The Fusion of Structural and Functional Connectivity and its Application in Autism

A thesis submitted to

University of Chinese Academy of Sciences

in partial fulfillment of the requirement

for the degree of

Master of Natural Science

in Cognitive Neuroscience

By

DENG Zhaoyu

Supervisor: Professor YAN Chao-Gan

Institute of Psychology, Chinese Academy of Sciences

June, 2023

Abstract

Autism Spectrum Disorder (ASD), as a neurodevelopmental disorder that appears in early childhood development, has an incidence rate of nearly 1.7%, and has a huge impact on children's families. However, the age of diagnosis is often 3-6 years old, but symptoms will appear at 1-2 years old. However, the current clinical diagnosis of ASD is still based on the subjective judgment of symptoms and lacks objective biomarkers, which seriously restricts the diagnosis and treatment of ASD. If objective diagnostic methods are used, children with ASD can be screened earlier, allowing children to receive earlier intervention treatment. Magnetic resonance imaging (Magnetic Resonance Image, MRI), as a non-invasive, relatively low-cost brain imaging method, has the potential to become an objective diagnostic method for ASD. In recent years, Diffusion Tensor Imaging (DTI) and Resting-state functional Magnetic Resonance Imaging (R-fMRI) have been widely used to find possible biomarkers of ASD. However, the existing DTI analysis and processing tools are diverse, and the processing methods also have their own advantages and disadvantages, and there is no unified standard process. Although the new tool QSIPrep integrates commonly used DTI analysis tools, it still needs further improvement. At the same time, due to the variety of structural connectivity tools and various structural connectivity analysis methods, which will have an impact on the research results, this study is dedicated to developing a standardized, automatic selection of optimal processing methods, using the most advanced, user-friendly Friendly toolbox for fiber tracing and structural connectivity analysis. In addition, most of the existing studies are unimodal analyzes using DTI or R-fMRI alone, and no consensus biomarkers have been found. The objective diagnostic criteria are unclear and need to be further clarified. In recent years, the emerging multimodal fusion analysis method reflects the comprehensive connection of the structure and function of brain regions, and has the potential to more sensitively discover the biomarkers of ASD. A novel multimodal MRI analysis method, called Structure-Function Coupling (SFC), has the potential to find robust biomarkers of ASD, but this fusion of structural and functional connectivity is lacking. Simple and easy to use tool.

This study has 3 sub-studies. Study 1 is the development of fiber tracing and structural connection toolbox. This sub-study combines the current commonly used toolkits, uses MATLAB for programming development, and develops DPABIFiber, a fiber tracing and structural connection analysis tool. It has a user-friendly graphical user

interface and can quickly and easily set parameters, so that researchers who are not familiar with computers and who are not proficient in fiber tracing methodologies can quickly get started, perform fiber tracing and structural connection quickly and accurately analysis. Study 2 is to look for single-modal biomarkers of ASD structure and functional connectivity. This sub-study uses the fiber tracing and structural connectivity analysis tool DPABIFiber developed in Study 1 and the cortical-based resting-state functional magnetic resonance analysis tool DPABISurf on ASD patients and DTI and R-fMRI data of typical development (TD) were analyzed to obtain Tract-Based Spatial Statistics (TBSS), structural connectivity (SC) and functional connectivity (FC) results. Among them, the fractional anisotropy (FA) of TBSS obtained ASD biomarkers abnormal in 5 left and right brain regions, and the apparent diffusion coefficient (ADC) of TBSS obtained ASD biomarkers abnormal in 8 regions. Structural connections were mostly low connections between networks, and only a few individual networks had intra-network connections; the default mode network (DMN) and other brain networks, especially the frontoparietal control network (FPN), with quite a few inter-network low connectivity. Functional connectivity has a low connection between the default mode network (DMN), frontoparietal control network (FPN) and dorsal attention network (VAN), and a low connection within the default mode network (DMN) , in the sensorimotor network (SMN) with 3 intra-network low connectivity. These features could serve as unimodal biomarkers for ASD. Study 3 explored biomarkers of structural and functional connectivity fusion in ASD, and this calculated SFC using the structural and functional connectivity matrices calculated in Study 2. The former of these two methods represents the information consideration of integrated structure and function, and the latter represents the relationship between structure and function. In SFC, 6 cortical brain networks and 2 subcortical nuclei had coupling changes, a total of 9 sites showed decreased flexibility, and 12 sites showed increased flexibility. Changes in these couplings may serve as multimodal biomarkers of ASD.

Overall, this study develops a fiber tracing and structural connectivity toolbox that provides researchers with fast and accurate fiber tracing and structural connectivity analysis. Based on the toolbox, this study conducted single-modal biomarker analysis on ASD, and further used the fusion method to conduct multi-modal biomarker analysis. Inspiring meaning. And hope that this new open source toolbox will help more novice and expert users and continue to support the development of advanced structural analysis methods and their application in clinical translational research.

Key Words: Autism Spectrum Disorder, Diffusion Tensor Imaging, Resting-state Functional Magnetic Resonance Imaging, Tractography, Multimodal

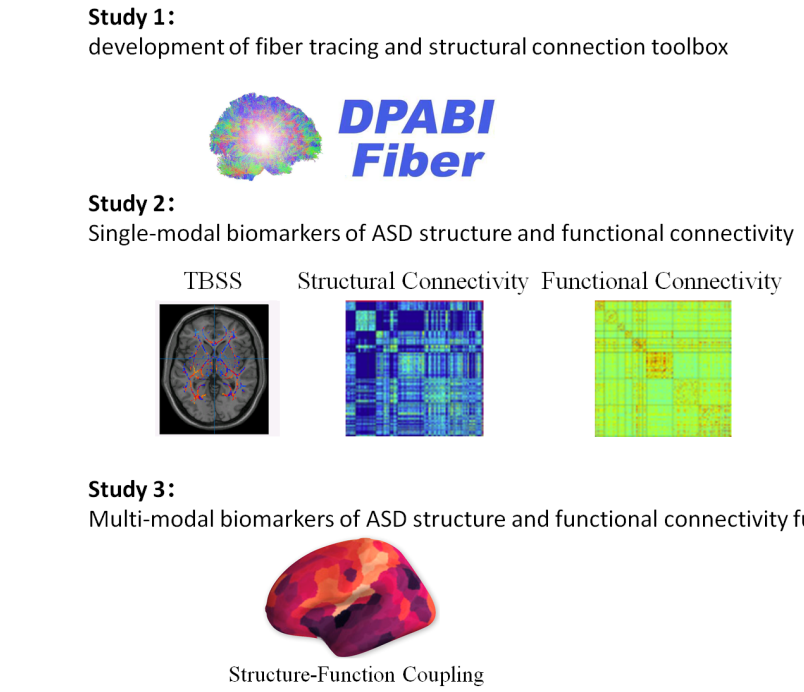

Figure 1-6 Overview of This Study

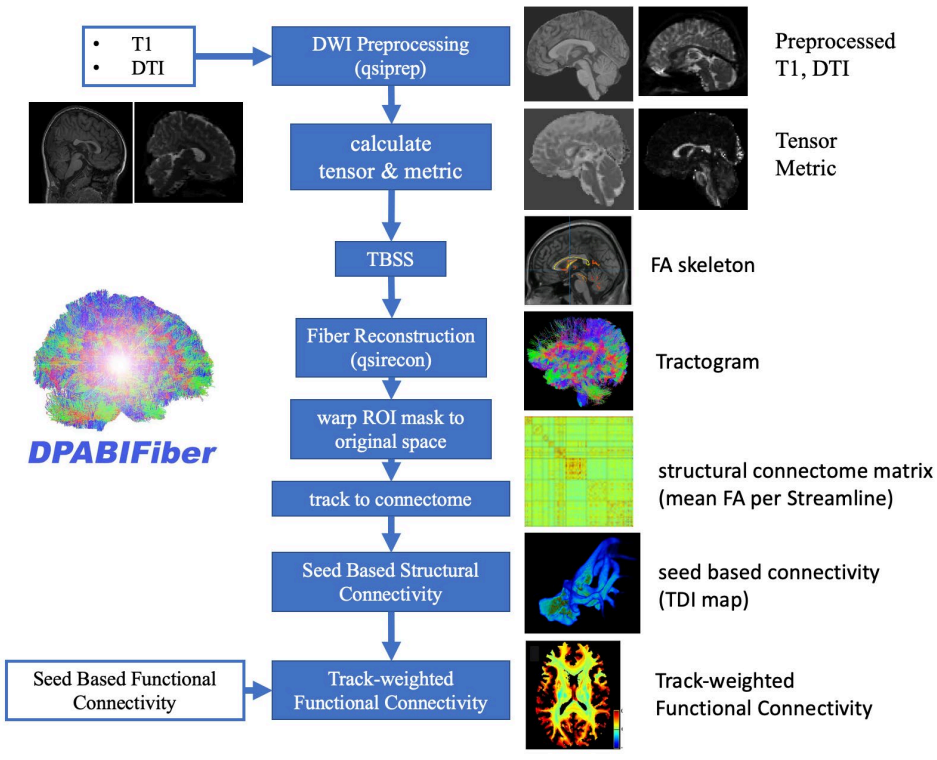

Figure 2-1 DPABIFiber Workflow

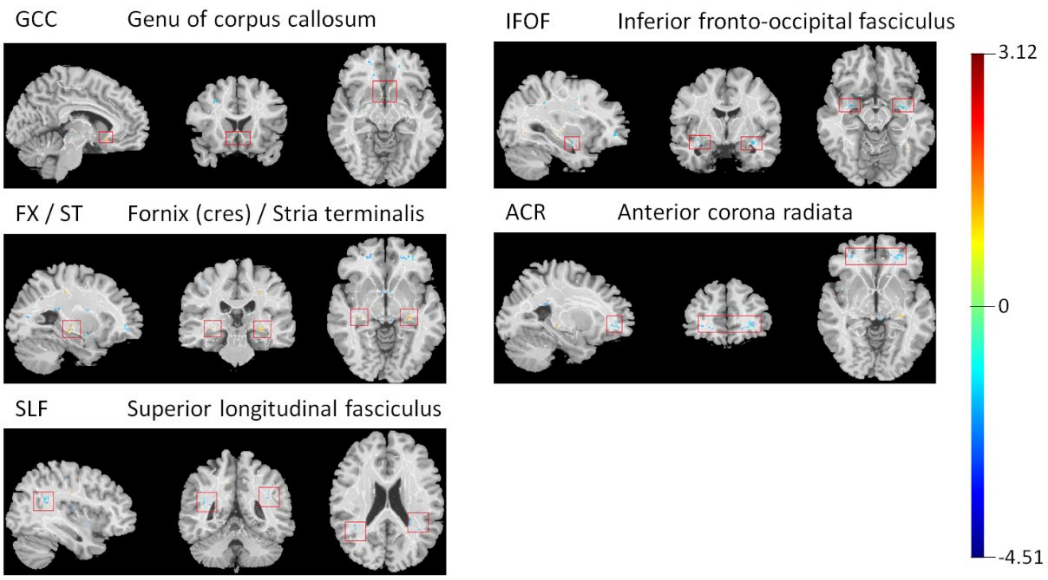

Figure 3-4 TBSS FA Result after Statistics

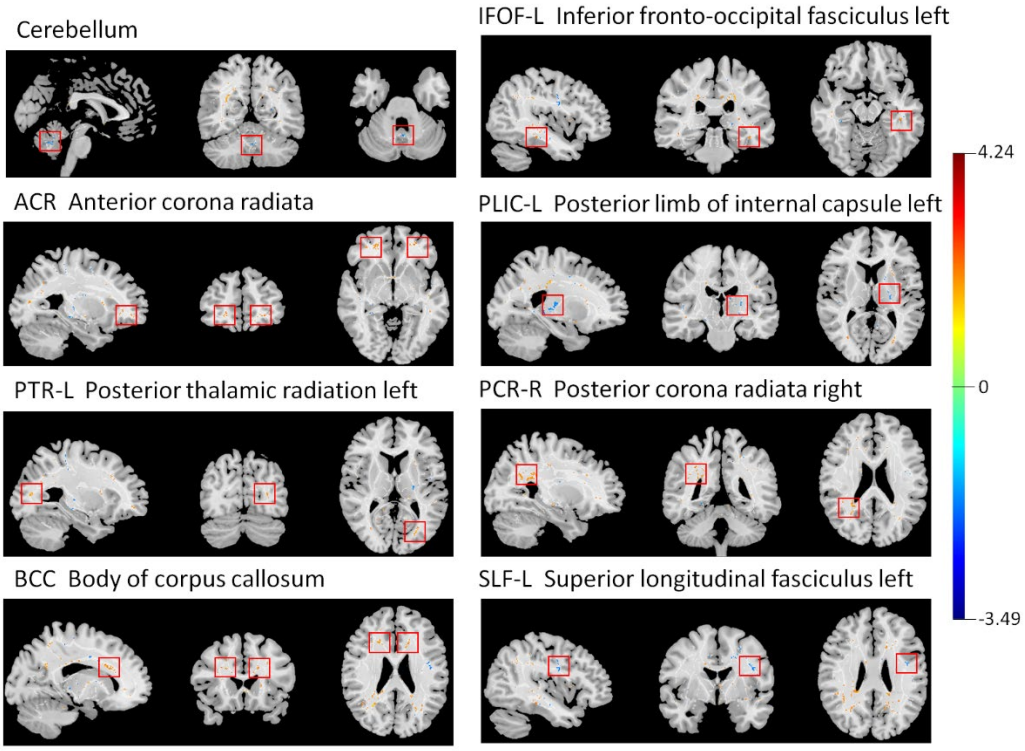

Figure 3-5 TBSS ADC Result after Statistics

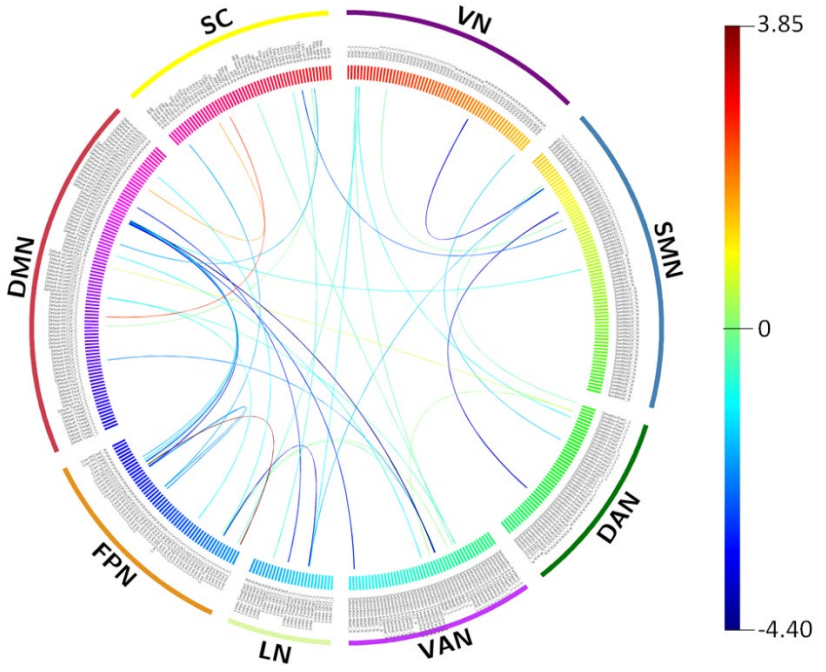

Figure 3-6 Structural Connectivity Network Circos Figure after Statistics

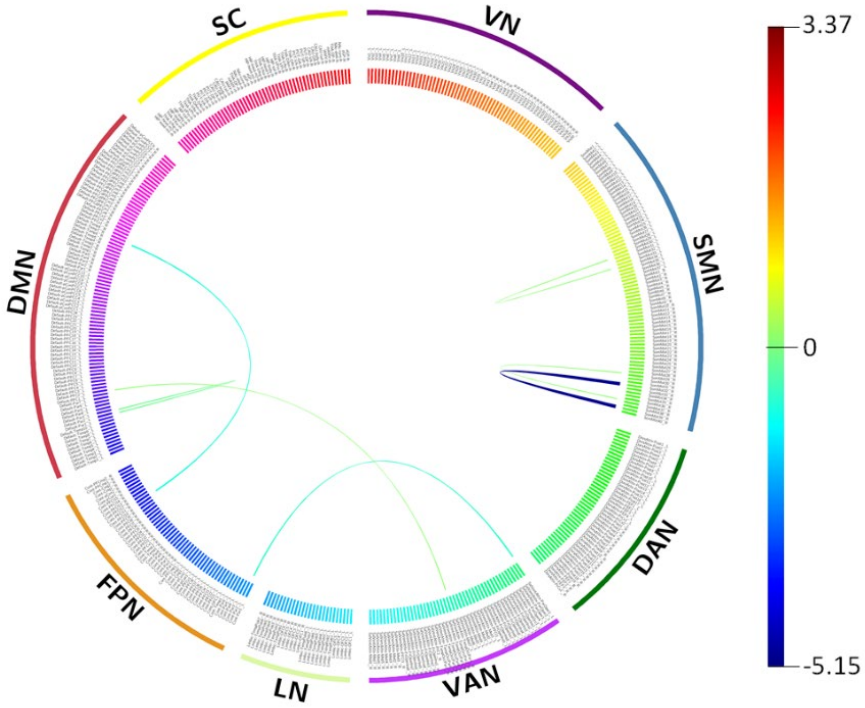

Figure 3-7 Functional Connectivity Network Circos Figure after Statistics

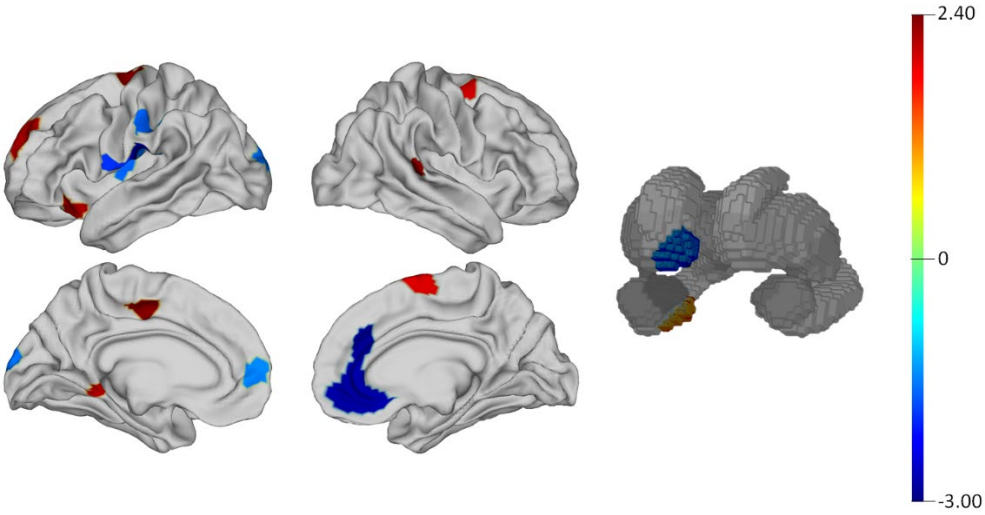

Figure 4-2 SFC Result

Table 3-1 Significant Regions in SFC and Corresponding T Value

Regions Label	Networks	Regions	Hemi	T Value
Vis13_L	Visual Network		L	2
Vis24_L	Visual Network		L	-2
SomMot4_L	Somatomotor Network		L	-2
SomMot9_L	Somatomotor Network		L	-2
SomMot10_L	Somatomotor Network		L	-2
SomMot11_L	Somatomotor Network		L	-3
SomMot15_L	Somatomotor Network		L	-2
SomMot18_L	Somatomotor Network		L	2.3
SomMot34_L	Somatomotor Network		L	2.2
DorsAttn-Post6_L	Dorsal Attention Network		L	-2
Default-PFC1_L	Default Mode Network	Prefrontal Cortex	L	2.1
Default-PFC8_L	Default Mode Network	Prefrontal Cortex	L	-2
Default-PFC14_L	Default Mode Network	Prefrontal Cortex	L	2
SomMot8_R	Somatomotor Network		R	2.4
DorsAttn-FEF3_R	Dorsal Attention Network	Frontal Eye Fields	R	2.1
SalVentAttn-Med7_R	Ventral Attention Network		R	2
Cont-PFCmp1_R	Frontoparietal Network	Medial Posterior Prefrontal Cortex	R	-2
Default-PFCdPFCm1_R	Default Mode Network	Dorsal & Medial Prefrontal Cortex	R	-2
Default-PFCdPFCm3_R	Default Mode Network	Dorsal & Medial Prefrontal Cortex	R	-2
HIP-head-m1-rh	Subcortex	Hippocampus (Head)	R	2.3
NAc-shell-rh	Subcortex	Nucleus Accumbens (Shell)	R	-2