mm³, putamen: 4915.39 \pm 630.88 mm³, globus pallidus: 1658.21 \pm 224.93 mm³), amygdala (left: 1294.87 \pm 165.42 mm³, right: 1477.87 \pm 179.84 mm³), and thalamus (left: 6811.93 \pm 691.86 mm³, right: 6557.80 \pm 750.39 mm³).

Table 1: Individual and Clinical Characteristics.

Variables	TOF	Variables	TOF
Age of surgery, mon	9 (7, 16)	Aortic override, %	0.5 (0.5, 0.5)
Male, %	18 (58%)	McGoon	1.71 ± 0.33
BMI	15.87 ± 1.95	Pre-RVOT-PG, mmHg	66.39 ± 14.78
Preoperative SpO2, %	100 (98, 100)	Post-RVOT-PG, mmHg	16 (12, 20)
Preoperative hypoxic spells, %	0	VT, mL	81.55 ± 19.44
Time of surgery, min	185 (160, 220)	FiO2, %	80 (80, 80)
Time of CPB, min	75 (63, 90)	PEEP, cmH2O	3 (3, 3)
Time of ACC, min	54 (41, 67)	f, times per min	25.65 ± 2.90
Stay in ICU, day	5 (4, 6)	Duration of ventilation, day	5 (4, 6)
Stay in Hospital, day	26 (20, 29)	HR, times per min	157 (130, 168)
Height, cm	97 (94, 110)	T, °Ĉ	36.64 ± 0.32
Weight, kg	15 (14, 18)	Time of follow-up, mon	35.56 ± 17.96
Family annual income, thousand	6 (4, 10)	Age at neurodevelopment	3.5 (2.9, 5.1)
yuan per year	, ,	accessment, year	
Parental education, year	12 (9, 16)	SBP, mmHg	87.35 ± 13.46

 $M \pm SD$, n (%), Median (Range).

Table 2: Volume of subcortical nuclei in patients of TOF.

Variables	TOF
LTHA, mm ³	6811.93 ± 691.86
LAM, mm ³	1294.87 ± 165.42
RTHA, mm ³	6557.80 ± 750.39
RCAU, mm ³	3491.20 ± 409.66
RPU, mm ³	4915.39 ± 630.88
RPA, mm ³	1658.21 ± 224.93
RAM, mm ³	1477.87 ± 179.84

 $Mean \pm SD.$

After a mean follow-up period of 35.56 ± 17.96 months, neurodevelopmental outcomes assessed by the WPPSI-IV scales covered seven domains: FSIQ (90.10 ± 12.35), VCI (87.32 ± 13.90), VSI (95.32 ± 12.41), WMI (93.13 ± 11.81), VAI (91.13 ± 15.07), NVI (92.87 ± 12.31), and GAI (90.35 ± 12.68) (Table 3). Preliminary correlation analyses revealed that LTHA (r = 0.389, p = 0.031), RTHA (r = 0.395, p = 0.028), LAM (r = 0.439, p = 0.014) were positively correlated with WMI. Positive correlations were also observed between RTHA (r = 0.389, p = 0.031) and RPU (r = 0.357, p = 0.048) with VSI, and between RTHA and FSIQ (r = 0.364, p = 0.044). Additionally, RPU was correlated with VAI (r = 0.361, p = 0.046), while RTHA showed a significant association with NVI (r = 0.374, p = 0.038) (Fig. 4).

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Table 3: The WPPSI-IV results in patients of TOF.

Variables	TOF
Verbal comprehension index	87.32 ± 13.90
Visual-spatial index	95.32 ± 12.41
Working memory index	93.13 ± 11.81
Full-scale IQ	90.35 ± 12.68
Vocabulary acquisition index	91.13 ± 15.07
Non-verbal index	92.87 ± 12.31
General ability index	90.10 ± 12.35

 $\overline{\text{Mean} \pm \text{SD}}$.

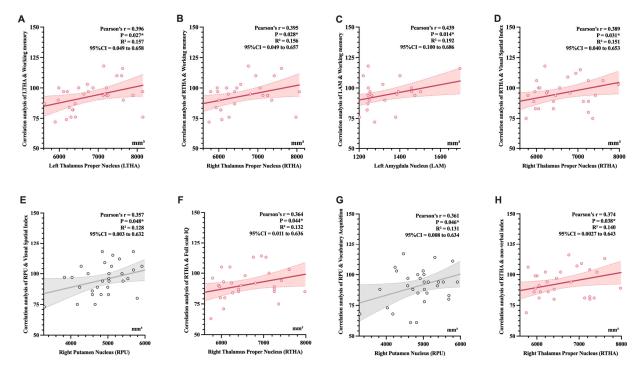


Figure 4: Correlation analysis between subcortical nuclei subregions and domain scores of the WPPSI-IV. (A) LTHA & WMI; (B) RTHA & WMI; (C) LAM & WMI; (D) RTHA & VSI; (E) RPU & VSI; (F) RTHA & FSIQ; (G) RPU & VAI; (H) RTHA & NVI; Pearson correlation was used to analyze the associations. Gray indicates marginal significance, while pink represents statistical significance. We observed significant positive correlations between specific subcortical nuclei and WPPSI-IV domain scores. *indicates statistical significance (p < 0.05).

5 Discussion

The long-term NDDs associated with CHD have been increasingly recognized over the past decade. However, several fundamental questions remain unanswered, including the mechanisms underlying NDDs, as well as limitations in long-term neurodevelopmental follow-up and assessment [26]. These unresolved issues hinder the application of current knowledge to clinical practice. In this study, we created the TOF Dataset, an evidence-based, manually curated knowledgebase for TOF, which links surgical and neurodevelopmental outcomes with brain MRI. Users can easily access MRI or clinical data for exploring the mechanism through our user-friendly data search interface. Thus, the TOF dataset provides a "one-stop" solution, offering a comprehensive landscape of TOF clinical data, MRI images, and cognitive evaluations.

TOF is the most common subtype of CCHD. The anatomical abnormalities of TOF include VSD, overriding aorta, right ventricular outflow tract obstruction, and right ventricular hypertrophy. These features lead to abnormal hemodynamics, resulting in a range of ischemic and hypoxic manifestations [27]. Given the heightened susceptibility of brain tissue to ischemia and hypoxia, MRI has revealed a spectrum of injury-related alterations [28,29]. These alterations include reductions in whole-brain gray matter volume, white matter injury, microstructural abnormalities, abnormal sulcal and gyral patterns, and disrupted neural network connectivity [18,30-32]. Research indicates that white matter injury detected by MRI is significantly correlated with neurodevelopmental cognitive scores [25,33], while ischemic-hypoxic damage exerts a pronounced negative impact on FSIQ and motor performance metrics [34-36]. Consequently, children with TOF are predisposed to a range of NDDs, including impaired executive functioning, deficits in gross and fine motor skills, and language impairments [36-38]. The precise pathogenic mechanisms underlying these deficits remain elusive, thereby constraining the scope of current interventional strategies, which primarily revolve around early surgical intervention, minimizing operative duration, and reducing the incidence of adverse events such as low cardiac output syndrome [39,40]. Therefore, elucidating the underlying mechanisms of NDDs in TOF and identifying reliable imaging biomarkers are pressing issues that need to be addressed to facilitate early clinical identification, diagnosis, and targeted intervention for NDDs.

At present, data for CHD are anchored by two international registries: the Society of Thoracic Surgeons Congenital Heart Surgery Database and the European Congenital Heart Surgeons Association Congenital Cardiac Database, which rank as the largest and second-largest CHD surgical repositories worldwide, respectively. Collectively, they capture nearly all pediatric cardiac surgical centers in North America and Europe, stratifying cases by age group and benchmark procedure categories while systematically recording key performance indicators such as operative mortality and length of stay, with periodic dissemination of quality-improvement reports [41,42]. In the imaging field, the publicly available Whole-Heart Segmentation in Congenital Heart Disease-2.0 database provides 3D cardiovascular magnetic resonance whole-heart segmentations specifically curated for CHD, serving as a critical resource for algorithm development and validation [43]. Although several centers have released brain MRI datasets in children with CHD [44,45], these resources have yet to be integrated into a systematic, large-scale repository.

Given the impact of TOF on children's neurodevelopment, establishing a "TOF Neurodevelopmental Imaging Dataset" is particularly important. The main purpose of this dataset is to integrate and make public the neurodevelopmental imaging data and related metadata of patients with TOF, aiming to provide a data sharing and communication platform for scholars in the field of congenital heart disease neurodevelopmental research worldwide. The significance of launching this open-source dataset by our center lies in promoting global research and collaboration. By providing a centralized data resource, we aim to accelerate the exploration of the mechanisms by which CHD affects children's neurodevelopment. This research lays the groundwork for further development of customized treatments for congenital heart disease, improving the quality of life for affected children.

6 Limitations

Our dataset has some limitations. Firstly, as a single-center dataset, the relatively small sample size limits generalizability to the broader TOF population and introduces potential selection bias. Furthermore, the fact that none of the children in our cohort experienced preoperative hypoxic spells suggests that our sample may not be fully representative of the entire TOF population, which includes patients with a history of such events. Secondly, imaging and cognition assessments require prolonged follow-up; early attrition at different time-points compromises data continuity. Although the WPPSI-IV was administered, the precise

timing of neurodevelopment change could not be determined. Moreover, neurodevelopment is shaped by genetic, environmental, and socio-economic factors that are not fully captured, restricting interpretability. Finally, at the end of follow up, the oldest participant with TOF was 6 years old, whereas published series have reported follow-up to 16 years (non-contiguous) [46]. Therefore, ongoing longitudinal surveillance is essential to delineate long-term neurodevelopment outcomes and to generate a dynamic brain-development atlas for TOF. Consequently, the dataset will be updated regularly and maintained under version control to allow full traceability of historical data.

7 Usage Notes

This dataset is intended for researchers interested in exploring the relationship between neurodevelopment and the long-term hypoxia and risk factors associated with TOF. It includes clinical variables and imaging data from 31 cases of TOF during the perioperative period, collected by cardiothoracic surgeons and radiologists from a center that has been dedicated to studying neurodevelopment over a span of six years. Our previous research has confirmed that chronic hypoxia can lead to changes in brain volume, which is related to cognition and other factors. Children with TOF are relatively few in number, making this data suitable for multi-center analysis. We have previously analyzed a fraction of this dataset in earlier work.

Please be advised that this dataset is derived from a single study with a limited sample size (n = 31). Consequently, the findings may have limited generalizability across diverse populations or settings. The dataset is publicly available on the Open Neuro platform. Users should acknowledge the original authors' contributions. Appropriate citation of this paper is required when using this dataset. We hope this resource will contribute to elucidating the relationship between neurodevelopment and long-term hypoxia and risk factors in TOF.

Acknowledgement: None.

Funding Statement: This work was supported by the National Natural Science Foundation of China (82270310), Noncommunicable Chronic Diseases-National Science and Technology Major Project (No. 2024ZD0527000 and No. 2024ZD0527005), Jiangsu Provincial key research and development program (BE2023662), General project of Nanjing Health Commission (YKK22166).

Author Contributions: The authors confirm contribution to the paper as follows: Yang Xu and Yaqi Zhang contributed equally to this manuscript. Yang Xu, Yaqi Zhang and Xuming Mo: conceived the project. Yang Xu and Yaqi Zhang: wrote the manuscript text and prepared figures and tables. Meijiao Zhu and Ming Yang: provided MRI images and performed preprocessing. Pengcheng Xue: uploaded the data and carried out subsequent version updates. Siyu Ma, Di Yu, Liang Hu and Yuxi Zhang: critically revising the work for intellectual content. Wei Peng, Jirong Qi, Xuyun Wen, Xuming Mo: gave approval of the final manuscript and agree to be accountable for all aspects of the work. All authors reviewed the results and approved the final version of the manuscript.

Availability of Data and Materials: All datasets mentioned in the article are publicly available on OpenNeuro (https://openneuro.org) under a CC0 1.0 Universal license. The data may be downloaded free of charge and reused without restriction, provided that this paper is cited.

Ethics Approval: All procedures performed in studies involving human participants were in accordance with the Ethical Standards of the Institutional and National research Committee, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This research was approved by the Institutional Review Board in Children's Hospital of Nanjing Medical University and the approval number is 202507014-1 and informed consent was acquired. Long-term data updates and access can be obtained by visiting https://openneuro.org/datasets/ds006556 (accessed on 22 August 2025).

Conflicts of Interest: The authors declare no conflicts of interest to report regarding the present study.

Abbreviations

ACC Aortic Cross-Clamp
BMI Body Mass Index
CPB Cardiopulmonary By

CPB Cardiopulmonary Bypass DBP Diastolic Blood Pressure

f Frequency
FSIQ Full-scale IQ

GAI General ability index

HR Heart Rate

ICUIntensive Care UnitLAMLeft Amygdala NucleusLTHALeft Thalamus Proper Nucleus

NVI Non-verbal index

Post-RVOT-PG Postoperative pressure in the right ventricular outflow tract

Pre-RVOT-PG Preoperative pressure gradient in the right ventricular outflow tract
WPPSI-IV Wechsler Pre-school and Primary School Intelligence Scale-Fourth Edition

RAM Right Amygdala Nucleus
RCAU Right Caudate Nucleus
RPA Right Pallidum Nucleus
RPU Right Putamen Nucleus

RTHA Right Thalamus Proper Nucleus

SBP Systolic Blood Pressure

T Temperature TOF Tetralogy of Fallot

VAI Vocabulary acquisition index
VCI Verbal comprehension index
VSD Ventricular Septal Defect
VSI Visual-spatial index
VT Tidal Volume

WMI Working memory index

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